## Current Research

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*Meets Learning Need Codes 4000, 5370, 9000, and 9020*

# Weight-Loss Outcomes: A Systematic Review and Meta-Analysis of Weight-Loss Clinical Trials with a Minimum 1-Year Follow-Up

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**ABSTRACT**

**Objective** To assist health professionals who counsel patients with overweight and obesity, a systematic review was undertaken to determine types of weight-loss interventions that contribute to successful outcomes and to define expected weight-loss outcomes from such interventions.

**Design** A search was conducted for weight-loss–focused randomized clinical trials with ≥1-year follow-up. Eighty studies were identified and are included in the evidence table.

**Outcomes measures** The primary outcomes were a measure of weight loss at 6, 12, 24, 36, and 48 months. Eight types of weight-loss interventions—diet alone, diet and exercise, exercise alone, meal replacements, very-low-energy diets, weight-loss medications (orlistat and sibutramine), and advice alone—were identified. By using simple pooling across studies, subjects mean amount of weight loss at each time point for each intervention was determined.

**Statistical analyses performed** Efficacy outcomes were calculated by meta-analysis and provide support for the pooled data. Hedges' gu was combined across studies to obtain an average effect size (and confidence level).

**Results** A mean weight loss of 5 to 8.5 kg (5% to 9%) was observed during the first 6 months from interventions involving a reduced-energy diet and/or weight-loss medications with weight plateaus at approximately 6 months. In studies extending to 48 months, a mean 3 to 6 kg (3% to 6%) of weight loss was maintained with none of the groups experiencing weight regain to baseline. In contrast, advice-only and exercise-alone groups experienced minimal weight loss at any time point.

**Conclusions** Weight-loss interventions utilizing a reduced-energy diet and exercise are associated with moderate weight loss at 6 months. Although there is some regain of weight, weight loss can be maintained. The addition of weight-loss medications somewhat enhances weight-loss maintenance.

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In 1998 the National Institutes of Health issued its first clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults (1), recommending weight loss for persons with a body mass index of 30 or more and for persons with a body mass index between 25 and 29.9 with two or more risk factors. The National Institutes of Health guidelines were intended to provide direction to health care professionals for counseling patients with overweight and obesity. However, professionals and the public often have conflicting views on the efficacy of weight-loss interventions—either believing that if individuals have "will-power" and diet they can lose an unlimited amount of weight or

believing that weight-loss attempts are rarely successful and weight regain invariably occurs.

From a health care perspective, addressing overweight and obesity is an important strategy in the primary and secondary prevention of disease. Obesity is associated with an increased prevalence of chronic diseases, including type 2 diabetes, hypertension, dyslipidemia, and cardiovascular disease (1). Sustained modest weight loss is associated with improvements in related clinical indicators, such as decreased risk for diabetes (2), reductions in blood pressure (3), and improved lipid profiles (3). Clinical improvements begin to appear with relatively small amounts of weight loss (approximately 5% to 7%), suggesting the importance of emphasizing modest weight loss for health benefits rather than for cosmetic reasons (3,4).

The prevalence of adult overweight and obesity increased dramatically between 1960 and 2000 (5,6). At the same time, the number of adults trying to lose weight and the amount of money spent on weight-loss interventions also increased. Using 2001-2002 National Health and Nutrition Examination Survey data, it was reported that approximately half of all adults are trying to control weight, with about one third of men and nearly one half of women trying to lose weight. Furthermore, more than $50 billion per year are spent by adults on weight-loss efforts (7). Consumers of these services often have unrealistic expectations for success. Women participating in a weight-loss program reported their goal weight as an average 32% reduction in body weight (8). A 17-kg weight loss was defined as a disappointing weight loss and a 25-kg loss was an acceptable weight loss. After 48 weeks of treatment and a 16-kg weight loss, 47% of women did not achieve weight loss they associated with success. Thus, the questions of what are effective weight-loss interventions and what are realistic long-term outcomes take on added importance for all health professionals counseling patients with overweight and obesity, as well as for the general public.

To answer these questions, HealthPartners Health Behavior Group in collaboration with Kaiser Permamente's Care Management Institute completed a systematic review of long-term weight-loss interventions and outcomes published after the release of the National Institutes of Health guidelines for the treatment of overweight and obesity. Weight-loss studies reviewed were categorized into eight types of interventions: advice alone, diet alone, diet and exercise, exercise alone, meal replacements, very-low-energy diets, and weight-loss medications (orlistat and sibutramine). In addition, a meta-analysis was carried out on interventions, including diet, exercise, diet and exercise, meal replacements, and weight-loss medications. The purpose of the systematic review was to assess weight-loss outcomes in studies with a minimum follow-up of 12 months and to determine treatment interventions that contribute to sustained (ie, ≥6 to 12 months) weight-loss maintenance. The purpose of the meta-analysis was to derive an empirically based estimate of the difference in weight loss among subjects participating in a weight-loss intervention (relative to another intervention arm). Although other systematic reviews have examined two or three weight-loss interventions, this is the first systematic review to examine all interventions (except bariatric surgery) described in the literature and to apply the findings to the question of what interventions health care professionals should provide to patients with overweight and obesity.

## METHODS

### Data Sources

For the purpose of conducting the systematic review, the central research question to be addressed was stated as: "Do weight-loss interventions (advice alone, diet alone, exercise alone, diet and exercise, meal replacements, very-low-energy diets, orlistat, and sibutramine) contribute to sustained weight loss/maintenance over time (ie, 6, 12, 24, 36, and 48 months)?" The PubMed (www.ncbi.nlm,nih.gov/entrez/query.fcgi) online database, along with the bibliographies of selected studies, was searched to produce relevant articles to answer this question. Medical Subject Headings used in the online search included *obesity*, *weight loss*, *nutrition*, *exercise movement techniques*, and *drug therapy*. To limit and focus the review, secondary outcomes such as blood pressure, lipids, glucose, quality-of-life, and treatment satisfaction, although recognized as important, were not described.

### Study Selection

The primary outcome of interest was weight loss and the therapies were selected based on the most common weight-loss interventions found in previous research. Study inclusion criteria were: published between January 1, 1997 and September 1, 2004; English language; overweight or obese adults (aged 18 years or older); randomized clinical trial with ≥1 year follow-up; and ≥1 intervention arm using at least one of the eight weight-management therapies already identified. Because no randomized trials employing bariatric surgery were identified, it is not included in the systematic review and meta-analyses. Measures of weight loss included absolute weight loss, percentage of weight loss, and body mass index changes relative to baseline.

### Data Synthesis

Data were pooled across studies for each of the eight identified conditions based on the following definitions: advice alone, where participants were given verbal or written advice on how to lose weight or participated in a single education session per year; diet alone, where a reduced-energy diet was the primary focus of the intervention along with behavioral strategies and with or without general advice to increase physical activity; exercise alone, where participants were given exercise recommendations or assistance as the primary weight-loss intervention and minimal or no advice on food and meal planning; diet and exercise, where a reduced-energy diet along with behavioral strategies was recommended and specific goals for physical activity were given and measured; meal replacements, where meal replacements were used for two or more meals per day and as an adjunct to a reduced-energy diet; very-low-energy diet, where a diet of 800 kcal or less per day, usually in the

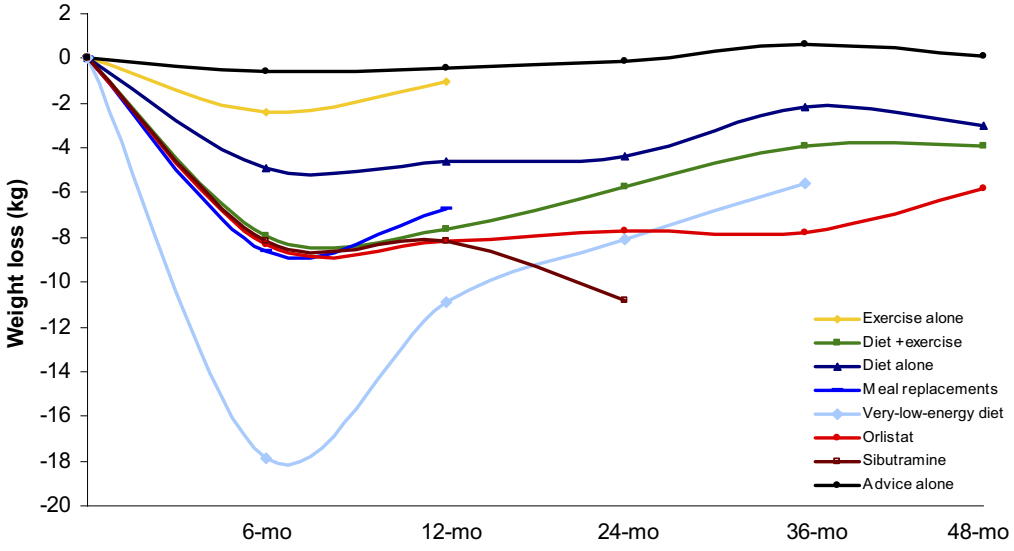
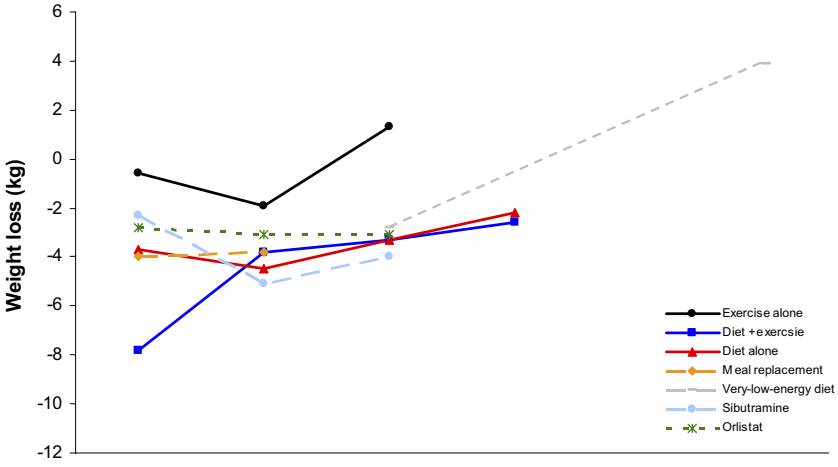



**Figure 1.** Average weight loss of subjects completing a minimum 1-year weight-management intervention; based on review of 80 studies (N=26,455; 18,199 completers [69%]).

form of a liquid diet, was used as the initial weight-loss intervention; orlistat, where a prescription for orlistat, a weight-management medication, was used in combination with lifestyle interventions; sibutramine, where a prescription for sibutramine, a weight-management medication, was used typically in combination with advice on lifestyle. A mean weight loss by type of therapy was determined from the pooled intervention data. Data points for Figure 1 were not determined if the pooled intervention had fewer than 50 subjects.




| | 6-mo | 12-mo | 24-mo | 36-mo | 48-mo | 60-mo |
|---|---|---|---|---|---|---|
| Exercise [a] | 33 (0.17) | 174 (0.52) | 31 (-0.28) | | | |
| Diet\Exercise [a] | 31 (1.52) | 305 (0.82) | 334 (0.64) | 231 (0.50) | | |
| Diet [a] | 1332 (0.85) | 834 (1.12) | 474 (0.56) | 1390 (0.36) | | |
| Meal Replacements [b] | 416 (0.89) | 239 (0.60) | | | | |
| Very-Low-Energy Diet [b] | | | 43 (0.24) | | | 13 (-0.77) |
| Sibutramine [b] | 590 (0.78) | 883 (1.27) | 352 (0.52) | | | |
| Orlistat [b] | 3007 (0.33) | 3802 (0.37) | 999 (0.29) | | | |

Number of participants (Hedges' gu effect size)

**Figure 2.** Meta-analysis: Average weight loss relative to the comparison group. [a]Advice-only comparison group. [b]Reduced-energy diet comparison group.

