Screening and Interventions for Obesity in Adults: Summary of the Evidence for the U.S. Preventive Services Task Force

Kathleen M. McTigue, MD, MPH; Russell Harris, MD, MPH; Brian Hemphill, MD, MPH; Linda Lux, MPA; Sonya Sutton, BSPH; Audrina J. Bunton, BA; and Kathleen N. Lohr, PhD

Background: **Obesity poses a considerable and growing health burden. This review examines evidence for screening and treating obesity in adults.**

Data Sources: **MEDLINE and Cochrane Library (January 1994 through February 2003).**

Study Selection: **Systematic reviews; randomized, controlled trials; and observational studies of obesity's health outcomes or efficacy of obesity treatment.**

Data Extraction: **Two reviewers independently abstracted data on study design, sample, sample size, treatment, outcomes, and quality.**

Data Synthesis: **No trials evaluated mass screening for obesity, so the authors evaluated indirect evidence for efficacy. Pharmacotherapy or counseling interventions produced modest (generally 3 to 5 kg) weight loss over at least 6 or 12 months, respectively. Counseling was most effective when intensive and combined with behavioral therapy. Maintenance strategies helped retain weight loss. Selected surgical patients lost substantial weight (10 to 159 kg over 1 to 5 years). Weight reduction improved blood pressure, lipid levels, and glucose metabolism and decreased diabetes incidence. The internal validity of the treatment trials was fair to good, and external validity was limited by the minimal ethnic or gender diversity of volunteer participants. No data evaluated counseling harms. Primary adverse drug effects included hypertension with sibutramine (mean increase, 0 mm Hg to 3.5 mm Hg) and gastrointestinal distress with orlistat (1% to 37% of patients). Fewer than 1% (pooled samples) of surgical patients died; up to 25% needed surgery again over 5 years.**

Conclusions: **Counseling and pharmacotherapy can promote modest sustained weight loss, improving clinical outcomes. Pharmacotherapy appears safe in the short term; long-term safety has not been as strongly established. In selected patients, surgery promotes large amounts of weight loss with rare but sometimes severe complications.**

Ann Intern Med. 2003;139:933-949. www.annals.org

For author affiliations, see end of text.

See related article on pp 930-932.

Obesity is an increasingly significant U.S. health problem. Over 4 decades, the prevalence of obesity (a body mass index [BMI] $\geq$30 kg/m^2) has increased from 13% to 31% in adults and the prevalence of overweight (a BMI of 25 to 29.9 kg/m^2) has increased from 31% to 34% (1). Concurrent increases occurred in adolescents and children (2–4). Obesity is especially common in African-American persons, some Hispanic persons, and Native American persons, and some health sequelae reflect similar ethnic differences (5, 6). Obesity is more common in women, and overweight is more common in men (5). Obesity is a risk factor for major causes of death, including cardiovascular disease, numerous types of cancer, and diabetes (7), and is linked with markedly diminished life expectancy (8, 9). Osteoarthritis, gall bladder disease, sleep apnea, respiratory impairment, diminished mobility, and social stigmatization are associated with obesity (10).

Health risk is better established for obese persons than for overweight persons. However, overweight status also carries risk (11). Even mild to moderate overweight in young adults predicts subsequent obesity (12), and weight gain is associated with adverse outcomes (13). Visceral fat versus subcutaneous fat is particularly linked with adverse cardiovascular profiles in diverse ethnic and racial groups (14–20). Body composition varies with race and ethnicity. For example, Asian persons may be more likely (21) and African-American persons may be less likely to accumulate visceral fat than white persons (15, 22, 23). Health implications may also vary (14–20).

Estimated direct obesity costs are 5.7% of total U.S. health expenditures (24). Expected lifetime costs for cardiovascular disease and its risk factors increase by 20% with mild obesity, by 50% with moderate obesity, and by nearly 200% with severe obesity (25).

We reviewed the medical literature to determine the effectiveness of adult obesity screening—the conscious measurement of weight status to clinically address body weight—and treatment. Although obesity may seem to be an obvious condition, only 42% of obese U.S. adults report that health care professionals have advised them to lose weight (26). In 1996, the U.S. Preventive Services Task Force (USPSTF) recommended periodic height and weight measurement (7). Because of increased obesity prevalence, therapeutic changes, and accumulating evidence of associated health risk, this recommendation needed to be updated. The Research Triangle Institute–University of North Carolina Evidence-based Practice Center developed a systematic review of evidence to assist the USPSTF in this process.

METHODS

We developed an analytic framework of obesity screening components with key questions and eligibility criteria (**Appendix Table 1**, available at www.annals.org). Randomized, controlled trials (RCTs) or systematic reviews of RCTs were preferred evidence. When these were lacking, we evaluated cohort and nonrandomized con-

trolled studies. Because long-term data were limited, we accepted pharmacotherapy efficacy trials with a minimum of 6 months' follow-up; otherwise, we required at least 12 months' follow-up. Study quality was rated by using USPSTF criteria (**Appendix Table 2**, available at www.annals.org) (27).

We examined the USPSTF's 1996 review (7) and then searched MEDLINE and the Cochrane Library for articles published in English between January 1994 and February 2003 (27). We evaluated well-done systematic reviews from the U.S. National Institutes of Health (NIH) (11), the Canadian Task Force on Preventive Health Care (CTFPHC) (28), the University of York for the U.K. National Health Service (NHS) (29), the U.S. National Task Force on the Prevention and Treatment of Obesity (30), and the *British Medical Journal*'s *Clinical Evidence* (31). We used the last as the sole systematic review source for drug efficacy because the comprehensive reviews were outdated. To compare treatment efficacy across reviews, we extracted data from each review's evidence tables on studies with current interventions and at least 1 year of follow-up. We also drew from their general conclusions.

We then reviewed primary literature not covered by previous reviews. At least 2 authors independently reviewed abstracts and articles, excluded those that did not meet eligibility criteria, and abstracted eligible articles. We abstracted or calculated 95% CIs for treatment efficacy from available data whenever possible. When sample size was not reported with variance (32, 33), the baseline sample was used.

The U.S. Agency for Healthcare Research and Quality funded this research. Agency staff and USPSTF members participated in the initial study design and reviewed interim analyses and the final manuscript.

Results

Although no RCTs evaluated the efficacy of obesity screening, we found studies that addressed the health risks of obesity, treatment efficacy, and the health implications of weight loss.

Weight and Health Risk

Longitudinal data showed J-shaped or U-shaped relationships between absolute mortality and BMI (34–45). Elevated risk at low BMI may partly reflect smoking (35, 37, 42) or the limitations of BMI in approximating fat mass (46). The BMI that carried the lowest mortality risk varied but was generally within the normal range for men and the normal-to-overweight range for women (34–45). Morbidity risk increased fairly linearly with BMI. Risk was strongest for cardiovascular disorders (37, 43, 47). Breast, colon, uterine, and ovarian cancer incidence increased with BMI (44, 48).

In the United States, the association between excess body weight and mortality may be weaker for African-American persons than for white persons (41, 42, 49). However, race-specific data are rare, and concerns about sample size limit conclusions. Mortality risk from excess weight may lessen with age; health risks from obesity are unclear beyond age 74 years (50).

Approaches to Screening

Body mass index, the most common screening test for obesity, is easy to measure, highly reliable, and closely correlated ($r = 0.7$ to 0.8) with adult body fat (7, 51, 52). Validity may vary by demographic characteristics, including ethnicity (53–55) and possibly age (51, 56). Clinical relevance is established by prospective links with diverse health outcomes (37, 40–43, 47, 57).

Waist circumference and the waist-to-hip ratio may capture increased cardiovascular risk for central adiposity, even among nonobese persons (44, 58–61). Waist circumference more closely approximates visceral adiposity, particularly in African-American persons (15, 20). Skinfold thickness measurement requires training for accuracy and so was judged undesirable (7). We focused on BMI because 1) it is linked with the broadest range of health outcomes, 2) entry criteria for most treatment studies are BMI-based, and 3) such trials typically report weight or BMI change.

Effect of Counseling and Behavioral Interventions on Body Weight

Counseling aims to promote change in diet, exercise, or both. Behavioral interventions are strategies to help patients acquire the skills, motivations, and support to change diet and exercise patterns. For comparison with other treatments, we considered counseling for diet, exercise, or some combination, potentially with behavioral theory, in aggregate. Of importance, each counseling component included diverse options, possibly in combination. Also, although primary care–based physical activity counseling has uncertain efficacy (62), physical activity has diverse health benefits (63) and fitness may reduce obesity's cardiovascular risk (64). Previous systematic reviews found modest effects of counseling and behavioral interventions, while more recent RCTs showed consistent findings (**Table 1**).

In 29 trials with at least 1 year of follow-up, the U.S. NIH review found that average weight change in diet or physical activity groups (some including behavioral therapy) was 1.9 to −8.8 kg (mean, −3.3 kg), corrected for change in controls (**Table 1**) (11). Counseling for low-calorie diets (1000 to 1200 kcal per day) reduced body weight by an average of 8% over 3 to 12 months and decreased abdominal fat. Although very-low-calorie diets produced greater initial weight loss than low-calorie diets, results were similar beyond 1 year. Counseling for physical activity in 24 RCTs led to weight loss of 2% to 3% and reduced abdominal fat. A combination of diet and physical activity counseling produced greater reduction of weight and abdominal fat than either approach alone. Behavior therapy was a useful adjunct to diet or physical activity

Table 1. **Summary of Findings from Previous Systematic Reviews and the Authors' Updated Searches of Obesity Treatment Efficacy***

Intervention Type	Evidence Source (Reference)	Median Follow-up (Range)	RCTs	Treatments Compared with Control	Mean Weight Change (Range)	
					Intervention Group	Intervention Group − Control Group
		mo	*n*		*kg*	
Counseling and behavioral therapy	U.S. NIH (11)	12 (12 to 60)	29	54	−5.7 (8 to −21.6)	−3.3 (1.9 to −8.8)
	U.K. NHS (29)	12 (12 to 60)	24	51	−4.5 (5.4 to −12.9)	−3.0 (1.4 to −10.6)
	CTFPHC (28)	24 (24 to 60)	6	12	−3.3 (2.7 to −9.2)	−2.1 (−0.2 to −4.5)
	Updated searches [1]	12 (12 to 54)	12	22	−3.7 (9.2 to −17)	−2.0 (0.88 to −5.8)
	Updated searches [2]	12 (12 to 54)	13	24	−4.6 (9.2 to −17.9)	−2.6 (0.88 to −12.3)
Pharmacotherapy (orlistat or sibutramine)	BMJ Clin Evid (31)	NA (0.5 to 24)	17†	NR	NR	NR (−2.5 to −4.4)
	Updated searches	6 (6 to 12)	10	11	−6.5 (−3.3 to −13.1)	−4.0 (−2.8 to −5.8)
Surgery	U.S. NIH (11)	24 (12 to 48)	5	7	−76.0 (−9.7 to −159)	NA
	U.K. NHS (29)	30 (12 to 48)	6	8	−45.1 (−9.7 to −57.9)	NA
	CTFPHC (28)	36 (24 to 60)	4	9	−29.9 (−17 to −45.5)	NA
	Updated searches	18 (18 to 18)	2	4	NA (−34 to <−46)	NA

* Data reflect RCTs of weight loss that have at least 1 year of follow-up; the longest follow-up reported is shown. Only counseling and pharmacotherapy trials that provided data on treatment effect with and without adjustment for control are included. Weight maintenance studies are not shown. Surgery data reflect only current procedures (gastric bypass, adjustable gastric banding, vertical banded gastroplasty); because trials compared 2 techniques (i.e., no comparison with nonsurgical control), results are unadjusted for control. Results of updated searches for counseling trials are shown with [1] and without [2] inclusion of a trial combining alternative counseling strategies with pharmacotherapy (65). BMJ Clin Evid = *British Medical Journal*'s *Clinical Evidence*; CTFPHC = Canadian Task Force on Preventive Health Care; NA = data not available to do appropriate calculation; NHS = National Health Service; NIH = National Institutes of Health; NR = not reported; RCT = randomized, controlled trial.
† Data presented are for 7 studies of sibutramine and 10 studies of orlistat only.

counseling. Longer-term efficacy depended on continued intervention.

The U.K. NHS review found that behavioral interventions, combined with diet or exercise, appeared effective, and long-term maintenance strategies were useful (29). In 24 studies, mean net weight change (intervention groups corrected for controls) was −3 kg over 12 to 60 months (**Table 1**). The CTFPHC review found that weight reduction was most effective during supervised dietary treatment and that patients then gradually regained weight (28). In 6 trials, net weight change was −0.2 to −4.5 kg after 24 to 84 months.

We identified 17 additional RCTs of counseling (65–82). We examined weight loss and weight loss maintenance trials separately (68, 73). Limitations included loss to follow-up (rates varied from 5% to 38%) and differential attrition between treatments. External validity concerns included volunteer enrollment versus random community sampling and poor gender and ethnic diversity.

To compare diverse programs (**Appendix Table 3**, available at www.annals.org), we assessed intervention mode (group or individual), components (diet, exercise, behavior), and intensity (low, moderate, high). Intensity was rated by using frequency of person-to-person contact in the first 3 months. Moderate intensity was defined as monthly contact, high intensity was defined as more frequent contact, and low intensity was defined as less frequent contact.

Figure 1 shows a summary of trials for which the difference in mean weight change between intervention and control groups could be calculated as close as possible to 1-year follow-up. High-intensity trials were most likely to be successful, generally achieving weight loss of 3 to 5 kg. Two intensive trials reported success frequency. In 1 trial (67), mean weight loss due to intervention was 3.4 kg (95% CI, 2.6 to 4.2 kg), and 30% more persons in the treatment group than in the control group lost at least 5% of their body weight. In the other trial, a net loss of 5.5 kg ($P < 0.001$) corresponded to a loss of 7% of total body weight in 38% of persons in the intervention group (81).

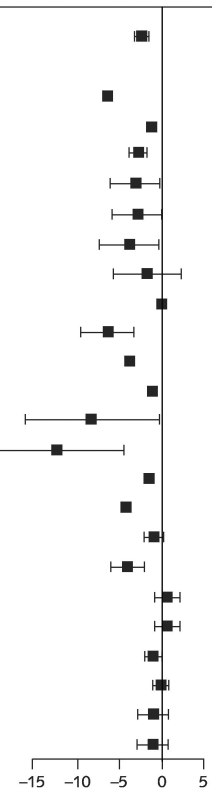
Because not all trials used a null control (many compared one counseling intervention with another), our treatment efficacy estimates (intervention effect minus control) may be conservative. Of 11 high-intensity interventions to promote weight loss, 6 used a true control. Four were successful (loss of 2.5 to 5.5 kg beyond controls in 12 to 54 months) (66, 67, 70, 81), and 2 showed borderline (76) or transient (69) weight reduction (**Table 2**). In 5 trials, 1 high-intensity intervention led to more weight loss than another (65, 72, 74, 78, 82). Moderate-intensity interventions showed mixed results (71, 79), and 2 of the 3 low-intensity weight loss interventions were ineffective (77, 83).

Successful interventions typically included 2 to 3 components (diet, exercise, and behavioral therapy). Only 1 trial (65) examined a combination of counseling and pharmacotherapy. In this trial, adding lifestyle counseling to sibutramine therapy led to a mean weight reduction of 7.3 kg (CI, 1.6 to 13.0 kg), and adding a low-calorie diet to counseling and sibutramine therapy led to a mean weight reduction of 12.8 kg (CI, 8.2 to 17.4 kg) (65).

Twelve- to 18-month and prolonged follow-up was reported in 3 high-intensity weight loss studies (67, 70, 76), 2 of which included long-term maintenance strategies (67, 76). Although participants regained weight, modest net loss (≥2 kg) was maintained for 24 to 36 months in 3 of 4 interventions (67, 70, 76).

