

The Long-term Effectiveness of Weight Reduction Interventions in Patients with Obesity: A Critical Review of the Literature

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- **Objectives:** (1) To critically evaluate the evidence relating to the long-term (ie, ≥ 2 years) effectiveness of weight reduction interventions in adults with obesity; and (2) to discuss the implications of these findings for the clinical management of patients with obesity.
- **Methods:** A MEDLINE search identified articles published between 1966 and November 1999 relating to the treatment of obesity. Selection criteria were used to limit the analysis to studies of the highest methodologic quality and with a follow-up duration of at least 2 years.
- **Results:** 37 studies were included in the analysis and separated into 4 categories: dietary therapy ($n = 16$); pharmacologic therapy ($n = 7$); surgical therapy ($n = 5$); and dietary counseling or behavioral therapy ($n = 9$). In most studies, there was a pattern whereby weight reduction was effective during the initial 6 to 12 months, followed by a period of gradual weight regain in a large proportion of patients. The effectiveness of long-term weight reduction was dependent on ongoing treatment with a pharmacologic agent or dietary or behavioral counseling. Surgical therapy is the most effective weight reduction intervention, with results usually sustained over the long term. However, this treatment is reserved for a small proportion of adults with morbid obesity.
- **Conclusions:** In obese adults without obesity-related diseases, there is a lack of evidence as to the long-term effectiveness of weight reduction methods. In obese adults with obesity-related diseases (eg, diabetes, hypertension, coronary artery disease, hyperlipidemia, obstructive sleep apnea), there is sufficient evidence indicating that weight reduction is effective because it can alleviate symptoms and reduce medication requirements, at least in the short term.

Obesity is becoming an increasingly prevalent condition, currently affecting about one third of all men and women in North America between the ages of 18 and 65 years [1,2]. Obesity has traditionally been defined by a weight/height² ratio (kg/m²) or body mass index (BMI)

greater than 27 [3,4]. More recent guidelines have classified adults with a BMI of 25 to 29.9 as overweight, those with a BMI of 30 to 39.9 as obese, and those with a BMI of 40 or greater as morbidly obese [5,6]. The BMI is a reliable measure of body adiposity because it is maximally correlated with weight and minimally correlated with height [7-10]. One limitation of the BMI is that it cannot distinguish between increased weight due to fluid retention or increased adiposity, although this should be clinically apparent. In addition, adults with central or android obesity, defined by an increased waist circumference (ie, > 102 cm for men or > 88 cm for women) [6], are at increased risk for obesity-related diseases independent of the BMI [11-16].

It is well established that obesity is associated with a substantial burden of illness and health care costs. Obesity is associated with an increased risk of hypertension [17,18], diabetes mellitus [19,20], hyperlipidemia [21,22], coronary artery disease [23-25], obstructive sleep apnea [26,27], osteoarthritis [28], cholelithiasis [29], and cancers of the breast [30,31], uterus [30,32], prostate [33], and colon [34]. It is also associated with disorders such as depression [35,36], low self-esteem [37], anorexia nervosa, and bulimia [35,38]. Furthermore, obesity is an independent risk factor for increased mortality [39-41], with an estimated reduction in life expectancy of about 1 year [42]. The economic costs associated with the management of obesity and obesity-related diseases represent 3% to 7% of the total health care expenditures in the United States and Canada [43,44].

To date, numerous studies have investigated weight reduction interventions for the treatment of obesity. However, most weight reduction intervention studies have been limited by a short follow-up duration (ie, < 1 year) [45-47]. Because obesity is considered by several authorities to be a chronic disease that is similar to hypertension or hyperlipidemia [48-50], it follows that the effectiveness of weight

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reduction interventions should be evaluated over the long term. Against this background, a systematic review of the literature was conducted. This review critically evaluates the evidence relating to the long-term (ie, ≥ 2 years) effectiveness of weight reduction interventions in adults with obesity and discusses the implications of these findings for the clinical management of patients with obesity.

