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Systematic Evidence Review
Number 21

Screening and Interventions for Overweight and Obesity in Adults

Prepared for*:*
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Preface

The Agency for Healthcare Research and Quality (AHRQ) sponsors the development of Systematic Evidence Reviews (SERs) through its Evidence-based Practice Program. With guidance from the U.S. Preventive Services Task Force* (USPSTF) and input from Federal partners and primary care specialty societies, the Evidence-based Practice Center at the Oregon Health Sciences University systematically review the evidence of the effectiveness of a wide range of clinical preventive services, including screening, counseling, and chemoprevention, in the primary care setting. The SERs—comprehensive reviews of the scientific evidence on the effectiveness of particular clinical preventive services—serve as the foundation for the recommendations of the USPSTF, which provide age- and risk-factor-specific recommendations for the delivery of these services in the primary care setting. Details of the process of identifying and evaluating relevant scientific evidence are described in the "Methods" section of each SER.

The SERs document the evidence regarding the benefits, limitations, and cost-effectiveness of a broad range of clinical preventive services and will help further awareness, delivery, and coverage of preventive care as an integral part of quality primary health care.

AHRQ also disseminates the SERs on the AHRQ Web site (http://www.ahrq.gov/clinic/uspstfix.htm) and disseminates summaries of the evidence (summaries of the SERs) and recommendations of the USPSTF in print and on the Web. These are available through the AHRQ Web site and through the National Guideline Clearinghouse (http://www.ncg.gov).

We welcome written comments on this SER. Comments may be sent to: Director, Center for Practice and Technology Assessment, Agency for Healthcare Research and Quality, 540 Gaither Road, Suite 3000, Rockville, MD 20850.

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*The USPSTF is an independent panel of experts in primary care and prevention first convened by the U.S. Public Health Service in 1984. The USPSTF systematically reviews the evidence on the effectiveness of providing clinical preventive services--including screening, counseling, and chemoprevention--in the primary care setting. AHRQ convened the USPSTF in November 1998 to update existing Task Force recommendations and to address new topics.

Acknowledgments

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The investigators deeply appreciate the contributions of Loraine Monroe at RTI, for superior secretarial assistance. In addition, we are indebted to Timothy S. Carey, MD, MPH, Co-Director of the RTI-UNC Evidence-based Practice Center at the University of North Carolina Cecil G. Sheps Center for Health Services Research.

We also owe our thanks to the following external peer reviewers, who provided constructive feedback and insightful suggestions for improvement of this systematic evidence review: David Arterburn, MD, University of Washington, Seattle, WA; James D. Douketis, MD, McMaster University, Hamilton, Onatario, Canada; Evelyn L. Lewis-Clark, MD Bowie, MD, representing the American Academy of Family Physicians; F. Xavier Pi-Sunyer, MD, MPH, St Luke's/Roosevelt Hospital Center, New York, NY; Walter J. Pories, MD, East Carolina School of Medicine, Greenville, NC; Bruce A. Reeder, University of Saskatchewan, Saskatoon, Canada and representing the Canadian Task Force on Preventive Health Care; and Vincenza Snow, MD, American College of Physicians-American Society of Internal Medicine, Philadelphia, PA.

Structured Abstract

Background

Obesity, a condition characterized by excess body fat, carries substantial health implications for both chronic disease and mortality. This fact and its increasing prevalence make obesity an important health problem.

Purpose

To examine the evidence of the benefits and harms of screening and earlier treatment in reducing morbidity and mortality from overweight and obesity.

Data Sources

We developed an analytic framework and 6 key questions that represent a logical chain between screening and sustained weight reduction and reduced morbidity and mortality. We searched MEDLINE from January 1, 1994 (the end date for prior USPSTF searches), to July 31, 2001, using the Medical Subject Heading obesity and overweight and combining this term with predefined strategies to identify relevant English-language studies. We also searched the Cochrane Library, contacted experts, and scanned review bibliographies. We found 4 recent, well-conducted systematic reviews and relied on their analyses of the studies they included.

Study Selection

We included: (1) large, population-based surveys of the prevalence of overweight and obesity; (2) randomized controlled trials (RCTs) with at least 1 year follow-up (6 months for pharmacological studies) reporting weight reduction or health outcomes for treatment and harms questions. The shorter follow-up period for pharmacological studies was driven by the available literature: weight loss trials were frequently only of 6 months' duration but were complemented by studies designed specifically to evaluate maintenance of that loss. When we found few or no RCTs, we examined cohort studies concerning the efficacy or harms of treatment. Two reviewers examined all abstracts and articles to determine which met inclusion criteria.

Data Extraction

Two reviewers abstracted relevant information from each article, using standardized abstraction forms. We graded the quality of all included articles according to criteria established by the U.S. Preventive Services Task Force.

Data Synthesis

No RCT of screening for obesity has been performed. Obesity is most commonly measured as body mass index (BMI, weight in kilograms [kg] divided by height in meters squared). Although other measures have been developed, BMI is the most consistently used in the literature, and so we focused on it as the preferred screening tool. The prevalence of obesity (BMI $\geq$30) has been increasing; currently; at least 27% of the adult population is obese. The prevalence of overweight (BMI 25-29.9) is about 34%. Among people with BMI of about 30 or

greater, intensive counseling and behavioral treatment for obesity is effective in reducing mean weight by about 3 kg to 5 kg after 1 year. Pharmacotherapy with sibutramine or orlistat is also effective in reducing mean weight by about 3 to 5 kg. For people with BMI of 35 or greater, surgical therapy leads to dramatic reductions in weight of 20 kg or more.

Both counseling-based and drug-based maintenance interventions were helpful in retaining weight loss. Weight reduction of 5% to 7% body weight is associated with lower incidence of diabetes, reduced blood pressure, and improved dyslipidemia. Larger weight loss has been linked with more dramatic improvements in glycemic control and lipids in limited surgical outcomes data.

We did not find evidence evaluating potential harms of counseling-based interventions. Sibutramine is sometimes associated with increased blood pressure (mean increase of 0-3.5 mm Hg); orlistat causes gastrointestinal distress in 15% to 37% of people taking the drug. Surgical procedures lead to mortality in less than 1% of patients in pooled samples, but in up to 25% patients re-operation is necessary over 5 years.

Conclusions

Screening with BMI would detect a large percentage of adults who are obese or overweight. Limited evidence suggests that counseling interventions may promote modest weight loss in the overweight (BMI 25-29.9). Effective treatments for people with BMI >30 include intensive counseling and behavioral interventions for lifestyle change, and pharmacotherapy. Surgery is effective in reducing weight for people with BMI of 35 or greater. Adverse effects include increased blood pressure and gastrointestinal distress with drugs and a small percentage of serious side effects with surgery

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1. Introduction

Background

Obesity, a condition characterized by excess body fat, carries significant health implications for both chronic disease and mortality. In the setting of escalating prevalence, the importance of obesity as a health problem in the United States is increasingly evident – as emphasized by the recent Surgeon General's "Call to Action to Prevent and Decrease Overweight and Obesity."[1]

Obesity is usually defined in terms of the body mass index (BMI, calculated by dividing kilograms of weight by meters of height squared), which is a measure of weight adjusted for height. Although numerous techniques are available for evaluating body fat, the variables for BMI are easy to measure. BMI has been shown to correlate closely with body fat content in adults and children.[2]

Adults with a BMI of 25 to 29.9 are identified as overweight and those with a BMI $\geq$ 30 as obese. These cutoffs are based on epidemiologic evidence of discernible, then substantial, increases in mortality.[3] For example, if a 5'6" women weighs 155 pounds, her BMI is 25 (overweight); if she weighs 186 pounds, her BMI is 30 (obese). BMI calculations can be tedious, so electronic BMI calculators (eg, from the National Institutes of Health [NIH], http://www.nhlbisupport.com/bmi/) or tables of BMI by height and weight (eg, from NIH, http://www.nhlbi.nih.gov/guidelines/obesity/bmi_tbl.htm) may be useful tools for clinicians and patients. Waist circumference and the waist-to-hip ratio are common adjuvant measures used to

classify the distribution of body fat in people who are overweight, as obesity-related complications are most closely correlated with abdominal fat distribution.[4-6]

The prevalence of obesity is increasing. Data from the National Center for Health Statistics show that, over the past 40 years, obesity prevalence increased from 13% to 27% of the U.S. adult population; the prevalence of the less severe overweight category increased from 31% to 34%.[7,8] Concurrently, a rise in prevalence of obesity has been noted in adolescent and pediatric populations.[9,10] Self-report data from the Behavioral Risk Factor Surveillance Survey (BRFSS) show the increase in prevalence continuing into the year 2000.[11]

Obesity prevalence is higher in women; overweight is more common in men.[7] Obesity is especially common in certain minority ethnic groups, including African Americans, some Hispanic populations, Native Americans, and Native Hawaiians.

All classes of excess body weight have substantial prevalence among U.S. adults. In the National Health and Nutrition Examination Survey III (NHANES III, 1988-1994), the prevalence of BMI 25 to 29.9 was 44% for people ages 55 years and older and 41% for people ages 25 to 54.9 years.[12,13] For these older (55 years of age and older) and younger (25-54.9 years) groups, the prevalence of BMI 30 to 34.9 was 18% and 14%, respectively. The prevalence of BMI 35 to 39.9 was 4% and 3%, respectively, and for BMI 40 or above, 1% and 2%.

Obesity is a risk factor for major causes of death, including cardiovascular disease, some cancers, and diabetes. Obesity has also been linked with many sources of morbidity, including osteoarthritis, gall bladder disease, sleep apnea, and respiratory impairment. Excess weight is a risk factor for cancers of the colon, rectum, prostate, gall bladder, biliary tract, breast, cervix, endometrium, and ovary.[2] It is associated with concerns of quality of life, including diminished mobility and social stigmatization.[14]

Most studies have found that mortality assumes a J-shaped or U-shaped relationship with BMI, with elevated risk at low BMI being attributable, at least in part, to the effect of smoking or concurrent disease. The BMI associated with the lowest risk varies among studies and populations. For example, in our review of cohort studies with at least 10 years of follow-up data,[15-26] the BMI range associated with the lowest overall mortality risk was generally within the "normal" BMI range for men, but in the normal-to-overweight range for women (Table 1).

Risk associated with specific morbidity tends to increase more linearly with BMI than the risk associated with total mortality. This trend has been demonstrated most frequently for cardiovascular disorders, so we focus on those health outcomes in this systematic evidence review (SER). In a study of a British cohort of men, the incidence of major coronary events was 9.1 per 1,000 person-years for those with a baseline BMI of 24 to 25.9.[18] By contrast, coronary heart disease incidence in Framingham heart participants was 18 per 1,000 person-years for men with a baseline BMI of 23.8 to 25.9.[27] In both these cohorts, and in a third from Sweden,[24] cardiovascular risk generally increased with increasing baseline BMI for men (Figure 1). A similar rise in cardiovascular health risk is seen with increasing baseline BMI in cohort studies of women (Figure 2).

Excess body weight has been linked to increased mortality for patients up to 74 years in age. The risk lessens with age:[28] however, the relationship between weight and health risk is unclear beyond that point.[3,29]

The association between obesity and health outcomes may vary by ethnic group. Figures 3 and 4 present data from 2 long (>10 year) cohort studies that reported data on more than 1 racial group.[22,23] These studies suggested that the association between excess body weight and mortality may be weaker for black populations than for white. One review of these and other

studies found that only tentative conclusions could be reached about mortality at elevated levels of BMI in black men, with the best evidence showing only modest increases in risk.[30] Likewise, the BMI-mortality association appears weaker in black women than in white women. These ethnic-specific studies assessed only all-cause mortality, not disease-specific mortality or morbidity. Evidence about obesity and other outcomes for black populations and about the association of obesity and health outcomes in general in other ethnic groups is insufficient to draw conclusions.