Figure 1. **Differences in mean weight loss between intervention and control groups for counseling and behavioral interventions.**

Study, Year (Reference)	Intervention	Control	Internal Validity	Timing of Measurement
Stevens et al., 2001 (70) (18-mo data)	D, E, B+++	Usual care	Good	18 mo
Knowler et al., 2002 (81)	D, E, B+++*	D, E+	Good	34 mo
Kuller et al., 2001 (66)	D, E, B+++*	Assessment only	Good	54 mo
Tuomilehto et al., 2001 (67)	D, E, B+++	D, E+	Good	12 mo
Fogelholm et al., 2000 (1-y data) (76)	D, EP2, B+++	D, B+	Fair	12 mo
	D, EP1, B+++	D, B+		
Jakicic et al., 1999 (72)	D, short-bout EP with EQ, B+++	D, short-bout EP, B+++	Fair	18 mo
	D, long-bout EP, B+++	D, short-bout EP, B+++		
Jones et al., 1999 (69)	D, B+++	Told to lose weight+	Fair	30 mo
Sbrocco et al., 1999 (74)	D, E, B1+++	D, E, B2+++	Fair	12 mo
Ashley et al., 2001 (82)	D (dietitian) with MR, E, B+++	D (dietitian), E, B+++	Fair	12 mo
	D (primary care), E, B+++	D (dietitian), E, B+++		
Wadden et al., 2001 (65)	B, sibutramine+++	Sibutramine	Fair	12 mo
	D, B, sibutramine+++	Sibutramine		
Wing and Anglin, 1996 (78)	Black patients: D1, E, B+++	D2, E, B+++	Fair	12 mo
	White patients: D1, E, B+++	D2, E, B+++		
Lindholm et al., 1995 (79)	D, E++	Usual care+	Good	18 mo
Swinburn et al., 1999 (71)	D, B++	D+	Fair	12 mo
Jeffery and French, 1997 (77)	Low SES women, D, E, L	No contact	Good	12 mo
	Low SES women, D, E	No contact		
	High SES women, D, E, L	No contact		
	High SES women, D, E	No contact		
	Low SES men, D, E, L	No contact		
	Low SES men, D, E	No contact		



Only studies for which the difference in mean weight loss could be calculated are included. Error bars represent 95% CIs and are presented for studies in which those data were available. Data presented are as close as possible to 1-year follow-up. An asterisk indicates that the difference was statistically significant ($P < 0.05$) but there were insufficient data to calculate CIs. B = behavioral therapy; D = diet; E = exercise; EP = exercise program; EQ = exercise equipment; L = lottery entry; MR = meal replacement; SES = socioeconomic status. +++ = high intensity; ++ = moderate intensity; + = low intensity.

Trials designed to maintain weight loss showed some success (68, 73). One promoted an additional 5-kg loss over 1 year (68). In another, weight-focused counseling promoted weight maintenance in 36% more participants than exercise-focused counseling (73). Overall, counseling promoted modest average weight loss (3 to 5 kg). Multicomponent, intensive interventions that included behavioral therapy most often led to weight loss. Maintenance strategies helped sustain loss.

Effect of Pharmacotherapy Interventions on Body Weight

Pharmacologic obesity treatment has changed substantially in the past decade. Safety concerns have eliminated several options. Evidence of the efficacy of sibutramine (a dopamine, norepinephrine, and serotonin reuptake inhibitor) and orlistat (a gastrointestinal lipase inhibitor) has increased. Both of these drugs, in combination with lifestyle change, are approved for people with BMIs of 30 kg/m^2 or more or people who have BMIs greater than 27 kg/m^2 along with other risk factors (for example, hypertension, diabetes, or dyslipidemia). Efficacy trials have also examined several drugs developed for non–weight-related purposes.

A recent systematic review of pharmacotherapy for obesity found that in 7 RCTs, sibutramine promoted weight loss of 2.8 to 4.2 kg over 8 to 52 weeks in healthy adults and those with controlled hypertension (31). However, participants regained weight after the treatment was discontinued. Orlistat had similar efficacy (mean loss of 3.5 kg in 10 RCTs of 1 to 2 years' duration). Phentermine (7.4-kg average loss in 1 RCT) and mazindol (3.8-kg average loss in 1 RCT) caused modest weight loss in adults who were more than 15% overweight; however, mazindol is no longer manufactured in the United States. Other small RCTs showed limited and inconsistent efficacy of diethylpropion (2 RCTs) and fluoxetine (2 RCTs).

We identified 18 additional RCTs meeting eligibility criteria (**Appendix Table 4**, available at www.annals.org). Seven evaluated sibutramine (32, 33, 84–88), 8 evaluated

(text continued on page 941)

Table 2 Top. **Randomized, Controlled Trials of Counseling and Behavioral Interventions***

Study, Year (Reference)	Goal and Components	Sample Size	Race	Women	Age†	Baseline Body Mass Index‡
		n		%	*y*	kg/m^2
High intensity						
Stevens et al., 2001 (70)	L + M D, E, B G + I	1191	White: 79 Black: 18	34	43	31
Kuller et al., 2001 (66)	L + M D, E, B G + I	535	White: 92	100	47	25
Tuomilehto et al., 2001 (67)	L D, E, B G	522	NR	67	55	31
Fogelholm et al., 2000 (76)	L + M D, E, B G	82	NR	100	Range, 30–45	34
Knowler et al., 2002 (81)	L + M D, E, B G + I	3234	White: 55 Black: 20 Hispanic: 16 Native American: 5 Asian: 4	68	51	34
Jakicic et al., 1999 (72)	L D, E, B G	148	NR	100	Range, 25–45	Weight 20%–75% higher than ideal body weight
Jones et al., 1999 (69)	L D, B G + I	102	White: 60 Black: 40	52	Intervention: 57 Control: 59	34
Sbrocco et al., 1999 (74)	L D, E, B G	24	NR	100	40–43 (varied by group)	33
Wadden et al., 2001 (65)	L D, E, B G	53	NR	100	Drug: 46 Drug + L: 41 Drug + D + L: 40	36–39
Ashley et al., 2001 (82)	L D, E, B G + I	113	NR	100	41–42 (varied by group)	25–35
Wing and Anglin, 1996 (78)	L D, E, B G	93	Black: 17 White: 80 Other: 2	Black: 75 White: 66	Black: 49 White: 52	Black: 37 White: 38

Table 2 Top—**Continued**

Study Duration	Groups§	Weight Change	Between-Group Difference§	*P* Value	Patients Lost to Follow-up	Study Quality
					%	
18 mo	Weight loss Control	−2 kg 0.7 kg	−2.7 kg	≤0.001	8 at 36 mo	Good
36 mo	Weight loss Control	−0.2 kg 1.8 kg	−2.0 kg	≤0.001		
54 mo	Lifestyle change assessment only	−0.09 kg 2.4 kg	−2.5 kg	≤0.001	5	Good
1 y	Intervention Control	−4.2 kg −0.8 kg	−3.4 kg	≤0.001	8	Good
2 y	Intervention Control	−3.5 kg −0.8 kg	−2.7 kg	≤0.001		
1 y	Intervention Control	Frequency of 5% loss NR NR	30%	0.001		
1 y	1st PA program 2nd PA program Control	−0.7 kg −0.6 kg 2.0 kg	−2.7 kg −2.6 kg	0.06	10	Fair
2 y	1st PA program 2nd PA program Control	5.9 kg 9.2 kg 9.7 kg	−3.8 kg −0.5 kg	0.07		
2.8 y	Metformin Lifestyle Placebo	−2.1 kg −5.6 kg −0.1 kg	−2.0 kg −5.5 kg	≤0.001	7.5	Good
	Metformin Lifestyle Placebo	Frequency of > 7% loss NR 38% NR				
18 mo	Long-bout PA Short-bout PA + EQ Short-bout PA	−5.8 kg −7.4 −3.7	−2.1 kg −3.7 kg (Referent)	≤0.05 NS all other pairs	22 (13–29 per group)	Fair
6 mo	Weight loss Control	−3.2 −1.8	−1.4 kg	0.05	9	Fair
12, 18, 24, 30 mo		NR	NR	NS		
12 mo	Behavioral choice Traditional behavioral treatment	−10.1 kg −4.3 kg	−5.76 kg	0.01	17	Fair
1 y	Sibutramine + diet + lifestyle Sibutramine + lifestyle Sibutramine	−16.6 −11.1 −3.8 59% of drug + diet + lifestyle participants had lost ≥ 15% of weight at 1 y	−12.8 kg −7.3 kg (Referent)	≤0.05 ≤0.05	32	Fair
1 y	Primary care visit, meal replacement Nutritionist, meal replacement Nutritionist alone	−3.5 kg −7.7 kg −3.4 kg	−0.1 kg −3.7 kg (Referent)	NS ≤0.05	32–38	Fair
1 y	Behavioral therapy with very-low-calorie diet Behavioral therapy with low-calorie diet	Black: −13 kg White: −17 kg Black: −11 kg White: −13 kg Weight loss is approximate, from graphic data	Black: −2 kg White: −4 kg (Referent) Weight loss is approximate, from graphic data	NR	19	Fair

Table 2 Bottom

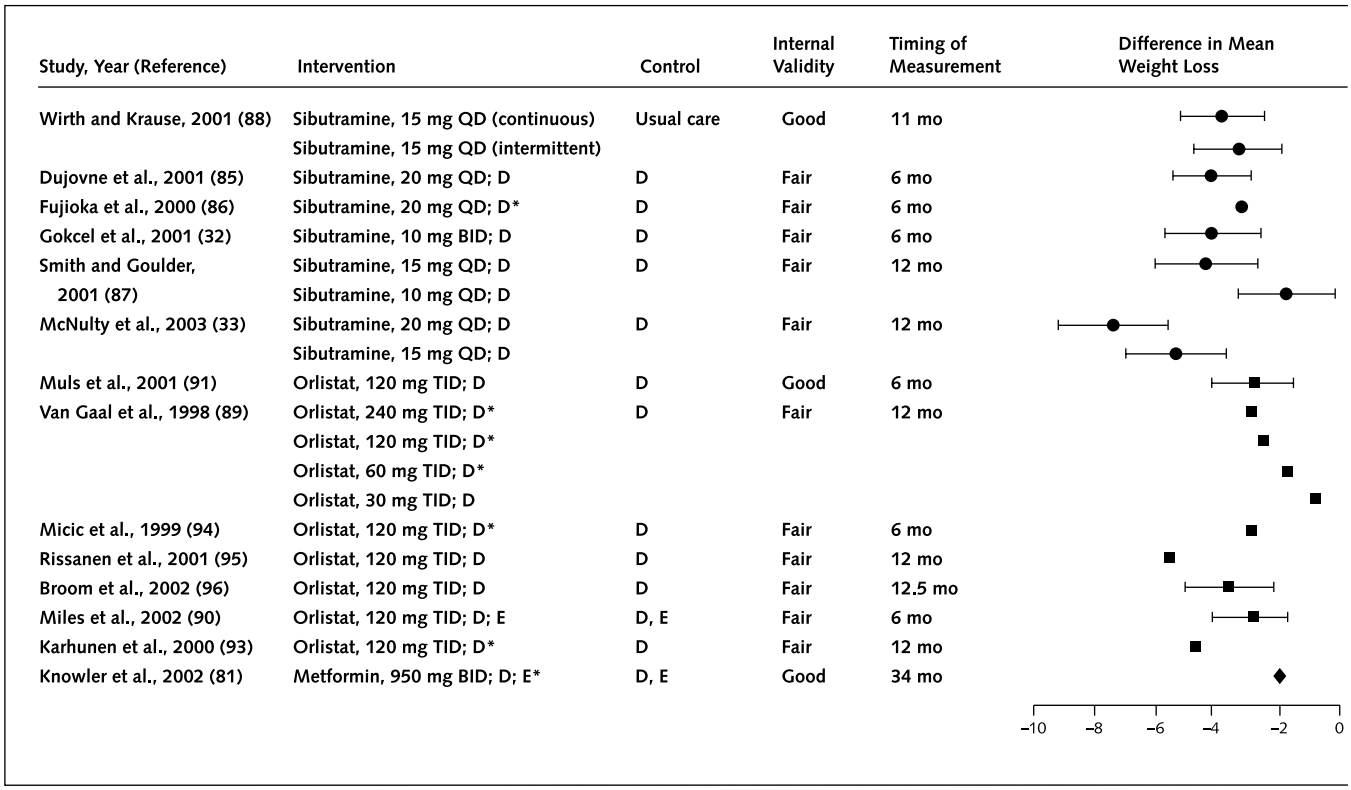
Study, Year (Reference)	Goal and Components	Sample Size	Race	Women	Age†	Baseline Body Mass Index‡
		n		%	*y*	kg/m^2
Leermakers et al., 1999 (73)	M D, E, B G	67	White: 94	80	50.8	31
Moderate intensity						
Lindholm et al., 1995 (79)	L D, E G	681	NR	15	Range, 30–59	Intervention Men: 27 Women: 30 Control Men: 27 Women: 29
Swinburn et al., 1999 (71)	L D, B G	176	Intervention European: 69 Maori: 12 Pacific Islander: 14 Other: 4 Control European: 75 Maori: 7 Pacific Islander: 4 Other: 3	Intervention: 21 Control: 35	Intervention: 53.2 Control: 52.3	Intervention: 84 kg Control: 85 kg
Low intensity						
Jeffery and French, 1997 (77)	L D, E G	822	White: 76–94 (range for each group)	81	31–37 (varied by group)	Men: 28 Women: 26–28
Bemelmans et al., 2000 (83)	L D G	266	NR	Intervention: 51 Control: 63	54–55 (varied by group)	30
Rothacker et al., 2001 (68)	M D I	75	NR	100	Range, 18–55	25
OXCHECK Study Group 1995 (80)	L D I	2205	NR	47	Range, 35–64	NR

* B = behavioral therapy; D = diet; E = exercise; EQ = exercise equipment; G = group-based; I = individual-based; L = weight loss; M = maintenance of weight loss; NR = not reported; NS = not significant; OXCHECK = OXford and Collaborators HEalth ChecK; PA = physical activity; SES = socioeconomic status.
† Mean values unless otherwise noted.
‡ Baseline mean or range unless otherwise noted.
§ See **Appendix Table 3** for details.
‖ Compared with control unless otherwise noted.

Table 2 Bottom—**Continued**

Study Duration	Groups§	Weight Change	Between-Group Difference§	*P* Value	Patients Lost to Follow-up	Study Quality
					%	
18 mo	Weight-focused maintenance program	3.1 kg	−2.1 kg	≤0.05	15 at 6 mo; 28 at 18 mo	Fair
	PA-focused maintenance program	5.2 kg		≤0.01		
	Weight-focused program	90% original weight loss maintained	−36%			
	PA-focused program	54% original weight loss maintained				
18 mo	6 sessions of health care advice	NR	−0.25 kg	NS	6	Good
	Usual care	NR				
12 mo	Reduced-fat diet	−3.1 kg	−3.5 kg	≤0.001	38	Fair
	Usual diet	0.4 kg				
12 mo		Men			14	Good
	Lifestyle education	0.72 lb	−1.22 lb	NS		
	Education + lottery	0.21 lb	−1.73 lb	NS		
	Control	1.94 lb				
		Women (High SES)				
	Lifestyle education	1.03 lb	−0.35 lb	NS		
	Education + lottery	0.51 lb	−0.87 lb	NS		
	Control	1.38 lb				
		Women (Low SES):				
	Lifestyle education	2.11 lb	0.81 lb	NS		
	Education + lottery	3.23 lb	1.93 lb	NS		
	Control	1.30 lb				
52 wk	Dietary interventions with group meetings and mailings	Men 0.5 kg/m^2 Women: 0.3 kg/m^2	Men: 0.1 kg/m^2 Women: 0 kg/m^2	NS NS	8	Fair (but non-randomized)
	Leaflet of Dutch nutritional guidelines	Men: 0.4 kg/m^2 Women: 0.3 kg/m^2				
1 y	Premeasured low-calorie liquid supplements	−6.3 kg	−5 kg	≤0.001	17	Fair
	Low-energy, low-fat foods	−1.3 kg				
3 y	Health checks	NR	At follow-up, those with health checks weighed 0.38 kg/m^2 less than controls	≤0.05	25	Fair
	Standard care					

Figure 2. **Differences in mean weight loss between intervention and control groups for pharmacotherapy interventions.**



Only studies for which the difference in mean weight loss could be calculated are included; each arm is represented by a data point. Error bars represent 95% CIs and are presented for studies in which those data were available. Intensity of co-interventions was not assessed because most trials provided insufficient information for evaluation. An asterisk indicates that the difference was statistically significant ($P < 0.05$) but there were insufficient data to calculate CIs. B = behavioral therapy; BID = twice daily; D = diet; E = exercise; QD = daily; TID = 3 times daily.

(continued from page 936)

orlistat (89–96), 2 evaluated metformin (81, 97), and 1 evaluated several drugs (98). Three trials examined maintenance strategies (84, 92, 93). Attrition (3% to 50%) and poor adherence data were primary quality limitations. Generalizability issues were similar to those in the counseling trials.