Methods

The English-language MEDLINE database was searched for articles published between 1966 and November 1999 relating to the treatment of obesity. The key search terms used were *obesity* and *BMI*. Subheadings used were *diet therapy*, *drug therapy*, *surgery*, *therapy*, *randomized controlled trial*, and *prospective cohort study*. Additional articles were identified by scanning the bibliographies of review articles or other relevant articles and the listings of *Current Contents: Clinical Medicine*. To limit the analysis to studies with the highest methodologic quality, study selection criteria were developed a priori. Inclusion criteria were as follows: (1) the study is either a prospective cohort study or a randomized controlled trial investigating the treatment of obesity with one or more of dietary, pharmacologic, surgical, dietary counseling or behavioral weight reduction methods; (2) the duration of patient follow-up is at least 2 years (1 year of follow-up was allowed for studies of pharmacologic therapy because an initial scan of these studies showed that only 2 had a follow-up of at least 2 years); (3) the main outcome is the effect of the weight reduction intervention on body weight or BMI; (4) at least 50 patients are included in the study. Exclusion criteria were as follows: (1) nonconsecutive patients are included; (2) the number of patients lost to follow-up is not reported; (3) the weight reduction intervention is considered unsafe and is not recommended for use (ie, total fasting, jaw wiring, intestinal bypass surgery); (4) the weight reduction intervention includes a drug that has been withdrawn from the North American market (eg, fenfluramine, dexfenfluramine). In studies with multiple publications, the version with the longest duration of patient follow-up was evaluated. Studies were separated into 4 categories as follows: (1) dietary therapy, (2) pharmacologic therapy, (3) surgical therapy, (4) dietary counseling or behavioral therapy. In studies where patients received multiple weight reduction interventions, studies were classified according to the intervention that was being tested (eg, pharmacologic vs. placebo; all patients receive dietary and physical exercise therapy).

Results

Of 870 retrieved studies, 178 satisfied the inclusion criteria. Of these, 141 were excluded because of one or more exclusion criteria, leaving 37 studies in the analysis [51–87]. Of these studies, 16 investigated dietary therapy [51–66], 7 stud-

ies investigated pharmacologic therapy [67–73], 5 studies investigated surgical therapy [74–78], and 9 studies investigated dietary counseling or behavioral therapy [79–87].

Dietary Therapy (Table 1)

Dietary therapy for obesity usually is combined with other weight reduction methods that include behavioral therapy, dietary counseling, and physical exercise. The 3 main types of dietary therapy are a low-calorie diet (LCD), which provides 800 to 1500 kcal of energy daily; a very-low-calorie diet (VLCD), which provides less than 800 kcal of energy daily and usually consists of a protein-enriched liquid; and an energy-restricted or hypocaloric diet (HCD), which is based on a person's estimated daily energy requirement (ie, basal metabolic rate $\times 1.3$). Eight randomized controlled trials and 8 prospective cohort studies of dietary therapy were evaluated.

In 8 randomized controlled trials [51–58], weight reduction was most effective during the period of supervised dietary treatment, but across studies there was a pattern of gradual weight regain during the subsequent unsupervised follow-up period. At the end of the follow-up period, the mean weight reduction in most study populations was relatively modest (ie, 2 to 6 kg). One study reported a considerable mean weight reduction of 8.7 kg after a 7-year follow-up period in men who received an LCD and long-term dietary and lifestyle counseling [54]. However, women allocated to the same treatment achieved a mean weight reduction of only 3.5 kg.

Of 8 prospective cohort studies, 5 studies with a similar follow-up duration (ie, 2 to 2.5 years) reported highly varied weight loss, with reported mean weight reductions of 5.8 to 20.4 kg [60–62,65,66]. In one study with a 42-month follow-up duration [63], the mean weight reduction was about 7.3 kg, with a mean weight regain of about 62%. In another study with a 5-year follow-up [59], one patient group that received a VLCD and behavioral therapy had a mean weight reduction of 16.9 kg, but this was observed in a minority of patients (13 of 59) that completed follow-up. In patients that did not complete the 5-year follow-up, there was a mean weight gain of 5.2 kg. One study was noteworthy because of its long follow-up duration (ie, 10 to 12 years) [64]. In this study, 56 patients received a VLCD, behavioral therapy, and dietary counseling throughout the follow-up period and had a reported mean weight reduction of 10.6 kg. Overall, the magnitude of weight reduction and the proportion of patients with sustained weight reduction was better in the cohort studies. However, across studies there was a consistent pattern of initial weight loss followed by gradual weight regain in a considerable proportion of patients.