Weight cycling – cycles of weight loss followed by weight regain – potentially carries health risk, but the relationship has not been clearly established. Weight cycling has been linked with increases of mortality;[31-34] this association is not, however, found consistently,[35] and these studies do not distinguish between intentional and unintentional weight loss. The evidence is mixed about the relationship between weight cycling associated with intentional weight loss (on the one hand) and coronary artery disease risk factors (on the other). One observational study showed 7% lower high-density lipoprotein (HDL) cholesterol levels among women with coronary risk factors,[36] and another showed a 4-fold increased risk of hypertension (odds ratio [OR], 4.1; confidence interval [CI], 2.4 – 6.9) in Italian women.[37] However, in 46,224 women of the Nurses Health Study II, adjusting for BMI and weight gain, mild or severe weight cycling was not associated with increased risk of hypertension incidence.[38] Likewise, in a large cohort of men, those who weight cycled did not have smaller improvements in total cholesterol, HDL, or blood pressure compared with noncyclers.[39] The psychological impact of weight cycling is also unclear: weight fluctuation has been linked with covert hostility[40] in one study and not associated with measures of depression, stress, anxiety, and anger in another.[41]

Cost of Obesity and Overweight

Financially, obesity incurs substantial cost. Recent analyses estimate that direct costs of obesity are 5.7% of total U.S. health expenditures[42] and 2.4% of the total health care budget of Canada.[43] A U.S.-based study looking at the impact of obesity on the cost of expected lifetime medical care on 5 diseases (hypertension, hypercholesterolemia, diabetes mellitus, coronary heart disease, and stroke) found that costs increased by 20% with mild obesity, by 50% with moderate obesity, and nearly 200% with severe obesity.[44]

At least 2 types of interventions might be considered for reducing the burden of suffering from obesity: public health measures for the population at large or screening and intervention in the individual patient's clinical encounter. This systematic evidence review considers the question of efficacy and effectiveness of screening and intervention in the clinical setting.

Some might ask why the issue of screening for obesity arises at all, as the diagnosis of obesity may seem obvious. Clinicians, however, frequently do not address the issue of obesity with obese patients. In a large national study of adults with a BMI of 30 or greater, for example, only 42% reported that their health care professional advised them to lose weight.[45] Thus, by screening we refer here to the conscious measurement of BMI by the clinician, with the purpose of addressing body weight in the clinical setting.

Obesity is a difficult problem to treat. This difficulty is the main concern that led prior systematic reviews to have reservations about screening for obesity. Our SER focuses primarily on the efficacy of potential interventions that might be initiated within the clinical setting. These interventions include counseling and behavioral therapy for calorie reduction and increasing physical activity, pharmacotherapy, and surgical approaches.

Prior Recommendations about Obesity Screening

In 1996, the U.S. Preventive Services Task Force (USPSTF) recommended periodic measurement of height and weight for all patients.[2] Since then, 3 large systematic reviews have examined screening for obesity; they are evidence reports from National Institutes of Health (NIH),[3] the Canadian Task Force on Preventive Health Care,[46]and the University of York for the UK National Health Service (NHS).[47]

Although all 3 reviews promoted clinical attention to obesity, their specific recommendations varied. Since their completion, the prevalence of obesity has continued to climb precipitously, new medications have become available, and more studies have addressed the role of weight loss on health outcomes. To assist the USPSTF in updating its recommendation, the RTI-UNC Evidence-based Practice Center undertook a systematic review of the evidence concerning screening for obesity. In our analysis, we combined the findings of the prior reviews with an assessment of more recent or not previously covered studies of fair to good quality.

In our SER, we address screening for adult populations. Obesity in childhood and adolescence is a significant and compelling issue that requires an evidence review dedicated to that age group.[9,10] The USPSTF regards the issue as sufficiently important that it expects to review screening for obesity in children and adolescents separately in the future.

Organization of This Review

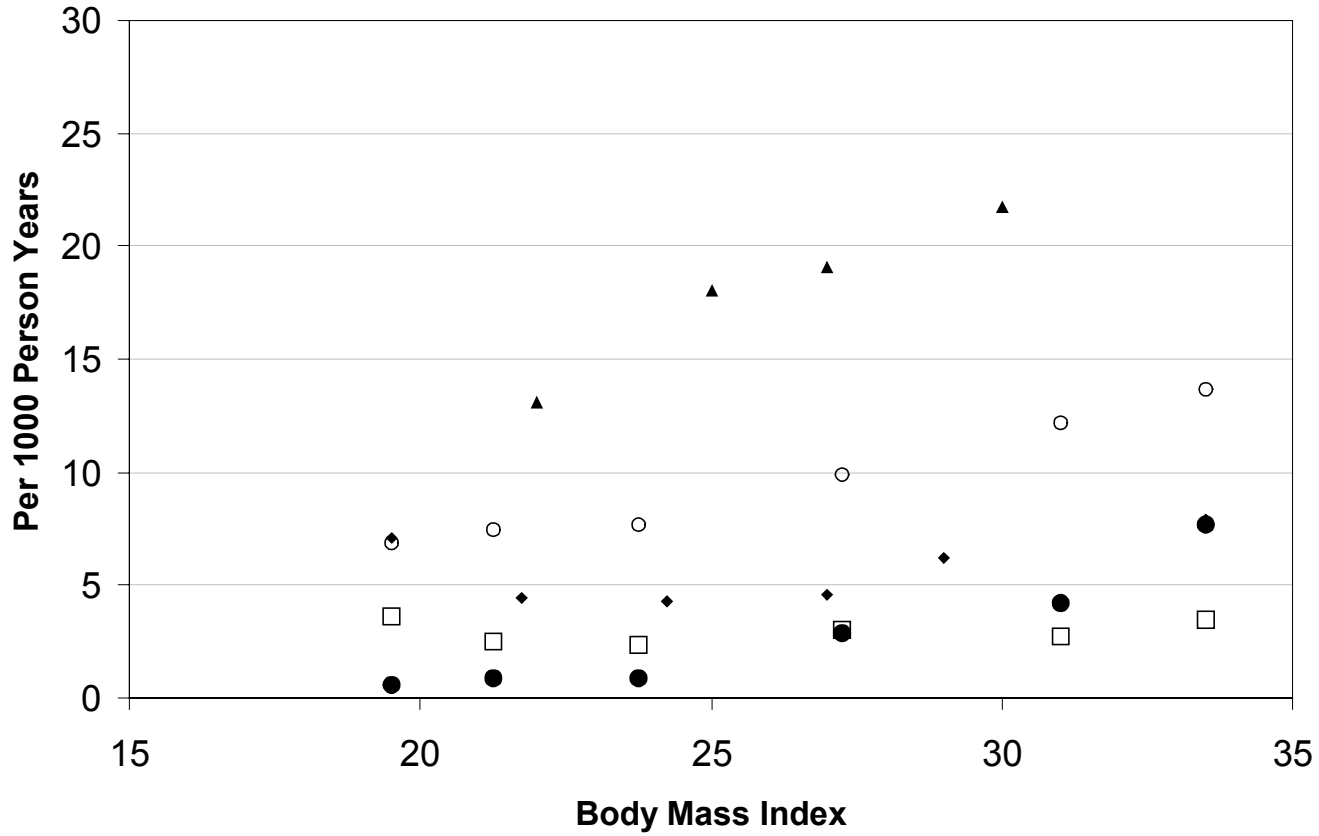
Chapter 2 of the SER documents our methods. Results appear in Chapter 3; Chapter 4 discusses the implications of our findings and offers suggestions about future research. Figures and tables are found at the end of chapters where they are first called out. Appendix A acknowledges the assistance of USPSTF liaisons to this project, the work of EPC staff, and the helpful comments from external peer reviewers. Evidence tables are presented in Appendix B.

Table 1. Ranges of Body Mass Index with Minimal Absolute Risk for Mortality in Men and Women

Men	BMI Range
Calle et al, 1999[23] Healthy nonsmoking U.S. white men	22.0-23.4
Calle et al, 1999[23] Healthy nonsmoking U.S. black men	23.5-24.9
Chyou et al, 1997[19] Japanese American men, age adjusted	24.6-26.3
Durazo-Arvizu et al, 1998[22] NHEFS* white men, age adjusted	25.6-28.7
Durazo-Arvizu et al, 1998[22] NHFES black men, age adjusted	24.0-26.1
Rosengren et al, 1999[24] Swedish men	22.5-25.0
Shaper et al, 1997[18] British men, age adjusted	22.0-23.9
Song and Sung, 2001[26] Korean men	24.0-25.0
Sorkin et al, 1994[15] Seventh Day Adventist men	24.3-25.7
Wannamethee et al, 1998[20] British men	22.0-23.9
Women	
Manson et al, 1995[16] U.S. nurses without cardiovascular disease or cancer	19-21.9
Folsom et al, 2000[25] Healthy Iowans	26.2-30.2
Laara and Rantakallio, 1996[17] Finnish women	25-28.9
Calle et al, 1999[23] Healthy nonsmoking U.S. white women	22-23.4
Calle et al, 1999[23] Healthy nonsmoking U.S. black women	25-26.4
Durazo-Arvizu et al, 1998[22] NHEFS white women, age adjusted	23.1-25.4
Durazo-Arvizu, et al, 1998[22] NHFES black women, age adjusted	26.6-28.8

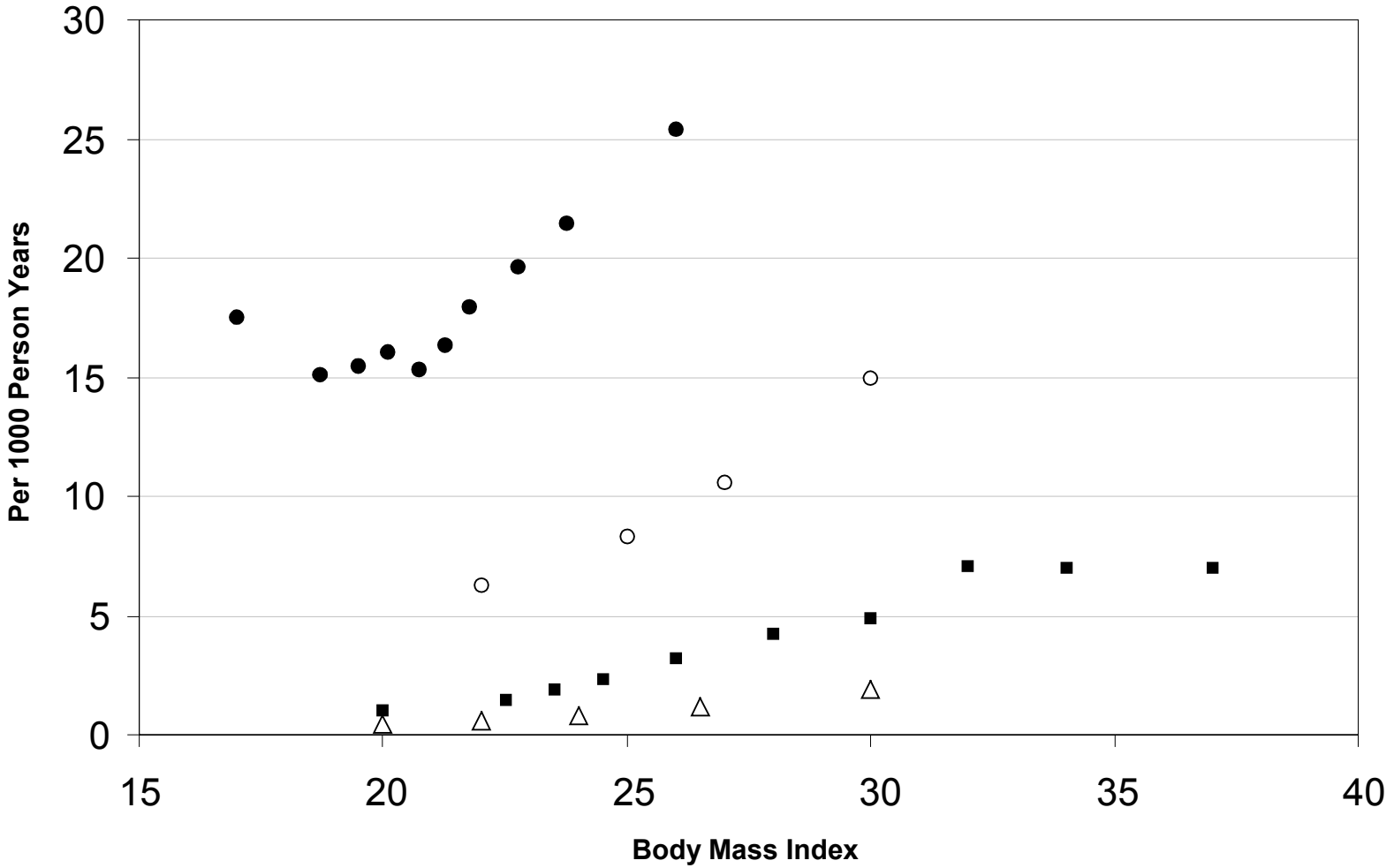
*NHEFS: National Health and Nutrition Epidemiolic Survey-I (NHANES-1) epidemiologic follow-up study.