In 6 weight loss trials (**Figure 2**) (32, 33, 85–88), sibutramine-treated participants lost 2.8 kg (CI, 1.6 to 4.0 kg) to 7.8 kg (CI, 5.9 to 9.7 kg) more than patients given a placebo (**Appendix Table 4**, available at www.annals.org). Frequency of response, when recorded, was high. Twenty-seven percent (CI, 18% to 36%) to 65% (CI, 60% to 70%) of sibutramine-treated patients lost 5% of their body weight and 6% (CI, 1% to 10%) to 34% (CI, 26% to 40%) lost 10% (33, 85–88). Nineteen percent (CI, 9% to 29%) to 53% (CI, 36% to 70%) more drug-treated participants than control participants lost 5% of body weight, and 5% (CI, 1% to 10%) to 27% (CI, 18% to 36%) lost more than 10% of body weight.

In 6 trials (90, 91–94, 96), participants treated with a typical dosage of orlistat (120 mg 3 times daily) lost statistically significantly more weight than controls (2.8 kg [CI, 1.8 to 3.7 kg] to 4.5 kg [CI not calculable]). In a 6th trial (95), orlistat-treated participants lost 5.8 kg more than controls, but the difference was not statistically significant. In the 3 trials reporting response rates (89, 91, 96), 14% (CI, 10% to 19%) to 38% (CI, 29% to 47%) of orlistat-treated participants lost 10% of body weight. Such response was 9% (CI, −2% to 20%) to 19% (CI, 8% to 30%) more common in orlistat-treated participants than controls.

In 1 trial comparing drug and lifestyle interventions, participants treated with metformin lost 2 kg more than those given a placebo but lost less than participants in the lifestyle group (81). Another trial showed no metformin effect (97). A multidrug trial showed that persons treated with sibutramine lost statistically significantly more weight (13.4 kg) than those treated with orlistat (8 kg) or metformin (9 kg) (98).

Maintenance studies showed moderate success. In 1 (84), sibutramine, taken 6 months for weight loss and 18 months for weight maintenance, promoted a net loss of 4 kg (CI, 2.4 to 5.6 kg) versus placebo. A corresponding 44% (CI, 37% to 50%) of sibutramine-treated participants versus 16% (CI, 6% to 25%) of placebo participants maintained 80% of initial weight loss. Likewise, successful dieters treated with orlistat lost more weight and over 1 year

were more likely to maintain 75% of the initial amount lost than those treated with placebo ($P < 0.05$) (92). In a 3rd trial, participants treated with 1 or 2 years of orlistat lost "significantly more" weight over 2 years than placebo participants (93). However, during the second year, continuous orlistat was no more effective than continuous placebo, and discontinuing therapy with the drug led to excess weight gain (for example, during the second year, mean weight gain in those who discontinued orlistat therapy was 6.3 kg compared with 3.1 kg in those who took placebo throughout) (93).

Overall, pharmacotherapy with sibutramine and orlistat promoted modest mean weight loss (3 to 5 kg) beyond that of controls, and prolonged drug courses helped sustain this loss up to 2 years. Phentermine and mazindol had similar short-term efficacy but are not approved for long-term use (31). Metformin, diethylpropion, and fluoxetine showed mixed efficacy.

Surgical Approaches

Surgical obesity treatment is limited to patients with BMIs exceeding 40 kg/m^2 or patients with BMIs of 35 kg/m^2 or more who have associated severe health complications and have not responded to other treatment methods (99). Bariatric surgery is restrictive or malabsorptive, and current techniques are primarily restrictive. Gastric bypass involves complete gastric partitioning with anastomosis of the proximal gastric segment to a jejunal loop. Adjustable gastric banding involves placing an inflatable band around the stomach that can be adjusted to different diameters (100). Vertical banded gastroplasty entails partial gastric partitioning at the proximal gastric segment with placement of a gastric outlet stoma of fixed diameter (28). Practice patterns appear to be shifting away from this technique. These procedures can be performed open or laparoscopically. Although the duodenal switch procedure—a relatively new malabsorptive technique—is fairly common in practice, we found no RCTs evaluating its effectiveness.

Because of practical and ethical constraints to a true randomized, blinded, placebo-controlled trial of surgery for obesity, high-quality evidence is limited. The 3 previous systematic reviews of obesity therapy primarily examined randomized unblinded trials comparing surgical techniques (that is, trials that included no nonsurgical controls).

The U.S. NIH reviewed 5 randomized trials and found that patients who received obesity surgery lost 10 to 159 kg over 12 to 48 months (**Table 1**) (11). Of 7 trials reviewed by the U.K. NHS (29), 6 showed weight loss with both gastric bypass (mean reduction, 45 to 65 kg) and gastroplasty (mean reduction, 30 to 35 kg). The CTFPHC (28) analyzed 4 surgical randomized trials and 1 prospective cohort study and found a mean weight loss of 17 to 46 kg after 2 to 5 years.

We identified 3 additional randomized trials that evaluated gastric banding over 1 to 2 years (**Appendix Table 5**, available at www.annals.org) (100–102). In addition to lack of nonsurgical controls, quality concerns included lack of cointerventions and comorbidity information. None of the trials showed statistically significantly different weight loss between groups, but all treatments promoted considerable loss (17 to >40 kg). In addition, we identified a large, controlled cohort study evaluating surgery efficacy: the Swedish Obese Subjects (SOS) study (103, 104). This study was a multicenter trial of surgical patients (equally divided among gastric banding, vertical banded gastroplasty, and gastric bypass) and nonrandomized, matched, nonsurgical controls (104). At 2 years, surgical patients had lost 28 kg (CI, 26.9 to 29.1 kg) and controls had lost 0.5 kg (CI, −0.2 to 1.2 kg). Mean weight reduction (±SD) after gastric banding, vertical banded gastroplasty, and gastric bypass was 21% ± 12%, 23% ± 10%, and 33% ± 10%, respectively. After 8 years, subset analysis showed an average weight loss of 20 kg (CI, 18.0 to 22.0 kg) in 251 surgical patients and 0.7 kg (CI, −0.8 to 2.2 kg) in 232 controls (104). Overall, surgery promoted substantial, prolonged weight loss (10 to 159 kg over 1 to 5 years) in patients with extreme obesity.

Intermediate Health Outcomes and Sustained Weight Loss

The U.S. NIH systematic review established that counseling-based weight loss (generally approximately 5 to 10 kg) can improve intermediate health outcomes such as blood pressure, glycemic control, and serum lipid levels (11). We assessed the effect of pharmacotherapy-associated weight loss on serum lipids and glucose. Since the previous drug review did not cover these outcomes, we abstracted these data from the primary literature covered by the review, in addition to more recent articles. We found mixed evidence for improved glucose tolerance with sibutramine-induced weight loss (32, 33, 84, 86, 87, 105). Orlistat generally (90, 96, 106–109) but not always (110) improved glucose levels. This inconsistency may be due in part to medication alterations accompanying weight loss. In 1 trial (90), orlistat-treated patients with diabetes were more likely to decrease or discontinue diabetes medications than controls (17% vs. 8%; $P < 0.05$), and glycosylated hemoglobin level decreased only when adjusted for these alterations.

Seven trials and 1 review linked orlistat with total cholesterol reduction (90, 92, 106–111). Sibutramine showed less consistent total cholesterol findings. No statistically significant drug versus placebo effect was found in 6 trials (33, 84, 86, 87, 112, 113), and improvement was found in 3 others (32, 114, 115). Orlistat was frequently but not always (116) associated with reduced low-density lipoprotein cholesterol level (90, 92–94, 96, 106–108, 110, 115), and sibutramine had inconsistent effects (32, 84–86, 90, 96, 113, 114). Neither drug consistently affected high-density lipoprotein cholesterol level (32, 33, 90, 96, 105,

113, 114, 116, 117) or triglyceride level (33, 84–87, 90, 94, 96, 105, 107, 110, 112–114).

Surgical cohort studies suggest that extensive weight loss may lead to dramatic improvements in glucose metabolism (118), lipid profiles (119, 120), and blood pressure. Of note, hypertension tended to recur within 3 to 10 years in the SOS study (121). Although weight regain accompanied this recurrence, all surgical groups had maintained at least a 20-kg average loss.

Ultimate Health Outcomes and Sustained Weight Loss

We found less evidence for effects of weight loss on ultimate (generally symptomatic) health outcomes. Limited observational data suggest that intentional weight loss in obese persons (particularly those with comorbid conditions) can reduce mortality (122, 123). Two large RCTs showed that behaviorally mediated weight loss can prevent diabetes among those with glucose intolerance (58% reduction; $P < 0.05$) (67, 81). A smaller reduction in diabetes incidence (31% [CI, 17% to 43%]) was seen among similar metformin-treated patients (81).

Diabetes may resolve in patients treated surgically. For example, in 2 trials (118, 120), 90% follow-up of 300 surgical patients, 50% of whom were initially glucose intolerant and 50% of whom initially had diabetes, showed that 91% had normal fasting glucose and glycosylated hemoglobin levels. However, these data are not from RCTs. Likewise, in the SOS, lower diabetes incidence over 2 years (odds ratio, 0.10 [CI, 0.03 to 0.28]) was seen in surgical patients versus nonsurgical patients (121).

Harms of Screening and Treatment

Difficulty sustaining weight loss has raised concern that cycles of loss followed by regain potentially carry risk. Observational studies examining weight cycling and mortality show mixed results (124–130). Conclusions are primarily limited by failure to distinguish between intentional and unintentional weight loss. Some studies examining weight cycling with intentional weight loss have found unfavorable effects on coronary heart disease and its risk factors (131, 132), but others have not (133, 134). This literature is further limited by joint consideration of participants with diverse baseline age or weight and measurement issues, such as self-recalled weight and problems characterizing cycling (135–137). For example, in studies not restricted to those with excess weight, some data suggest that weight-cycling risk increases inversely with BMI and so is minimized among obese persons. We did not find studies or previous reviews addressing harms of screening or counseling interventions. Some risk is probably present, particularly since stigma associated with obesity is well established (138–140).

Sibutramine and orlistat both have frequent, although not usually serious, adverse effects. Common side effects of sibutramine include insomnia, nausea, hypertension, dry mouth, dizziness, and confusion (31). In the previously reviewed studies, common adverse effects occurred in 10% to 30% of sibutramine-treated patients versus 8% to 19% of controls (31). Among recent RCTs, side effects were common (11% to 79%) (86–88), but incidence was similar across treatments. The most worrisome side effects of sibutramine are cardiovascular, including increased blood pressure (mean increase, 0 to 3.5 mm Hg [31, 86–88] or 5% [84, 88]) and heart rate (mean increase, 4 to 6.8 beats/min) (31–33, 85, 87). In 1 study (33), elevated diastolic blood pressure ($\geq$ 5 mm Hg) or pulse ($\geq$10 beats/min) occurred in 18% more sibutramine-treated participants than controls. In people with controlled hypertension, clinically significant blood pressure increases were similar across treatment groups (31), but some persons experienced marked increase in blood pressure (31, 86). When reported, dropout due to hypertension was up to 3.9% higher among those treated with sibutramine than among those not treated; overall, dropout rates for adverse events were similar in drug and placebo groups (84, 86–88).

Adverse events were reported in 7.4% to 18% more participants receiving orlistat than participants receiving placebo (31, 89, 91, 94). Most symptoms were gastrointestinal, including oily spotting, flatulence, and fecal urgency, and were reported by 22% to 95% of orlistat users (1% to 37% more often than controls) (89–92, 96). Other problems have included need for vitamin supplementation and reduced absorption of contraceptive pills (31). In recent trials, dropout due to side effects was 0% to 12% more common in orlistat-treated participants (89, 90, 92, 94, 96). The RCTs of metformin that we reviewed did not report dropouts due to drug effects. Gastrointestinal symptoms were noted to be more common (77.8 per 100 person-years vs. 30.7 per 100-person years) in 1 trial (141) and were present but transient in 4% of patients in another (97). In the latter trial, mean lactic acid levels did not rise. Previous review of other weight loss medications found no evidence of serious adverse reactions for phentermine. However, case reports suggested potentially serious side effects of pulmonary hypertension with mazindol and diethylpropion therapy and psychosis with mazindol therapy (142).

Because of data from RCTs of surgery were limited, we evaluated surgical adverse effects in case series. Adverse effects were both general (for example, need for prolonged follow-up, multivitamin supplementation) and procedure-specific. The RCTs on gastric banding did not report mortality. One showed fewer surgical complications with laparoscopic versus open procedures (100), while the 2 evaluating the site of band placement presented conflicting data about the relative safety of esophagogastric versus gastric placement (101, 102) (**Appendix Table 5**, available at www.annals.org). Reported symptoms suggest low rates of dysphagia, hunger, vomiting, and esophagitis (101, 102). In the nonrandomized, controlled SOS study, complications were not reported by procedure (104). The postoperative mortality rate was 0.2%, and morbidity included bleeding (0.9%), wound complications (1.8%), abdominal

infection (2.1%), thromboembolic events (0.8%), pulmonary symptoms (6.2%), and miscellaneous events (4.8%).

In 38 surgical case series, at least 3 evaluating vertical banded gastroplasty and gastric bypass included patients with substantial comorbid conditions (143–145). Many studies included patients with modest health problems. Generally, mortality rates were low. In 12 cohorts receiving vertical banded gastroplasty (143, 145–155), the perioperative mortality rate ranged from 0% to 1.5% (6 deaths in 1165 patients [pooled data]). Similar rates were seen among patients who underwent gastric bypass (0% to 1.5% per series) (118, 144, 149, 156–161) and those who had adjustable gastric banding (0% to 1.5%) (155, 162–176).

Morbidity was more common. The main complications of vertical banded gastroplasty were reoperation (20% to 25% over 3 to 5 years) (148, 151) and wound infection (8% to 32% of patients) (145, 148, 149). Less frequent events (<6%) included gastric leaks, stomal stenosis, and pouch dilatations. Wound infection was reported in 8% to 20% of patients who underwent gastric bypass (149, 159, 160). Single studies noted staple failure (15%) (118), vitamin B_{12} deficiency (40%) (118), diarrhea (13%) (160), and gastrointestinal hemorrhage (3%) (149). Among patients who underwent adjustable gastric banding, morbidity often involved reoperation (1% to 20%) (102, 162, 165, 168–170, 175, 177, 178) or band dislocation, leakage, or slippage (0.4% to 8%) (100, 163–165, 167, 168, 170–172, 177, 178).

Discussion

Efficacy of Therapeutic Interventions for Obesity

Obesity is common and easy to screen for, poses a substantial health burden in the United States, and has treatment options. Although RCT evidence for long-term improved health with weight loss is limited, weight loss–associated changes in intermediate health variables suggest benefit. In the setting of escalating obesity prevalence, the importance of considering body weight in clinical practice seems clear.

With counseling, obese patients can achieve modest but clinically significant, sustained (1 to 2 years) weight loss (for example, 3 to 5 kg). Because control groups also frequently received some intervention, this estimate may be conservative. More intense programs were generally more successful, as were those incorporating behavioral therapy. Treating patients on an individual rather than a group basis appeared less important.

Sibutramine and orlistat have modest potentially prolonged effects (weight loss of 3 to 5.5 kg). These estimates do not reflect the effects of lifestyle interventions, which should accompany pharmacotherapy. Weight maintenance trials suggest that prolonged therapy with these drugs confers some benefit but that discontinuation may lead to rapid weight regain. Other drugs show inconsistent or short-term benefit. In both counseling and pharmacotherapy trials, a relatively high number of participants have achieved clinically significant (5% to 10%) weight loss.

Surgical options can promote substantial weight loss (10 to 159 kg over 1 to 5 years). Evidence from case series suggests that such loss can be achieved in patients with multiple comorbid conditions and may be prolonged. Although surgical options are appropriate only for the very obese, between 5% and 6% of U.S. adults have a BMI of 35 kg/m^2 or greater (179), so the number of potentially eligible persons may be substantial.

Limitations of the Literature

Limitations of previous systematic reviews included different eligibility criteria, treatment classifications, and approaches to data synthesis. In addition, aggregate values of their findings do not reflect variations in RCT sample size, length of follow-up, or treatment differences (for example, counseling intensity). There was partial but incomplete overlap in the literature covered by each review. Overall, however, findings were consistent.