**Table.** Baseline data, number of study completers, study duration, type of weight-loss intervention, and weight-loss outcomes reported in studies reviewed to determine type of weight-loss interventions that contribute to successful outcomes

| Study | No. enrolled | No. of completers | Mean baseline weight (kg) | Mean baseline BMI[a] | Mean baseline age (y) | Sex (% male) | Total study duration (wks) | Treatment duration (wks) | Interventions[b] | Mean Weight Loss (kg) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | 6 mo | 12 mo | Final |
| **Diet alone**[c] | | | ← mean±standard deviation → | | | | | | | | | |
| Bacon and colleagues, 2002 (10) | 78 | 54 | 99.0±11.4 | 35.7±3.6 | 39.3±4.5 | 0 | 52 | 26 | DA | −4.6 | −5.9 | |
| | | | | | | | | | AA | +0.5 | +1.3 | |
| Brinkworth and colleagues, 2004 (11) | 58 | 43 | 93.6±5.5 | 34.1±1.8 | 50.4±5.3 | 22 | 68 | 12 | DA | −8.7 | −3.7 | −2.7 |
| | | | | | | | | | DA (high-protein diets) | −7.2 | −3.2 | −3.8 |
| Burke and colleagues, 2002 (12) | 63 | 63 | 86.1±8.2 | 30.6±2.9 | 54.8±7.3 | 33 | 64 | 17 | DA | −5.5 | −5.1 | −6.6 |
| | | | | | | | | | AA | −1.9 | −1.9 | −0.3 |
| Djuric and colleagues, 2002 (13) | 48 | 39 | 95.4±13.6 | 35.5±3.9 | 51.7±8.4 | 0 | 52 | NA[d] | DA | −7.9 | −8.0 | |
| | | | | | | | | | DA+Weight Watchers (WW) | −9.3 | −9.4 | |
| | | | | | | | | | AA (referred to WW) | −3.0 | −2.6 | |
| | | | | | | | | | AA | −1.0 | +0.9 | |
| Foster and colleagues, 2003 (14) | 63 | 37 | 98.5±19.5 | 34.3±3.8 | 44.0±9.4 | 32 | 52 | NA | DA (low CHO,[e] high protein diet) | −9.6 | −7.2 | |
| | | | | | | | | | AA | −5.2 | −4.4 | |
| Heshka and colleagues, 2003 (15) | 423 | 309 | 93.6±14.4 | 33.7±3.7 | 44.5±10 | 15 | 104 | NA | DA (WW) | −5.8 | −5.0 | −3.0 |
| | | | | | | | | | AA | −1.8 | −1.4 | −0.1 |
| Jones and colleagues, 1999 (16) | 112 | 102 | 94.5±18 | 34±6 | 58±7 | 48 | 150 | 12 | DA | −3.2 | −1.7 | −1.2 |
| | | | | | | | | | AA | −1.8 | −1.4 | −2.2 |
| Manning and colleagues, 1998 (17) | 205 | 145 | 99 (96.3-104)[f] | 32 (29.8-34.3)[f] | 56 (50.5-62.7)[f] | 49 | 208 | 26 | DA | −2.7 | −2.3 | −1.7 |
| | | | | | | | | | AA | NA | +1.2 | NA |
| McManus and colleagues, 2001 (18) | 101 | 61 | 91±32 | 33±5 | 44±10 | 6 | 78 | 26 | DA | −5.1 | −5.0 | −2.9 |
| | | | | | | | | | DA (moderate fat: 35%) | −4.9 | −4.8 | −4.8 |
| Pritchard and colleagues, 1998 (19) | 270 | 177 | 89.1±NA | NA | NA | 27 | 52 | 52 | DA | NA | −6.2 | |
| | | | | | | | | | AA | NA | +0.7 | |
| Ramirez and colleagues, 2001 (20) | 88 | 65 | 96±22.9 | 33.8±5.1 | 44±9.7 | 22 | 52 | 16 | DA | NA | −6.6 | |
| | | | | | | | | | DA+body image therapy | NA | −5.6 | |
| Rapoport and colleagues, 2000 (21) | 75 | 63 | 94.4±16.3 | 35.4±6.3 | 46.5±12 | 0 | 52 | 10 | DA | −3.5 | −3.6 | |
| | | | | | | | | | AA | −2.0 | −1.9 | |
| Sbroco and colleagues, 1999 (22) | 24 | 21 | 89.6±11.6 | 32.6±3.6 | 41.4±10.7 | 0 | 52 | 15 | DA | −4.5 | −4.3 | |
| | | | | | | | | | DA+cognitive behavioral program | −7.0 | −10.1 | |
| Stern and colleagues, 2004 (23) | 132 | 126 | 131±27 | 42.9±7.7 | 54±9 | 82 | 52 | 4 | DA | −1.9 | −3.1 | |
| | | | | | | | | | DA (low CHO diet) | −5.8 | −5.1 | |
| Toubro and colleagues, 1997 (24) | 43 | 37 | 98.4 (91.9-105.7)[e] | 36.5 (33.8-37.7)[f] | 43.6 (39.8-47.7)[f] | 5 | 121 | 17 | DA (follow-up: fixed energy intake) | −13.1 | −9.7 | −2.5 |
| | | | | | | | | | DA (follow-up: ad lib, low fat, high CHO diet) | −15.8 | −15.5 | −8.0 |
| Trials of Hypertension 1997 (25) | 2.382 | 2.202 | 93.6±14.2 | NA | 43.6±6.2 | 66 | 156 | 26 | DA | −4.3 | NA | −0.3 |
| | | | | | | | | | AA | −0.6 | NA | +1.8 |
| Turnin and colleagues, 2001 (26) | 557 | 341 | NA | 33.3±0.5[g] | 41.2±0.6[g] | 8 | 52 | NA | DA | NA | NA | NA |
| | | | | | | | | | DA+follow-up, Internet program | NA | NA | NA |
| Whelton and colleagues, 1998 (27) | 585 | 532 | 86.8±10 | 31.2±2.5 | 66±4 | 47 | 150 | 35 | DA | −5.0 | −4.7 | −4.7 |
| | | | | | | | | | AA | −1.1 | −1.1 | −0.9 |
| Wolf and colleagues, 2004 (28) | 147 | 117 | 106.9±25.5 | 37.6±7.7 | 53.4±8.6 | 41 | 52 | 52 | DA | −3.8 | −2.4 | |
| | | | | | | | | | AA | +0.7 | +0.6 | |
| Womble and colleagues, 2004 (29) | 47 | 31 | 90.6±12.6 | 33.4±3.2 | 43.7±11.1 | 0 | 52 | NA | DA (eDiets.com) | −1.2 | −2.0 | |
| | | | | | | | | | AA | −3.5 | −3.9 | |
| Wylie-Rosett and colleagues, 2001 (30) | 588 | 476 | 97.4±20 | 35.6±6.5 | 52.2±12.1 | 18 | 52 | NA | DA | NA | −3.4 | |
| | | | | | | | | | AA+computer kiosks | NA | −2.1 | |
| | | | | | | | | | AA | NA | +3.4 | |

*(continued)*

**Table.** Baseline data, number of study completers, study duration, type of weight-loss intervention, and weight-loss outcomes reported in studies reviewed to determine type of weight-loss interventions that contribute to successful outcomes (continued)