Figure 1. Cardiovascular Morbidity in Men



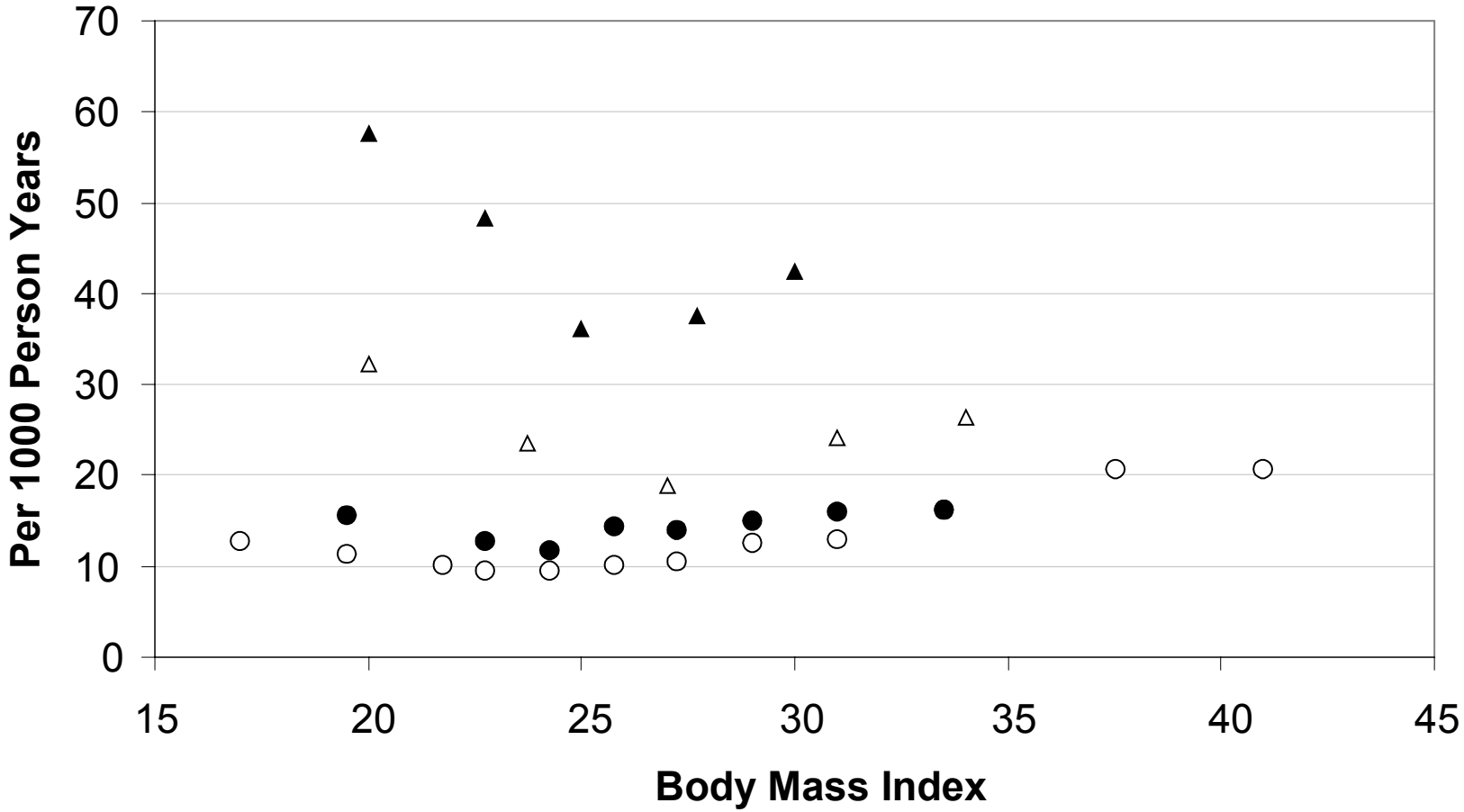
○ Shaper et al[18] – Major coronary event in British men
● Shaper et al[18] – Diabetes in British men
▲ Kim et al[27] – Coronary heart disease in Framingham heart participants
□ Shaper et al[18] – Major stroke event in British men
♦ Rosengren et al[24] – Coronary disease in Swedish men

Figure 2. Cardiovascular Morbidity in Women



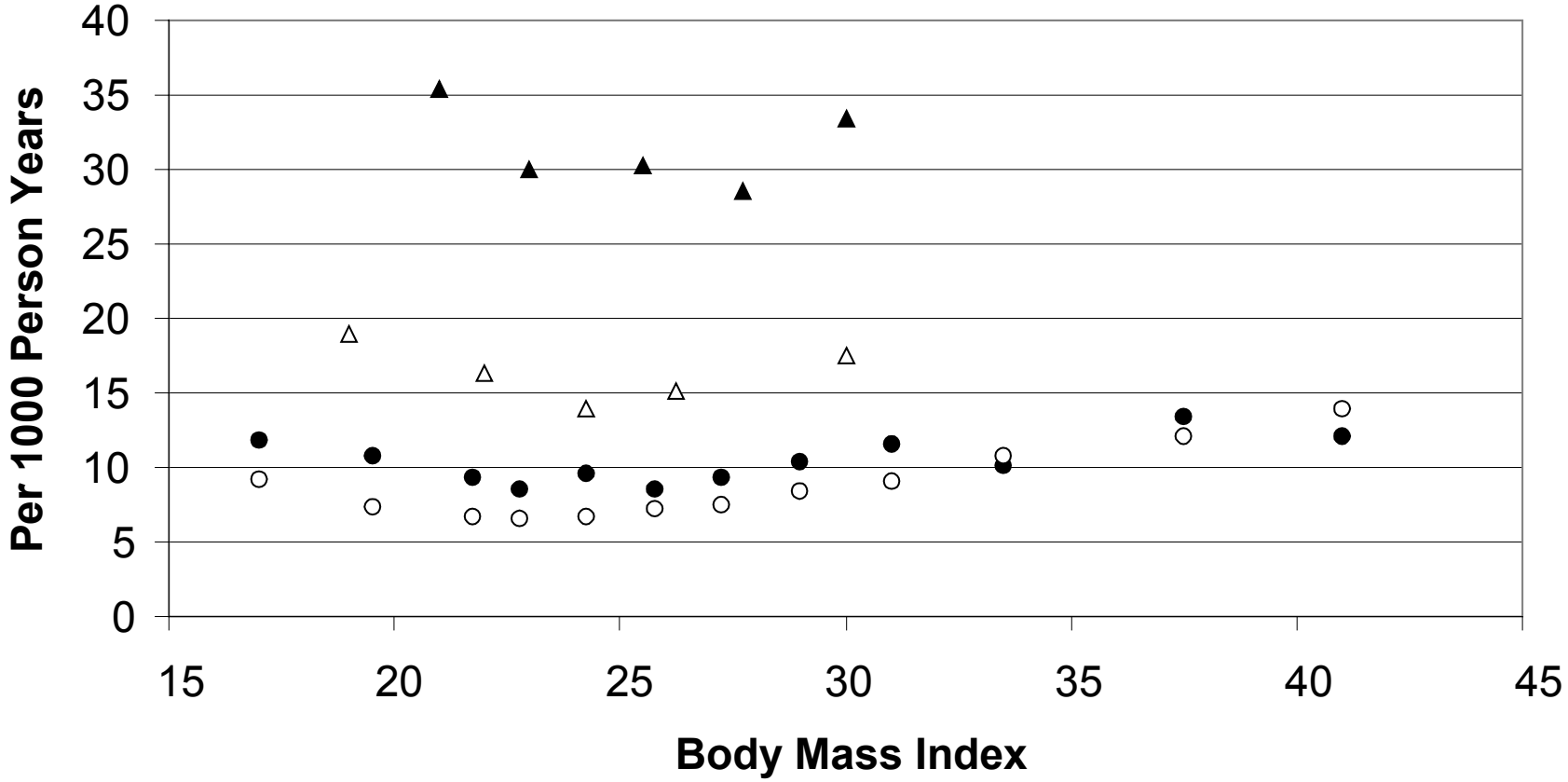
■ Colditz et al[48] – Incidence of diabetes in healthy Nurses' Health Study participants
▲ Willet et al[49] – Onset of coronary heart disease in Nurses' Health Study participants (by BMI in 1976)
○ Kim et al[27] – Incidence of coronary heart disease in Framingham heart participants
● Huang et al[21] – Hypertension in Nurses' Health Study participants

Figure 3. All-cause Mortality in Men: Studies with Race Differentials



□ Durazo-Arvizu et al[22] – White U.S. men, age adjusted
▲ Durazo-Arvizu et al[22] – Black U.S. men, age adjusted
○ Calle et al[23] – Healthy nonsmoking white U.S. men, age adjusted
● Calle et al[23] – Healthy nonsmoking black U.S. men, age adjusted

Figure 4. All-cause Mortality in Women: Studies with Race Differentials



□ Durazo-Arvizu et al[22] – White U.S. women, age adjusted
▲ Durazo-Arvizu et al[22] – Black U.S. women, age adjusted
○ Calle et al[23] – Healthy nonsmoking white U.S. women, age adjusted
● Calle et al[23] – Healthy nonsmoking black U.S. women, age adjusted

2. Methods

Analytic Framework and Key Questions

Analytic Framework

Using methods of the U.S. Preventive Services Task Force (USPSTF),[50] we developed an analytic framework (Figure 5) and 6 key questions (KQs) (Table 2) to guide the literature searches and analyses for this systematic evidence review (SER). The analytic framework begins with a population at risk (in this case, adults) and moves through screening to identification of individuals as either obese or overweight. Those so defined may receive one or more treatments that affect weight loss or maintenance of weight loss (the top intermediate outcomes) or glucose tolerance, blood pressure, or lipids (the bottom set of intermediate outcomes). The treatments include various counseling and behavioral interventions, medications, and surgery. The intermediate outcomes in turn may be related not only to each other but also to a set of health outcomes, here mortality and morbidity, mental health, physical functioning, or various other outcomes. One overarching relationship concerns a direct relationship between screening and health outcomes. In addition, the figure notes (the two ovals) our concerns with harms of both screening and treatment. Numbers in parentheses refer to our main key clinical questions.