Pharmacologic Therapy (Table 2)

Pharmacologic weight reduction therapy is usually combined with some form of dietary therapy, with or without other

interventions that include behavioral and physical exercise therapy. Currently available appetite-suppressant (anorectic) drugs that have been investigated for the treatment of obesity include fluoxetine, a selective serotonin reuptake inhibitor; sibutramine, a serotonin and norepinephrine reuptake inhibitor; and mazindol, a noradrenergic agent. In recent years, a gastrointestinal lipase inhibitor (orlistat) has been developed that promotes weight reduction by inhibiting fat absorption. Seven randomized controlled trials that investigated the effectiveness of 12 to 24 months of an anorectic or lipase-inhibiting drug were evaluated [67–73]. In 3 studies investigating the use of an anorectic drug, patients received an LCD and were randomized to placebo or to one of fluoxetine, mazindol, or sibutramine for 1 year [67–69]. In general, weight reduction varied from 1.7 to 14.1 kg, depending on the anorectic drug that patients received, and was sustained as long as patients continued to receive anorectic drug therapy.

In 4 studies investigating the use of orlistat as part of a weight reduction intervention, patients received an HCD and were randomized to receive orlistat or placebo for 1 to 2 years [70–73]. These studies found that weight reduction was sustained over a 1- to 2-year period while patients received this treatment. However, in 2 studies with a 2-year follow-up, there was a trend towards weight regain during the second year of follow-up, although a mean weight loss of 7% to 8% of the baseline body weight was still maintained.

Surgical Therapy (Table 3)

Bariatric or weight reduction surgery is usually reserved for patients with morbid obesity who are refractory to other non-surgical weight reduction interventions. Bariatric surgery is usually combined with dietary and/or behavioral therapy and is separated into 2 main categories: (1) gastric bypass, which involves complete gastric partitioning with anastomosis of the proximal gastric segment to a jejunal loop; and (2) gastropasty, which involves partial gastric partitioning at the proximal gastric segment and placement of a gastric outlet stoma. Both methods are intended to create an upper gastric pouch that reduces gastric luminal capacity, thereby resulting in early satiety. Four randomized controlled trials and 1 prospective cohort study were evaluated [74–78]. All studies reported long-term success in sustaining the weight reduction that occurred during the initial 3 to 6 months after surgery. The magnitude of weight loss with surgical therapy was greater than that observed with dietary or drug treatments. In studies that reported mean weight loss in the study population, the mean weight loss was between 28.4 and 44.2 kg. In these studies, postoperative mortality was low, with one surgery-related death in all studies. Postoperative morbidity was usually secondary to infection (eg, wound-related, pneumonia) or pulmonary complications (eg, atelectasis) and occurred in less than 5% of patients. The need for

re-operation varied widely, from 1.7% to 7.1% in 3 studies and from 20.3% to 33.3% in 2 studies.

Dietary Counseling and Behavioral Therapy (Table 4)

Dietary counseling usually consists of individual or group sessions that deal with dietary and lifestyle modifications coupled with reinforcement of these changes using behavioral therapy. Behavioral therapy, which consists of cognitive behavior modification and behavior skills training, is aimed at modifying eating and physical activity habits as a means of preventing weight regain and is used as an adjunct to dietary therapy. Five randomized trials and 4 prospective cohort studies were evaluated [79–87]. The mean weight reduction across studies was modest (1 to 5 kg), with a pattern of weight loss during the initial 6 to 12 months followed by gradual weight regain during the subsequent follow-up period. However, in 2 studies that reported the proportion of patients who achieved a predetermined weight reduction goal, 34% and 39% of patients maintained a 4.5-kg weight loss during a 4-year period [81,83]. In these studies, modest weight loss was sustainable over the long term in a small proportion of patients who were receiving continuous dietary counseling with or without behavioral therapy.