| Study | No. enrolled | No. of completers | Mean baseline weight (kg) | Mean baseline BMI[a] | Mean baseline age (y) | Sex (% male) | Total study duration (wks) | Treatment duration (wks) | Interventions[b] | Mean Weight Loss (kg) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | 6 mo | 12 mo | Final |
| **Diet and exercise**[h] | | | | | | | | | | | | |
| Anderson and colleagues, 1999 (31) | 40 | 33 | 87.0±13.5 | 31.9±4.5 | 43.0±9.1 | 0 | 68 | 16 | DE (structured aerobic exercise) | −8.3 | NA | −6.7 |
| | | | | | | | | | DE (moderate lifestyle activity) | −7.9 | NA | −7.8 |
| Ashutosh and colleagues, 1997 (32) | 37 | 31 | 94.8±14.1 | NA | 43±7 | 0 | 52 | 25 | DE | NA | −15.8 | |
| | | | | | | | | | DA | NA | −14.5 | |
| DPP 2002 (33) | 3,234 | 2,991 | 94.2±20.8 | 34.0±6.7 | 50.6±11.3 | 32 | 208 | 24 | DE | −7.0 | −7.0 | −4.0 |
| | | | | | | | | | AA | −0.1 | +0.1 | −0.1 |
| Esposito and colleagues, 2003 (34) | 120 | 112 | 94.5±9.4 | 34.9±2.4 | 34.6±5.1 | 0 | 104 | 52 | DE | NA | NA | −14.0 |
| | | | | | | | | | AA | NA | NA | −3.0 |
| Fleming and colleagues, 2002 (35) | 120 | 100 | 105.5±33.6 | NA | 43±8 | 47 | 52 | NA | DE | NA | −17.2 | |
| | | | | | | | | | AA | NA | −2.7 | |
| Harvey-Berino and colleagues, 2002 (36) | 122 | 90 | 88.7±15.3 | 32.4±4.8 | 48.4±11.1 | 15 | 78 | 24 | DE (in-persons support) | −9.8 | −9.8 | −10.4 |
| | | | | | | | | | DE (Internet support) | −8.0 | −6.0 | −5.7 |
| | | | | | | | | | DE (minimal in-person support) | −11.0 | −10.6 | −10.4 |
| Harvey-Berino and colleagues, 2004 (37) | 255 | 176 | 89.4±15.2 | 31.8±4.1 | 45.8±8.9 | 18 | 78 | 26 | DE (in-person support) | −7.6 | −7.5 | −5.1 |
| | | | | | | | | | DE (Internet support) | −8.4 | −10.1 | −7.6 |
| | | | | | | | | | DE (minimal in-person support) | −7.6 | −7.1 | −5.5 |
| Jakicic and colleagues, 1999 (38) | 148 | 115 | 90.0±12.0 | 32.8±4.3 | 36.7±6.0 | 0 | 78 | 26 | DE (long bout exercise) | −10.2 | −8.0 | −7.6 |
| | | | | | | | | | DE (short bout exercise) | −9.3 | −6.0 | −5.2 |
| | | | | | | | | | DE (short bout and exercise equipment) | −10.2 | −11.0 | −8.4 |
| Jakicic and colleagues, 2003 (39) | 201 | 184 | 87.4±13.3 | 32.6±4.2 | 37.0±5.7 | 0 | 52 | 26 | DE (vigorous intensity/high duration exercise) | −9.4 | −8.8 | |
| | | | | | | | | | DE (moderate intensity/high duration exercise) | −8.0 | −8.2 | |
| | | | | | | | | | DE (moderate intensity/moderate intensity exercise) | −7.1 | −6.4 | |
| | | | | | | | | | DE (vigorous intensity/moderate duration exercise) | −7.5 | −6.9 | |
| Jeffery and colleagues, 2003 (40) | 202 | 168 | 91.1±10.0 | 31.1±2.5 | 41.1±6.1 | 42 | 78 | 26 | DE (2,500 kcal/wk exercise) | −9.0 | −8.5 | −6.7 |
| | | | | | | | | | DE (1,000 kcal/wk exercise) | −8.1 | −6.1 | −4.1 |
| Leemakers and colleagues, 1999 (41) | 67 | 57 | 85.2±15.9 | 30.8±4.5 | 60.8±11.1 | 20 | 78 | 26 | DE (weight maintenance exercise-focused) | −9.6 | −7.9 | −6.9 |
| | | | | | | | | | DE (weight maintenance weight-focused) | −8.7 | −8.5 | −8.1 |
| Perri and colleagues, 1997 (42) | 49 | 40 | 88.5±11.7 | 33.6±4.5 | 48.8±6.2 | 0 | 65 | 26 | DE (moderate exercise in groups) | −10.9 | −10.1 | −9.2 |
| | | | | | | | | | DE (moderate exercise at home) | −10.6 | −12.4 | −11.9 |
| Racette and colleagues, 2001 (43) | 69 | 36 | 107±5 | 40±2 | 48±1 | 15 | 52 | 1 | DE | −5.3 | −4.6 | |
| | | | | | | | | | AA | NA | +0.3 | |
| Rejeski and colleagues, 2002 (44) | 278 | 222 | 93.8±18.8 | 34.5±5.8 | 68.5±6.6 | 28 | 78 | 26 | DE | NA | NA | −4.0 |
| | | | | | | | | | DA | NA | NA | −5.4 |
| | | | | | | | | | AA | NA | NA | −1.2 |
| | | | | | | | | | EA | NA | NA | −2.4 |
| Tuomilehto and colleagues, 2001 (45); Lindstrom and colleagues, 2003 (46) | 522 | 471 | 86.1±14.4 | 31.2±4.6 | 55±7 | 33 | 156 | 52 | DE | NA | −4.2 | −3.5 |
| | | | | | | | | | AA | NA | −1.0 | −0.9 |
| Wing and colleagues, 1998 (47) | 154 | 129 | 98.8±16.0 | 36.0±5.4 | 45.5±4.9 | 21 | 104 | 52 | DE | −10.3 | −7.4 | −2.5 |
| | | | | | | | | | DA | −9.1 | −5.5 | −2.1 |
| | | | | | | | | | AA | −1.5 | −0.3 | −0.3 |
| | | | | | | | | | EA | −2.1 | −0.1 | +1.0 |
| Wing and colleagues, 1999 (48) | 166 | 136 | 84.8±13.1 | 31.2±4.0 | 42.2±9.2 | 49 | 60 | 52 | DE | −5.3 | NA | −3.0 |
| | | | | | | | | | DE+social support | −6.1 | NA | −3.0 |
| | | | | | | | | | DE+3 friends | −8.8 | NA | −4.7 |
| | | | | | | | | | DE+social support | −8.7 | NA | −4.7 |

*(continued)*

**Table.** Baseline data, number of study completers, study duration, type of weight-loss intervention, and weight-loss outcomes reported in studies reviewed to determine type of weight-loss interventions that contribute to successful outcomes (continued)

| Study | No. enrolled | No. of completers | Mean baseline weight (kg) | Mean baseline BMI[a] | Mean baseline age (y) | Sex (% male) | Total study duration (wks) | Treatment duration (wks) | Interventions[b] | Mean Weight Loss (kg) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | 6 mo | 12 mo | Final |
| **Exercise alone**[j] | | | | | | | | | | | | |
| Donnelly and colleagues, 2000 (49) | 22 | 22 | 83.6±13.1 | 31.2±5.1 | 51±9 | 0 | 78 | 78 | EA (continuous exercise) | NA | −0.5 | −1.7 |
| | | | | | | | | | EA (intermittent exercise) | NA | −1.9 | −0.8 |
| Donnelly and colleagues, 2003 (50) | 131 | 74 | 86.3±12.6 | 29.2±3.2 | 22.8±5 | 58 | 78 | 78 | EA | −2.6 | −1.9 | −2.3 |
| | | | | | | | | | AA | −0.4 | +0.9 | +1.2 |
| Irwin and colleagues, 2003 (51) | 173 | 168 | 81.7 (78.4-84.7)[f] | 30.5±(29.6-31.4)[f] | 60.8±(59.1-62.5)[f] | 0 | 52 | 52 | EA | NA | −1.3 | |
| | | | | | | | | | AA | NA | +0.1 | |
| Pritchards and colleagues, 1997 (52) | 68 | 58 | 87.6±10.5 | 28.9±2.8 | 43.6±6.5 | 100 | 52 | NA | EA | NA | −2.6 | |
| | | | | | | | | | AA | NA | +0.9 | |
| | | | | | | | | | DA | NA | −6.4 | |
| **Meal replacement**[j] | | | | | | | | | | | | |
| Ditschuneit and colleagues, 1999 (53) | 100 | 75 | 96.4±12.9 | 33.3±4.1 | 45.8±12.0 | 21 | 108 | 12 | MR | −9.1 | −9.1 | −9.5 |
| | | | | | | | | | DA | −3.5 | −3.7 | −4.1 |
| Rothacker and colleagues, 2001 (54) | 75 | 64 | 76.5±7.5 | 28.9±1.7 | 36.8±7.2 | 0 | 52 | 12 | MR | −6.3 | −6.4 | |
| | | | | | | | | | DA | −3.8 | −1.2 | |
| Hensrud, 2001 (55) | 33 | 24 | 87.1±14.7 | 31.0±4.2 | 46.1±11.3 | 39 | 52 | 12 | MR | −4.7 | −1.3 | |
| | | | | | | | | | DA | −3.0 | −1.0 | |
| Ashley and colleagues, 2001 (56) | 74 | 74 | 83.2±9.8 | 30.0±3.1 | 41.4±4.7 | 0 | 52 | NA | MR | −5.8 | −5.6 | |
| | | | | | | | | | DA | −2.3 | −3.4 | |
| Ahrens and colleagues, 2000 (57) | 95 | 51 | 87.1±14.7 | 31.0±4.2 | 46.1±11.3 | 13 | 52 | NA | MR | −4.9 | −8.2 | |
| | | | | | | | | | DA | −4.4 | −9.5 | |
| Metz and colleagues, 2000 (58) | 302 | 250 | NA | 33.1±4.9 | 54.4±9.5 | 44 | 52 | NA | MR | −7.8 | −5.8 | |
| | | | | | | | | | DA | −2.4 | −1.7 | |
| Wadden and colleagues, 2004 (59) | 123 | 82 | 97.3±13.0 | 35.9±4.5 | 44.2±10.2 | 0 | 65 | 40 | MR | −12.2 | −9.6 | −8.3 |
| | | | | | | | | | DA | −7.8 | −7.5 | −6.2 |
| | | | | | | | | | AA | −0.1 | −0.1 | +0.1 |
| **Very-low-energy diet**[k] | | | | | | | | | | | | |
| Borg and colleagues, 2002 (60) | 90 | 68 | 106.0±9.9 | 32.9±2.6 | 42.6±4.6 | 100 | 134 | 8 | 2 mo VLED followed by DA | −13.0 | −12.1 | −5.3 |
| | | | | | | | | | 2 mo VLED followed by wt maintenance walking group | −14.0 | −12.3 | −4.0 |
| | | | | | | | | | 2 mo VLED followed by wt maintenance resistance training group | −15.5 | −14.9 | −6.1 |
| Fogelholm and colleagues, 1999 (61) | 85 | 80 | 91.9±2.3[g] | 34.0 (29-46)[l] | 29-46[l] | 0 | 52 | 12 | 12 wk VLED followed by DA | −13.5 | +1.7 | |
| | | | | | | | | | 12 wk VLED followed by weight maintenance walking group | −12.6 | −0.5 | |
| Lantz and colleagues, 2003 (62) | 334 | 117 | 114.3±18.9 | 40.0±5.7 | 41.6±11.3 | 26 | 104 | 16 | 16 wk VLED with VLED 2 wks every 3 mo | −20.6 | −15.0 | −7.0 |
| | | | | | | | | | 16 wk VLED with VLED on-demand with wt regain | −22.0 | −17.0 | −9.1 |
| Paisey and colleagues, 2002 (63) | 45 | 25 | 105±21 | 36.8±9.9 | 52.8±12.2 | 40 | 260 | 6 | 6 wk VLED followed by DA | | | |
| | | | | | | | | | DA | −14.5 | −13.5 | −8.9 |
| | | | | | | | | | AA | −3.0 | −2.0 | −1.0 |
| Pasman and colleagues, 1997 (64) | 44 | 31 | 88.7±10.4 | 33.2±3.7 | 41.4±7.4 | 0 | 69 | | 6 wks VLED followed by DA with fiber supplement | −9.8 | −5.3 | −1.4 |
| | | | | | | | | | 6 wks VLED followed by DA without fiber | −11.0 | −8.3 | −4.4 |
| Rössner and colleagues, 1997 (65) | 98 | 93 | 113.6±18.6 | 38.7±5.2 | 20-65[l] | 32 | 52 | 6 | 6 wks VLED followed by DA | −20.1 | −15.1 | |
| | | | | | | | | | 6 wks 880 kcal/d followed by DA | −18.3 | −12.1 | |
| Ryttig and colleagues, 1997 (66) | 81 | 42 | 114.7±20.8 | 37.7±5.7 | 41.8±10 | 45 | 104 | 8 | 2 mo VLED followed by DA | −18.2 | −12.3 | −5.8 |
| | | | | | | | | | DA | −10.2 | −5.5 | −5.5 |
| Stenius-Aarniala and colleagues, 2000 (67) | 38 | 38 | NA | 30-42[l] | 18-60[l] | 76 | 52 | 8 | 8 wk VLED followed by DA | −14.2 | −11.1 | |
| | | | | | | | | | AA | −0.3 | +2.3 | |
| Torgerson and colleagues, 1997 (68) | 113 | 87 | 116.4±16.7 | 40.4±4.3 | 47.1±6.7 | 35 | 104 | 12 | 12 wks VLED followed by DA | −17.0 | −14.0 | −9.2 |
| | | | | | | | | | DA | −7.0 | −7.0 | −6.3 |
| Torgerson and colleagues, 1999 (69) | 121 | 73 | 109.3±16.0 | 38.0±5.0 | 42.6±11.7 | 22 | 52 | 16 | 16 wk VLED followed by DA | −19.1 | −12.3 | |
| | | | | | | | | | 16 wk VLED in metabolic ward followed by DA | −14.0 | −10.2 | |
| | | | | | | | | | 16 wk VLED plus 2 meals/wk followed by DA | −13.2 | −8.6 | |