Key Questions

As noted in Table 2, the first KQ examined direct evidence connecting screening and reduced morbidity or mortality or other outcomes (marked 1 as in Figure 1). KQs 2 through 5 dealt with indirect evidence of the various relationships depicted in the figure.

KQ 2 concerned the prevalence of overweight and obesity in the population and KQ 3 concerned the accuracy of screening tests. KQ 4 examined the efficacy of 3 treatments for overweight and obesity (counseling and behavioral interventions, medications, and surgery) for sustained weight reduction and for improved measures of glucose tolerance, blood pressure, and lipid status; KQ 5 examined the impact of these interventions (perhaps mediated through weight reduction or improvement in glucose intolerance, blood pressure, and lipid levels) on the 4 sets of health outcomes. Finally, KQ 6 concerned the harms of screening and treatment.

Literature Search Strategy and Synthesis

Search Terms

We examined the critical literature reviewed in the 1996 *Guide to Clinical Preventive Services* from the USPSTF.[2] We also searched the MEDLINE database and Cochrane Library for reviews and relevant studies published in the English language between January 1, 1994, and February 2002, using search terms consistent with the inclusion criteria. All searches were constrained to human populations and English language.

Inclusion and Exclusion Criteria

We developed inclusion and exclusion criteria for selecting the evidence relevant to answer the key questions. Table 3 documents the number of articles meeting these criteria for each key question, except KQ 3; because all relevant studies measured weight directly or by BMI, we did not conduct searches for KQ3. Articles were excluded that did not meet USPSTF criteria for at least "fair" quality.[50]

Article Review and Data Abstraction

We found 3 well-conducted, recent systematic reviews relevant to the issue of screening for obesity.[3,46,47] A fourth systematic review of good quality examined pharmacotherapy for obesity.[51] These studies are presented in Table 4, along with a comparison to our review. Inclusion criteria for prior reviews were based on USPSTF criteria for systematic review methods.[50] After checking studies from our searches against the studies in these reviews, we reviewed in detail only those studies that had not been included in at least 1 of the systematic reviews.

At least 2 authors reviewed abstracts and articles to find those that met inclusion criteria. For these included studies, a primary reviewer then abstracted relevant information using standardized abstraction forms. Key data appear in the evidence tables in Appendix B. We graded the quality of all included articles according to USPSTF criteria.[50]

Preparation of this Systematic Evidence Review

The authors worked with 3 members of the USPSTF throughout the review (see Acknowledgments in Appendix A) and, during 2001 and early 2002, presented a work plan and interim reports to the full USPSTF. After Task Force feedback and any necessary revisions, we distributed a draft of this systematic review for broad-based external peer review, including experts in the field and relevant professional organizations and federal agencies. Following peer review, we revised the evidence report and presented it to the Task Force for it to use in making final recommendations on this topic.

Table 2. Screening for Obesity: Key Questions

(Overarching): Is there direct evidence that screening for obesity improves health outcomes?
What is the prevalence of overweight and obesity?
Is there a reliable and valid screening test?
Do any of the interventions below lead to sustained weight reduction or improved glucose tolerance, lipid status, or blood pressure: Counseling and behavioral treatments? Medications? Surgery?
Do any of these interventions lead to improved health outcomes?
What are the harms of screening and treatment?

Table 3. Screening for Obesity: Inclusion Criteria and Results of Searches

	Key Question	Inclusion Criteria*	Number of Articles Meeting Inclusion Criteria and Not in Prior Systematic Review†
1.	Efficacy of screening	RCT Mass screening	0
2.	Prevalence of overweight and obesity	Large U.S. population-based surveys	1
4. - 5.	Efficacy of treatment for wt reduction or intermediate outcomes		
	a. Counseling and behavioral treatment	Counseling and behavioral interventions: - RCT (of fair or good quality) - Outcome: wt loss or BMI reduction; glucose tolerance, blood pressure, lipid disorders - Duration: ≥ 1 yr - BMI ≥ 25 - 12 mo follow-up	21
	b. Medications	Medications: - RCT (of fair or good quality) - Outcome: wt loss or BMI reduction; glucose tolerance, blood pressure, lipid disorders - Duration: ≥ 6 mos - Population: generalizable to typical U.S. primary care population	10
	c. Surgery	Surgery: - RCT (of fair or good quality) - Outcome: wt loss or BMI reduction; glucose tolerance, blood pressure, lipid disorders - Duration: ≥ 1 yr - Cohort - Initial BMI ≥ 25 - Surgical procedure	2
6.	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 one nonrandomized controlled trial	21 counseling 10 medication 2 surgery

* BMI, body mass index; RCT, randomized controlled trial.
† Prior systematic reviews[3,46,47,51]

Table 4. Summary of Findings from Prior Systematic Reviews and Our Updated Searches of Obesity Treatment Efficacy*

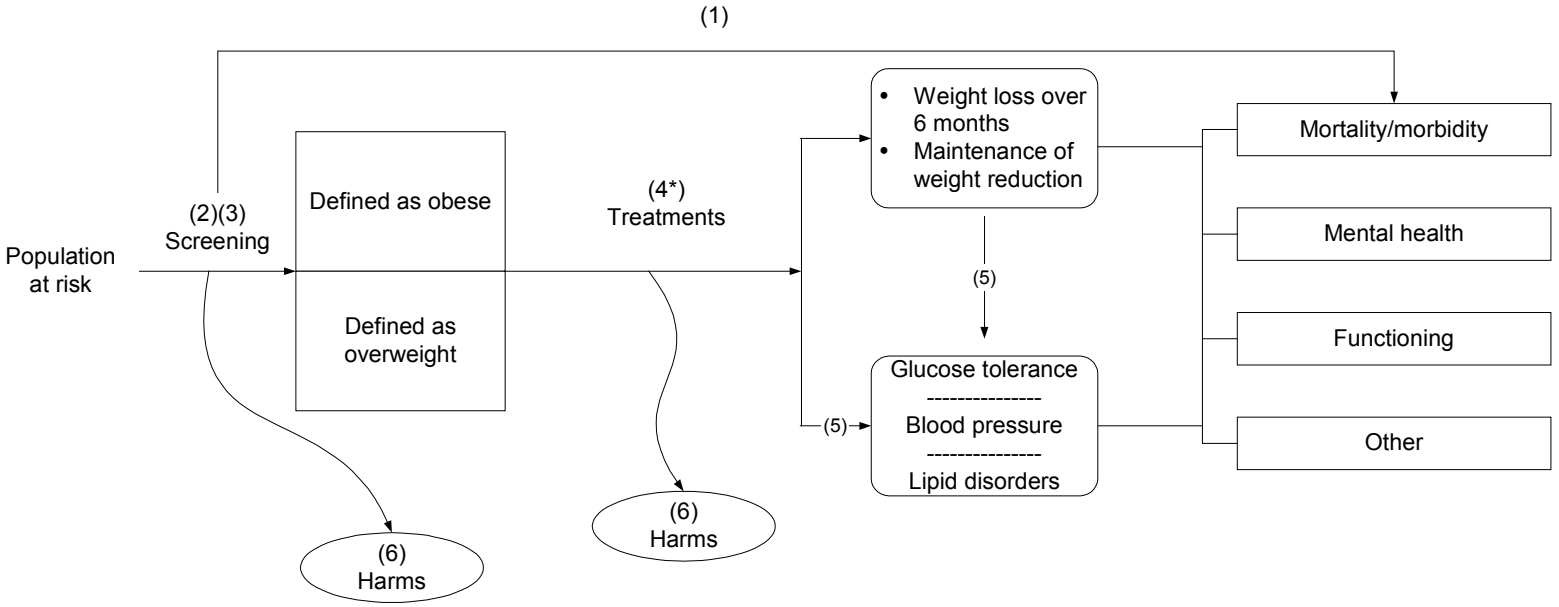
Intervention Type	Evidence Source	Months of Follow-up		RCTs	Treatments Compared to Control	Wt Change: Intervention Group (kg)		Wt Change: Intervention Control (kg)	
		Range	Median	Number	Number	Range	Mean	Range	Mean
Counseling and behavioral therapy	NIH[3]	12-60	12	29	54	8 to -21.6	-5.7	1.9 to -8.8	-3.3
	NHS[47]	12-60	12	24	51	5.4 to -12.9	-4.5	1.4 to -10.6	-3.0
	CTFPHC[46]	24-60	24	6	12	2.7 to -9.2	-3.3	-0.2 to-4.5	-2.1
	Updated searches - 1	12-54	12	12	22	9.2 to -17	-3.7	0.88 to -5.8	-2.0
	Updated searches - 2	12-54	12	13	24	9.2 to -17.9	-4.6	0.88 to -12.3	-2.6
Pharmacotherapy (orlistat or sibutramine)	BMJ *Clinical Evidence*[51]	0.5-24	NA	17†	NR	NR	NR	-2.5 to -4.4	NR
	Updated searches	6-12	6	10	11	-3.3 to -13.1	-6.5	-2.8 to -5.8	-4.0
Surgery	NIH[3]	12-48	24	5	7	-9.7to -159	-76.0	NA	
	NHS[47]	12-48	30	6	8	-9.7 to -57.9	-45.1	NA	
	CTFPHC[46]	24-60	36	4	9	-17 to -45.5	-29.9	NA	
	Updated searches	18-18	18	2	4	-34 to <-46	NA	NA	

Note: CTFPHC, Canadian Task Force on Preventive Health Care; NA, data not available to do appropriate calculation; NHS, UK National Health Service; NIH, National Institute of Health; NR, not reported; RCT, randomized controlled trials.

* Data extracted from prior reviews' evidence tables reflect those RCTs that have at least 1 year of follow-up; the longest follow-up reported is shown. Only those counseling and pharmacotherapy trials that provided data on treatment effect with and without adjustment for control are included. Surgery data reflect only current procedures. Updates searches for counseling and behavioral therapy are shown without (number 1) and with (number 2) a trial combining alternative counseling strategies with pharmacotherapy.[52]

† Data presented are for sibutramine (n = 7) and orlistat (n = 10) studies only.

Figure 5. Analytic Framework: Screening and Interventions for Overweight and Obesity in Adults



***Treatments**

4a. Counseling and Behavioral Interventions:
--Diet
--Physical activity
--Diet and physical activity

4b. Medications

4c. Surgery

3. Results

We present in this chapter the findings from our review according to each key question of the analytic framework (Table 2 and Figure 5). Tables and figures called out for the first time in this chapter can be found at the end of the chapter; evidence tables appear in Appendix B.

Key Question No. 1: Does Screening for Overweight and Obesity Affect Health Outcomes?

We found no randomized controlled trials (RCTs) evaluating the efficacy of obesity screening programs (the overarching key question). Lacking direct evidence linking screening and mortality, morbidity, mental health outcomes, or functioning, we turned to indirect evidence on the components that a screening and intervention initiative would involve. These are the internal linkages depicted in the analytic framework.

Key Question No. 2: What is the Prevalence of Overweight and Obesity?