Recent primary literature also had deficiencies. Among counseling and pharmacotherapy trials, internal validity was typically fair (with limitations including loss to follow-up and differential attrition between groups), although a few trials were judged to have good validity. Studies tended to report mean weight change but not frequency of response. External validity was an issue: Participants were frequently volunteers, and diversity in sex and ethnicity was limited. No counseling RCT lasted for more than 54 months. Pharmacotherapy trials were accepted with shorter follow-up periods than trials evaluating other treatment methods. Although 6- and 12-month efficacy appeared similar among these trials, their shorter duration could have inflated estimates of sustained weight loss. Surgical data were limited by lack of placebo-controlled RCT evidence; available studies often did not report response frequency, participant comorbid conditions, or co-interventions.

Finally, some studies (particularly those examining pharmacotherapy) used a "last-observation-carried-forward" analytic approach, that is, the final weight outcome available was used as the final weight for participants who dropped out of the study. Because maximal weight loss tends to occur within 6 months of intervention, this technique may overestimate the ability to sustain weight loss. Although this technique is common when a true intention-to-treat analysis is not possible, it should be combined with alternate analyses (180, 181). Many trials showed parallel analyses of trial enrollees and those who completed the trials, but few authors presented parallel "worst-case" analyses.

Harms of Intervention

Treatment appeared reasonably safe. We identified no evidence evaluating harms of counseling. Both sibutramine and orlistat had clinically significant, often mild, adverse

effects in trials lasting at most 2 years; long-term adverse effects are less defined. Surgical options clearly have the highest risk. They led to death in less than 1% of patients in pooled samples, but up to 25% of patients may need reoperation over 5 years.

A systematic review of intervention costs was beyond the scope of this project. However, it is important to note that treatment options for obesity may entail considerable cost. Intensive counseling programs require a large amount of time and a substantial staffing commitment. Based on average wholesale price, 1-year supplies of orlistat (120 mg 3 times daily) and sibutramine (15 mg daily) cost $1445.40 and $1464.78 U.S., respectively (182). Surgical costs reflect both the invasive procedure and long-term follow-up. It is possible that long-term health improvements may offset these costs to some extent.

Implications for Clinical Practice and Research

Most efficacy trials reviewed here were not performed in clinical settings. Some interventions, in particular intense counseling, may be difficult to incorporate into medical practice. One option may be referral to programs that offer intense counseling with behavioral therapy. Another may be combining office-based counseling with innovative delivery of behavioral approaches, such as videotapes or Internet-delivered adjuncts. Other topics requiring future research include longer-term follow-up of the efficacy and harms of weight loss strategies (including better characterization of weight-cycling risks), postmarketing safety records of drugs, ability of interventions to alter body fat distribution, race- and ethnicity-specific health effects of purposeful reduction of central adiposity, and efficacy of weight maintenance strategies. In the interest of obesity prevention, treatment efficacy and health effects of lifestyle modification should be clarified for patients who are overweight but not obese. Finally, better estimates of the cost-effectiveness of obesity screening and treatment, including their impact on long-term health outcomes, are needed.

Long-term research on combined treatment methods in more generalized populations is also necessary. We were unable to assess treatment effectiveness by sex or ethnicity. Intervention efficacy trials have focused on white women, and observational evidence for health outcomes is derived mostly from patients of European origin. Treatment efficacy may differ with race (11, 78), and because some ethnic groups have a disproportionate prevalence of obesity, this area needs further attention.

All obesity therapies carry promise and burden, which must be balanced in clinical decision making. Counseling approaches appear the least harmful and produce modest, clinically important weight loss but entail cost in time and resources. Pharmacotherapy promotes modest additional weight loss, but long-term drug use may be needed to sustain this benefit, and long-term adverse events and appreciable cost are unknown. Only surgical options consistently result in substantial long-term weight reduction; however, they carry a low risk for severe complications and are expensive. Body size, health status, and weight loss history all may influence obesity treatment.

From University of Pittsburgh, Pittsburgh, Pennsylvania; University of North Carolina School of Medicine, Chapel Hill, North Carolina; and RTI International, Research Triangle Park, North Carolina.

Disclaimer: The authors of this article are responsible for its contents, including any clinical or treatment recommendations. No statement in this article should be construed as an official position from the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services.

Acknowledgments: The authors thank David Atkins, MD, MPH, Medical Officer, Center for Outcomes and Evidence, and Eve Shapiro, Managing Editor, USPSTF, Agency for Healthcare Research and Quality. They also thank Loraine Monroe of RTI International.

Grant Support: This study was developed by the RTI International–University of North Carolina Evidence-based Practice Center under contract to the Agency for Healthcare Research and Quality (contract no. 290-97-0011), Rockville, Maryland. Dr. McTigue was supported by the University of North Carolina Robert Wood Johnson Clinical Scholars Program.

Potential Financial Conflicts of Interest: None disclosed.

Requests for Single Reprints: Reprints are available from the AHRQ Web site at www.ahrq.gov/clinic/uspstfix.htm and in print through the AHRQ Publications Clearinghouse (call 1-800-358-9295).

Current author addresses are available at www.annals.org.

References

1. **National Center for Health Statistics, Division of Data Services.** Health, United States, 2002, with Chartbook on Trends in the Health of Americans. Hyattsville, MD: National Center for Health Statistics, Division of Data Services; 2002.

2. **Dietz WH.** Overweight and precursors of type 2 diabetes mellitus in children and adolescents [Editorial]. J Pediatr. 2001;138:453-4. [PMID: 11295702]

3. **Strauss RS, Pollack HA.** Epidemic increase in childhood overweight, 1986-1998. JAMA. 2001;286:2845-8. [PMID: 11735760]

4. **Ogden CL, Flegal KM, Carroll MD, Johnson CL.** Prevalence and trends in overweight among US children and adolescents, 1999-2000. JAMA. 2002;288:1728-32. [PMID: 12365956]

5. **National Center for Health Statistics.** Health, United States, 2001. With Urban and Rural Health Chartbook. Hyattsville, MD: National Center for Health Statistics; 2001.

6. **Harwell TS, Gohdes D, Moore K, McDowall JM, Smilie JG, Helgerson SD.** Cardiovascular disease and risk factors in Montana American Indians and non-Indians. Am J Prev Med. 2001;20:196-201. [PMID: 11275446]

7. **U.S. Preventive Services Task Force.** Guide to Clinical Preventive Services. 2nd ed. Alexandria, VA: International Medical Publishing; 1996:219-29.

8. **Fontaine KR, Redden DT, Wang C, Westfall AO, Allison DB.** Years of life lost due to obesity. JAMA. 2003;289:187-93. [PMID: 12517229]

9. **Peeters A, Barendregt JJ, Willekens F, Mackenbach JP, Al Mamun A, Bonneux L, et al.** Obesity in adulthood and its consequences for life expectancy: a life-table analysis. Ann Intern Med. 2003;138:24-32. [PMID: 12513041]

10. **Roe DA, Eickwort KR.** Relationships between obesity and associated health factors with unemployment among low income women. J Am Med Womens Assoc. 1976;31:193-4, 198-9, 203-4.

11. NHLBI Obesity Education Initiative. Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults: the Evidence Report. Bethesda, MD: U.S. Department of Health and Human Services, Public

Health Service, National Institutes of Health, National Heart, Lung, and Blood Institute; 1998. NIH publication no. 98-4083.

12. **McTigue KM, Garrett JM, Popkin BM.** The natural history of the development of obesity in a cohort of young U.S. adults between 1981 and 1998. Ann Intern Med. 2002;136:857-64. [PMID: 12069559]

13. **Juhaeri, Stevens J, Chambless LE, Tyroler HA, Rosamond W, Nieto FJ, et al.** Associations between weight gain and incident hypertension in a bi-ethnic cohort: the Atherosclerosis Risk in Communities Study. Int J Obes Relat Metab Disord. 2002;26:58-64. [PMID: 11791147]

14. **Lovejoy JC, de la Bretonne JA, Klemperer M, Tulley R.** Abdominal fat distribution and metabolic risk factors: effects of race. Metabolism. 1996;45: 1119-24. [PMID: 8781299]

15. **Albu JB, Murphy L, Frager DH, Johnson JA, Pi-Sunyer FX.** Visceral fat and race-dependent health risks in obese nondiabetic premenopausal women. Diabetes. 1997;46:456-62. [PMID: 9032103]

16. **Casas YG, Schiller BC, DeSouza CA, Seals DR.** Total and regional body composition across age in healthy Hispanic and white women of similar socioeconomic status. Am J Clin Nutr. 2001;73:13-8. [PMID: 11124743]

17. **Conway JM, Yanovski SZ, Avila NA, Hubbard VS.** Visceral adipose tissue differences in black and white women. Am J Clin Nutr. 1995;61:765-71. [PMID: 7702017]

18. **Dowling HJ, Pi-Sunyer FX.** Race-dependent health risks of upper body obesity. Diabetes. 1993;42:537-43. [PMID: 8454103]

19. **Lear SA, Chen MM, Frohlich JJ, Birmingham CL.** The relationship between waist circumference and metabolic risk factors: cohorts of European and Chinese descent. Metabolism. 2002;51:1427-32. [PMID: 12404193]

20. **Wajchenberg BL, Giannella-Neto D, Da Silva ME, Santos RF.** Depot-Specific Hormonal Characteristics of Subcutaneous and Visceral Adipose Tissue and their Relation to the Metabolic Syndrome. Horm Metab Res. 2002;34:616-21. [PMID: 12660870]

21. **Park YW, Allison DB, Heymsfield SB, Gallagher D.** Larger amounts of visceral adipose tissue in Asian Americans. Obes Res. 2001;9:381-7. [PMID: 11445659]

22. **Hill JO, Sidney S, Lewis CE, Tolan K, Scherzinger AL, Stamm ER.** Racial differences in amounts of visceral adipose tissue in young adults: the CARDIA (Coronary Artery Risk Development in Young Adults) study. Am J Clin Nutr. 1999;69:381-7. [PMID: 10075320]

23. **Bacha F, Saad R, Gungor N, Janosky J, Arslanian SA.** Obesity, regional fat distribution, and syndrome X in obese black versus white adolescents: race differential in diabetogenic and atherogenic risk factors. J Clin Endocrinol Metab. 2003;88:2534-40. [PMID: 12788850]

24. **Wolf AM, Colditz GA.** Current estimates of the economic cost of obesity in the United States. Obes Res. 1998;6:97-106. [PMID: 9545015]

25. **Thompson D, Edelsberg J, Colditz GA, Bird AP, Oster G.** Lifetime health and economic consequences of obesity. Arch Intern Med. 1999;159:2177-83. [PMID: 10527295]

26. **Galuska DA, Will JC, Serdula MK, Ford ES.** Are health care professionals advising obese patients to lose weight? JAMA. 1999;282:1576-8. [PMID: 10546698]

27. **Harris RP, Helfand M, Woolf SH, Lohr KN, Mulrow CD, Teutsch SM, et al.** Current methods of the US Preventive Services Task Force: a review of the process. Am J Prev Med. 2001;20:21-35. [PMID: 11306229]

28. **Douketis JD, Feightner JW, Attia J, Feldman WF.** Periodic health examination, 1999 update: 1. Detection, prevention and treatment of obesity. Canadian Task Force on Preventive Health Care. CMAJ. 1999;160:513-25. [PMID: 10081468]

29. NHS Centre for Reviews and Dissemination University of York. The prevention and treatment of obesity. Eff Health Care. 1997;3:1-12.

30. National Task Force on the Prevention and Treatment of Obesity. Long-term pharmacotherapy in the management of obesity. JAMA. 1996;276:1907-15.

31. **Arterburn D, Noel PH.** Effects of drug treatment for obesity in adults. Clin Evid. 2001;412-9.

32. **Gokcel A, Karakose H, Ertorer EM, Tanaci N, Tutuncu NB, Guvener N.** Effects of sibutramine in obese female subjects with type 2 diabetes and poor blood glucose control. Diabetes Care. 2001;24:1957-60. [PMID: 11679464]

33. **McNulty SJ, Ur E, Williams G.** A randomized trial of sibutramine in the management of obese type 2 diabetic patients treated with metformin. Diabetes Care. 2003;26:125-31. [PMID: 12502668]

34. **Sorkin JD, Muller D, Andres R.** Body mass index and mortality in Seventh-day Adventist men. A critique and re-analysis. Int J Obes Relat Metab Disord. 1994;18:752-4. [PMID: 7866475]

35. **Manson JE, Willett WC, Stampfer MJ, Colditz GA, Hunter DJ, Hankinson SE, et al.** Body weight and mortality among women. N Engl J Med. 1995; 333:677-85. [PMID: 7637744]

36. **Laara E, Rantakallio P.** Body size and mortality in women: a 29 year follow up of 12,000 pregnant women in northern Finland. J Epidemiol Community Health. 1996;50:408-14. [PMID: 8882224]

37. **Shaper AG, Wannamethee SG, Walker M.** Body weight: implications for the prevention of coronary heart disease, stroke, and diabetes mellitus in a cohort study of middle aged men. BMJ. 1997;314:1311-7. [PMID: 9158466]

38. **Chyou PH, Burchfiel CM, Yano K, Sharp DS, Rodriguez BL, Curb JD, et al.** Obesity, alcohol consumption, smoking, and mortality. Ann Epidemiol. 1997;7:311-7. [PMID: 9177115]

39. **Wannamethee SG, Shaper AG, Walker M, Ebrahim S.** Lifestyle and 15-year survival free of heart attack, stroke, and diabetes in middle-aged British men. Arch Intern Med. 1998;158:2433-40. [PMID: 9855381]

40. **Huang Z, Willett WC, Manson JE, Rosner B, Stampfer MJ, Speizer FE, et al.** Body weight, weight change, and risk for hypertension in women. Ann Intern Med. 1998;128:81-8. [PMID: 9441586]

41. **Durazo-Arvizu RA, McGee DL, Cooper RS, Liao Y, Luke A.** Mortality and optimal body mass index in a sample of the US population. Am J Epidemiol. 1998;147:739-49. [PMID: 9554415]

42. **Calle EE, Thun MJ, Petrelli JM, Rodriguez C, Heath CW Jr.** Body-mass index and mortality in a prospective cohort of U.S. adults. N Engl J Med. 1999; 341:1097-105. [PMID: 10511607]

43. **Rosengren A, Wedel H, Wilhelmsen L.** Body weight and weight gain during adult life in men in relation to coronary heart disease and mortality. A prospective population study. Eur Heart J. 1999;20:269-77. [PMID: 10099921]

44. **Folsom AR, Kushi LH, Anderson KE, Mink PJ, Olson JE, Hong CP, et al.** Associations of general and abdominal obesity with multiple health outcomes in older women: the Iowa Women's Health Study. Arch Intern Med. 2000;160: 2117-28. [PMID: 10904454]

45. **Song YM, Sung J.** Body mass index and mortality: a twelve-year prospective study in Korea. Epidemiology. 2001;12:173-9. [PMID: 11246577]

46. **Allison DB, Moonseong H, Fontaine KR, Hoffman DJ.** Body weight, body composition and longevity. In: Björntorp P, ed. International Textbook of Obesity. New York: J Wiley; 2001: 31-48.