Methodologic Limitations of Studies

There were several methodologic limitations identified across studies that limit the interpretation of results and the strength of the study conclusions. First, in all but 2 of the 37 studies the effectiveness of weight reduction, as determined by the change in weight or BMI, was reported only for patients who remained in the study until the end of the follow-up period [59,67]. This has the potential to exaggerate the effectiveness of weight reduction methods if patients who achieved greater weight reduction were more likely to remain in the study [88]. Second, methods of patient recruitment were not clearly specified in the studies of dietary, drug and dietary counseling, and behavioral therapy. In 18 studies that specified methods of patient recruitment, 9 studies recruited patients from tertiary-care obesity clinics [57,70–73,79,81–83], 11 studies recruited patients using media advertisements [51,56,58,60,61,66,67,70,80,85,87], and 4 studies provided patients with a financial incentive to remain in a weight reduction program [61,85–87]. Furthermore, 4 studies excluded patients who did not demonstrate a pre-study weight reduction goal [70,72,73] or who were less compliant during a pre-study lead-in phase [69]. These factors might have resulted in preferential selection of patients who would be more likely to achieve greater weight reduction, who are better motivated, and who are not representative of the general population of obese patients. Third, the interpretation of the effectiveness of weight reduction treatments was limited because in all but 7 studies

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Table 1. Studies of the Effectiveness of Dietary Therapy for Obesity

Study	No. of Patients (No. of Women)	Length of Follow-up	Patients Lost to Follow-up (%)	Intervention Groups	Mean Baseline BMI or Weight, kg
Randomized controlled trials					
Hakala et al [51]	60 (40)	5 yr	7 (8.6)	A: LCD + group counseling B: LCD + individual counseling	BMI 41.7–43.6
Miura et al [52]	70 (46)	2 yr	0 (0)	A: VLCD B: VLCD + BT C: BT	Weight 37%–65% above ideal
Wadden et al [53]	76 (76)	5 yr	21 (28)	A: VLCD B: VLCD + BT C: BT	BMI 39.4
Karvetti et al [54]	189 (147)	7 yr	110 (58)	A: LCD B: LCD + counseling	A: BMI 33.5 B: BMI 34.3
Skender et al [55]	127 (61)	2 yr	66 (52)	A: LCD B: Exercise C: LCD + exercise	A: 98.5 B: 93.1 C: 100.1
Torgerson et al [56]	113 (74)	2 yr	26 (23)	A: VLCD + counseling B: Counseling	A: 116.2 B: 116.6
Ryttig et al [57]	81 (44)	26 mo	39 (48)	A: VLCD + BT B: VLCD + LCD C: VLCD + VLCD	A: 116.2 B: 113.2 C: 113.2
King et al [58]	103 (0)	2 yr	30 (29)	A: LCD + counseling B: LCD C: Exercise + counseling D: Exercise	A: 85.7 B: 83.4 C: 91.0 D: 86.2
Prospective cohort studies					
Pekkarinen et al [59]	59 (34)	5 yr	8 (14)	A: VLCD + BT B: BT	A: 131.2 B: 134.2
Pekkarinen et al [60]	62 (57)	2 yr	5 (8.1)	VLCD	99.0
Nunn et al [61]	60 (44)	2.5 yr	3 (0.5)	VLCD + BT	104.3
Anderson et al [62]	80 (55)	2 yr	34 (43)	VLCD + BT + counseling	BMI > 40
Anderson et al [63]	100 (71)	42 mo	42 (42)	VLCD + BT + counseling	Women 93.7; men 115.7
Bjorvell et al [64]	68 (53)	10–12 yr	12 (18)	VLCD + BT + counseling + exercise	BMI 41.0
Ditschuneit et al [65]	100 (79)	27 mo	47 (44)	A: LCD (self-selected diet) B: LCD (meal replacements)	A: 92.6 B: 92.6
James et al [66]	112 (41)	2 yr	21 (19)	LCD	108.1 (men) 88.8 (women)

BMI = body mass index; BT = behavioral therapy; LCD = low-calorie diet; VLCD = very-low-calorie diet.