*(continued)*

**Table.** Baseline data, number of study completers, study duration, type of weight-loss intervention, and weight-loss outcomes reported in studies reviewed to determine type of weight-loss interventions that contribute to successful outcomes (continued)

| Study | No. enrolled | No. of completers | Mean baseline weight (kg) | Mean baseline BMI[a] | Mean baseline age (y) | Sex (% male) | Total study duration (wks) | Treatment duration (wks) | Interventions[b] | Mean Weight Loss (kg) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | 6 mo | 12 mo | Final |
| Van Aggel-Leijssen and colleagues, 2002 (70) | 37 | 22 | 103.0±2.6 | 32.1±2.6 | 33.9±7.7 | 100 | 52 | 12 | 12 wk VLED followed by DE | −14.8 | −8.9 | |
| | | | | | | | | | 12 wk VLED followed by DA | −15.4 | −7.1 | |
| **Orlistat and diet**[m] | | | | | | | | | | | | |
| Bakris and colleagues, 2002 (71) | 532 | 270 | 101.3±1.0 | 35.6±4.0 | 52.9±0.5 | 39 | 52 | NA | O | −5.5 | −5.4 | |
| | | | | | | | | | DA | −2.8 | −2.7 | |
| Broom and colleagues, 2002 (72) | 522 | 327 | 101.4±20.5 | 37.0±6.4 | 46.0±11.5 | 22 | 54 | 54 | O | −6.0 | −5.8 | |
| | | | | | | | | | DA | −2.0 | −2.3 | |
| Davidson and colleagues, 1999 (73) | 880 | 403 | 100.6±0.9 | 36.3±0.9 | 43.8±0.7 | 16 | 104 | 52 | O | −7.8 | −8.8 | −5.6 |
| | | | | | | | | | DA | −6.2 | −5.8 | −2.1 |
| Finer and colleagues, 2000 (74) | 228 | 139 | 98.2±15.0 | 36.8±3.7 | 41.4±10.5 | 11 | 52 | NA | O | −9.0 | −8.8 | |
| | | | | | | | | | DA | −6.7 | −5.4 | |
| Hanefeld and colleagues, 2002 (75) | 383 | 264 | 98.9±18.5 | 34.0±5.6 | 56.2±8.9 | 49 | 52 | NA | O | −4.5 | −5.3 | |
| | | | | | | | | | DA | −3.5 | −3.4 | |
| Hauptman and colleagues, 2000 (76) | 635 | 328 | 100.9±1.0[g] | 36.0±0.3[g] | 42.5±0.8[g] | 22 | 104 | 52 | O | −8.5 | −8.4 | −4.9 |
| | | | | | | | | | DA | −5.5 | −4.3 | −1.5 |
| Hill and colleagues, 1999 (77) | 1313 | 537 | 90.6±0.9[g] | 32.8±0.2[g] | 46.4±0.8[g] | 16 | 76 | 24 | O | −10.0 | NA | −6.2 |
| | | | | | | | | | DA | −10.0 | NA | −5.9 |
| Hollander and colleagues, 1998 (78) | 322 | 254 | 99.7±15.4 | 34.3±3.4 | 55.0±9.7 | 51 | 52 | NA | O | −5.0 | −6.3 | |
| | | | | | | | | | DA | −3.7 | −4.2 | |
| Kelley and colleagues, 2002 (79) | 535 | 265 | 101.9±1.0[g] | 35.7±0.3[g] | 57.9±1.0[g] | 44 | 52 | NA | O | −4.3 | −3.9 | |
| | | | | | | | | | DA | −1.8 | −1.3 | |
| Krempf and colleagues, 2003 (80) | 696 | 425 | 97.3±0.9[g] | 36.1±0.3[g] | 41.0±0.6[g] | 14 | 78 | NA | O | −7.0 | −7.3 | −6.4 |
| | | | | | | | | | DA | −4.0 | −4.4 | −2.7 |
| Miles and colleagues, 2002 (81) | 516 | 311 | 101.6±1.1[g] | 35.4±0.3[g] | 53.1±0.4[g] | 52 | 52 | NA | O | −5.0 | −4.7 | |
| | | | | | | | | | DA | −2.1 | −1.8 | |
| Sjöström and colleagues, 1998 (82) | 743 | 435 | 99.4 (61.0-146.6)[l] | 36.1 (28.3-47.2)[l] | 44.8 (18.0-77.0)[l] | 17 | 104 | 52 | O | −10.0 | −10.3 | −8.0 |
| | | | | | | | | | DA | −8.0 | −6.1 | −5.0 |
| Torgerson and colleagues, 2004 (83) | 3305 | 1414 | 110.5±16.5 | 37.4±4.5 | 43.4±8.0 | 45 | 308 | 26 | O | −10.1 | −10.6 | −5.8 |
| | | | | | | | | | DA | −6.4 | −6.2 | −3.0 |
| **Sibutramine**[n] | | | | | | | | | | | | |
| Apfelbaum and colleagues, 1999 (84) | 205 | 108 | 104.3±20 | 38.3±6.8 | 37.7±9.5 | 20 | 52 | 4 | S | −14.5 | −14.0 | |
| | | | | | | | | | DA | −9.8 | −7.5 | |
| James and colleagues, 2000 (85) | 467 | 261 | 102.6±15.5 | 36.6±4.1 | 40.5±10.3 | 17 | 104 | 26 | S 24 wk followed by S | −12.0 | −12.0 | −10.2 |
| | | | | | | | | | S 24 wk followed by DA | −12.0 | −9.0 | −4.7 |
| McMahon and colleagues, 2000 (86) | 224 | 211 | 96.3±17.1 | 34.3±4.0 | 52.5±10.0 | 39 | 52 | NA | S | −4.3 | −4.4 | |
| | | | | | | | | | AA | −0.5 | −0.5 | |
| McNulty and colleagues, 2003 (87) | 195 | 144 | 102.8±2.9[g] | 36.7±1.0[g] | 50.0±1.1[g] | 44 | 52 | NA | S | −6.2 | −6.8 | |
| | | | | | | | | | DA | −0.5 | −0.3 | |
| Redmon and colleagues, 2002 (88) | 61 | 54 | 110.8±3.9[g] | 38.2±0.9[g] | 53.5±5.0[g] | 46 | 52 | 52 | S | −6.3 | −7.3 | |
| | | | | | | | | | DA | −1.0 | −0.8 | |
| Smith and colleagues, 2001 (89) | 485 | 256 | 87 (60-136)[l] | 32.7±4.1 | 41.9±12.1 | 17 | 52 | NA | S | −5.4 | −5.4 | |
| | | | | | | | | | AA | −2.0 | −1.6 | |
| Wadden and colleagues, 2001 (90) | 53 | 43 | 102.1±11.0 | 37.2±3.3 | 40.1±8.8 | 0 | 52 | 24 | S+4-wk VLED followed by DA | −18.1 | −16.6 | |
| | | | | | | | | | S+DA | −11.4 | −11.1 | |
| | | | | | | | | | S+AA | −5.1 | −3.8 | |

[a]BMI=body mass index.
[b]DA=diet alone; AA=advice alone; DE=diet and exercise; EA=exercise alone; MR=meal replacement; VLED=very-low-energy diet; O=orlistat; S=sibutramine.
[c]Studies have diet alone (reduced energy intake, basic behavioral strategies, and general advice for exercise) as the primary weight-loss intervention.
[d]NA=not available.
[e]CHO=carbohydrate.
[f]Means±95% confidence intervals.
[g]Means±standard error of the mean.
[h]Studies have diet and exercise (reduced energy intake, basic behavioral strategies, and specific goals for exercise) as the primary weight-loss intervention.
[i]Studies have exercise alone (specific guidelines for exercise, no specific recommendations for diet) as the primary weight-loss intervention.
[j]Studies have meal replacements as the primary weight-loss intervention.
[k]Studies have a very-low-energy diet as the primary weight-loss intervention.
[l]Range.
[m]Studies use orlistat and diet as the primary weight-loss intervention.
[n]Studies use sibutramine as the primary weight-loss intervention.

### Data Analysis

All data analysis for this research was generated using SAS software (version 9.1, 2003, SAS Institute Inc, Cary, NC). To complement the systematic review, a meta-analysis was conducted to derive an empirically based estimate of the difference in weight loss between treatments at each time point. For each study, Hedges' gu was used to approximate the population standardized mean differences between groups (ie, difference of population means in the two groups divided by the population standard deviation for the mean difference). The Hedges' gu estimate of effect size has a correction factor that accounts for sample bias and can be interpreted as the number of standard deviations difference between the compared groups (9). Hedges' gu was computed for each study using the SAS macros COMPEFF and COVTEFST. Hedges' gu estimates were combined across studies to obtain an average effect size (and confidence interval) using the SAS macro WAVGMETA. Homogeneity of effect sizes was assessed using the SAS macro WITHIN.