47. **Kim KS, Owen WL, Williams D, Adams-Campbell LL.** A comparison between BMI and Conicity index on predicting coronary heart disease: the Framingham Heart Study. Ann Epidemiol. 2000;10:424-31. [PMID: 11018345]

48. **Nilsen TI, Vatten LJ.** Prospective study of colorectal cancer risk and physical activity, diabetes, blood glucose and BMI: exploring the hyperinsulinaemia hypothesis. Br J Cancer. 2001;84:417-22. [PMID: 11161410]

49. **Stevens J.** Obesity and mortality in Africans-Americans. Nutr Rev. 2000;58: 346-53. [PMID: 11140906]

50. **Heiat A, Vaccarino V, Krumholz HM.** An evidence-based assessment of federal guidelines for overweight and obesity as they apply to elderly persons. Arch Intern Med. 2001;161:1194-203. [PMID: 11343442]

51. **Deurenberg P, Weststrate JA, Seidell JC.** Body mass index as a measure of body fatness: age- and sex-specific prediction formulas. Br J Nutr. 1991;65:105-14. [PMID: 2043597]

52. **Gray DS, Fujioka K.** Use of relative weight and Body Mass Index for the determination of adiposity. J Clin Epidemiol. 1991;44:545-50. [PMID: 2037859]

53. **Wang J, Thornton JC, Russell M, Burastero S, Heymsfield S, Pierson RN Jr.** Asians have lower body mass index (BMI) but higher percent body fat than do whites: comparisons of anthropometric measurements. Am J Clin Nutr. 1994; 60:23-8. [PMID: 8017333]

54. **Deurenberg P, Yap M, van Staveren WA.** Body mass index and percent body fat: a meta analysis among different ethnic groups. Int J Obes Relat Metab Disord. 1998;22:1164-71. [PMID: 9877251]

55. **Gurrici S, Hartriyanti Y, Hautvast JG, Deurenberg P.** Relationship between body fat and body mass index: differences between Indonesians and Dutch Cau-

casians. Eur J Clin Nutr. 1998;52:779-83. [PMID: 9846588]

56. **Deurenberg P, van der Kooy K, Hulshof T, Evers P.** Body mass index as a measure of body fatness in the elderly. Eur J Clin Nutr. 1989;43:231-6. [PMID: 2661215]

57. **Colditz GA, Willett WC, Rotnitzky A, Manson JE.** Weight gain as a risk factor for clinical diabetes mellitus in women. Ann Intern Med. 1995;122:481-6. [PMID: 7872581]

58. **Rexrode KM, Carey VJ, Hennekens CH, Walters EE, Colditz GA, Stampfer MJ, et al.** Abdominal adiposity and coronary heart disease in women. JAMA. 1998;280:1843-8. [PMID: 9846779]

59. **Liese AD, Mayer-Davis EJ, Tyroler HA, Davis CE, Keil U, Duncan BB, et al.** Development of the multiple metabolic syndrome in the ARIC cohort: joint contribution of insulin, BMI, and WHR. Atherosclerosis risk in communities. Ann Epidemiol. 1997;7:407-16. [PMID: 9279450]

60. **Baik I, Ascherio A, Rimm EB, Giovannucci E, Spiegelman D, Stampfer MJ, et al.** Adiposity and mortality in men. Am J Epidemiol. 2000;152:264-71. [PMID: 10933273]

61. **Janssen I, Katzmarzyk PT, Ross R.** Body mass index, waist circumference, and health risk: evidence in support of current National Institutes of Health guidelines. Arch Intern Med. 2002;162:2074-9. [PMID: 12374515]

62. **Eden KB, Orleans CT, Mulrow CD, Pender NJ, Teutsch SM.** Does counseling by clinicians improve physical activity? A summary of the evidence for the U.S. Preventive Services Task Force. Ann Intern Med. 2002;137:208-15. [PMID: 12160371]

63. U.S. Department of Health and Human Services. Physical Activity and Health: A Report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion; 1996. Accessed 23 July 2003 at www.cdc.gov/nccdphp/sgr/pdf/sgrfull.pdf.

64. **Stevens J, Cai J, Evenson KR, Thomas R.** Fitness and fatness as predictors of mortality from all causes and from cardiovascular disease in men and women in the lipid research clinics study. Am J Epidemiol. 2002;156:832-41. [PMID: 12397001]

65. **Wadden TA, Berkowitz RI, Sarwer DB, Prus-Wisniewski R, Steinberg C.** Benefits of lifestyle modification in the pharmacologic treatment of obesity: a randomized trial. Arch Intern Med. 2001;161:218-27. [PMID: 11176735]

66. **Kuller LH, Simkin-Silverman LR, Wing RR, Meilahn EN, Ives DG.** Women's Healthy Lifestyle Project: A randomized clinical trial: results at 54 months. Circulation. 2001;103:32-7. [PMID: 11136682]

67. **Tuomilehto J, Lindstrom J, Eriksson JG, Valle TT, Hamalainen H, Ilanne-Parikka P, et al.** Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med. 2001;344:1343-50. [PMID: 11333990]

68. **Rothacker DQ, Staniszewski 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;101:345-7. [PMID: 11269616]

69. **Jones DW, Miller ME, Wofford MR, Anderson DC Jr, Cameron ME, Willoughby DL, et al.** The effect of weight loss intervention on antihypertensive medication requirements in the hypertension Optimal Treatment (HOT) study. Am J Hypertens. 1999;12:1175-80. [PMID: 10619579]

70. **Stevens VJ, Obarzanek E, Cook NR, Lee IM, Appel LJ, Smith West D, et al.** Long-term weight loss and changes in blood pressure: results of the Trials of Hypertension Prevention, phase II. Ann Intern Med. 2001;134:1-11. [PMID: 11187414]

71. **Swinburn BA, Woollard GA, Chang EC, Wilson MR.** Effects of reduced-fat diets consumed ad libitum on intake of nutrients, particularly antioxidant vitamins. J Am Diet Assoc. 1999;99:1400-5. [PMID: 10570677]

72. **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;282:1554-60. [PMID: 10546695]

73. **Leermakers EA, Perri MG, Shigaki CL, Fuller PR.** Effects of exercise-focused versus weight-focused maintenance programs on the management of obesity. Addict Behav. 1999;24:219-27. [PMID: 10336103]

74. **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 Consult Clin Psychol. 1999;67:260-6. [PMID: 10224737]

75. **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 Relat Metab Disord. 1999;23:203-10. [PMID: 10078857]

76. **Fogelholm M, Kukkonen-Harjula K, Nenonen A, Pasanen M.** Effects of walking training on weight maintenance after a very-low-energy diet in premenopausal obese women: a randomized controlled trial. Arch Intern Med. 2000;160:2177-84. [PMID: 10904461]

77. **Jeffery RW, French SA.** Preventing weight gain in adults: design, methods and one year results from the Pound of Prevention study. Int J Obes Relat Metab Disord. 1997;21:457-64. [PMID: 9192229]

78. **Wing RR, Anglin K.** Effectiveness of a behavioral weight control program for blacks and whites with NIDDM. Diabetes Care. 1996;19:409-13. [PMID: 8732700]

79. **Lindholm LH, Ekbom T, Dash C, Eriksson M, Tibblin G, Schersten B.** The impact of health care advice given in primary care on cardiovascular risk. CELL Study Group. BMJ. 1995;310:1105-9. [PMID: 7742677]

80. Effectiveness of health checks conducted by nurses in primary care: final results of the OXCHECK study. Imperial Cancer Research Fund OXCHECK Study Group. BMJ. 1995;310:1099-104. [PMID: 7742676]

81. **Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, et al.** Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med. 2002;346:393-403. [PMID: 11832527]

82. **Ashley JM, St Jeor ST, Schrage JP, Perumean-Chaney SE, Gilbertson MC, McCall NL, et al.** Weight control in the physician's office. Arch Intern Med. 2001;161:1599-604. [PMID: 11434791]

83. **Bemelmans WJ, Broer J, de Vries JH, Hulshof KF, May JF, Meyboom-De Jong B.** Impact of Mediterranean diet education versus posted leaflet on dietary habits and serum cholesterol in a high risk population for cardiovascular disease. Public Health Nutr. 2000;3:273-83. [PMID: 10979147]

84. **James WP, Astrup A, Finer N, Hilsted J, Kopelman P, Rossner S, et al.** Effect of sibutramine on weight maintenance after weight loss: a randomised trial. STORM Study Group. Sibutramine Trial of Obesity Reduction and Maintenance. Lancet. 2000;356:2119-25. [PMID: 11191537]

85. **Dujovne CA, Zavoral JH, Rowe E, Mendel CM.** Effects of sibutramine on body weight and serum lipids: a double-blind, randomized, placebo-controlled study in 322 overweight and obese patients with dyslipidemia. Am Heart J. 2001;142:489-97. [PMID: 11526363]

86. **Fujioka K, Seaton TB, Rowe E, Jelinek CA, Raskin P, Lebovitz HE, et al.** Weight loss with sibutramine improves glycaemic control and other metabolic parameters in obese patients with type 2 diabetes mellitus. Diabetes Obes Metab. 2000;2:175-87. [PMID: 11220553]

87. **Smith IG, Goulder MA.** Randomized placebo-controlled trial of long-term treatment with sibutramine in mild to moderate obesity. J Fam Pract. 2001;50:505-12. [PMID: 11407998]

88. **Wirth A, Krause J.** Long-term weight loss with sibutramine: a randomized controlled trial. JAMA. 2001;286:1331-9. [PMID: 11560538]

89. **Van Gaal LF, Broom JI, Enzi G, Toplak H.** Efficacy and tolerability of orlistat in the treatment of obesity: a 6-month dose-ranging study. Orlistat Dose-Ranging Study Group. Eur J Clin Pharmacol. 1998;54:125-32. [PMID: 9626916]

90. **Miles JM, Leiter L, Hollander P, Wadden T, Anderson JW, Doyle M, et al.** Effect of orlistat in overweight and obese patients with type 2 diabetes treated with metformin. Diabetes Care. 2002;25:1123-8. [PMID: 12087008]

91. **Muls E, Kolanowski J, Scheen A, Van Gaal L.** The effects of orlistat on weight and on serum lipids in obese patients with hypercholesterolemia: a randomized, double-blind, placebo-controlled, multicentre study. Int J Obes Relat Metab Disord. 2001;25:1713-21. [PMID: 11753595]

92. **Hill JO, Hauptman J, Anderson JW, Fujioka K, O'Neil PM, Smith DK, et al.** Orlistat, a lipase inhibitor, for weight maintenance after conventional dieting: a 1-y study. Am J Clin Nutr. 1999;69:1108-16. [PMID: 10357727]

93. **Karhunen L, Franssila-Kallunki A, Rissanen P, Valve R, Kolehmainen M, Rissanen A, et al.** Effect of orlistat treatment on body composition and resting energy expenditure during a two-year weight-reduction programme in obese Finns. Int J Obes Relat Metab Disord. 2000;24:1567-72. [PMID: 11126207]

94. **Micic D, Ivkovic-Lazar T, Dragojevic R, Jorga J, Stokic E, Hajdukovic Z.**

Orlistat, a gastrointestinal lipase inhibitor, in therapy of obesity with concomitant hyperlipidemia. Med Pregl. 1999;52:323-33. [PMID: 10624380]

95. **Rissanen P, Vahtera E, Krusius T, Uusitupa M, Rissanen A.** Weight change and blood coagulability and fibrinolysis in healthy obese women. Int J Obes Relat Metab Disord. 2001;25:212-8. [PMID: 11410822]

96. **Broom I, Wilding J, Stott P, Myers N.** 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;56:494-9. [PMID: 12296610]

97. **Giugliano D, Quatraro A, Consoli G, Minei A, Ceriello A, De Rosa N, et al.** Metformin for obese, insulin-treated diabetic patients: improvement in glycaemic control and reduction of metabolic risk factors. Eur J Clin Pharmacol. 1993; 44:107-12. [PMID: 8453955]

98. **Gokcel A, Gumurdulu Y, Karakose H, Melek Ertorer E, Tanaci N, Bascil-Tutuncu N, et al.** Evaluation of the safety and efficacy of sibutramine, orlistat and metformin in the treatment of obesity. Diabetes Obes Metab. 2002;4:49-55. [PMID: 11874442]

99. **Hubbard VS, Hall WH.** Gastrointestinal surgery for severe obesity. Obes Surg. 1991;1:257-265. [PMID: 10775921]

100. **de Wit LT, Mathus-Vliegen L, Hey C, Rademaker B, Gouma DJ, Obertop H.** Open versus laparoscopic adjustable silicone gastric banding: a prospective randomized trial for treatment of morbid obesity. Ann Surg. 1999;230:800-5; discussion 805-7. [PMID: 10615935]

101. **Weiss HG, Nehoda H, Labeck B, Peer-Kuehberger R, Oberwalder M, Aigner F, et al.** Adjustable gastric and esophagogastric banding: a randomized clinical trial. Obes Surg. 2002;12:573-8. [PMID: 12194554]

102. **Weiner R, Bockhorn H, Rosenthal R, Wagner D.** A prospective randomized trial of different laparoscopic gastric banding techniques for morbid obesity. Surg Endosc. 2001;15:63-8. [PMID: 11178766]

103. **Sjostrom L, Larsson B, Backman L, Bengtsson C, Bouchard C, Dahlgren S, et al.** Swedish obese subjects (SOS). Recruitment for an intervention study and a selected description of the obese state. Int J Obes Relat Metab Disord. 1992; 16:465-79. [PMID: 1322873]

104. **Torgerson JS, Sjostrom L.** The Swedish Obese Subjects (SOS) study—rationale and results. Int J Obes Relat Metab Disord. 2001;25 Suppl 1:S2-4. [PMID: 11466577]

105. **McMahon FG, Fujioka K, Singh BN, Mendel CM, Rowe E, Rolston K, et al.** Efficacy and safety of sibutramine in obese white and African American patients with hypertension: a 1-year, double-blind, placebo-controlled, multicenter trial. Arch Intern Med. 2000;160:2185-91. [PMID: 10904462]

106. **Sjostrom L, Rissanen A, Andersen T, Boldrin M, Golay A, Koppeschaar HP, et al.** Randomised placebo-controlled trial of orlistat for weight loss and prevention of weight regain in obese patients. European Multicentre Orlistat Study Group. Lancet. 1998;352:167-72. [PMID: 9683204]

107. **Hollander PA, Elbein SC, Hirsch IB, Kelley D, McGill J, Taylor T, et al.** Role of orlistat in the treatment of obese patients with type 2 diabetes. A 1-year randomized double-blind study. Diabetes Care. 1998;21:1288-94. [PMID: 9702435]

108. **Lindgarde F.** The effect of orlistat on body weight and coronary heart disease risk profile in obese patients: the Swedish Multimorbidity Study. J Intern Med. 2000;248:245-54. [PMID: 10971792]

109. **Rossner S, Sjostrom L, Noack R, Meinders AE, Noseda G.** Weight loss, weight maintenance, and improved cardiovascular risk factors after 2 years treatment with orlistat for obesity. European Orlistat Obesity Study Group. Obes Res. 2000;8:49-61. [PMID: 10678259]

110. **Hauptman J, Lucas C, Boldrin MN, Collins H, Segal KR.** Orlistat in the long-term treatment of obesity in primary care settings. Arch Fam Med. 2000;9: 160-7. [PMID: 10693734]

111. **Scheen AJ, Lefebvre PJ.** Pharmacological treatment of obesity: present status. Int J Obes Relat Metab Disord. 1999;23 Suppl 1:47-53. [PMID: 10193862]

112. **Luque CA, Rey JA.** Sibutramine: a serotonin-norepinephrine reuptake-inhibitor for the treatment of obesity. Ann Pharmacother. 1999;33:968-78. [PMID: 10492502]

113. **Apfelbaum M, Vague P, Ziegler O, Hanotin C, Thomas F, Leutenegger E.** Long-term maintenance of weight loss after a very-low-calorie diet: a randomized blinded trial of the efficacy and tolerability of sibutramine. Am J Med. 1999;106:179-84. [PMID: 10230747]

114. **Bray GA.** Drug treatment of obesity. Baillieres Best Pract Res Clin Endocrinol Metab. 1999;13:131-48. [PMID: 10932681]

115. Orlistat. No hurry... Can Fam Physician. 1999;45:2331-3, 2336-8, 2343-5 passim. [PMID: 10540693]

116. **Finer N, James WP, Kopelman PG, Lean ME, Williams G.** One-year treatment of obesity: a randomized, double-blind, placebo-controlled, multicentre study of orlistat, a gastrointestinal lipase inhibitor. Int J Obes Relat Metab Disord. 2000;24:306-13. [PMID: 10757623]

117. **Sjostrom L.** Surgical intervention as a strategy for treatment of obesity. Endocrine. 2000;13:213-30. [PMID: 11186223]

118. **Pories WJ, Swanson MS, MacDonald KG, Long SB, Morris PG, Brown BM, et al.** Who would have thought it? An operation proves to be the most effective therapy for adult-onset diabetes mellitus. Ann Surg. 1995;222:339-50; discussion 350-2. [PMID: 7677463]

119. **Brolin RE, Bradley LJ, Wilson AC, Cody RP.** Lipid risk profile and weight stability after gastric restrictive operations for morbid obesity. J Gastrointest Surg. 2000;4:464-9. [PMID: 11077320]

120. **Sjostrom CD, Lissner L, Wedel H, Sjostrom L.** Reduction in incidence of diabetes, hypertension and lipid disturbances after intentional weight loss induced by bariatric surgery: the SOS Intervention Study. Obes Res. 1999;7:477-84. [PMID: 10509605]

121. **Sjostrom CD, Peltonen M, Sjostrom L.** Blood pressure and pulse pressure during long-term weight loss in the obese: the Swedish Obese Subjects (SOS) Intervention Study. Obes Res. 2001;9:188-95. [PMID: 11323444]