Mean Weight Loss/Gain at Follow-up, kg	Comments
A: -2.1 to -3.0 B: -3.4 to -12.9	A: 86% of weight loss regained among women, 80% among men B: 71% of weight loss regained among women, 50% among men
A: -4.5 B: -1.3 C: No change	—
A: +1.0 B: +2.7 C: +2.9	64% regained all weight loss, 18% maintained loss of 0.1-5.0 kg, 18% maintained loss of > 5 kg
A: N/A B: -3.5 women; -8.7 men	—
A: +0.9 B: -2.7 C: -2.2	—
A: -9.2 B: -6.3	A: 45% of women, 75% of men had weight loss > 5 kg B: 50% of women, 40% of men had weight loss > 5 kg
A: -5.5 B: -5.9 C: -5.7	—
A: -4.4 B: -3.3 C: -3.7 D: -1.6	—
A: -16.9 B: -4.9	Mean weight gain among patients who did not complete treatment (A: +5.2 kg [n = 12], B: +13.0 kg [n = 3])
-5.8	19 patients did not regain weight, 24 regained 70% lost weight, and 13 regained 100% of lost weight
-13.1	—
N/A	Mean regain 52% of lost weight
Women -7.3 Men -7.2	Mean regain 61% of lost weight among women and 64% among men
-10.6	—
	A: Mean weight loss = 5.9% B: Mean weight loss = 11.3%
N/A	8% weight loss (men) 13% weight loss (women)

[53,56,57,75,81,83,87], results were expressed as the change in the mean weight or BMI for all study patients rather than the proportion of patients who achieved a predetermined weight reduction target. Fourth, only 3 studies investigated the effects of weight reduction on the incidence of major clinical outcomes [81,82,84]. In these studies, deaths and major morbid events (eg, myocardial infarction, stroke) were infrequent, with no significant difference in rates between weight reduction and control groups. Finally, few studies have investigated the long-term (≥ 2 years) effectiveness and safety of pharmacologic weight reduction interventions, which highlights the need for further long-term prospective studies. Because obesity may be considered a chronic disease [48-50] that may require an indefinite duration of treatment to prevent weight regain, pharmacologic therapy will prove to be beneficial only if long-term effectiveness and safety is demonstrated. Given that several pharmacologic weight reduction interventions introduced in the past 30 years have not withstood the test of time, physicians should consider pharmacologic therapy of obesity with some caution and with careful patient monitoring.

Practical Considerations in the Treatment of Obesity

What Are the Health Benefits Associated With the Treatment of Obesity?

In obese adults with concurrent diseases that might be causally linked with obesity, there is sufficient evidence that weight reduction can provide health benefits, at least in the short term (ie, within 2 years of starting a weight reduction program). In patients with obesity and diabetes, 3 prospective cohort studies found that weight reduction with dietary treatment was associated with improved glycemic control and a reduction in oral hypoglycemic drug and insulin requirements [88-90]. In patients with obesity and hypertension, 3 randomized controlled trials and 4 prospective cohort studies found that weight reduction resulted in reduced blood pressure and decreased antihypertensive drug requirements [81-83, 91-95]. In patients with obesity and hyperlipidemia, 4 prospective cohort studies found that weight reduction improved the serum lipid profile [89,96-98]. Further, improvements in blood pressure control, blood glucose levels, and serum lipid levels were found to occur with modest weight reductions (ie, 5 to 10 kg) [81-83,98,99]. Two randomized controlled trials involving obese and nonobese adults with coronary artery disease found that a risk reduction program that included a low-fat diet, aerobic exercise, and smoking cessation was associated with fewer anginal symptoms [100,101]. Three prospective cohort studies found that weight reduction in obese adults alleviated symptoms of obstructive sleep apnea [26, 102, 103].

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Table 2. Randomized Controlled Trials of the Effectiveness of the Pharmacologic Treatment of Obesity

Study	No. of Patients (No. of Women)	Length of Follow-up	Patients Lost to Follow-up (%)	Intervention Groups	Mean Baseline BMI or Weight, kg
Goldstein et al [67]	45 8 (371)	12 mo	245 (53)	A: LCD + fluoxetine 60 mg once daily B: LCD + placebo	A: BMI 36.2 B: BMI 35.8
Enzi et al [68]	158 (47)	12 mo	49 (31)	A: Mazindol B: LCD C: Placebo (multiphase crossover study)	Weight > 50% above ideal
Hollander et al [69]	321 (157)	12 mo	67 (21)	A: HCD + orlistat 120 mg b.i.d. B: HCD + placebo	A: 99.6 B: 99.7
Sjostrom et al [70]	743 (567)	24 mo	308 (41)	A: HCD + orlistat 120 mg t.i.d. B: HCD + placebo	A: 99.1 B: 99.8
Davidson et al [71]	892 (741)	24 mo	403 (45)	A: HCD + orlistat 120 mg t.i.d. B: HCD + placebo	A: 100.7 B: 100.6
Hill et al [72]	729 (605)	12 mo	192 (26)	A: HCD + orlistat 120 mg t.i.d. B: HCD + orlistat 60 mg t.i.d. C: HCD + orlistat 30 mg t.i.d. D: HCD + placebo	A: 89.7 B: 92.4 C: 89.3 D: 90.3
Apfelbaum et al [73]	205 (N/A)	12 mo	97 (46)	VLCD for 4 weeks, then A: HCD + sibutramine 10 mg daily B: HCD + placebo	A: 95.7 B: 97.7

BMI = body mass index; HCD = hypocaloric diet LCD = low-calorie diet.