## RESULTS

### Systematic Review

The initial literature review identified 1,797 citations for screening. Of these, 59 studies met inclusion criteria. During the screening process, another 21 articles were identified using the study bibliographies. Thus, a total of 80 studies were ultimately included in the review with 26,455 subjects enrolled and randomized. At the 1-year follow-up, the average participant attrition rate across studies was 29%. Overall, attrition was 31% at study end regardless of follow-up length.

Diet alone was an intervention strategy in 51 studies (in 21 studies it was the primary intervention and an additional 30 studies had a diet-alone comparison arm). Exercise alone was the primary intervention in four studies, with two other studies having an exercise-alone intervention arm. Diet and exercise was the primary intervention in 17 studies. Seven studies used meal replacements and 11 studies used very-low-energy diets. Thirteen studies used orlistat and seven used sibutramine in intervention arms. In addition, 28 studies had an advice-alone arm. Most investigators excluded dropouts from the final data analysis; thus, weight loss by condition is reported primarily for study completers (although intent-to-treat data were included in the meta-analysis where possible). Table 1 presents study characteristics including baseline data, number of study completers, study duration, type of weight loss intervention, and weight-loss outcomes.

Figure 1 provides a visual comparison of the mean weight loss per subject by intervention. Weight loss was observed during the first 6 months of all interventions involving a reduced-energy diet and/or weight-management medication. After 6 months, weight-loss plateaus but none of the groups experienced complete regression to baseline weights by study end. Participants who were simply advised to lose weight with minimal support or in the exercise-alone group experienced minimal weight loss across all time points.

Participants who received diet alone as an intervention experienced a mean weight loss at 6 months of 4.9 kg (5%), maintaining a mean weight loss of 4.6 to 4.4 to 3.0 kg (4.6%, 4.4%, 3.0%) at 12, 24, and 48 months, respectively. When specific recommendations for exercise were added to the dietary interventions, it resulted in a mean weight loss of 7.9 kg (8.5%) at 6 months; weight-loss plateaus to 12 months and at 36 and 48 months is maintained at 3.9 kg (4%). A more structured dietary intervention (ie, meal replacements) resulted in a mean weight loss of 8.6 to 6.7 kg (9.6% to 7.5%) at 6 and 12 months, respectively. Very-low-energy diet use resulted in a major mean weight loss of 17.9 kg (16%) at 6 months followed by a rapid regain so that at 12 months the mean weight loss was 10.9 kg (10%) and by 36 months 5.6 kg (5%). Exercise alone, without a focus on food intake, was not very effective, resulting in a mean 2.4 kg (2.7%) weight loss at 6 months and a mean 1.0 kg (1.0%) at 24 months.

Most of the weight loss from orlistat and sibutramine trials is also observed during the first 6 months. Subjects taking orlistat at 6 months experienced a mean 8.3 kg (8%) weight loss, and a mean 8.2 kg, 7.7 kg, 7.8 kg, and 5.8 kg (8%, 7%, 7%, and 5.3%) at 12, 24, 36, and 48 months, respectively. Subjects taking sibutramine at 6 months experienced a mean 8.2 kg (8.4%) weight loss and a mean 8.2 kg and 10.8 kg (8.4% and 11%) at 12 and 24 months, respectively.

### Meta-Analysis

The dependent variable of interest for the meta-analysis was difference in weight loss in a treatment vs control study arm (eg, diet and exercise vs advice alone) and was treated as a normally distributed variable. Of 80 studies included in the systematic review, 47 provided enough information to calculate Hedges' gu for at least one time point and thus are included in the meta-analysis: 13 studies on diet alone (10,13-16,19,21,25,27,28,30,47,55); four studies on diet and exercise (34,42,45,48); four studies on exercise alone (47,50-52); seven studies on meal replacements (53-59); 12 studies on orlistat (67-78); five studies on sibutramine (80,81,83-85); and two studies on very-low-energy diets (59,64). Figure 2 illustrates the average weight loss in each treatment relative to the comparison group for time points at which Hedges' gu was computed.

For diet-alone interventions compared to advice alone, the average effect size estimates were gu=0.85, 1.12, 0.56, and 0.36 at 6 (seven studies), 12 (10 studies), 24 (three studies), and 36 (two studies) months, respectively, all of which were significantly greater than zero. These corresponded to about 3.7±4.3, 4.5±4.1, 3.3±5.9, and 2.2±6.2 kg more weight loss in the diet-alone groups at 6, 12, and 36 months, respectively. The homogeneity tests showed that effect sizes were significantly heterogeneous across studies at 6 months, ($Q_{6mo}(6)=22.05$, $P<0.001$ and 12, $Q_{12mo}(9)=364.27$, $P<0.001$).

The meta-analyses comparing diet and exercise to advice alone were based on data from four studies. The average effect size estimates were gu=1.52, 0.82, 0.64, and 0.50 at 6 (one study), 12 (three studies), 24 (three studies), and 36 (one study) months, respectively, and all of which were significantly greater than zero. These corresponded to averages of about 7.8±5.2, 3.8±4.6, 3.3±5.1, and 2.6±5.2 kg more weight loss in the diet plus exercise groups at 6, 12, 24, and 36 months, respectively.

Homogeneity tests were not conducted due to the low sample size.

For exercise-alone treatments relative to advice alone, four studies provided sufficient information to be included in the meta-analyses. The average effect size estimates were gu=0.17 (one study), 0.52 (four studies), and −0.28 (one study) at 6, 12, and 24 months, respectively. Only the 12-month effect size estimate was statistically significant and it corresponded to about 1.9±3.6 kg more weight loss among the exercise only groups relative to advice-alone groups. Homogeneity tests were not conducted due to the low sample size.

Seven meal-replacement vs diet-alone studies provided sufficient information to be included in the meta-analyses. Information for five of these studies came from a previous meta-analysis of meal replacements vs a diet comparison group (91). The average effect size estimates were gu=0.89 (seven studies) and 0.60 (six studies) at 6 and 12 months. These corresponded to about 4.0±4.5 and 3.8±6.3 kg more weight loss among the meal-replacement groups relative to the comparison groups at 6 and 12 months, and both were statistically significant. Both the 6- and 12-month effect sizes were heterogeneous across studies ($Q_{6mo}(8)=44.9$, $P<0.001$; $Q_{12mo}(5)=10.9$, $P=0.053$).

Only two studies comparing very-low-energy diets to diet alone provided sufficient information to be included in the meta-analyses; most of the reviewed studies in this area only provided a figure or line graph (without explicit means or standard deviations denoted) to report weight outcomes. Hedges' gu could be calculated for only two studies, each at only one time point (gu=0.24 at 24 months and −0.77 at 60 months) and neither was statistically significant. These effect sizes translated into additional weight loss of 2.8±11.8 kg at 24 and 3.9±5.0 kg weight gain at 60 months in the very-low-energy diet group. These results should be interpreted with caution because each estimate is based on a single small study.

For orlistat treatments relative to diet alone, 12 studies provided sufficient information to be included in the meta-analyses. The average effect size estimates were gu=0.33 (10 studies), 0.37 (12 studies), and 0.29 (three studies) at 6, 12, and 24 months, respectively, and all were statistically significant. These corresponded to an average of about 2.8±8.7, 3.1±8.4, and 3.1±10.5 kg more weight loss among the orlistat groups at 6, 12, and 24 months relative to the comparison groups. The 6- and 12-month homogeneity tests all showed that the effect sizes were heterogeneous ($Q_{6mo}(9)=21.2$, $P<0.012$; $Q_{12mo}(11)=38.24$, $P<0.001$).

The meta-analyses comparing sibutramine treatments to diet alone included data from six studies. The average effect size estimates were 0.78 (four studies) at 6 months, 1.27 (five studies) at 12 months, and 0.52 (one study) at 24 months, and all three were statistically significant. These effect sizes translate into an additional weight loss of about 2.3±3.0 kg at 6 months, 5.1±4.0 kg at 12 months, and 4.0±7.6 kg at 24 months in the sibutramine groups relative to comparison groups. The 6- and 12-month homogeneity tests showed that the effect sizes were heterogeneous ($Q_{6mo}(3)=39.7$, $P<0.001$; $Q_{12mo}(4)=304.5$, $P<0.001$).

## DISCUSSION

Based on the results of a systematic review of the literature, this study provides evidence that among completers of weight-loss clinical trials, interventions that include food and meal planning strategies—diet alone, diet and exercise, and meal replacements—resulted in a mean weight loss of approximately 5 to 8.5 kg (5% to 9%) from starting weight during the first 6 months. Weight-loss plateaus at approximately 6 months and stabilized to a weight loss of approximately 4.5 to 7.5 kg (4.8% to 8%) at 12 months. Weight loss of approximately 3 to 4 kg (3% to 4.3%) was maintained at 24, 36, and 48 months with none of the groups experiencing weight regain to baseline. Numerous reports have concluded that this amount of weight loss contributes to important health benefits (1,3,4). The pattern of weight loss and maintenance with the use of weight-management medications is similar to diet plus exercise at 6 months, but at 24 months participants maintained a mean weight loss of approximately 2 to 5 kg (2% to 5%) above diet and exercise interventions. Very-low-energy diets resulted in a dramatic weight loss followed by rapid and substantial weight regain. Exercise alone or just providing advice, even when accompanied by weight-loss information such as booklets, brochures, weight-loss manuals, or even by one individualized session, did not result in successful weight loss, although no further weight gain was observed in either in these two types of interventions.

Because weight loss appears to plateau at approximately 6 months, the emphasis of a weight-management program should evolve from a focus on weight loss only to weight loss with continued weight-loss maintenance (92). Participants must continue with a lower-energy diet and regular physical activity to prevent weight regain. Health care professionals and participants often express frustrations believing that if a reduced energy intake is maintained (or decreased even further as was done in some studies), weight loss should continue. This appears not to happen even when weight-loss interventions are continued. However, if weight-loss interventions are discontinued entirely, weight regain is likely to occur.

In a recent systematic review of long-term weight loss after diet and exercise clinical trials, Curioni and colleagues (93) reported that individuals in a diet and exercise group had a mean weight loss of 13 kg after intervention compared to a mean weight loss of 9.9 kg in individuals in diet groups. After 1 year, individuals in the diet and exercise groups maintained a weight loss of 6.7 kg compared to 4.5 kg in individuals in the diet groups. This is similar to our data in which at 12 months individuals in the diet and exercise group maintained a weight loss of 7.6 kg and individuals in the diet-alone group 4.6 kg.