122. **Williamson DF, Pamuk E, Thun M, Flanders D, Byers T, Heath C.** Prospective study of intentional weight loss and mortality in never-smoking overweight US white women aged 40-64 years. Am J Epidemiol. 1995;141:1128-41. [PMID: 7771451]

123. **Singh RB, Rastogi SS, Verma R, Laxmi B, Singh R, Ghosh S, et al.** Randomised controlled trial of cardioprotective diet in patients with recent acute myocardial infarction: results of one year follow up. BMJ. 1992;304:1015-9. [PMID: 1586782]

124. **Lissner L, Odell PM, D'Agostino RB, Stokes J 3rd, Kreger BE, Belanger AJ, et al.** Variability of body weight and health outcomes in the Framingham population. N Engl J Med. 1991;324:1839-44. [PMID: 2041550]

125. **Blair SN, Shaten J, Brownell K, Collins G, Lissner L.** Body weight change, all-cause mortality, and cause-specific mortality in the Multiple Risk Factor Intervention Trial. Ann Intern Med. 1993;119:749-57. [PMID: 8363210]

126. **Andres R, Muller DC, Sorkin JD.** Long-term effects of change in body weight on all-cause mortality. A review. Ann Intern Med. 1993;119:737-43. [PMID: 8363208]

127. **Williamson DF.** "Weight cycling" and mortality: how do the epidemiologists explain the role of intentional weight loss? J Am Coll Nutr. 1996;15:6-13. [PMID: 8632117]

128. **Reynolds MW, Fredman L, Langenberg P, Magaziner J.** Weight, weight change, mortality in a random sample of older community-dwelling women. J Am Geriatr Soc. 1999;47:1409-14. [PMID: 10591233]

129. **Williamson DF, Pamuk ER.** The association between weight loss and increased longevity. A review of the evidence. Ann Intern Med. 1993;119:731-6. [PMID: 8363207]

130. Weight cycling. National Task Force on the Prevention and Treatment of Obesity. JAMA. 1994;272:1196-202. [PMID: 7741844]

131. **Olson MB, Kelsey SF, Bittner V, Reis SE, Reichek N, Handberg EM, et al.** Weight cycling and high-density lipoprotein cholesterol in women: evidence of an adverse effect: a report from the NHLBI-sponsored WISE study. Women's Ischemia Syndrome Evaluation Study Group. J Am Coll Cardiol. 2000;36:1565-71. [PMID: 11079659]

132. **Guagnano MT, Ballone E, Pace-Palitti V, Vecchia RD, D'Orazio N, Manigrasso MR, et al.** Risk factors for hypertension in obese women. The role of weight cycling. Eur J Clin Nutr. 2000;54:356-60. [PMID: 10745288]

133. **Field AE, Wing RR, Manson JE, Spiegelman DL, Willett WC.** Relationship of a large weight loss to long-term weight change among young and middle-aged US women. Int J Obes Relat Metab Disord. 2001;25:1113-21. [PMID: 11477495]

134. **Petersmarck KA, Teitelbaum HS, Bond JT, Bianchi L, Hoerr SM, Sowers MF.** The effect of weight cycling on blood lipids and blood pressure in the Multiple Risk Factor Intervention Trial Special Intervention Group. Int J Obes Relat Metab Disord. 1999;23:1246-55. [PMID: 10643680]

135. **Bouchard C.** Is weight fluctuation a risk factor? [Editorial]. N Engl J Med. 1991;324:1887-9. [PMID: 2041553]

136. **Kuller L, Wing R.** Weight loss and mortality [Editorial]. Ann Intern Med. 1993;119:630-2. [PMID: 8363176]

137. Variability of body weight and health outcomes [Letter]. N Engl J Med. 1991;325:1745-6. [PMID: 1944478]

138. **Gortmaker SL, Must A, Perrin JM, Sobol AM, Dietz WH.** Social and economic consequences of overweight in adolescence and young adulthood. N Engl J Med. 1993;329:1008-12. [PMID: 8366901]

139. **Teachman BA, Brownell KD.** Implicit anti-fat bias among health professionals: is anyone immune? Int J Obes Relat Metab Disord. 2001;25:1525-31. [PMID: 11673776]

140. **Myers A, Rosen JC.** Obesity stigmatization and coping: relation to mental health symptoms, body image, and self-esteem. Int J Obes Relat Metab Disord. 1999;23:221-30. [PMID: 10193866]

141. **Knowler WC, Narayan KM, Hanson RL, Nelson RG, Bennett PH, Tuomilehto J, et al.** Preventing non-insulin-dependent diabetes. Diabetes. 1995; 44:483-8. [PMID: 7729603]

142. **Arterburn D, Noel PH.** Extracts from "Clinical Evidence". Obesity. BMJ. 2001;322:1406-9. [PMID: 11397749]

143. **Melissas J, Christodoulakis M, Spyridakis M, Schoretsanitis G, Michaloudis D, Papavasiliou E, et al.** Disorders associated with clinically severe obesity: significant improvement after surgical weight reduction. South Med J. 1998;91: 1143-8. [PMID: 9853727]

144. **Schauer PR, Ikramuddin S, Gourash W, Ramanathan R, Luketich J.** Outcomes after laparoscopic Roux-en-Y gastric bypass for morbid obesity. Ann Surg. 2000;232:515-29. [PMID: 10998650]

145. **Bloomston M, Zervos EE, Camps MA, Goode SE, Rosemurgy AS.** Outcome following bariatric surgery in super versus morbidly obese patients: does weight matter? Obes Surg. 1997;7:414-9. [PMID: 9730495]

146. **Balsiger BM, Poggio JL, Mai J, Kelly KA, Sarr MG.** Ten and more years after vertical banded gastroplasty as primary operation for morbid obesity. J Gastrointest Surg. 2000;4:598-605. [PMID: 11307094]

147. **Davila-Cervantes A, Ganci-Cerrud G, Gamino R, Gallegos-Martinez J, Gonzalez-Barranco J, Herrera MF.** Open vs. laparoscopic vertical banded gastroplasty: a case control study with a 1-year follow-up. Obes Surg. 2000;10:409-12. [PMID: 11054244]

148. **Alper D, Ramadan E, Vishne T, Belavsky R, Avraham Z, Seror D, et al.** Silastic ring vertical gastroplasty- long-term results and complications. Obes Surg. 2000;10:250-4. [PMID: 10929157]

149. **Choi Y, Frizzi J, Foley A, Harkabus M.** Patient satisfaction and results of vertical banded gastroplasty and gastric bypass. Obes Surg. 1999;9:33-5. [PMID: 10065578]

150. **Papakonstantinou A, Alfaras P, Komessidou V, Hadjiyannakis E.** Gastrointestinal complications after vertical banded gastroplasty. Obes Surg. 1998;8: 215-7. [PMID: 9730397]

151. **Baltasar A, Bou R, Arlandis F, Martinez R, Serra C, Bengochea M, et al.** Vertical banded gastroplasty at more than 5 years. Obes Surg. 1998;8:29-34. [PMID: 9562483]

152. **Stoner J, Stoner P, Sytsma J.** 42-month preliminary follow-up of the silastic ring vertical banded gastroplasty. Obes Surg. 1997;7:513-5. [PMID: 9730510]

153. **Yashkov YI, Timoshin AD, Oppel TA.** Vertical banded gastroplasty: first experience in Russia. Obes Surg. 1997;7:317-20; discussion 321. [PMID: 9730517]

154. **Goulding ST, Hovell BC.** Anaesthetic experience of vertical banded gastroplasty. Br J Anaesth. 1995;75:301-6. [PMID: 7547048]

155. **Lundell L, Ruth M, Olbe L.** Vertical banded gastroplasty or gastric banding for morbid obesity: effects on gastro-oesophageal reflux. Eur J Surg. 1997;163: 525-31. [PMID: 9248987]

156. **Nguyen NT, Ho HS, Palmer LS, Wolfe BM.** A comparison study of laparoscopic versus open gastric bypass for morbid obesity. J Am Coll Surg. 2000;191:149-55; discussion 155-7. [PMID: 10945358]

157. **Choban PS, Onyejekwe J, Burge JC, Flancbaum L.** A health status assessment of the impact of weight loss following Roux-en-Y gastric bypass for clinically severe obesity. J Am Coll Surg. 1999;188:491-7. [PMID: 10235576]

158. **Jones KB Jr.** Roux-en-Y gastric bypass: an effective antireflux procedure in the less than morbidly obese. Obes Surg. 1998;8:35-8. [PMID: 9562484]

159. **Crampton NA, Izvornikov V, Stubbs RS.** Silastic ring gastric bypass: results in 64 patients. Obes Surg. 1997;7:489-94. [PMID: 9730506]

160. **Freeman JB, Kotlarewsky M, Phoenix C.** Weight loss after extended gastric bypass. Obes Surg. 1997;7:337-44. [PMID: 9730521]

161. **Oh CH, Kim HJ, Oh S.** Weight loss following transected gastric bypass with proximal Roux-en-Y. Obes Surg. 1997;7:142-7; discussion 148. [PMID: 9730542]

162. **Abu-Abeid S, Szold A.** Laparoscopic management of Lap-Band erosion. Obes Surg. 2001;11:87-9. [PMID: 11361174]

163. **Nowara HA.** Egyptian experience in laparoscopic adjustable gastric banding (technique, complications and intermediate results). Obes Surg. 2001;11:70-5. [PMID: 11361172]

164. **De Luca M, de Werra C, Formato A, Formisano C, Loffredo A, Naddeo M, et al.** Laparotomic vs laparoscopic lap-band: 4-year results with early and intermediate complications. Obes Surg. 2000;10:266-8. [PMID: 10929160]

165. **Suter M, Bettschart V, Giusti V, Heraief E, Jayet A.** A 3-year experience with laparoscopic gastric banding for obesity. Surg Endosc. 2000;14:532-6. [PMID: 10890959]

166. **Wiesner W, Schob O, Hauser RS, Hauser M.** Adjustable laparoscopic gastric banding in patients with morbid obesity: radiographic management, results, and postoperative complications. Radiology. 2000;216:389-94. [PMID: 10924559]

167. **Holeczy P, Novak P, Kralova A.** Complications in the first year of laparoscopic gastric banding: is it acceptable? Obes Surg. 1999;9:453-5. [PMID: 10605902]

168. **Dargent J.** Laparoscopic adjustable gastric banding: lessons from the first 500 patients in a single institution. Obes Surg. 1999;9:446-52. [PMID: 10605901]

169. **Suter M, Giusti V, Heraief E, Jayet C, Jayet A.** Early results of laparoscopic gastric banding compared with open vertical banded gastroplasty. Obes Surg. 1999;9:374-80. [PMID: 10484296]

170. **Abu-Abeid S, Szold A.** Results and complications of laparoscopic adjustable gastric banding: an early and intermediate experience. Obes Surg. 1999;9:188-90. [PMID: 10340776]

171. **Miller K, Hell E.** Laparoscopic adjustable gastric banding: a prospective 4-year follow-up study. Obes Surg. 1999;9:183-7. [PMID: 10340775]

172. **Forsell P, Hallerback B, Glise H, Hellers G.** Complications following Swedish adjustable gastric banding: a long-term follow-up. Obes Surg. 1999;9: 11-6. [PMID: 10065574]

173. **Doherty C, Maher JW, Heitshusen DS.** Prospective investigation of complications, reoperations, and sustained weight loss with an adjustable gastric banding device for treatment of morbid obesity. J Gastrointest Surg. 1998;2:102-8. [PMID: 9841975]

174. **Forestieri P, Meucci L, De Luca M, Formato A, De Werra C, Chiacchio C.** Two years of practice in adjustable silicone gastric banding (LAP-BAND): evaluation of variations of body mass index, percentage ideal body weight and percentage excess body weight. Obes Surg. 1998;8:49-52. [PMID: 9562487]

175. **Forsell P, Hellers G.** The Swedish Adjustable Gastric Banding (SAGB) for morbid obesity: 9 year experience and a 4-year follow-up of patients operated with a new adjustable band. Obes Surg. 1997;7:345-51. [PMID: 9730522]

176. **Horchner R, Tuinebreijer W.** Improvement of physical functioning of morbidly obese patients who have undergone a Lap-Band operation: one-year study. Obes Surg. 1999;9:399-402. [PMID: 10484301]

177. **Doldi SB, Micheletto G, Lattuada E, Zappa MA, Bona D, Sonvico U.** Adjustable gastric banding: 5-year experience. Obes Surg. 2000;10:171-3. [PMID: 10782180]

178. **Weiner R, Datz M, Wagner D, Bockhorn H.** Quality-of-life outcome after laparoscopic adjustable gastric banding for morbid obesity. Obes Surg. 1999;9: 539-45. [PMID: 10638479]

179. **Must A, Spadano J, Coakley EH, Field AE, Colditz G, Dietz WH.** The disease burden associated with overweight and obesity. JAMA. 1999;282:1523-9. [PMID: 10546691]

180. **Friedman LM, Furberg CD, DeMets DL.** Fundamentals of Clinical Trials. 3rd ed. New York: Springer; 1998.

181. **Jadad A.** Randomized Controlled Trials. London: BMJ Books; 1998.

182. 2002 Drug Topics Red Book: The Pharmacist's Trusted Companion for More Than a Century. Montvale, NJ: Medical Economics; 2002.

Current Author Addresses: Dr. McTigue: Departments of Medicine and Epidemiology, 3459 5th Avenue, Suite 933 West/MUH, Pittsburgh, PA 15213.
Dr. Harris and Ms. Bunton: Department of Medicine and Cecil G. Sheps Center for Health Services Research, CB #7590, 725 Airport Road, University of North Carolina School of Medicine, Chapel Hill, NC 27599.
Dr. Hemphill: 7725 Pinewood Drive, Albuquerque, NM 87120.
Ms. Lux, Ms. Sutton, and Dr. Lohr: RTI International, 3040 Cornwallis Road, Research Triangle Park, NC 27709-2194.

Appendix Table 1. **Screening for Obesity: Eligibility Criteria and Results of Searches***

Key Question	Eligibility Criteria	Articles That Met Eligibility Criteria and Were Not in Previous Systematic Review, *n*†
Efficacy of screening	RCT Mass screening	0
Epidemiology of obesity		
Prevalence	Large U.S. population-based surveys	1
Health risks	Prospective cohort studies with absolute rates of health risk reported over ≥ 10 years	14
Efficacy of treatment for weight reduction or intermediate outcomes		
Counseling and behavioral treatment	RCT (of fair or good quality) Outcome: weight loss or BMI reduction; glucose tolerance, blood pressure, lipid disorders Duration ≥ 1 y BMI ≥ 25 kg/m^2 12-mo follow-up	21
Medications	RCT (of fair or good quality) Outcome: weight loss or BMI reduction; glucose tolerance, blood pressure, lipid disorders Duration ≥ 6 mo Sample generalizable to typical U.S. primary care population	10
Surgery	RCT (of fair or good quality) Outcome: weight loss or BMI reduction; glucose tolerance, blood pressure, lipid disorders Duration: ≥ 1 y Cohort Initial BMI ≥ 25 kg/m^2 Surgical procedure	2
Harms of screening and treatment	Same studies as efficacy of counseling/behavioral and medication interventions For surgery, same studies as efficacy plus multiple cohorts and 1 non-RCT	Counselling: 21 Medication: 15 Surgery: 2

* BMI = body mass index; RCT = randomized, controlled trial.
† References 11, 28, 29, 31.

Appendix Table 2. **Criteria for Grading the Internal Validity of Individual Studies***

Study Design	Criteria
Systematic reviews	Comprehensiveness of sources and search strategy used Standard appraisal of included studies Validity of conclusions Recency and relevance
Case–control studies	Accurate ascertainment of cases Nonbiased selection of cases and controls with exclusion criteria applied equally to both Response rate Diagnostic testing procedures applied equally to each group Appropriate attention to potential confounding variables
RCTs and cohort studies	Initial assembly of comparable groups: For RCTs: adequate randomization, including concealment and whether potential confounders were distributed equally among groups For cohort studies: consideration of potential confounders with either restriction or measurement for adjustment in the analysis; consideration of inception cohorts Maintenance of comparable groups (includes attrition, crossovers, adherence, contamination) Important differential loss to follow-up or overall high loss to follow-up Measurements: equal, reliable, and valid (includes masking of outcome assessment) Clear definition of interventions All important outcomes considered Analysis: adjustment for potential confounders for cohort studies, or intention-to-treat analysis for RCTs
Diagnostic accuracy studies	Screening test relevant, available for primary care, adequately described Study uses a credible reference standard, performed regardless of test results Reference standard interpreted independently of screening test Handles indeterminate results in a reasonable manner Spectrum of patients included in study Sample size Administration of reliable screening test

* Based on reference 27. RCT = randomized, controlled trial.