Data from the National Center for Health Statistics show that, over the past 40 years, obesity prevalence, estimated from measured height and weight, has increased from 13% to 27% of the U.S. adult population.[7,8] The prevalence of overweight, a less severe problem, rose from 31% to 34%. Thus, an estimated 61% of the U.S. population has a problem of excess weight or body fat. Age, sex, and ethnic prevalence differentials exist, as discussed in Chapter 1.

Key Question No. 3: Is There a Reliable and Valid Screening Test?

The most commonly used screening test for obesity, and the one upon which the clinical definition is based, is the body mass index (BMI, calculated as weight in kilograms divided by height in meters squared). BMI is thus a measure of weight adjusted for height.

In 1996, the U.S. Preventive Services Task Force (USPSTF) reviewed literature showing that BMI is easy to measure, highly reliable, and closely correlated (0.7-0.8) with body fat content in adults and children.[2] BMI is correlated with percentage of body fat (R^2 = 0.68-0.74[53] and R^2 = 0.47-0.92, depending on age)[54] and with body fat mass (R^2 = 0.95, in men; R^2 = 0.98, in women).[53] Validity may vary by characteristics of the population. For example, the degree of body fat and BMI differ somewhat by ethnicity.[55-57] The elderly generally show a higher proportion of internal fat, and BMI correlates least strongly with body fat percentage in elderly adults;[54] however, estimates of body fat percentage from BMI for the elderly have shown an error comparable to that for young adults (approximately 4%).[58] The clinical relevance of BMI measurement is clear from an established prospective link between BMI and multiple adverse health outcomes.[18,21-24,27,48,49]

Some limitations of BMI do exist. For example, the correlation between body fat and BMI is age dependent and does not incorporate body fat distribution, which is an independent risk factor for health outcomes.[59,60] In addition, BMI does not take into account "fitness" (the weight of muscle vs the weight of fat in a heavily muscled individual), which is also associated with mortality independent of BMI.[61]

Other measures of adiposity (eg, waist-to-hip ratio, waist circumference) have been proposed to capture the increased cardiovascular risk seen with central adiposity. Central, or

abdominal, adiposity has been most closely linked with cardiovascular risk in several prospective studies.

In the Atherosclerosis Risk in Communities (ARIC) study, either BMI ≥30 (odds ratio [OR], 1.7; 95% confidence interval [CI], 1.4-2.0) or a waist-hip ratio >0.98 (OR,1.5; 95% CI, 1.3-1.8) was linked with increased risk of the multiple metabolic syndrome, adjusted for age, sex, ethnicity, and center.[62] Ten-year death rates from the Health Professional Follow-up Study suggest that the relationship between central adiposity and mortality may be age dependent in men. In this study, overall and cardiovascular mortality in men increased linearly with baseline BMI in younger men (initially <65 years of age) and had no relationship with BMI in older men (initially at least age 65); by contrast, waist circumference predicted risk of overall and cardiovascular mortality in younger men and cardiovascular death among the older men.[63] In a cohort of Iowa women, the waist-hip ratio was a better predictor of total or coronary heart disease mortality than BMI; hypertension incidence was more strongly linked with general obesity than with abdominal obesity; and all measures of obesity were strongly linked with diabetes incidence.[25] Of particular note, even women in the lowest BMI quintile had marked increased risk of diabetes if they also had a high waist-hip ratio.[25] In another prospective study of women, waist-hip ratio and waist circumference were independently associated with increased risk of coronary heart disease, even among those with BMI < 25.[64]

As BMI has been linked with a wider range of health outcomes, entry criteria for most studies are based on BMI. Obesity treatment trials typically reported either change in weight (directly proportional to BMI) or BMI; they did not reliably report measures of fat distribution. Because of these factors, we focused our analysis of screening tools on BMI.

Key Question No. 4a: Do Any Interventions Lead to Sustained Weight Reduction?

We identified 3 major forms of treatment for obesity that can be offered through various health care settings: counseling and behavioral interventions aimed at lifestyle intervention, pharmacotherapy, and surgery. We present results on these types of interventions below; details of the main studies cited appear in the evidence tables in Appendix B. As reflected in the analytic framework, our interest is both in intermediate outcomes such as sustained weight loss and maintenance of weight loss or those related to glucose tolerance, blood pressure, and lipid status, and in various health outcomes (discussed below).

Counseling and Behavioral Interventions

Counseling and behavioral interventions include a variety of approaches, all aimed at promoting a change in diet or exercise. These treatments can be delivered with or without behavioral intervention. The latter comprises strategies to help patients acquire the skills, motivations, and supports to change their diet and exercise patterns.

Prior Systematic Reviews

The National Institutes of Health (NIH) panel reviewed 29 counseling-based trials, with follow-up of at least 12 months, in which net weight loss (weight loss in intervention group minus weight loss in control group) could be calculated from evidence table data (Table 4). They found that average weight change in the intervention groups varied from a gain of 8 kg to a loss of 21.6 kg; corrected for change in control groups, weight change was +1.9 kg to –8.8 kg. In considering trials of ≥ 1 month duration, they found 38 in which counseling for low-calorie diets

(1,000-1,200 kilo-calorie [kcal] per day) could reduce body weight by an average of 8% over 3 to 12 months and decrease abdominal fat.[3] While very-low-calorie diets produced greater initial weight loss than low-calorie diets, effects were similar over follow-up beyond 1 year. Counseling for physical activity (in 24 RCTs) led to modest weight loss (2% to 3% of weight) and reduction in abdominal fat independent of the effect of caloric reduction. The combination of counseling for a reduced calorie diet and increased physical activity produced greater weight loss and reduction in abdominal fat than either approach alone. Review of 36 studies indicated that behavior therapy was a useful adjunct to other weight loss approaches over 1 year and that longer-term efficacy depended on continuing the intervention.

Upon review of 13 diet or behavioral therapy trials, the Canadian Task Force on Preventive Health Care found that weight reduction was most effective during supervised dietary treatment, with subsequent gradual weight regain. In 6 trials, with 24 to 60 months of follow-up, net weight change was 0 kg to -4.5 kg.[46]

The UK National Health Service (NHS) likewise found that behavioral interventions, combined with diet or exercise, appear to be effective and may be more so if of longer duration.[47] In 24 studies, net weight change was similar to that found in other reviews: +1.4 to -10.6 kg over 12 to 60 months. The authors concluded that long-term follow-up and maintenance strategies should be an integral part of a weight loss program.[47]

Studies of Efficacy of Counseling and Behavioral Interventions

We identified 17 randomized trials of fair or good quality in which interventions were based on counseling (including diet, exercise, or some combination of the 2) and delivered with or without behavioral therapy.[52,65-80] In 1 additional trial, the intervention or control activity was delivered by county of residence in a nonrandom fashion.[81] Evidence Table 1, Appendix B,

records details of these 18 studies. Sustained weight loss was defined as a change in body weight (in pounds, kilograms, or kilograms per meter squared of height [ie, BMI]) for at least 1 year.

We recorded the mode of intervention in Evidence Table 1 as well as the degree of intensity of the intervention. We considered interventions to be of moderate intensity if they involved monthly person-to-person contact with the participant, during the first 3 months of the intervention. Those with more frequent contact were considered high intensity and those with less frequent contact low intensity; cut-offs were driven by the distribution of program intensity we found represented in the literature. The following discussion takes up trials of high, medium, and low intensity in that order. We classified trials according to the type of intervention – ie, type of behavior counseled (diet or exercise [D, E respectively in Evidence Table 1]) and presence of a behavioral therapy component in the delivery of the intervention (B in Evidence Table 1). More detail on counseling interventions is presented in Appendix C.

Trials often entailed both weight loss and maintenance phases. These were analyzed separately from trials that involved either only a loss phase or only a maintenance phase (following successful weight loss). We break out the 2 maintenance-only trials in the discussion below.[67,72]

Comparison of effects is summarized in Figure 6. For this, we plotted the difference in mean weight change between intervention and control groups, at end-points as close as possible to 1 year, for all trials for which we could calculate the difference or the investigators could report the difference. If variance data were available in the articles or we could calculate them, we also depicted the 95% confidence intervals. Data are arrayed for high-, then moderate-, and

then low-intensity studies; those with good internal validity are listed ahead of those with fair internal validity.

High-Intensity Interventions for Weight Loss. In all, 11 RCTs employed high-intensity interventions at the group or individual level.[52,65,66,68,69,71,73,74,76,79,80] Of these, 6 RCTs compared high-intensity counseling intervention with a true control (no-intervention) group. Four achieved significant reductions in weight in the treatment groups (average loss: 2.7-5.5 kg improvement over controls at 12 months to more than 2 years of follow-up).[65,66,69,79]

Of these, a Finnish trial is of particular note: individual-based diet and exercise advice with a behavioral component (7 sessions over the first year) led the intervention group to lose 3.4 kg more than controls over the first year.[66] The investigators noted a high frequency of response (where response was defined as 5% weight loss): 43% of the intervention group versus 5% of the controls.[66] Similar results were subsequently found for the participants in the Diabetes Prevention Program in the United States: high-intensity counseling for diet and exercise, with behavioral therapy, led to an average 5.5 kg loss in the intervention group versus controls over an average of 2.8 years.[79]

Two trials with a true control were less successful. One, with a group-based approach, showed borderline-significant reduction in weight in the treatment groups.[74] Another combined an intense individual and group approach; the treatment group had improved weight at 6 months, but did not differ significantly from controls at 12 to 30 months of follow-up.[68]

Because prior studies have shown that combinations of diet, exercise, and behavioral therapy tend to be more effective than a single treatment, we evaluated 5 additional trials in which 1 combination of treatments was found to be superior to another, even in the setting of no true control (ie, no treatment) arm.[52,71,73,76,80] One study evaluating choice of behavioral

interventions found that a diet and exercise approach combined with behavioral choice treatment led to, on average, 5.8 kg of additional weight loss compared with traditional behavioral therapy.[73] Another trial examined different exercise regimens in the setting of diet and behavioral therapy: people who were supplied with treadmill machines for use at home, and instructed to do short bouts of exercise, lost more weight (4.3 kg more) over 18 months than those with similar instructions but no home equipment.[71] A trial comparing various 1-year, 26-session counseling programs found that combining meal replacements with a dietician-led group intervention was more effective than such counseling alone; short counseling sessions (10 to 15 minutes) with a health care provider combined with meal replacements led to similar degrees of weight loss as 1-hour dietician-led group sessions.[80]

A single trial examined the combination of counseling and behavioral therapy with pharmacotherapy for obesity.[52] Compared with sibutramine alone, the addition of a lifestyle intervention (behavioral therapy) led to a 7.3 kg weight reduction, and the further addition of a portion-controlled low-calorie diet led to weight loss of 12.8 kg over 1 year. Finally, Wing and Anglin studied weight change by race, rather than weight loss per se. The data in Figure 6 thus reflect differences between black and white populations estimated from their graph-based results.[76] Graphical data (significance not noted) suggest that weight loss was greater with behavioral therapy and an intermittent very-low-calorie diet than with behavioral therapy with a continuous low-calorie diet for white and black participants. However, over the 1-year follow-up, weight loss was lower in blacks than whites, primarily from faster regain.