Douketis and colleagues (94) also reported on long-term weight loss in subjects with obesity. Data were extracted for weight loss after 1 year (pharmacologic studies only), 2 years, 3 years, and 4 years. Dietary/lifestyle interventions provided <5 kg weight loss after 2 to 4 years, and pharmacologic therapy provided 5 to 10 kg weight loss after 1 to 2 years. Douketis and colleagues' (94) results corroborate the reported results of the review presented here. In addition, Douketis and colleagues (94) noted that a major methodologic limitation of weight-loss studies

involves the reporting of only mean group weight changes. Although means give clues to expected outcomes from interventions at the group level, they do not evaluate how many people attained a significant weight loss, making application to individuals in a weight-management program difficult.

In a systematic review of prospective randomized weight reduction studies with physical activity measured at baseline, Fogelhom and Kukkonen-Harjula (95) reported that at a mean 20-month follow-up, the difference between exercise and control groups' mean weight regain was 1.8 kg. Similarly, we found a difference between mean weight change at 24 months in diet alone and diet and exercise favoring diet and exercise by 1.3 kg. Despite the modest effect of physical activity on weight-loss maintenance, they concluded that physical activity should be recommended as one part of a healthful lifestyle. Aside from weight, physical activity has important positive effects on lipid levels (96), insulin sensitivity (97), and all-cause mortality and cardiovascular disease mortality (98).

Our data related to use of weight-loss medications is supported by a meta-analysis by Haddock and colleagues (99) of obesity pharmacotherapy. They reported the absolute placebo-subtracted weight losses associated with single drugs never reached more than 4 kg. Increasing the length of drug treatment did not lead to more weight loss; thus, longer treatments appear to assist with weight maintenance, but further weight loss beyond the typical plateau at 6 months is unlikely. Similarly, Glazer (100), in a review of efficacy and safety of pharmacotherapy for obesity, reported that subjects receiving sibutramine had a weight loss attributable to the drug (ie, in excess of placebo) in trials lasting 36 to 52 weeks of 4.3 kg and for those receiving orlistat of 3.4 kg. In our review, subjects taking orlistat at 6 months experienced a 3.3 kg weight loss above lifestyle controls, 3.7 kg at 12 months, and approximately 3 kg at 24, 26, and 48 months. Subjects taking sibutramine at 6 months experienced a 3.9 kg weight loss above controls, and 4.9 kg and 6.1 kg at 12 and 24 months, respectively.

The primary diet intervention implemented in 75 intervention arms was a lower-energy, lower-fat diet; three studies used a reduced-energy, moderate-fat diet (Mediterranean type diet); and three studies used some combination of low carbohydrate, high-protein diets. However, at 12 months there were no differences in weight loss based on the macronutrient content of the diet implemented. In general, in the diet-alone studies, the energy intake was approximately 500 kcal or more less than estimated energy need and fat intake was $\leq$30% of total energy intake. In the diet and exercise studies, 1,200 kcal for women and 1,500 kcal for men were generally prescribed. In the orlistat studies at 6 months energy intake was reduced another 200 to 500 kcal to compensate for the reduced energy requirements; however, a minimum of 1,200 kcal/day was prescribed. Advice-alone groups were prescribed the same lifestyle interventions. Our data on meal replacements are supported by a meta-analysis by Heymsfield and colleagues (91) and on very-low-energy diets by a meta-analysis by Tsai and Wadden (101).

In the diet-alone studies, general guidelines for physical activity were suggested. However, in the diet and exercise studies, specific goals for physical activity/exercise were implemented. Continuous or intermittent moderate intensity exercise of 30 to 40 minutes 3 to 5 days per week or 150 minutes per week of moderate intensity physical activity/exercise was recommended. Time spent in physical activity was recorded and monitored.

Basic behavioral weight-loss methods that are identified as being core to behavioral treatment and are used in nearly all weight-loss interventions include self-monitoring, goal setting, stimulus control, reinforcement, and cognitive change (3). Other behavioral strategies shown to be beneficial are problem solving, relapse prevention, and stress management. Social support from partners, family, friends, or others has also been shown to be helpful (12). Study participants in the clinical trials appeared to benefit from the continued professional support they received; 43 studies report monthly follow-up, 14 biweekly or weekly, and 14 quarterly. Support was generally provided in face-to-face encounters, but telephone consults (13,18), and the Internet (26,29,30,36,37) also slowed the rate of weight regain.

The findings of this review are consistent and provide support for the American Dietetic Association's Adult Weight Management Evidence-Based Nutrition Practice Guideline (102). The guidelines recommend that weight-loss and weight-maintenance therapy should be based on a comprehensive weight-management program, including diet, physical activity, and behavioral therapy; that medical nutrition therapy for weight loss should last at least 6 months with implementation of a weight-maintenance program after that time; and that individualized goals of weight-loss therapy should be to reduce body weight at an optimal rate of 0.5 to 1 kg per week for the first 6 months and to achieve an initial weight-loss goal of up to 10% from baseline. Our review also provides support for the statement that food and nutrition professionals are effective counseling interventionists. Interventions and follow-up were provided by registered dietitians in 51 studies, by behavioral specialists in 17 studies, and in three studies by nurses or physicians. Support and involvement when needed from behavioral therapists, exercise physiologists, and physicians is essential. Extended care teams that include registered dietitians and other allied health professionals and that are integrated with clinic-based care should be considered.

As with all systematic reviews and meta-analyses we are limited to abstracting the data reported in the primary studies. It is difficult to account for the potential bias of publishing studies that favor successful interventions and for enrolling participants most likely to be successful. Bias, if any, would likely favor reporting successful interventions and enrolling participants with the greatest potential to complete the trial. Large clinical and community weight-management programs tend to experience a higher dropout rate as compared to published studies. However, if one assumes that the tendency to enroll subjects likely to be successful is evenly distributed across all intervention types, then the program comparison analyses would be appropriate. In many of the studies the number of subjects screened before enrollment is not reported. If all subjects screened were accurately

reported, the percentages of completers in all studies would likely be dramatically reduced.

Many studies could not be included in the meta-analysis because integral measures, such as the standard deviation, were missing and could not be inferred from other information provided. Also, some studies did not include an acceptable comparison group (eg, studies that only included two levels of the same diet). The source of heterogeneity observed in some interventions was not tested, but likely stems from the interstudy differences in areas such as participant populations and treatments.

Most weight-loss outcomes were based on study completers. Such data are invaluable to clinicians because they highlight what can be expected if individuals complete a weight-management program. On the other hand, if a health care provider is looking to determine what percentage of patients who enroll in a particular weight-management program will meet expected outcomes, the data will be less helpful. Unfortunately, due to the design of the systematic review, we were unable to provide more insight into this limitation but future research should address this issue as a component of effective translation of research into recommendations for practical application.

Despite the limitations, this systematic review provides a set of results that represents the longest-term studies of weight loss and maintenance available in the literature and places them in a context that is meaningful to practitioners; that is, by type of weight-management therapy.

## CONCLUSIONS

Based on a systematic review of the literature, weight-management completers can expect to lose a modest amount of weight that will decrease their risk for developing chronic health problems. Weight-loss interventions involving attention to food intake—diet alone, diet and exercise, meal replacements, and weight-loss medications combined with diet—seem to produce the most encouraging short-term results. At approximately 6 months, weight loss begins to plateau across nearly all interventions, but with continued professional support such as was provided in the clinical trials, weight loss can be maintained.

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## References

1. National Institute of Health. National Heart, Lung, and Blood Institute. Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults. The evidence report. *Obes Res*. 1998;6(suppl 2):51S-209S.
2. American Diabetes Association and National Institute of Diabetes, Digestive, and Kidney Diseases. The prevention or delay of type 2 diabetes. *Diabetes Care*. 2002;25:742-749.
3. Klein S, Burke LE, Bray GA, Blair S, Allison DB, Pi-Sunyer X, Hong Y, Eckel RH. Clinical implications of obesity with specific focus on cardiovascular disease. A statement for professionals from the American Heart Association Council on Nutrition, Physical Activity, and Metabolism. *Circulation*. 2004;110:2952-2967.
4. Katz DL, O'Connell M, Yeh MC, Nawaz H, Njike V, Anderson LM, Cory S, Dietz W. Public health strategies for preventing and controlling overweight and obesity in school and worksite settings: A report on recommendations of the Task Force on Common Preventive Services. *MMWR Recomm Rep*. 2005;54:1-12.
5. Flegal KM, Carroll MD, Ogden CL, Johnson CL. Prevalence and trends in obesity among US adults, 1999-2000. *JAMA*. 2002;288: 1723-1727.
6. Flegal KM, Carroll MD, Kuczmarski RJ, Johnson CL. Overweight and obesity in the United States: Prevalence and trends, 1960-1994. *Int J Obes Relat Metab Disord*. 1998;22:39-47.
7. Weis EC, Galuska DA, Khan LK, Serdula MK. Weight-control practices among US adults, 2001-2002. *Am J Prev Med*. 2006;31:18-24.
8. Foster GD, Wadden TA, Vogt RA, Brewer G. What is a reasonable weight loss? Patients' expectations and evaluations of obesity treatment outcomes. *J Consult Clin Psychol*. 1997;65:79-85.
9. Hedges LV. Distribution theory for Glass's estimator of effect size and related estimators. *J Educ Stat*. 1981;6:107-128.
10. Bacon L, Keim NL, Van Loan MD, Derricote M, Gale B, Kazaks A, Stern JS. Evaluating a non-diet wellness intervention for improvement of metabolic fitness, psychological well-being, and eating and activity behaviors. *Int J Obes*. 2002;26:854-865.
11. Brinkworth GD, Noakes M, Keogh JB, Luscome 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*. 2004;28:661-670.
12. Burke V, Mori TA, Giangiulio N, Gillam HF, Heilin LJ, Houghton S, Cutt HE, Mansour J, Wilson A. An innovative program for changing health behaviours. *Asian Pacific J Clin Nutr*. 2002;11(suppl 3):S586-S597.
13. Djuric Z, DiLaura NM, Jenkins I, Darga L, Jen CK-L, Mood D, Bradley E, Hryniuk WM. Combining weight-loss counseling with the Weight Watchers plan for obese breast cancer survivors. *Obes Res*. 2002;10:657-665.
14. Foster GD, Wyatt HR, Hill JO, McGuckin BG, Brill C, Mohammed S, Szapary PO, Rader DJ, Edman JS. Klein S. A randomized trial of a low-carbohydrate diet for obesity. *N Eng J Med*. 2003;348:2082-2090.
15. Heshka S, Anderson JW, Atkinson RL, Greenway FL, Hill JO, Phinney SD, Kolotkin RL, Miller-Kovach K, Pi-Sunyer FX. Weight loss with self-help compared with a structured commercial program. *JAMA*. 2003;289:1792-1798.
16. Jones DW, Miller ME, Wofford MR, Anderson DC, Cameron ME, Willoughby DL, Adair CT, King NS. The effect of weight loss intervention on antihypertensive medication requirements in the Hypertension Optimal Treatment (HOT) Study. *Am J Hypertens*. 1999;12: 1175-1180.
17. Manning RM, Jung RT, Leese GP, Newton RW. The comparison of four weight reduction strategies aimed at overweight patients with diabetes mellitus: Four-year follow-up. *Diabetic Med*. 1998;15:497-502.
18. McManus K, Antinoro L, Sacks F. A randomized controlled trial of a moderate-fat, low-energy diet compared with a low fat, low-energy diet for weight loss in overweight adults. *Int J Obes*. 2001;25:1503-1511.
19. Pritchard DA, Hyndman J, Taba F. Nutritional counseling in general practice: A cost-effective analysis. *J Epidemiol Community Health*. 1999;53:311-316.
20. Ramirez EM, Rosen JC. A comparison of weight control and weight control plus body image therapy for obese men and women. *J Consul Clin Psychol*. 2001;3:440-446.
21. Rapoport L, Clark M, Wardle J. Evaluation of a modified cognitive-behavioural programme for weight management. *Int J Obes Relat Metab Disord*. 2000;12:1726-1737.
22. Sbrocco T, Nedegaard RC, Stone JM, Lewis EL. Behavioral choice treatment promotes continuing weight loss: Preliminary results of a cognitive-behavioral decision-based treatment for obesity. *J Consul Clin Psychol*. 1999;67:260-266.
23. Stern L, Iqbal N, Seshadri P, Chicano KL, Daily DA, McGrory J, Williams M, Gracely EJ, Samaha FF. The effects of low-carbohydrate vs conventional weight loss diets in severely obese adults:

One-year follow-up of a randomized trial. *Ann Intern Med.* 2004; 140:778-785.
24. Toubro S, Astrup A. Randomised comparison of diets for maintaining obese subjects' weight after major weight loss: ad lib, low fat, high carbohydrate diet vs fixed energy intake. *BMJ*. 1997;314:29-34.
25. The Trials of Hypertension Prevention Collaborative Research Group. Effects of weight loss and sodium restriction on blood pressure and hypertension incidence in overweight people with high-normal blood pressure. The Trials of Hypertension Prevention, Phase II. *Arch Intern Med*. 1997;157:657-667.
26. Turnin MC, Bourgeois O, Cathelineau G, Leguerrier AM, Halimi S, Sandre-Banon D, Coliche V, Breux M, Verlet E, Labrousee F, Bensoussan D, Grenier JL, Poncet MG, Gordjmann F, Brun JM, Blickle JF, Mattei C, Bolzonella C, Buisoon JC, Fabaare D, Tauber JP, Hanaire-Broutin H. Multicenter randomized evaluation of a nutritional education software in obese patients. *Diabetes Metab.* 2001; 27:139-147.
27. Whelton PK, Appel LJ, Espeland MA, Applegate WB, Ettinger WH, Kostis JB, Kumanyika S, Lacy CR, Johnson KC, Folmar S, Cutler JA, for the TONE Collaborative Research Group. Sodium restriction and weight loss in the treatment of hypertension in older persons: A randomized controlled trial of nonpharmacologic interventions in the elderly (TONE). TONE Collaborative Research Group. *JAMA*. 1998; 279:839-846.
28. Wolf AM, Conaway MR, Crowther JQ, Hazen KY, Nadler JL, Onedia B, Bovbjerg VE. Translating lifestyle intervention to practice in obese patients with type 2 diabetes. *Diabetes Care.* 2004;27:1570-1576.
29. 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;12:1011-1018.
30. Wylie-Rosett J, Swencionis C, Ginsberg M, Cimino C, Wassertheil-Smoller S, Caban A, Segal-Isaacson CJ, Martin T, Lewis J. Computerized weight loss intervention optimizes staff time: The clinical and cost results of a controlled clinical trial conducted in a managed care setting. *J Am Diet Assoc*. 2001:101:1155-1162.
31. Anderson RE, Wadden TA, Bartlett SJ, Zemel B, Verde TJ, Franckowiak SC. Effects of lifestyle activity vs structured aerobic exercise in obese women. A randomized trial. *JAMA*. 1999;281:335-340.
32. Ashutosh K, Methrotra K, Fragale-Jackson J. Effects of sustained weight loss and exercise on aerobic fitness in obese women. *J Sports Med Phys Fitness*. 1997;37:252-257.
33. Diabetes Prevention Program Research Program. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med*. 2002;346:393-403.
34. Esposito K, Pontillo A, DiPalo C, Giugliano G, Masella M, Marfella R, Marfella R, Giugliano D. Effect of weight loss and lifestyle changes on vascular inflammatory markers in older obese women. *JAMA*. 2003;289:1799-1804.
35. Fleming RM. The effect of high-, moderate-, and low-fat diets on weight loss and cardiovascular disease risk factors. *Prev Cardiol.* 2002;5:110-118.
36. Harvey-Berino J, Pintauro S, Buzzell P, DiGiulio M, Gold BC, Moldovan C, Ramirez E. Does using the Internet facilitate the maintenance of weight loss? *Int J Obes Relat Metab Disord.* 2002;9:1254-1260.
37. Harvey-Berino J, Pintauro S, Buzzell P, Gold EC. Effect of internet support on the long-term maintenance of weight loss. *Obes Res*. 2004;12:320-329.
38. Jakicic JM, Winters C, Lang W, Wing RR. Effects of intermittent exercise and use of home exercise equipment on adherence, weight loss, and fitness in overweight women, a randomized trial. *JAMA*. 1999;282:1554-1560.
39. Jakicic JM, Marcus BH, Gallagher KI, Napolitano M, Lang W. Effect of exercise duration and intensity on weight loss in overweight, sedentary women. A randomized trial. *JAMA*. 2003;290:1323-1330.
40. Jeffery RW, Wing RR, Sherwood NE, Tate DF. Physical activity and weight loss: Does prescribing higher physical activity goals improve outcomes? *Am J Clin Nutr*. 2003;78:684-689.
41. Leermakers EA, Perri MG, Shigaki CL, Fuller PR. Effects of exercise-focused vs weight focused maintenance programs on the management of obesity. *Addict Behav.* 1999;24:219-227.
42. Perri MG, Martin D, Leermakers EA, Sears SF, Notelovitz M. Effects of group- vs home-exercise in the treatment of obesity. *J Consul Clin Psychol.* 1997;65:278-285.
43. Racette SB, Weiss EP, Obert KA, Kohrt WM, Holloszy. Modest lifestyle intervention and glucose tolerance in obese African Americans. *Obes Res*. 2001;9:348-355.
44. Rejeski WJ, Focht BC, Messier SP. Obese, older adults with knee osteoarthritis: Weight loss, exercise, and quality of life. *Health Psychol.* 2002;21:419-426.
45. Tuomilheto J, Lindström J, Eriksson JG, Valle TT, Hämäläinen H, Ilanne-Parikka P, Keinanen-Kiukaanniemia S, Laakso M, Louheranta A, Rastas M, Uusitupa M. for the Finnish Diabetes Prevention Study Group. Prevention of type 2 diabetes by changes in lifestyle among subjects with impaired glucose tolerance. *N Eng J Med*. 2001;344:1343-1350.
46. Lindström J, Louheranta A, Mannelin M, Rastas M, Salminen V, Eriksson J, Uusitupa M, Tuomilehto J. for the Finnish Diabetes Prevention Study Group. The Finnish Diabetes Prevention Study. Lifestyle intervention and 3-year results on diet and physical activity. *Diabetes Care*. 2003;26:3230-3236.
47. Wing RR, Venditti E, Jakicic JM, Polley BA, Lang W. Lifestyle intervention in overweight individuals with a family history of diabetes. *Diabetes Care*. 1998;21:350-359.
48. Wing RR, Jeffrey RW. Benefits of recruiting participants with friends and increasing social support for weight loss and maintenance. *J Consul Clin Psychol*. 1999;67:132-138.
49. Donnelly JE, Jacobsen DJ, Heelan KS, Seip R, Smith S. The effects of 18 months of intermittent vs continuous exercise on aerobic capacity, body weight and composition, and metabolic fitness in previously sedentary, moderately obese females. *Int J Obes*. 2000;24:566-572.
50. Donnelly JE, Hill JO, Jacobsen DJ, Potteiger J, Sullivan DK, Johnson SL, Heelan K, Hise M, Fennessey PV, Sonko B, Sharp T, Jakicic JM, Blair SN, Tran ZV, Mayo M, Gibson C, Washburn RA. Effects of 16-month randomized controlled exercise trial on body weight and composition in young, overweight men and women. The Midwest Exercise Trial. *Arch Intern Med.* 2003;163:1343-1350.
51. Irwin ML, Yasui Y, Ulrich CM, Bowen D, Rudolph RE, Schwartz RS, Yukawa M, Aiello E, Potter JD, McTierman A. Effect of exercise on total and intra-abdominal body fat in postmenopausal women. *JAMA*. 2003;289:323-330.
52. Pritchard JE, Nowson CA, Wark JD. A worksite program for overweight middle-aged men achieves lesser weight loss with exercise than with dietary change. *J Am Diet Assoc.* 1997;97:37-42.
53. Ditshuneit HH, Flechtner-Mor M, Johnson TD, Adler G. Metabolic weight-loss effects of long-term dietary intervention in obese patients. *Am J Clin Nutr*. 1999;69:198-204.
54. Rothacker DQ, Satanieszewski BA, Ellis PK. Liquid meal replacement vs traditional food: A potential model for women who cannot maintain eating habit change. *J Am Diet Assoc*. 2001;101:345-347.
55. Hensrud DD. Dietary treatment and long-term weight loss and maintenance in type 2 diabetes. *Obes Res*. 2001;9:3485-3535.
56. Ashley JM, St Jeor S, Schrage JP, Perumean-Chaney SE, Gilbertson MC, McCall NL, BoVee V. Weight control in the physician's office. *Arch Intern Med*. 2001;161:1599-1604.
57. Ahrens R, Hower M. Evaluation of the effectiveness of an OTC weight loss product vs traditional diet methods in a rural community pharmacy setting. *J Am Pharm Assoc*. 2000;40:275-278.
58. Metz JA, Stern JS, Kris-Etherton P, Reusser ME, Morris CD, Hatton DC, Oparil S, Haynes B, Resnick LM, Pi-Sunyer X, Clark S, Chester L, McMahon M, Snyder GW, McCarron DA. A randomized trial of improved weight loss with a prepared meal plan in overweight and obese patients. *Arch Intern Med.* 2000;160:2150-2158.
59. Wadden TA, Foster GD, Sarwer DB, Anderson DA, Gladis M, Sanderson RS, Letchak RV, Berkowitz RI, Phelan S. Dieting and the development of eating disorders in obese women: Results of a randomized controlled trial. *Am J Clin Nutr.* 2004;80:560-568.
60. Borg P, Kukkonen-Harjula K, Fogelholm M, Pasanen M. Effects of walking or resistance training on weight loss maintenance in obese, middle-aged men: A randomized trial. *Int J Obes.* 2002;26:676-683.
61. Fogelholm M, Kukkonen-Harjula K, Oja P. Eating control and physical activity as determinants of short-term weight maintenance after a very-low-calorie diet among obese women. *Int J Obes*. 1999;23:203-210.
62. Lantz H, Peltonen M, Agren L, Torgerson JS. Intermittent vs on-demand use of very low calorie diet: A randomized 2-year clinical trial. *J Intern Med*. 2003;253:463-471.
63. Paisey RB, Frost J, Harvey P, Paisey A, Bower L, Paisey M, Taylor P, Belka I. Five-year results of a prospective very low calorie diet or conventional weight loss programme in type 2 diabetes. *J Hum Nutr Diet.* 2002;15:121-127.
64. Pasman WJ, Westerterp-Plantenga MS, Muls E, Vansant G, van Ree J, Saris WHM. The effectiveness of long-term fibre supplementation on weight maintenance in weight reduced women. *Int J Obes.* 1997; 21:548-555.