Appendix Table 3. **Descriptions of Intensive Counseling Interventions***

Study, Year (Reference)	Intervention	Intervention Setting	Intervention Delivery	Counseling and Behavioral Description
Stevens et al., 2001 (70)	Control	Not noted	Not noted	Usual care (details not noted)
	Weight loss only	Not noted	Dietitians or health educators	One individual counseling session, then 14 weekly group meetings, then 6 biweekly group meetings, then monthly group meetings. After 18 mo, alternative options were offered, including individual counseling and special group sessions focused on selected weight loss topics. Focus included self-directed behavior change, nutrition and physical activity education, and social support for making and maintaining behavior changes. Behavior change techniques included self-monitoring, setting explicit short-term goals, developing action plans to achieve those objectives, and alternative strategies for situations triggering problem eating. Dietary intervention focused on reduced calorie intake by less consumption of fat, sugar, and alcohol, with a minimum daily calorie intake of 1500 kcal for men and 1200 kcal for women, and moderate weight loss goals of $\leq$ 0.9 kg/wk. Physical activity goal was for gradually increased activity to moderate-intensity activity (40%–55% of heart rate reserve) 30 to 45 min/d, 4 to 5 d/wk. Primary exercise was brisk walking.
Knowler et al., 2002 (81)	Standard lifestyle + placebo	Not noted	Not noted	Written information and an annual 20- to 30-min individual session emphasizing importance of healthy lifestyles. Advice included encouragement to follow the USDA Food Guide Pyramid and equivalent of National Cholesterol Education Program Step I diet, reduce weight, and increase physical activity.
	Standard lifestyle + metformin	Not noted	Not noted	Same as placebo, but with metformin titrated up to 875 mg twice per day.
	Intensive lifestyle	Not noted	Case managers	16-session curriculum covering diet, exercise, and behavior modification taught by case managers on a 1-to-1 basis in the first 24 wk. Flexible, culturally sensitive, and individualized. Subsequent individual (typically monthly) and group sessions with case managers to reinforce behavioral change.
Kuller et al., 2001 (66)	Assessment only	Large research clinic	Psychologists (PhD level)	Clinical assessment, with baseline health education pamphlet on reducing cardiovascular risk factors, and advice to quit smoking.
	Lifestyle intervention	Large research clinic	Psychologists (PhD level), nutritionists, exercise physiologists	Cognitive–behavioral program aimed at preventing increases in LDL cholesterol level and weight gain and increasing leisure-time activity. Intensive group program in the first 6 mo, then follow-up individual and group sessions from mo 6 to 54. Weight loss goal was 5 to 15 lb, depending on baseline weight. Participants were asked to lower dietary fat intake and daily caloric intake. Lifestyle approach to increasing physical activity to expenditure of 1000 to 1500 kcal/wk.
Tuomilehto et al., 2001 (67)	Control	Not noted	Not noted	General oral and written information about diet and exercise at baseline and at subsequent annual visits. 3-d food diary at baseline and at each annual visit.
	Intervention	Not noted	Nutritionist	Detailed advice about how to achieve weight loss, diet, and exercise goals. Participants met with nutritionist 7 times over first year, then every 3 mo. Dietary advice was tailored to each participant on the basis of quarterly food diaries and included behavioral modification tips. Participants received individual guidance on increasing physical activity level. Endurance exercise (walking, jogging, swimming, aerobic ball games, or skiing) was recommended as a way of increasing aerobic capacity. Supervised, progressive, individualized circuit-type resistance training also offered for improving functional capacity and strength.

Appendix Table 3—**Continued**

Study, Year (Reference)	Intervention	Intervention Setting	Intervention Delivery	Counseling and Behavioral Description
Fogelholm et al., 2000 (76)	Control (40-wk follow-up after 12-wk weight reduction program)	Not noted	Nutritionist (weight loss phase)	12-wk weight reduction program (wk 1: low-energy diet based on meal exchange; wk 2 to 9: VLCD; weeks 10 to 12: low-energy diets), with weekly small groups (5 to 12 participants) receiving instruction on diet, weight maintenance, relapse prevention. No increase in habitual exercise in the 40-wk follow-up.
	Walking program (4.2 MJ/wk target expenditure) following 12-wk weight reduction program	Not noted	Nutritionist (weight loss phase); exercise instructor (maintenance phase)	12-wk weight reduction program as above. In maintenance program, each participant had a weekly walking time prescribed and walked with a heart rate monitor. One weekly walking session was supervised. All persons participated in weekly meetings in small groups throughout the maintenance program, conducted by an exercise instructor. Educational material was distributed monthly. Weekly homework included monitoring of high-risk situations for overeating. Problems in diet and prevention of relapse were discussed in the meetings.
	Walking program (8.4 MJ/wk target expenditure) following 12-wk weight reduction program	Not noted	Nutritionist (weight loss phase), exercise instructor (maintenance phase)	12-wk weight reduction program, then 40-wk walking weight maintenance program as described in the 4.2-MJ program above; only difference was increased targeted energy expenditure.
Jakicic et al., 1999 (72)	Short-bout exercise	Not noted	Nutritionists, exercise physiologists, and behavioral therapists	Behavioral weight loss program: group treatment meetings of diminishing frequency (weekly in mo 1 to 6, biweekly in mo 7 to 12, monthly in wk 13 to 18). Meetings focused on behavioral strategies for modifying eating and exercise behaviors. Participants were instructed to reduce daily energy and fat intake. Caloric goal based on baseline weight, with goal of 0.45 to 0.9 kg loss per wk. Fat intake goal was 20% of total intake. Food diaries reviewed weekly, with feedback from interventionists. Exercise: Same volume of exercise, all home based, in all 3 groups. Participants instructed to exercise 5 d/wk, initially 20 min/d (wk 1 to 4), increasing to 40 min/d by wk 9. Exercise was divided into multiple 10-min bouts performed at convenient times in the day.
	Long-bout exercise	Not noted	Nutritionists, exercise physiologists, and behavioral therapists	Behavioral weight loss program as in the short-bout exercise group. Exercise: daily total exercise amounts as described in the short-bout exercise group. Exercise was to be performed in 1 long bout.
	Short-bout exercise with equipment	Not noted	Nutritionists, exercise physiologists, and behavioral therapists	Behavioral weight loss program as in the short-bout exercise group. Exercise: daily total exercise amounts as described in the short-bout exercise group. Participants were provided with motorized treadmills in their homes.
Jones et al., 1999 (69)	Control	Not noted	Study nurse	Participants were told that they should lose weight, but received no formal diet counseling or group support.
	Weight loss	Not noted	Registered dietitian	Patients were individually counseled within 10 d of randomization and 2 to 4 wk later. Content focused on food selection and preparation, and weight reduction goals were established. No exercise advice was given. Participants met in groups twice monthly for 3 mo, then every 3 to 6 mo.

Appendix Table 3—**Continued**

Study, Year (Reference)	Intervention	Intervention Setting	Intervention Delivery	Counseling and Behavioral Description
Sbrocco et al., 1999 (74)	Behavioral choice treatment	Not noted	Clinical psychologist or clinical social worker (also a psychology graduate student) with extensive experience in the behavior treatment of obesity. Two inexperienced graduate students (psychology) were co-leaders.	13 weekly 1.5-h group sessions with 5 to 7 members per group. Participants received 2-wk meal plans and recipe booklets for a low-fat (25%) diet, 1800 kcal/d. Diaries were reviewed, with immediate feedback each session, including graphs of daily fat and calorie intake and a list of highest-fat foods and some alternatives. Participants were encouraged to eat at a constant calorie level. Self-monitoring was phased out before acute treatment ended. Participants were encouraged to complete a walking program 30 min/d, 3 d/wk in a single bout. No formal exercise groups, but daily exercise logs. Stated purpose: to stop dieting and to view eating as a choice; to expect slower weight loss than they had experienced in the past, but more permanent change. Health behavior including food choice, avoiding exercise, eating behaviors discussed as choices designed to achieve certain outcomes. Individuals taught to identify their choices and the outcomes controlling these choices and to focus on learning to eat in a manner consistent with a reasonable eventual end-goal weight, rather than focusing on how quickly weight can be lost.
	Traditional behavioral treatment	Not noted	Clinical psychologist or clinical social worker (also a psychology graduate student) with extensive experience in the behavior treatment of obesity. Two inexperienced graduate students (psychology) were co-leaders.	Weekly group sessions, meal plans, recipes, food diaries and exercise as above, but with 1200-kcal/d diet. Stated purpose: to promote substantial weight loss and to help develop habits and strategies to maintain this loss. Standard behavioral weight management techniques (e.g., self-monitoring, stimulus control, and behavioral substitution) were taught. Participants were encouraged to avoid eating and purchasing high-calorie foods and to lose weight so they could then maintain these changes; they were taught to understand their reasons for eating and to engage in problem solving to determine other methods to respond to stress.
Ashley et al., 2001 (82)	Dietitian-led lifestyle intervention	Not noted	Registered dietitian	26 one-hour sessions over 1 y. Participants received instruction manuals that included lessons based on an established weight control program (LEARN). Diet included LCD (1200-kcal/d, with $\leq$ 30% of calories from fat), using standard recommendations for food groups and portion sizes. Activity instruction included walking up to 10 000 steps/d, measured by a supplied pedometer. Self-monitoring of food intake and energy expenditure in diaries. Specific to this group, participants attended small (8 to 10 people) classes led by a registered dietitian. Classes were weekly for 3 mo, then biweekly for 3 mo, then monthly for 4 mo. Diet was made up of conventional food items.
	Dietitian-led lifestyle intervention with meal replacements	Not noted	Registered dietitian	As in the traditional group above, instruction manuals for dieting, 1200-kcal diet, and exercise instructions with pedometer use and self-monitoring. Sessions with registered dietitian as above. However, 2 of the 3 main meals were replaced with meal-replacement shakes or bars (reduced to 1 main meal if goal reached and maintained).
	Primary care office intervention with meal replacements	Physician office	Primary care physician (two thirds of visits) or registered nurse (one third of visits)	26 biweekly 10- to 15-min individual sessions over 1 y, with a focus of helping patients lose weight (although other related medical problems were also discussed). Diet prescription with meal replacements as in the "dietitian-led with meal replacement" plan above. During each visit, diet, behavior modification and physical activity habits were reviewed, and questions were answered about the diet instructions.

Appendix Table 3—**Continued**

Study, Year (Reference)	Intervention	Intervention Setting	Intervention Delivery	Counseling and Behavioral Description
Wadden et al., 2001 (65)	Sibutramine alone	Not noted	Physician	Baseline meeting with a physician who described medication use and the importance of lifestyle modification. A balanced diet (1200 to 1500 kcal/d) was prescribed. Gradually increased exercise (typically walking) to 4 to 5 sessions/wk, each of 30 to 40 min duration. Literature supporting these instructions was disseminated. Over the trial, patients had 10 brief (5- to 10-min) follow-up visits with the physician (wk 2, 4, 8, 12, 16, 20, 24, 32, 40, 52). No lifestyle counseling or instruction for self-monitoring of lifestyle change was provided.
	Sibutramine + lifestyle	Not noted	Physician (outcomes monitoring), doctoral-level psychologists (counseling)	Physician visits on same schedule as sibutramine-alone group. In addition, in the first 20 wk, they attended weekly psychologist-led group lifestyle modification sessions. They were prescribed the same diet and exercise goals as the drug-only group but were given behavioral strategies for achieving them and were asked to self-monitor food intake and physical activity for at least 16 wk. Behavioral topics discussed at weekly sessions included stimulus control, slowed rate of eating, social support, and cognitive restructuring. During wk 24 to 52, sessions focused on skills for maintenance of weight loss.
	Sibutramine + lifestyle + diet	Not noted	Physician (outcomes monitoring), doctoral-level psychologists (counseling)	Identical intervention to the sibutramine plus lifestyle group, with the addition of the first 16 wk prescription of a 1000 kcal/d portion-controlled diet (4 servings/d of a liquid nutritional supplement with an evening balanced meal). After wk 16, gradually decreased consumption of liquid supplement, with 1200- to 1500-kcal diet of conventional food diet by wk 20 (similar to the patients in the other 2 groups).
Wing and Anglin, 1996 (78)	Behavior therapy with LCD	Not noted	Multidisciplinary team (all white)	1 y of weekly sessions, including review of self-monitoring records; weighing; and a lecture/discussion on nutrition, behavioral techniques, or exercise. Topics included stimulus control, goal setting, and self-monitoring of diet and exercise. Participants were encouraged to gradually increase activity until walking 2 miles/d, 5 d/wk. Participants followed a LCD (1000–1200 kcal/d), with $<$ 30% calories from fat.
	Behavior therapy with intermittent VLCD	Not noted	Multidisciplinary team (all white)	Counseling and behavioral therapy as above for diet and exercise. Intermittent VLCD in wk 1 to 12 and wk 24 to 36. During VLCD intervals, goal consumption of approximately 500 kcal/d, either as liquid formula or lean meat, fish, or fowl. After each VLCD, other foods were gradually reintroduced until consumption of 1000 to 1200 kcal/d was reached.

* Information was primarily obtained from the published sources listed. In selected cases (Tuomilehto et al. [67] and Kuller et al. [66]), additional information was obtained from study staff. LCD = low-calorie diet; LDL = low-density lipoprotein; USDA = U.S. Department of Agriculture; VLCD = very-low-calorie diet.

Appendix Table 4 Top. **Randomized, Controlled Trials of Pharmacotherapy Interventions***

Study, Year (Reference)	Drug Dose	Co-Interventions	Sample Size	Race	Women	Age†	Baseline BMI‡
			n	%		*y*	
Sibutramine							
Wirth and Krause, 2001 (88)	15 mg/d, continuous or intermittent	All participants: no formal diet, exercise, or behavioral program Written dietary information	1102	White: 99.8	77	Sibutramine Continuous: 43 Intermittent: 43 Placebo: 44	Sibutramine Continuous: 34.7 kg/m^2 Intermittent: 34.9 kg/m^2 Placebo: 35.0 kg/m^2
Dujovne et al., 2001 (85)	20 mg/d	D All participants: Step I American Heart Association Diet (1500 kcal/d for women, 1800 kcal/d for men)	322	White: 82 Black: 12 Indian or Pakistani: 1 Mexican American: 2 Other: 3	Drug: 56 Placebo: 51	Drug: 45 Placebo: 46	Sibutramine: 35.1 kg/m^2 Placebo: 35.5 kg/m^2
Fujioka et al., 2000 (86)	Titrated up to 20 mg/d	D All participants: 250 to 500 kcal/d caloric deficit diet with individual dietary counseling	175	White: 73 Black: 17 Other: 10	47	Sibutramine: 53.5 Placebo: 55.0	Sibutramine: 34.1 kg/m^2 Placebo: 33.8 kg/m^2
Gokcel et al., 2001 (32)	10 mg bid	D All participants: 25 kcal/kg ideal body weight diet, with counseling at baseline	60	NR	100	Sibutramine: 47 Placebo: 49	Sibutramine: 39.3 kg/m^2 Placebo: 37.4 kg/m^2
Smith and Goulder, 2001 (87)	10 mg/d or 15 mg/d	D All participants: Dietary advice	485	White: 99 Other: 1	80	Sibutramine 10 mg: 41 15 mg: 43 Placebo: 42	Sibutramine 10 mg: 32.9 kg/m^2 15 mg: 32.7 kg/m^2 Placebo: 32.4 kg/m^2