Table 3. Studies of the Effectiveness of Surgical Treatment of Obesity

Study	No. of Patients (No. of Women)	Length of Follow-up	Patients Lost to Follow-up (%)	Intervention Groups	Mean Baseline BMI or Weight, kg	Mean Weight Loss/Gain at Follow-up, kg
Randomized controlled trials						
Anderson et al [74]	57 (50)	5 yr	1 (1.8)	A: VLCD B: LCD + gastroplasty	A: 115 B: 120	A: -26.8 B: -18.2
Hall et al [75]	310 (288)	3 yr	52 (17)	A: Gastric bypass B: Gastroplasty C: Gastrogastrostomy	A: 110 B: 112 C: 115	A: -17 B: -31 C: -39
Naslund et al [76]	57 (51)	2 yr	0 (0)	A: Gastric bypass B: Gastroplasty	A: 117.7 B: 117.8	A: -42.9 B: -27.6
Lechner et al [77]	112 (N/A)			A: Gastric bypass B: Gastroplasty	A: 119.9 B: 118.6	A: -45.5 B: -28.8
Prospective cohort study						
Ashley et al [78]	114 (96)	6-48 mo	5 (4.4)	Gastroplasty	BMI 44.8	N/A

BMI = body mass index; LCD = low-calorie diet; VLCD = very low-calorie diet.

Mean Weight Loss/Gain at Follow-up, kg	Comments
A: -1.7 B: -2.1	—
A: -10.2 B: -7.2 C: -9.5	—
A: -6.2 B: -4.3	—
N/A	A: mean weight loss = 8.0%, 57.1% maintain > 5% weight loss B: mean weight loss = 4.6%, 37.4% maintain > 5% weight loss
N/A	A: mean weight loss = 7.6%, 34.4% maintain > 10% weight loss B: mean weight loss 4.5%, 17.5% maintain > 10% weight loss
A: -7.2 B: -6.2 C: -5.2 D: -5.9g	—
A: -14.1 B: -7.3	A: 96% maintain > 50% weight loss B: 33% maintain > 50% weight loss

Comments
A: 21/30 patients regained most weight loss (within 1 kg of baseline weight) B: 16/27 patients regained most weight loss (within 1 kg of baseline weight)
66% of patients in group A, 44% of group B, and 16% in group C had > 50% excess weight loss
—
—
31 of 47 patients followed for 2 yr regained > 50% of lost weight

Despite convincing evidence relating to the short-term effectiveness of obesity treatment, there is limited evidence that weight reduction is associated with a reduction in major clinical outcomes (eg, myocardial infarction, stroke, cardiovascular death). In cross-sectional population-based studies, a history of intentional weight loss in nonsmoking adults was associated with a 32% to 44% reduction in diabetes-related mortality, but intentional weight reduction was not associated with a reduction in total or cardiovascular mortality [104,105]. In a retrospective analysis of the Framingham population, people with a history of intentional weight loss of 10% or more of total body weight had, on average, a 6.6-mm Hg decrease in systolic blood pressure, a 0.28-mmol/L decrease in serum cholesterol, and a 20% decrease in fasting serum glucose [24]. It was postulated that these changes could result in a 20% reduction in the incidence of symptomatic coronary artery disease. One retrospective study of 263 obese diabetic patients found that those with a history of intentional weight reduction had a longer survival compared with a matched group without previous weight reduction [106]. Three randomized controlled trials that included non-obese and obese patients with recent myocardial ischemia found that a low-fat diet as part of a dietary, physical exercise, and lifestyle modification program was associated with a reduction in the rate of myocardial ischemia and cardiovascular death [107] and retarded progression of coronary atherosclerosis [108,109]. Thus, although there is indirect evidence that weight reduction might reduce the incidence of major cardiovascular outcomes, this has not been demonstrated in prospective studies when the effects of dietary, pharmacologic, or surgical weight reduction interventions are evaluated independent of other interventions such as an aerobic exercise program. Studies are ongoing that will use hard clinical endpoints to evaluate the long-term effectiveness of weight reduction interventions [110,111].