65. Rossner S, Flaten H. VLCD vs LCD in long-term treatment of obesity. *Int J Obes.* 1997;21:22-26.
66. Ryttig KR, Flaten H, Rossner S. Long-term effects of a very-low-calorie diet (Nutrilett) in obesity treatment. A prospective, randomized, comparison between VLCD and a hypocaloric diet + behavior modification and their combination. *Int J Obes.* 1997;21:574-579.
67. Stenius-Arniala B, Poussa T, Kvarnstrom J, Gronlund E-L, Ylikahri M, Mustajoki P. Immediate and long-term effects of weight reduction in obese people with asthma: Randomized controlled study. *BMJ.* 2000;320:827-832.
68. Torgerson JS, Lissner L, Lindroos AK, Kruijer H, Sjostrom L. VLCD plus dietary and behavioural support vs support alone in the treatment of severe obesity. A randomized two-year clinical trial. *Int J Obes.* 1997;21:987-994.
69. Torgerson JS, Agren L, Sjostrom L. Effects on body weight of strict or liberal adherence to an initial period of VLCD treatment. A randomized, one-year clinical trial of obese subjects. *Int J Obes.* 1999;23: 190-197.
70. Van Aggel-Leijssen DP, Saris WH, Hul GB, van Baak MA. Long-term effects of low-intensity exercise training on fat metabolism in weight-reduced obese men. *Metabolism.* 2002;51:1003-1010.
71. Bakris G, Calhoun D, Egan B, Hellmann C, Dolder M, Kingma I on behalf of the orlistat and resistant hypertension investigators. Orlistat improves blood pressure control in obese subjects with treated but inadequately controlled hypertension. *J Hypertens*. 2002;20: 2257-2267.
72. Broom I, Wilding J, Stott P, Myers N on behalf of the UK Multimorbidity Study Group. Randomised trial of the effect of orlistat on body weight and cardiovascular disease risk profile in obese patients: UK Multimorbidity Study. *Int J Clin Pract*. 2002;56:494-499.
73. Davidson MH, Hauptman J, DiGirolamo M, Foreyt JP, Halsted CH, Heber D, Heimburger DC, Lucas CP, Robbins DC, Chung J, Heymsfield SB. Weight control and risk factor reduction in obese subjects treated for 2 years with orlistat. A randomized controlled trial. *JAMA.* 1999;281:235-242.
74. Finer N, James WPT, Kopelman PG, Lean MEJ, Williams G. One-year treatment of obesity: A randomized, double-blind, placebo-controlled, multicentre study of orlistat, a gastrointestinal lipase inhibitor. *Int J Obes*. 2000;24:306-313.
75. Hanefeld M, Sachse G. The effects of orlistat on body weight and glycaemic control in overweight patients with type 2 diabetes: A randomized, placebo-controlled trial. *Diabetes Obes Metab.* 2002;4: 415-434.
76. Hauptman J, Lucas C, Boldrin MN, Collins H from the Orlistat Primary Care Study Group, Segal KR. Orlistat in the long-term treatment of obesity in primary care settings. *Arch Fam Med*. 2000; 9:160-167.
77. Hill JO, Hauptman J, Anderson JW, Fujioka K, O'Neil PM, Smith DK, Zavoral JH, Aronne LJ. Orlistat, a lipase inhibitor, for weight maintenance after conventional dieting: A 1-y study. *Am J Clin Nutr.* 1999:69:1108-1116.
78. Hollander PA, Elbein SC, Hirsch IB, Kelley D, McGill J, Taylor T, Weiss SR, Crockett SE, Kaplan RA, Comstock J, Lucas CP, Lodewick PA, Canovatchel W, Chung J, Hauptman J. Role of orlistat in the treatment of obese patients with type 2 diabetes. *Diabetes Care*. 1998;21:1288-1289.
79. Kelley DE, Bray GA, Pi-Sunyer FX, Klein S, Hill J, Miles J, Hollander P. Clinical efficacy of orlistat therapy in overweight and obese pts with insulin-treated type 2 diabetes. *Diabetes Care*. 2002;25: 1033-1041.
80. Krempf M, Louvet J-P, Allanic H, Miloradovich T, Joubert J-M, Attali J-R. Weight reduction and long-term maintenance after 18 months treatment with orlistat for obesity. *Int J Obes*. 2003;27:591-597.
81. Miles JM, Leiter L, Hollander P, Wadden T, Anderson JW, Doyle M, Foreyt J, Aronne L, Klein S. Effect of orlistat in overweight and obese patients with type 2 diabetes treated with metformin. *Diabetes Care.* 2002;25:1123-1128.
82. Sjostrom L, Rissanen A, Andersen T, Boldrein M, Golay A, Koppeschaar HPF, Krempf M for the European Multicentre Orlistat Study Group. Randomised placebo-controlled trial of orlistat for weight loss and prevention of weight gain in obese patients. *Lancet*. 1998; 352:167-172.
83. Torgerson JS, Hauptman J, Boldrin MN, Sjostrom L. XENICAL in the prevention of diabetes in obese subjects (XENDOS) study. *Diabetes Care*. 2004;27:155-161.
84. Apfelbaum M, Vague P, Ziegler O, Hanotin C, Thomas F, Leutenegger E. Long-term maintenance of a weight loss after a very-low-calorie diet: A randomized blinded trial of the efficacy and tolerability of sibutramine. *Am J Med*. 1999;106:179-184.
85. James WPT, Astrup A, Finer N, Hilsted J, Kopelman P, Rossner S, Saris WHM, Van Gaal LF, STORM Study Group. Effect of sibutramine on weight maintenance after weight loss: A randomized trial. *Lancet*. 2000;356:2119-2125.
86. McMahon FG, Fujioka K, Singh BN, Mendel CM, Rowe E, Rolston K, Johnson F, Mooradian AD. Efficacy and safety of sibutramine in obese white and African American patients with hypertension. A 1-year, double-blind, placebo-controlled, multicenter trail. *Arch Intern Med*. 2000;160:2185-2191.
87. McNulty SJ, Ur E, Williams G for the Multicenter Sibutramine Study Group. A randomized trial of sibutramine in the management of obese type 2 diabetic patients treated with metformin. *Diabetes Care*. 2003;26:125-131.
88. Redmon JB, Raatz SK, Reck KP, Swanson JE, Kwong CA, Fan Q, Thomas W, Bantle JP. One-year outcome of a combination of weight loss therapies for subjects with type 2 diabetes. A randomized trial. *Diabetes Care*. 2003;26: 2505-2511.
89. Smith IG, Goulder MA on behalf of the members of the Sibutramine Clinical Study 1047 Team. Randomized placebo-controlled trial of long-term treatment with sibutramine in mild to moderate obesity. *J Fam Pract*. 2001;50:5005-512.
90. Wadden TA, Berkowitz RJ, Sarwer DB, Prus-Wisniewski R, Steinberg C. Benefits of lifestyle modification in the pharmacologic treatment of obesity. A randomized trial. *Arch Intern Med*. 2001;161:218-227.
91. Heymsfield SB, van Mierlo CAJ, van der Knaap HCM, Heo M, Frier HI. Weight management using a meal replacement strategy: Meta and pooling analysis from six studies. *Int J Obes*. 2003;27:537-549.
92. 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: 1563-1571.
93. Curioni CC, Lourenco PM. Long-term weight loss after diet and exercise: A systematic review. *Int J Obes.* 2005;29:1153-1167.
94. Douketis JD, Macie C, Thabane L, Williamson DF. Systematic review of long-term weight loss studies in obese adults: Clinical significance and applicability to clinical practice. *Int J Obes.* 2005;29: 1153-1167.
95. Fogelholm M, Kukkonen-Harjula K. Does physical activity prevent weight gain—a systematic review. *Obes Rev*. 2000;1:95-111.
96. Kraus EW, Houmard JA, Duscha BD, Kneitzger KJ, Wharton MB, McCartney JS, Bales CW, Henes S, Samsa GP, Otvos JD, Kulkarni KR, Slentz CA. Effects of the amount and intensity of exercise on plasma lipoproteins. *N Eng J Med.* 2002;347:1483-1492.
97. Duncan GE, Pern MG, Theriaque DW, Hutson AD, Eckel RH, Stacpoole PW. Exercise training without weight loss increases insulin sensitivity and postheparin plasma lipase activity in previously sedentary adults. *Diabetes Care.* 2003;26:557-562.
98. Lee DC, Blair SN, Jackson AS. Cardiorespiratory fitness, body composition, and all-cause and cardiovascular disease mortality in men. *Am J Clin Nutr*. 1999;69:373-380.
99. Haddock CK, Poston WSC, Dill PL, Foreyt JP, Ericsson M. Pharmacotherapy for obesity: A quantitative analysis of four decades of published randomized clinical trials. *Int J Obes.* 2002:26:262-273.
100. Glazer G. Long-term pharmacotherapy of obesity 2000. A review of efficacy and safety. *Arch Intern Med*. 2001;161:1814-1821.
101. Tsai AG, Wadden TA. The evolution of very-low-calorie diets: An update and meta-analysis. *Obesity*. 2006;14:1283-1293.
102. American Dietetic Association. Adult Weight Management Evidence-Based Nutrition Practice Guideline. Available at: http://www.adaevidencelibrary.com/topic.cfm?cat=2798&library=EBG. Accessed September 12, 2006.