Three studies (1 with 2 different physical activity interventions) reported weight change results first at 12 to 18 months, and then with prolonged follow-up.[66,69,74] As seen in prior reviews, subjects showed a tendency towards weight regain. However, in 3 of the 4

interventions, a modest statistically significant weight loss of at least 2 kg was maintained 24 to 36 months after initiation.[65,66,74] Two programs specifically included long-term maintenance interventions.[65,74]

Moderate-Intensity Interventions for Weight Loss. We identified 2 moderate-intensity, counseling-based weight loss interventions, both with a behavioral component.[70,77] A 1-year, group-focused intervention showed effectiveness similar to that of the nonpharmacological high-intensity interventions (3.5 kg).[70] A second intervention for multiple issues related to cardiac risk showed no significant improvement in weight at 18 months.[77]

Low-Intensity Interventions for Weight Loss. The low-intensity weight loss interventions that we reviewed were not effective. In 1 RCT, Jeffrey and French looked at the difference in weight change between intervention and control groups; this study was designed for weight gain prevention and showed no difference in men or in women of 2 socioeconomic strata at the end of 1 year.[75]

Two other studies (not shown in Figure 6) also investigated low-intensity approaches.[78,81] An RCT that did not measure baseline weight for controls found that, after 3 years, skilled manual laborers who underwent either a single or an annual nurse-run preventive medicine examination weighed 0.4 kg less than coworkers who received no health checks.[78] Finally, a group-based study, delivered according to nonrandomized intervention or control counties, was likewise ineffective.[81]

Interventions for Weight Loss in the Overweight. Limited data address the efficacy of counseling-based interventions in the overweight. A well-done high-intensity intervention on participants with baseline mean BMI levels of 25 promoted weight loss in a range similar to that found in trials including only obese participants.[65] However, 1 low- and 1 moderate-intensity

intervention in which participants' baseline BMI was in the upper range of overweight were ineffective.[75,77]

Interventions for Maintenance of Weight Loss. Two trials, neither with a true control group, evaluated counseling and behavioral plans for weight maintenance only.[67,72] In the high-intensity trial, members of a weight-focused treatment arm regained 2.1 kg less over 18 months than those receiving exercise-focused treatment.[72] Weight-focused participants maintained, on average, 90% of their weight loss over that time (compared with 54% in the exercise-focused arm). A low-intensity weight maintenance intervention also found a significant difference between treatments:[67] among self-selected women who had already lost more than 20 pounds, the prescription of pre-measured low-calorie liquid meal replacements led to an average of 5 kg lower weight over 1 year.

Summary of the Effectiveness of Counseling and Behavioral Treatment

Data on effectiveness of counseling and behavioral interventions must be understood in light of several caveats. Although several trials were of "good" quality (internal validity), most were judged only "fair," with limitations such as small sample size, potential selection bias (trials often enrolled volunteers), and high drop-out rates. Studies tended to report mean group weight change (eg, an average weight change of -5 kg in a group of 50 participants) and not frequency of response to the interventions (eg, 15 [30%] of 50 participants achieved loss of 10% of their initial body weight). We were not able to assess differences by sex or ethnic background in response to counseling and behavioral interventions; most trials included only women and either did not specify ethnicity or involved primarily white samples. One study did examine weight loss in black and white participants; initial weight loss in the black groups was followed by rapid weight regain, so that at the end of the study, sustained weight loss was considerably greater in

white participants.[76] Finally, the vast majority of these trials enrolled either only obese participants or samples in which average baseline BMI was in the high-overweight range. We were not able to assess the effectiveness of interventions specifically for those who are overweight but not obese.

Our findings agreed with those of the prior systematic reviews: generally, the counseling and behavioral interventions showed small to moderate degrees of weight loss sustained over at least 1 year. In the updated searches, higher-intensity trials and combinations of interventions appeared to promote better outcomes. However, treating patients with individual- versus group-based approaches did not appear to have a strong influence on success. As previous reviews have noted, trials with follow-up beyond 1 year tended to show a loss of effect; several studies, however, have shown modest weight loss maintained at 24 to 36 months. In addition, the success of weight maintenance trials is encouraging. Weight loss methods may need to be paired with longer-term maintenance interventions for sustained improvement.

Pharmacotherapy Interventions

Prior Systematic Reviews

Pharmacological treatment options for obesity are intended either to help promote or to sustain weight loss, in coordination with lifestyle change. Drug options have changed markedly since the major prior systematic reviews for obesity. The evidence concerning sibutramine (a dopamine, norepinephrine, and serotonin re-uptake inhibitor) and orlistat (a gastrointestinal lipase inhibitor) has increased. Both are approved by the U.S. Food and Drug Administration (FDA) for weight loss and weight maintenance after prior weight loss, in persons with BMI > 30

or persons with BMI > 27 with other risk factors such as hypertension, diabetes, or dyslipidemia; they should be used in conjunction with a reduced-calorie diet. FDA approval was based upon studies of up to 2 years' duration. Because of safety concerns, dexfenfluramine, fenfluramine, phenylpropanolamine, and the combination of fenfluramine/phentermine—previously central players in the pharmacotherapy of obesity—are no longer available in the United States.

Because available medications have changed so substantially since the publication of the 3 earlier large comprehensive obesity reviews, we do not present their findings here, although we did review relevant content. For example, we reviewed the 1996 National Task Force on the Prevention and Treatment of Obesity systematic review of clinical trials up to 6 months of drugs available at that time. Arterburn and Noel had also reviewed these same articles in 2001,[82] so we focused on the more recent review. In our data synthesis step, we included the findings of the systematic reviews along with the additional studies that we reviewed in detail.

Arterburn and Noel concluded that limited evidence shows that sibutramine is more effective than placebo in promoting modest weight loss (2.8-4.2 kg in 7 RCTs over 0.5-24 months) in healthy adults, and in those with controlled hypertension, but that subjects regain weight after stopping treatment.[51] Orlistat was found to have a modest effect on body weight (an average of 3.5 kg loss in 10 RCTs). Both medications lacked long-term evidence of safety. 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; again, these drugs lacked long-term evidence on safety. Small RCTs found limited and inconsistent evidence for the efficacy of diethylpropion (2 RCTs) and fluoxetine (2 RCTs) for weight loss compared with placebo.

Pharmacotherapy Intervention Studies Reviewed

We identified 13 RCTs of the efficacy of pharmacotherapy for weight loss that had been published since the 1996 USPSTF guidelines and that fit our inclusion criteria. Of these, 6 trials evaluated sibutramine,[83-88] 6 covered orlistat,[89-94] and 1 involved metformin.[95] We did not re-review any trials that Arterburn and Noel had covered.[51] We added 1 medication, metformin, to the list of drugs reviewed previously, as we had located several trials addressing its use specifically for weight loss. Evidence Tables 2, 3, and 4 in Appendix B present details on trials of sibutramine, orlistat, and metformin, respectively.

Inclusion criteria for our review included (a) fair or good quality, placebo-controlled RCTs on humans; (b) body weight or BMI as a primary trial outcome; (c) trial duration of at least 6 months; (d) trial population generalizable to a typical U.S. primary care population; (e) English language; and (f) no review by Arterburn and Noel. We categorized studies as either "weight loss" (minimum of 6-month follow-up) or "weight maintenance" (minimum of 1-year follow-up after successful weight loss). Eight weight-loss trials and 3 weight-maintenance trials were judged to be of fair or good quality (1 study had both a loss and a maintenance arm).

To depict the various findings from the trials focused on weight loss, we record in Figures 7 and 8 the mean weight changes and the percentage frequency of response (10% weight loss), respectively.

Pharmacotherapy Interventions for Weight Loss

Sibutramine. Of the 6 sibutramine trials (Evidence Table 2),[83-88] 5 concerned weight loss and lasted 6 to 12 months.[84-88] Sibutramine-treated participants achieved an average of 2.8 kg to 4.8 kg more weight loss than placebo (Figure 7). Four trials recorded frequency of response; for example, 27% to 65% of sibutramine-treated patients achieved 5% weight loss and

6% to 38% of patients lost 10% of their initial body weight.[84,86-88] Sibutramine-treated participants achieved 5% of total body weight loss 19% to 37% more often than controls (depending on drug dose). As shown in Figure 8, patients on sibutramine achieved a 10% weight loss 5% to 27% more often than controls (Figure 8, right hand panel). Differences by dose of drug or mode of use (Figure 8, left-hand panel) were also of interest; however, by and large dosage did not materially affect outcomes. For instance, in 1 trial, weight loss obtained with sibutramine therapy did not differ between people treated with continuous therapy and those treated with intermittent therapy.[87]

Orlistat. Of the 6 orlistat trials (see Evidence Table 3),[89-93,96] we reviewed 5 assessing weight loss over 6 to 12 months duration; orlistat-treated participants treated in the normal dosing range (120 mg 3 times a day [Figure 7]) lost significantly more weight than controls: on average, 2.8 kg to 4.5 kg (or 1.2-1.5 kg/m^2) more than control participants.[89-93] In 1 small study (n = 55), the average weight of orlistat treated patients dropped 5.8 kg more than that of controls, but the difference was not statistically significant.[94] Only 2 of the orlistat trials we reviewed reported frequency of response.[89,93] In these trials, a 10% weight loss response occurred in 23% to 38% of orlistat-treated participants depending on dose (Figure 8, left-hand panel). Between 9% and 19% more of orlistat group members were able to achieve 10% loss of their body weight than members of the control group (Figure 8, right-hand panel).

Metformin. Only 1 metformin trial met quality criteria (Evidence Table 4).[95] It included patients with diabetes who had inadequate blood glucose control despite oral therapy for at least 1 year. Metformin-treated patients did no better than controls in terms of weight loss.

Pharmacotherapy Interventions for Maintenance of Weight Loss

Sibutramine. James et al reported weight change from baseline through 6 months of successful treatment with sibutramine, followed by an 18-month period of sibutramine maintenance therapy.[83] Over the 2 years, sibutramine-treated participants lost, on average, 4 kg more than their placebo-treated counterparts. They were also more likely (41% of sibutramine vs 14% of placebo participants) to maintain 80% of their initial weight loss.

Orlistat. In the trial conducted by Karhunen et al, participants received 2 years of therapy: orlistat for 2 years, placebo for 2 years, or 1 year of each.[91] The investigators did not record orlistat versus placebo results. Patients who were treated with orlistat for 1 or 2 years obtained "significantly more" weight loss over 2 years than participants treated with placebo. During the second year of treatment, orlistat was no more effective than placebo, on average, and discontinuing orlistat appeared to lead to excess weight regain. That is, those treated with orlistat for the first year and then changed to placebo had a mean 6.3 kg weight gain during the second year, whereas those treated with placebo throughout gained, on average, only 3 kg over the second year of the study.

In another trial, initiated after 6 months of successful dieting, participants treated with an orlistat dose of at least 60 mg 3- times a day lost more weight over 1 year and were less likely to experience marked weight regain than placebo-treated patients.[90] Those treated with 120 mg 3-times daily also achieved a larger percentage of weight change and were more likely to maintain 75% of their initial weight loss than placebo-treated patients.

Summary of the Efficacy of Pharmacotherapy

Again, findings must be interpreted in light of several considerations. One is internal validity: most trials were of fair quality, although a few were judged to be of good quality. A

second is the degree to which participants were overweight in the trials. These trials did not assess drug effectiveness by degree of overweight. Some included participants with baseline BMI in the high 20s, but average baseline weight was consistently in the obese range (ie, BMI $\geq$ 30), and pharmacotherapy for weight loss is approved only for the obese. As with pharmacotherapy trials, participants were primarily women of European origin. We evaluated several pharmacotherapy trials with relatively short-term follow-up (less than 1 year); although their findings were generally within the range seen for the longer studies, sustained weight loss was not established in so short a time.