What Are the Health Risks Associated With Obesity Treatments?

A comprehensive evaluation of the adverse effects of weight reduction interventions is beyond the scope of this review. Briefly, treatment with a VLCD is associated with fatigue, dizziness, hair loss, menstrual irregularities, cholelithiasis, gouty arthritis, and cardiac arrhythmias [112,113]. Anorectic drugs are associated with drowsiness, fatigue, nausea, diarrhea, urinary retention, and xerostomia [114]. Some anorectic drugs (ie, dexfenfluramine, fenfluramine, phentermine) have been associated with a small but clinically important increased risk of pulmonary hypertension and valvular heart disease [115,116], which has resulted in the withdrawal of these

Table 4. Studies of the Effectiveness of Dietary Counseling and Behavioral Therapy for Obesity

Study	No. of Patients (No. of Women)	Length of Follow-up	Patients Lost to Follow-up (%)	Intervention Groups	Mean Baseline BMI or Weight, kg	Mean Weight Loss/Gain at Follow-up, kg	Comments
Randomized controlled trials							
Trials of Hypertension Prevention [79]	2382 (N/A)	36 mo	98.1%–99.3% completed trial	A: Counseling B: Sodium restriction C: Counseling + sodium restriction (D: Control)	N/A	A: -0.2 B: +1.7 C: -0.3 D: +1.8	—
Hakala [80]	52 (42)	5 yr	52 (100)	A: Counseling at rehabilitation center B: Individual counseling	A: Men 104.0; women 121.9 B: Men 104.3; women 120.2	A: Men +0.3; women -6.8 B: Men +0.5; women +0.2	—
Siamler et al [81]	189 (69)	4 yr	8 (4.2)	A: Counseling + stop antihypertensive drugs B: Stop antihypertensive drugs (C: Control)	A: 77.6 B: 76.7 C: 77.4	A: -1.8 B: +2.0 C: +2.0	39% of group A patients maintained 4.5 kg weight loss
Hypertension Prevention Trial [82]	841 (292)	3 yr	90%–94%	A: Counseling B: Sodium restriction C: Counseling + sodium restriction (D: Control)	A: 87.4 B: 84.2 C: 84.1 D: 83.4	A: -1.6 B: +0.7 C: -0.1 D: +1.9	—
Elmer et al [83]	902 (354)	4 yr	85% at 2 yr	Counseling + BT for all patients (randomly assigned to receive 1 of 4 antihypertensive drugs or placebo)	85.1	-2.6	After 4 yr, 70% of patients remained below baseline weight and 34% had at least 4.5 kg weight loss
Prospective cohort studies							
Eriksson et al [84]	222 (0)	5 yr	32 (14)	Exercise + counseling	BMI 26.6–27.7	-2.0 to -3.3	—
Jeffery et al [85]	89 (0)	2 yr	9 (10)	Exercise + counseling	100.4 kg	-5.1	—
Kramer et al [86]	200 (12)	4 yr	48 (24)	Exercise + counseling	101.1 kg	-2.8 to -4.0	—
Adams et al [87]	125 (108)	12–36 mo	83 (66)	BT	93.8 kg	N/A	33 patients regained weight; 25 sustained weight loss

BMI = body mass index; BT = behavioral therapy.

drugs from the North American market. Bariatric surgery is associated with several postoperative complications including gastric leakage, gastric outlet obstruction, staple line breakdown, and complications related to surgery in the morbidly obese patient (eg, wound dehiscence and infection, pneumonia, venous thromboembolism) [117,118]. Weight reduction interventions also are associated with an increased risk for major depression, bulimia, and other eating disorders [119,120]. Despite previous concerns that repeated episodes of weight loss followed by weight regain (weight cycling or “yo-yo” dieting) may be associated with increased mortality, several recent reviews have found that weight cycling is not associated with increased mortality [121,122].