Appendix Table 4 Top—**Continued**

Length, Goal	Groups	Weight Change	Between-Group Difference§	*P* Value	Patients Lost to Follow-up and Adverse Events	Trial Quality
44 wk, L	Sibutramine (continuous) Sibutramine (intermittent) Placebo	−3.8 kg −3.3 kg −0.2 kg	−3.6 kg −3.1 kg	<0.001	Sibutramine (continuous) Dropout: 79/405 Due to adverse event: 25/405 Adverse event rate: 303/405	Good
		5% loss			Sibutramine (intermittent)	
	Sibutramine (continuous) Sibutramine (intermittent) Placebo	65% 63% 35%	30% 28%	<0.001	Dropout: 80/395 Due to adverse event: 13/395 Adverse event rate: 283/395	
		10% loss			Placebo	
	Sibutramine (continuous) Sibutramine (intermittent) Placebo	32% 33% 13%	19% 20%	<0.001	Dropout: 55/201 Due to adverse event: 9/201 Adverse event rate: 151/201	
24 wk, L	Sibutramine Placebo	−4.9 kg −0.6 kg	−4.3 kg	≤0.05	Sibutramine Dropout: 29.6% Due to adverse event: 9.9% Due to hypertension: 0.6%	Fair
		5% loss			Placebo	
	Sibutramine Placebo	42% 8%	34%	<0.05	Dropout: 33.8% Due to adverse event: 6.9% Due to hypertension: 1.9%	
		10% loss				
	Sibutramine Placebo	12% 3%	9%	<0.05		
24 wk, L	Sibutramine Placebo	−3.7 kg −0.4 kg	−3.3 kg	≤0.5	Sibutramine Dropout: 29/89 Due to adverse event: 9/89	Fair
		5% loss			Placebo	
	Sibutramine Placebo	27% 1%	26%	<0.001	Dropout: 25/86 Due to adverse event: 10/86	
		10% loss				
	Sibutramine Placebo	6% 1%	5%	0.12		
24 wk, L	Sibutramine Placebo	−3.9 kg 0.36 kg	−4.3 kg	<0.0001	Sibutramine Dropout: 1/30 Due to adverse event: 1/30 Placebo Dropout: 5/30 Due to adverse event: NR	Fair
52 wk, L	Sibutramine: 10 mg Sibutramine: 15 mg Placebo	−4.4 kg −6.4 kg −1.6 kg	−2.8 kg −4.8 kg	<0.01	Sibutramine, 10 mg Dropout: 67/161 Due to adverse event: 2/161 Adverse event rate: 20/161	Fair
		5% loss			Sibutramine: 15 mg	
	Sibutramine: 10 mg Sibutramine: 15 mg Placebo	39% 57% 20%	19% 37%	<0.01	Dropout: 79/161 Due to adverse event: 2/161 Adverse event rate: 18/161	
		10% loss			Placebo	
	Sibutramine: 10 mg Sibutramine: 15 mg Placebo	19% 34% 7%	12% 27%	<0.01	Dropout: 83/163 Due to adverse event: 4/163 Adverse event rate: 24/163	

Appendix Table 4 Middle

Study, Year (Reference)	Drug Dose	Co-Interventions	Sample Size	Race	Women	Age†	Baseline BMI‡
			n	%		*y*	
McNulty et al., 2003 (33)	15–20 mg/d	D Standard dietary advice by a dietitian or nurse	195	NR	56	Sibutramine 15 mg: 49 20 mg: 48 Placebo: 51	Sibutramine 15 mg: 36.3 kg/m^2 20 mg: 37.5 kg/m^2 Placebo: 36.2 kg/m^2
James et al., 2000 (84)	10–20 mg/d	D, E, B All participants: High-intensity, individualized 600-kcal deficit diet	467	"Almost all" white Afro-Caribbean: 2 Asian: 1.5	84	Sibutramine: 41 Placebo: 40	Sibutramine: 36.5 kg/m^2 Placebo: 36.6 kg/m^2
Orlistat							
Muls et al., 2001 (91)	120 mg	D All participants: Moderate-intensity dietary advice from a dietitian (−600 kcal/d)	294	NR	Orlistat: 82 Placebo: 78	Orlistat: 50 Placebo: 48	33 kg/m^{2}s
Van Gaal et al., 1998 (89)	30, 60, 120, or 240 mg tid	D All participants: High-intensity dietary advice from a dietitian	613	NR	77	Range, 40–44 (varied by group)	34–35 kg/m^2 (varied by group)

Appendix Table 4 Middle—**Continued**

Length, Goal	Groups	Weight Change	Between-Group Difference§	*P* Value	Patients Lost to Follow-up and Adverse Events	Trial Quality
12 mo, L	Sibutramine: 15 mg Sibutramine: 20 mg Placebo	−5.5 kg −8.0 kg −0.2 kg	−5.3 kg −7.8 kg	<0.001 <0.001	Sibutramine, 15 mg Dropout: 19/68 Due to adverse event: NR	Fair
		5% loss			Sibutramine, 20 mg	
	Sibutramine: 15 mg Sibutramine: 20 mg Placebo	46% 65% 12%	34% 53%	Sibutramine "significantly more"	Dropout: 13/62 Due to adverse event: NR	
		10% loss			NR	
	Sibutramine: 15 mg Sibutramine: 20 mg Placebo	14% 27% 0%	14% 27%	NR	Placebo Dropout: 18/64 Due to adverse event: NR	
					NR	
80 wk, M (following 6-mo L phase)	Sibutramine Placebo	−8.9 kg −4.9 kg	−4 kg	<0.001	Sibutramine Dropout: 148/352 Due to adverse event: 48/352	Fair
		Maintaining >80% of original loss				
	Sibutramine Placebo	41% 14%	27%	<0.001	Placebo Dropout: 58/115 Due to adverse event: 6/115	
24 wk, L	Orlistat Placebo	−4.66 kg −1.88 kg	−2.78 kg	<0.001	Orlistat Dropout: 19/147 (13%) Adverse event rate: 80%‖	Good
		Mean change				
	Orlistat Placebo	−5.3% −2.3%	−3%	≤0.001	GI adverse event rate: 64% Placebo Dropout: 16/147 (11%)	
		5% loss				
	Orlistat Placebo	64% 39%	25%	NR	Adverse event rate: 67% GI adverse event rate: 38%	
		10% loss				
	Orlistat Placebo	23% 13%	10%	NR		
52 wk, L	Orlistat, 30 mg Orlistat, 60 mg Orlistat, 120 mg Orlistat, 240 mg Placebo	−8.5% −8.8% −9.8% −9.3% −6.5%	−2% −2.3% −3.3% −2.8%	<0.001	Orlistat, 30 mg Dropout: 29/122 Due to adverse event: 7/122 Adverse event rate: 79% Orlistat, 60 mg	
		10% loss				
	Orlistat, 30 mg Orlistat, 60 mg Orlistat, 120 mg Orlistat, 240 mg Placebo	28% 28% 37% 38% 19%	9% 9% 18% 19%	NR	Dropout: 29/124 Due to adverse event: 6/124 Adverse event rate: 83% Orlistat, 120 mg Dropout: 23/122 Due to adverse event: 2/122 Adverse event rate: 84% Orlistat, 240 mg Dropout: 20/120 Due to adverse event: 3/120 Adverse event rate: 87% Placebo Dropout: 27/125 Due to adverse event: 3/125 Adverse event rate: 69%	

Appendix Table 4 Middle a

Study, Year (Reference)	Drug Dose	Co-Interventions	Sample Size	Race	Women	Age†	Baseline BMI‡
			n	%		*y*	
Micic et al., 1999 (94)	120 mg tid	D All participants: Mildly hypocaloric diet with dietary advice	119	NR	Orlistat: 70 Placebo: 78	Orlistat: median, 46 Placebo: median, 45	Orlistat: 34.8 kg/m^2 Placebo: 35.2 kg/m^2
Rissanen et al., 2001 (95)	120 mg tid	D All participants: 600-kcal deficit diet	51	NR	100	44	36.2 kg/m^2
Broom et al., 2002 (96)	120 mg tid	D All participants: Mildly hypocaloric diet (minimum of 1200 kcal/d), with food and beverage diaries	531	NR	78	Orlistat: 46.7 Placebo: 45.3	Orlistat: 37.1 kg/m^2 Placebo: 37.0 kg/m^2
Miles et al., 2002 (90)	120 mg tid	D, E All participants: Recommended to increase physical activity and follow a diet (−600 kcal/day) with dietary counseling throughout the study	516	Orlistat White: 84 Black: 10 Other: 6 Placebo White: 79 Black: 14 Other: 7	48	Orlistat: 52.5 Placebo: 53.7	Orlistat: 35.2 kg/m^2 Placebo: 35.6 kg/m^2
Karhunen et al., 2000 (93)	120 mg tid	D All participants: Dietary advice (−600 kcal/d) individualized advice throughout the 1-y loss phase	96	NR	82	43	35.9 kg/m^2
Hill et al., 1999 (92)	30, 60, or 120 mg 3 times daily	D, E, B All participants: 4180-kJ/d deficit diet Multivitamin	729	White: 88 Black: 6 Hispanic: 5 Other: 1	84	Orlistat 30 mg: 47 60 mg: 46 120 mg: 46 Placebo: 46	Orlistat 30 mg: 32.6 kg/m^2 60 mg: 32.9 kg/m^2 120 mg: 32.8 kg/m^2 Placebo: 32.8 kg/m^2

Appendix Table 4 Middle a—**Continued**

Length, Goal	Groups	Weight Change	Between-Group Difference§	*P* Value	Patients Lost to Follow-up and Adverse Events	Trial Quality
24 wk, L	Orlistat Placebo	−10.8 kg −7.3 kg	−3.5 kg	0.001	Orlistat Dropout: 10/60 Due to adverse event: 1/60 Adverse event rate: 18/60 Placebo Dropout: 10/59 Due to adverse event: NR Adverse event rate: 7/59	Fair
12 mo, L	Orlistat Placebo	−13 kg −7.2 kg	−5.8 kg	NS	Dropout: 4/55	Fair
54 wk, L	Orlistat Placebo Orlistat Placebo Orlistat Placebo	−5.8 kg −2.3 kg >5% loss 55.6% 24.3% >10% loss 19.7% 11.0%	−3.5 kg 31.3% 8.7%	<0.001 <0.001 NS	Orlistat Dropout: 79/265 Due to adverse event: 20/265 Due to GI symptoms: 13/265 Serious adverse events: 13/265 Placebo Dropout: 105/266 Due to adverse event: 11/266 Due to GI symptoms: 6/266 Serious adverse events: 17/266	Fair
52 wk, L	Orlistat Placebo Orlistat Placebo Orlistat Placebo	−4.7 kg −1.8 kg >5% loss 39.0% 15.7% >10% loss 14.1% 3.9%	−2.9 kg 23.3% 10.2%	<0.001 0.008 0.003	Orlistat Dropout: 35% Due to adverse event: 10% Due to GI symptoms: NR GI event frequency: 83% Placebo Dropout: 44% Due to adverse event: 5% Due to GI symptoms: NR GI event frequency: 62%	Fair
2 y: 1 y of L, 1 y of M	Loss phase Orlistat Placebo Maintenance phase (Tx Year 1/Tx Year 2) Orlistat/orlistat Orlistat/placebo Placebo/orlistat Placebo/placebo	Year 1 −13.1 kg −8.6 kg Year 2 only 3.1 kg 6.3 kg 0.5 kg 3.5 kg	 −4.5 kg 	 0.007 	No data on adverse effects Dropout: 24/96 (25%) Due to adverse event: NR	Fair
52 wk, M (following 6 mo of L)	Orlistat, 30 mg Orlistat, 60 mg Orlistat, 120 mg Placebo	4.9 kg 3.8 kg 2.6 kg 4.4 kg	0.5 kg −0.6 kg −1.8 kg	<0.001	Orlistat, 30 mg Dropout: 47/187 Due to adverse event: 17/187 Orlistat, 60 mg Dropout: 40/173 Due to adverse event: 17/173 Orlistat, 120 mg Dropout: 55/181 Due to adverse event: 27/181 Placebo Dropout: 50/188 Due to adverse event: 5/188	Fair

Appendix Table 4 Bottom

Study, Year (Reference)	Drug Dose	Co-Interventions	Sample Size	Race	Women	Age†	Baseline BMI‡
			n	%		*y*	
Metformin							
Giugliano et al., 1993 (97)	850 mg bid	Counseling to maintain baseline diet and exercise patterns	50	NR	62	Metformin: 60 Placebo: 60.8	Metformin: 33 kg/m^2 Placebo: 32.7 kg/m^2
Knowler et al., (81)	850 mg bid (titrated up)	D, E Metformin and placebo participants: Written information plus annual 20- to 30-min individual session emphasizing low-fat diet and physical activity.	3234	White: 55 Black: 20 Hispanic: 16 Native American: 5 Asian: 4	68	Mean: 51	34 kg/m^2
Multiple drugs							
Gokcel et al., 2002 (98)	Sibutramine: 10 mg bid Orlistat: 120 mg tid Metformin: 850 mg bid	D 25-kcal per kg of ideal body weight with caloric distribution: 50% carbohydrates, 30% lipids, 20% protein	150	NR	100	Sibutramine: 42.3 Orlistat: 42.1 Metformin: 43.6	Sibutramine: 38.5 kg/m^2 Orlistat: 35.3 kg/m^2 Metformin: 37.9 kg/m^2

* B = behavioral therapy; bid = twice daily; BMI = body mass index; D = diet; E = exercise; GI = gastrointestinal; L = weight loss; M = maintenance of weight loss; NR = not reported; tid = three times daily.
† Values are means unless otherwise indicated.
‡ Presented as baseline mean or range unless otherwise noted.
§ Compared with control unless otherwise noted.
‖ $P = 0.02$ vs. placebo.

Appendix Table 4 Bottom—**Continued**

Length, Goal	Groups	Weight Change	Between-Group Difference§	*P* Value	Patients Lost to Follow-up and Adverse Events	Trial Quality
6 mo, L	Metformin Placebo	Data in graph form	Data in graph form	NS	NR	Fair
2.8 y, L + M	Metformin Lifestyle Placebo	−2.1 kg −5.6 kg −0.1 kg	−2.0 kg −5.5 kg	≤0.001	7.5%	Good
6 mo, L	Sibutramine Orlistat Metformin	−13.4 kg −8.0 kg −9.0 kg	−4.4 kg 1.0 kg (vs. metformin)	BMI loss significantly greater with sibutramine than either other group	Sibutramine Dropout: NR Due to adverse event: 2/50 Orlistat Dropout: NR Due to adverse event: 2/50 Metformin Dropout: NR Due to adverse event: NR	Fair

Appendix Table 5. **Randomized, Controlled Trials of Surgical Interventions**

Study, Year (Reference)	Goal	Sample Size	Race	Women	Co-Intervention	Mean Baseline BMI† (mean kg/m^2)	Duration
		n	%				
de Wit et al., 2002 (100)	L	50	NR	68	NR	51.3 (laparoscopic) 49.7 (open)	1 y
Weiner et al., 2001 (102)	L	101	NR	85	"Interdisciplinary obesity surgery program"	49.5 (esophagogastric) 48.5 (retrogastric)	18 mo
Weiss et al., 2002 (101)	L	52	NR	90	NR	42.5 (gastric) 41.8 (esophagogastric)	23–24 mo

* ASGB = adjustable silicone gastric banding; L = weight loss; NR = not recorded.

Appendix Table 5—**Continued**

Groups	Weight Change	Between-Group Difference	*P* Value	Patients Lost to Follow-up	Adverse Effects	Trial Quality
ASBG				2%	Surgical complications Laparoscopic: 0% Open: 16.7% (incisional hernias, migrating band) Access port complications Laparoscopic: 20% Open: 21% Mean hospital stay Laparoscopic: 7.8 d Open: 11.8 d Patients with readmission Laparoscopic: 20% Open: 29%	Fair
Laparoscopic Open	−35.0 kg −34.4 kg	−1.4 kg	NS			
Placement of laparoscopic ASGB: Esophagogastric Retrogastric	Data in graph form. > 40-kg loss in both groups	NR	NS	4%	Band slippage Esophagogastric: 0% Retrogastric: 2% Pouch dilation Esophagogastric: 0% Retrograde: 6% Esophageal dilation Esophagogastric: 4% Retrograde: 4% Hunger at 18 mo Esophagogastric: 2% Retrograde: 4% Dysphagia at 18 mo Esophagogastric: 2% Retrograde: 2% Recurrent vomiting at 18 mo Esophagogastric: 2% Retrograde: 2% Esophagitis at 18 mo Esophagogastric: 2% Retrograde: 2%	Fair
Placement of laparoscopic, ASGB	Median BMI			NR	Mortality: NR	Fair
Gastric Esophagogastric	−17.4 kg/m^2 −18.9 kg/m^2	1.5 kg/m^2	NS		Conversion to open surgery Gastric: 3.6% Esophagogastric: 3.8%	
	> 25% loss				Need for reoperation	
Gastric Esophagogastric	100% 100%	0%			Gastric: 10.7% Esophagogastric: 19.2%	
	Gain				Heartburn at 2 y	
Gastric Esophagogastric	0% 0%	0%			Gastric: 11.1% Esophagogastric: 14.3%	
					Dysphagia at 2 y Gastric: 0% Esophagogastric: 57.1%	