Finally, although most trials did employ a form of intention-to-treat analysis, typically the investigators analyzed their data according to a "last observation carried forward" protocol—the final weight outcome available was used as the final weight for those participants who dropped out of the study. As weight loss tends to be maximal within the first 6 months of therapy, failure to measure body weight at the endpoint of longer trials risks overestimating the tendency towards sustained weight loss. We would prefer to review such results alongside analysis of trial "completers," but such an approach was infrequent.

Overall, fairly long-term data for sibutramine and orlistat suggested that these drugs have modest but potentially prolonged effects. Although average weight loss was consistently modest, the percentage of patients achieving clinically significant loss (5%-10% of body weight) was frequently substantial. Weight maintenance trials suggested that prolonged drug therapy confers some benefit but that discontinuation of pharmacotherapy may lead to rapid weight regain.

Surgical Approaches

Bariatric surgical procedures are restrictive or malabsorptive in nature. The 3 techniques most commonly used in randomized trials 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.[97] Vertical banded gastroplasty entails partial gastric partitioning at the proximal gastric segment with placement of a gastric outlet stoma of fixed diameter.[46] Although this literature still reports on this technique, clinical practice patterns appear to be shifting away from it. Gastric bypass, adjustable gastric banding, and vertical banded gastroplasty can all be performed either laparoscopically or through an open technique.

The duodenal switch procedure is a relatively new malabsorptive technique; although fairly common in clinical practice, we did not find any RCTs evaluating its effectiveness. Another malabsorptive method, jejunoileal bypass, is no longer recommended because of excessive malabsorption.[47]

Prior Systematic Reviews

The 3 previous obesity reviews all evaluated the impact of surgery on people with obesity. Because of practical and ethical constraints to a true randomized, blinded, placebo-controlled surgical obesity trial, high-quality evidence for obesity surgery is limited. Reviews have relied primarily on randomized unblinded trials in which neither arm was a true control (eg, comparisons between surgical techniques). Here, we summarize their findings for current procedures with at least 1 year of follow-up. The Canadian Task Force on Preventive Health Care analyzed 4 randomized trials and 1 prospective cohort study.[46] In these studies, mean

weight loss following surgery was 17 kg to 46 kg after 2 to 5 years. Postoperative mortality and morbidity rates were low; 1 surgery-related death occurred (0.002% of subjects), and post-operative morbidity was less than 5%. The Centre for Reviews and Dissemination from the University of York's review of 6 trials showed weight loss of 9.7 kg to 57.9 kg.[47] In the NIH National Heart, Lung and Blood Institute review, 5 randomized surgical trials led to weight loss of 10 kg to 159 kg over 12 to 48 months.[3]

Studies of the Effectiveness of Surgical Interventions for Weight Loss

Randomized Trials. Our review of randomized trials with comparison arms included trials of fair to good quality with follow-up of at least 1 year and weight loss or BMI change as an outcome. We identified 2 trials that had not been reported by the previous systematic reviews.[97,98] Details are in Evidence Table 5. One compares laparoscopic versus open banding techniques,[97] and the other, 2 laparoscopic banding techniques.[98]

In the de Wit et al study, 50 obese (BMI >40) patients were randomized to either open or laparoscopic adjustable silicone gastric banding.[97] Both groups showed large average weight declines over 1 year: 35 kg in the laparoscopic and 34 kg in the open surgical group. Accordingly, BMI dropped from 51.3 to 39.7 in the laparoscopic group and from 49.7 to 39.1 in the open group. Complications included incisional hernias (14.3%), umbilical hernia (2%), and infection (2%); no subject died.

Weiner et al randomized 101 consecutive patients to 1 of 2 groups of laparoscopic gastric banding—retrogastric placement (RGP) or esophagogastric placement (EGP).[98] Weight loss was substantial in both groups: more than 40 kg in both groups at 18 months. Post-operative complications included 3 band slippages (3%, which were subsequently corrected with additional laparoscopic surgery), 1 pouch dilation (1%), vomiting in 6 patients (6%), and dysphagia in 6

patients (6%); no patient died. Of note, results from a quality-of-life questionnaire revealed that more than 96% of participants reported excellent well-being at the 18-month follow-up.

Cohort Studies. We used well-designed cohort studies as a second form of evidence for obesity surgery. RCTs are the preferable form of evidence, but because the constraints against a large RCT for obesity surgery are extensive, this may be a situation in which carefully evaluated cohort data are appropriate. We searched for controlled cohort studies with weight loss as a primary outcome, in which the patient population was well described, and identified a single large on-going study – the Swedish Obese Subjects (SOS) study.[99,100] In addition, we examined extensive uncontrolled cohort (case series) evidence to assess the safety of obesity surgical techniques and their applicability to primary care populations.

The SOS study provides the best cohort evidence: a large ongoing multi-center trial with nonrandomized matched controls involving volunteers at 750 primary health care centers and 26 county and university hospitals in Sweden. The surgical arm is divided equally among 3 surgical techniques: gastric banding, vertical banded gastroplasty, and gastric bypass. Controls are treated with "the best non-surgical options available" (p. S3).[100]

Two-year data revealed weight loss of 28 kg (23% of total weight) among the surgical patients and 0.5 kg among controls. The percentages of weight reduction after gastric banding, vertical banded gastroplasty, and gastric bypass were 21%, 23%, and 33%, respectively. Eight-year follow-up data showed a 20-kg weight loss (16.5% of total weight) for 251 patients in the surgical group; over this same period, the 232 control patients gained 0.7 kg.[100] The reported post-operative mortality rate was 0.2%. As in the randomized trials, morbidity was low; among 1,164 patients, complications 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%).[100]

Summary of Effectiveness of Surgical Treatment

Overall, considering RCTs, controlled cohort studies, and uncontrolled cohort studies, the degree of weight reduction obtained with surgical interventions is consistently dramatic. Cohort evidence suggests that this weight loss may be prolonged and that it can be achieved in patient populations with multiple comorbidities.

We must, however, note some limitations to this literature. Surgical data are limited by the lack of placebo-controlled RCT evidence, and the internal validity of the trials we reviewed was of only fair quality. Again, the investigators tended to report average treatment effect, rather than frequency of response.

Finally, obesity surgery has been performed for only a select group of patients; the NIH obesity panel recommends it only for those people with a BMI >40 or a BMI of 35 to 40 with at least 1 obesity-related comorbidity.[3] National data indicate that 5% to 6% of the general population has a BMI in this range,[12] so a substantial number of people may meet these criteria.

Key Question No. 4b: Do Interventions Improve Other Intermediate Health Outcomes?

Prior reviews have established that counseling-based weight loss can improve various intermediate health outcomes (in the analytic framework in Chapter 2, Figure 5, these are maintenance of weight loss, blood pressure, gylcemic control, and serum lipids). In this review, we did not attempt to re-establish either this link or that between our intermediate health outcomes and final health outcomes. The NIH review found that weight loss by lifestyle

modifications reduced blood pressure in overweight nonhypertensive patients.[3] Likewise, multiple trials of weight loss via lifestyle intervention in hypertensive patients – generally achieving 5 kg to 10 kg weight loss – led to reductions in systolic and diastolic blood pressure (3-7 mm Hg, and 3 mm Hg, respectively), less incident hypertension, and few antihypertensive medications. Only 1 RCT producing weight loss in hypertensive patients reported no significant change in blood pressure.

Trials reviewing weight loss in a similar range reduced serum triglycerides, increased high-density lipoprotein (HDL) cholesterol, and reduced low-density lipoprotein (LDL) cholesterol. In addition, weight loss from lifestyle modification lowered blood glucose levels in overweight and obese persons without diabetes and reduced blood glucose and hemoglobin A1c (HbA1c) in some subjects with diabetes.

Because pharmacotherapy can potentially alter body chemistry and thus affect physiology differently from other means of weight loss, we did assess new data looking specifically at the ability of drug-induced weight loss to affect intermediate health outcomes. Health outcomes for pharmacotherapy are limited to data from trials lasting no more than 2 years. Three trials assessed the effect of sibutramine treatment on HbA1c.[83-85] Two, lasting 24 to 104 weeks, found no significant drug versus placebo effect;[83,84] the third found that sibutramine-treated participants, over 24 weeks, had a 2.2% greater decline in HbA1c than placebo.[85] Three trials examined fasting or nonfasting serum glucose in relation to sibutramine therapy;[83,84,86] none found a significant difference compared with placebo.

Orlistat therapy was linked to slightly lower total cholesterol after 24 to 52 weeks: 8% lower in 2 trials,[90,93] and 2.7mg/dL to 8.5 mg/dL (0.07-0.22 mmol/L) lower in another.[92]

Sibutramine showed less consistent total cholesterol findings. Three trials found no significant drug versus placebo effect;[83,84,86] another found a 20.4 mg/dL improvement over 24 weeks.[85]

Sibutramine and orlistat showed inconsistent effects on triglycerides[83,84,86,88,92] and on HDL.[85,88] One trial found a significant decrease in HDL cholesterol with orlistat therapy (1.5-1.9 mg/dL with >90 mg daily dose),[90] and another a 3.49% increase in HDL cholesterol.[92] Two trials found a significant increase in HDL cholesterol (5 mg/dL in one and 2.1 mg/dL in the other) with sibutramine,[83,88] and 2 others reported no significant effect.[84,85] Orlistat was associated with reductions in LDL cholesterol (3.1-10 mg/dL reduction vs placebo) in 1 trial[90] and a 10% reduction in another.[93] Sibutramine, in 4 different trials, had no effect on LDL cholesterol.[83-85,88] Overall, we found mixed evidence of improvements of secondary health outcomes among the relatively short-term pharmacotherapy trials reviewed here; this inconsistency may be attributable to altered metabolism by medications or to inadequate length of follow-up.

In surgical cohort data, substantial weight loss was linked with dramatic improvements of intermediate health outcomes. In one cohort of 330 patients with baseline glucose abnormalities (half with impaired glucose tolerance and half with type 2 diabetes), 90% complete postsurgical follow-up revealed normal fasting blood glucose and glycosylated hemoglobin in 91% of subjects.[101] Long-term follow-up (>5 years) of a group of 109 surgical patients found the rate of development of diabetes to be 0.15 cases per 100 person years; in 27 controls (patients who qualified for surgery but subsequently declined the procedure), the rate was 2.72 cases per 100 person years.[102] Marked improvements in lipid profiles have also been noted.[103] In the SOS,[104] participants were initially matched on age, sex, height, weight, waist, blood pressure, cholesterol and triglyceride levels, and diabetes. In the 2-year follow-up, the investigators reported lower

odds of hypertension (odds ratio [OR], 0.38; CI, 0.22-0.65), diabetes (OR, 0.02; CI, 0.00-0.16), hypertriglyceridemia (OR, 0.10; CI, 0.04-0.25), and low HDL cholesterol (OR, 0.28; CI, 0.16-0.49) in the surgical patients compared with the controls. However, blood pressure slowly returned to levels similar to the control group. Thus, they did not report a long-term improvement in blood pressure.[105]

Key Question No. 5: Do Interventions Improve Final Health Outcomes

To examine the question of effects of sustained weight loss, we divided our analysis of health effects into intermediate outcomes (discussed above) and final health outcomes. Even moderate intentional weight loss (5%-10% of initial body weight) has been shown to reduce the severity of comorbidities associated with obesity. Limited observational data suggest that intentional weight loss in the obese can lead to reduced mortality.[106,107]

We looked for new evidence that weight loss can affect mortality, morbidity, mental health, and daily functioning. Two recent trials provide strong evidence that behaviorally mediated weight loss can prevent diabetes.[66,79] We found very limited evidence evaluating other outcomes in the setting of modest controlled weight loss: 1 trial evaluating 2 types of behavioral therapy showed borderline improved self-esteem in both treatment groups.[73] The National Task Force on the Prevention and Treatment of Obesity found that dieting did not lead to problems in psychological function or eating disorders.[60] The health benefits of weight loss in overweight patients are less clear.