What Is the Role of Physical Exercise in the Treatment of Obesity?

In general, physical exercise as an isolated weight reduction intervention results in only modest weight loss, since considerable energy needs to be expended for weight reduction in the absence of dietary therapy [123–125]. However, regular physical exercise is an integral component of obesity treatment and is an important determinant of long-term maintenance of weight loss [126–128]. Physical exercise that expends 1500 to 2000 kcal of energy per week is effective in maintaining more than 75% of weight loss resulting from a weight-reduction program [129]. A more comprehensive evaluation of the role of physical exercise in the treatment of obesity has been recently conducted [130].

How Well Do Patients Adhere to Weight Reduction Interventions?

Compliance with a weight reduction intervention is likely to vary depending on the type of weight reduction intervention, the availability and extent of supervision, the use of adjunctive treatments (ie, behavioral therapy, physical exercise), and the duration of treatment. In the studies that were reviewed, most of which were undertaken in a supervised clinical setting, the mean rate of patient drop-outs due to noncompliance or treatment intolerance following dietary, pharmacologic, surgical, and behavioral interventions was 32%, 39%, 9%, and 8%, respectively. In patients who are undertaking weight reduction interventions outside of a supervised clinical setting, noncompliance with a weight reduction program is likely to be greater, given that clinical trials tend to include volunteers who may be highly motivated to lose weight or patients who have previously demonstrated successful weight reduction. Although there are case series of patients who have demonstrated long-term weight reduction, there is little information as to the likelihood of long-term weight maintenance in unselected obese patients who are receiving weight reduction interventions.

Two factors that have been associated with an increased risk of weight regain are lack of regular physical exercise during a weight reduction intervention program and a lack of social support [131,132].

Summary and Guidelines for Clinical Management

This review evaluated the evidence relating to the effectiveness of methods used to prevent and treat obesity. The analysis suggests that weight reduction methods are ineffective over the long term (≥ 2 years) except in a small proportion of people who receive dietary, selected pharmacologic, and surgical treatments. In addition, in patients with obesity and obesity-related diseases (eg, diabetes, coronary artery disease, hypertension, hyperlipidemia, obstructive sleep apnea), weight reduction is effective at least in the short term to alleviate symptoms and to decrease drug therapy requirements. In most studies of obesity treatment, there was a general pattern observed in which weight reduction was effective in most patients during the initial 6 to 12 months after the start of treatment followed by a period of gradual weight regain in a large proportion of patients. In general, the effectiveness of long-term weight reduction was dependent on continuing treatment either with a pharmacologic agent or dietary and/or behavioral counseling. Surgical treatments for obesity were found to be associated with the greatest magnitude of weight reduction, which was often sustained over the long-term, but this treatment is reserved for a small proportion of obese adults with morbid obesity and can be associated with clinically important postoperative complications.

The following evidence-based clinical management guidelines are suggested for health care providers who are involved in the care of overweight or obese patients:

1. Overweight or obese patients without obesity-related diseases. In unselected patients who are overweight (BMI, 25 to 29.9) or obese (BMI > 30), in whom there is no concurrent obesity-related disease, there is insufficient evidence to recommend in favor of or against weight reduction interventions because of a lack of strong evidence that weight reduction methods are effective over the long term. Weight reduction interventions should be considered based on an assessment of a patient's risk of developing obesity-related diseases. If a weight reduction intervention is begun, modest weight reduction goals (ie, 5% to 10% of body weight) should be considered that are sufficient to reduce the risk of obesity-related diseases. In the absence of weight reduction interventions, maintenance of a stable weight is a reasonable long-term objective.
2. Patients who are overweight or obese with concurrent obesity-related diseases. In a high-risk group of overweight or

obese adults with concurrent diseases that may be causally linked to obesity (eg, diabetes, hypertension, coronary artery disease, hyperlipidemia, obstructive sleep apnea), there is sufficient evidence to recommend in favor of weight reduction interventions. In this patient group, even modest weight reduction (ie, 5 to 10 kg) may be beneficial, at least in the short term, to improve symptoms and to reduce drug therapy requirements.

3. Nonoverweight or nonobese patients. Given the considerable health risks associated with overweight or obesity and the limited long-term effectiveness of weight reduction interventions, the prevention of obesity through maintenance of a stable weight should be a priority for health care providers.

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