Key Question No. 6: What are the Harms of Screening and Treatment?

Screening or Counseling and Behavioral Interventions

We did not find studies evaluating the harms of screening or of counseling and behavioral interventions. Nonetheless, a potential risk does exist, particularly as the stigma of obesity is well established.

Medications

In their review of sibutramine harms, Arterburn and Noel found that common adverse effects occurred somewhat more frequently in drug than control arms (10%-30% vs 8%-19%), but no serious adverse events were reported.[51] They noted reports of mean increases in systolic and diastolic blood pressure (1-3 mm Hg) and heart rate (4-5 beats per minute); in people with controlled hypertension, the incidence of clinically significant increases in blood pressure was similar in intervention and control participants. They also found a 3.9% dropout for hypertension in the sibutramine trials they reviewed.

Among the sibutramine trials that we reviewed, several showed high dropout rates; however, attrition was generally lower for sibutramine patients than for those on placebo. Attrition attributable to an adverse event was almost identical in drug and placebo arms in 5 sibutramine trials;[83,84,86-88] it was not noted in the sixth.[85]

Even though reports of adverse events were common, when rates were specified they tended not to differ between drug and placebo participants. The most frequent side effects included insomnia, nausea, hypertension, dry mouth, dizziness, and confusion; side effects were

usually not severe. The most concerning side effect is hypertension; the average increase in blood pressure was small: 0 mm Hg to 3.5 mm Hg higher in drug-treated patients in 3 studies,[86-88] 2.1 mm Hg higher in a fourth,[84] and 5% higher in a fifth.[83] Two studies reported dropout because of hypertension, but it did not differ between drug and placebo arms.[84,88] One study noted that an average increase of 6.7 beats per minute in pulse rate was associated with sibutramine.[88]

Orlistat adverse effects are primarily gastrointestinal. Arterburn and Noel found that 22% to 27% of orlistat-treated participants reported oily spotting, flatulence, and fecal urgency (vs 1%-7% of control participants).[51] Of the RCTs they reviewed, 4 showed an increased incidence of vitamin deficiency with orlistat treatment; 1 suggested reduced intestinal absorption of contraceptive pills with this medication. In addition, in 1 RCT of participants with coronary heart disease risk factors, more serious adverse events (10% vs 2.6%; unidentified in nature) occurred with orlistat than placebo.

In the orlistat trials we reviewed, attrition rates were generally similar (within 5%) between drug and placebo arms. Dropout because of an adverse event generally was slightly more common (0%-7%) in orlistat-treated participants, although in 1 group it was an additional 12%.[90]

In the 3 trials that reported overall adverse event rates, 10% to 18% more of the drug-treated participants reported problems than did those in the placebo groups.[89,92,93] The most common side effects were gastrointestinal (flatus, abdominal pain, fecal urgency): 14% to 37% more orlistat patients than controls reported the problems in the 3 studies, but they were usually mild. One trial reported the frequency of severe gastrointestinal events to be 1% to 9% more in

drug-treated participants versus placebo.[89] Two studies noted that orlistat led to gastrointestinal disturbance leading to attrition in 1% to 10% of participants.

Adverse effects of other obesity medications may be of concern. Arterburn and Noel's review of harms of pharmacotherapy found no evidence of serious adverse reactions for phentermine, but unclear incidence rates of potentially serious side effects for mazindol and diethylpropion (pulmonary hypertension [mazindol and diethylpropion] and psychosis [mazindol]).[51] They found that fluoxetine has been linked with gastrointestinal symptoms, sleep disturbance, sweating, tremor, amnesia, and thirst, and systematic review evidence of 10% to 15% incidence of anxiety, diarrhea, dry mouth, headache, and nausea.[51] The single metformin trial we reviewed did not provide enough information to evaluate its profile of side effects.[95]

Surgical Approaches

We evaluated multiple surgical cohort studies, with follow-up of at least 1 year, to assess adverse effects. Adverse outcome data included 2 series in which patients had substantial comorbidity,[108,109] and multiple studies in which a modest degree of comorbidity was present. Generally, mortality rates were very low. In 12 cohorts treated with vertical banded gastroplasty, mortality ranged from 0% to 1.5%; if these rates were pooled, this represents a total of 3 deaths in 1,165 patients.[108-119] Two of those studies included patients with substantial comorbid conditions,[108,109] as did 2 of the gastric bypass cohorts.[109,120] Among 9 cohorts of gastric bypass patients, mortality was 0% to 1.5% (10 deaths in 1,397 patients).[101,113,120-126] Adjustable gastric banding mortality was similarly low: 0% to 1.6% in 16 cohorts.[119,127-141]

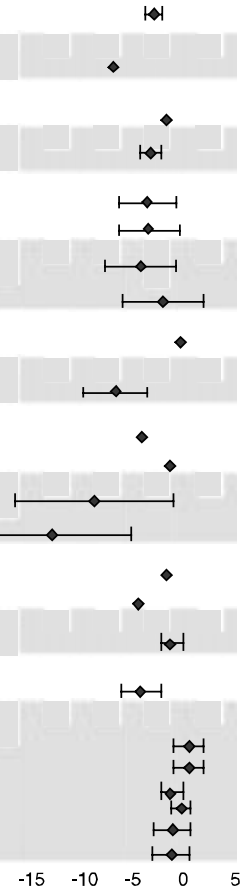
Vertical banded gastroplasty was associated with several types of complications. Re-operation rate was reported to be 20% to 25% over 3 to 5 years.[112,115] Wound infection was

noted in 8% to 32% of patients in 3 studies.[109,112,113] Less frequent adverse events (<6%) included gastric leaks, stomal stenosis, and pouch dilatations. In gastric bypass patients, wound infection was reported in 8% to 20% of patients.[113,124,125] Staple failure occurred in 15% of patients in 1 study with 14 years of follow-up;[101] the same cohort developed vitamin B12 deficiency in 40% of participants. Other notable morbidity included diarrhea in 13% of 1 group[125] and gastrointestinal hemorrhage in 3% of another.[113] In patients undergoing adjustable gastric banding, morbidity was often from re-operation (1%-20%),[127,130,133-136,140,142] band dislocation, leakage, or slippage (0.4%-8%).[128-130,132,133,135-137,142]

In addition to these procedure-specific adverse consequences, surgical patients require long-term follow-up and multivitamin supplementation. We found no evidence of psychological harms, but there is a suggestion of psychological benefit to weight reduction in surgery studies.

Figure 6. Differences in Mean Weight Loss Between Intervention and Control Groups for Counseling and Behavioral Interventions

Study & Intervention	Control	Intensity	Intensity Validity	Timing of Measurement
Stevens et al., 2001[69] (18-mo. data)				
D, E, B+++	Usual care	High	Good	18 mo
Knowler et al., 2002[79]				
D, E, B+++*	D, E+	High	Good	34 mo
Kuller et al., 2001[65]				
D, E, B+++*	Assessment only	High	Good	54 mo
Tuomilehto et al., 2001[66]				
D, E, B+++	D, E+	High	Good	12 mo
Fogelholm et al., 2000 (1-yr data)[74]				
D, EP2, B+++	D, B+	High	Fair	12 mo
D, EP1, B+++	D, B+			
Jakicic et al., 1999[71]				
D, Short-Bout EP with EQ, B+++	D, Short-bout EP, B+++	High	Fair	18 mo
D, Long-Bout EP, B+++	D, Short-bout EP, B+++			
Jones et al., 1999[68]				
D, B+++	Told to lose weight+	High	Fair	30 mo
Sbrocco et al., 1999[73]				
D, E, B1+++	D, E, B2+++	High	Fair	12 mo
Ashley et al., 2001[80]				
D (dietician) with MR, E, B+++	D (Dietician), E, B+++	High	Fair	12 mo
D (primary care), E, B+++	D (Dietician), E, B+++			
Wadden et al., 2001[52]				
B, Sibutramine+++	Sibutramine	High	Fair	12 mo
D, B, Sibutramine+++	Sibutramine			
Wing and Anglin, 1996[76]				
Black patients: D1, E, B+++	D2, E, B+++	High	Fair	12 mo
White patients: D1, E, B+++	D2, E, B+++			
Lindholm et al., 1995[77]				
D, E++	Usual Care+	Moderate	Good	18 mo
Swinburn et al., 1999[70]				
D, B++	D+	Moderate	Fair	12 mo
Jeffery and French, 1997[75]				
Low SES women: D, E, $	No contact	Low	Good	12 mo
Low SES women: D, E	No contact			
High SES women: D, E, $	No contact			
High SES women: D, E	No contact			
Low SES men: D, E, $	No contact			
Low SES men: D, E	No contact			

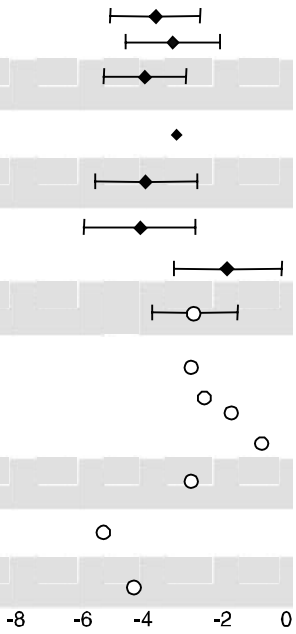


◆ = Mean weight change (kg) in intervention group - mean weight change (kg) in control group. Only studies for which this difference can be calculated are included. Error bars represent 95% confidence intervals and are presented for studies in which those data are available. Data presented are as close as possible to 1-year follow-up.

* = Statistically significant ($p < 0.05$) but with insufficient data to calculate 95% confidence intervals; D=diet; E=exercise; B=behavioral therapy; EP = exercise program; EQ = exercise equipment; MR = meal replacement; SES = socioeconomic status; $ = lottery entry ($100 drawing/month); +++ = high intensity; ++ = moderate intensity; + = low intensity.

Figure 7. Differences in Mean Weight Loss Between Intervention and Control Groups for Pharmacotherapy Interventions

Study & Intervention	Control	Internal Validity	Timing of Measurement
Wirth and Krause, 2001[87]			
Sibutramine 15 mg QD (continuous)	Usual Care	Good	11 mo
Sibutramine 15 mg QD (intermittent)			
Dujovne et al., 2001[88]			
Sibutramine 20 mg QD, D	D	Fair	6 mo
Fujioka et al., 2000[84]			
Sibutramine 20 mg QD, D*	D	Fair	6 mo
Gokcel et al., 2001[85]			
D Sibutramine 10 mg BID, D	D	Fair	6 mo
Smith et al., 2001[86]			
Sibutramine 15 mg QD, D	D	Fair	12 mo
Sibutramine 10 mg QD, D			
Muls et al., 2001[93]			
Orlistat 120 mg TID, D	D	Good	6 mo
Van Gaal et al., 1998 [89]			
Orlistat 240 mg TID, D*	D	Fair	12 mo
Orlistat 120 mg TID, D*			
Orlistat 60 mg TID, D*			
Orlistat 30 mg TID, D			
Micic et al., 1999[92]			
Orlistat 120 mg TID, D*	D	Fair	6 mo
Rissanen et al., 2001[96]			
Orlistat 120 mg TID, D	D	Fair	12 mo
Karhunen et al., 2000[91]			
Orlistat 120 mg TID, D*	D	Fair	12 mo



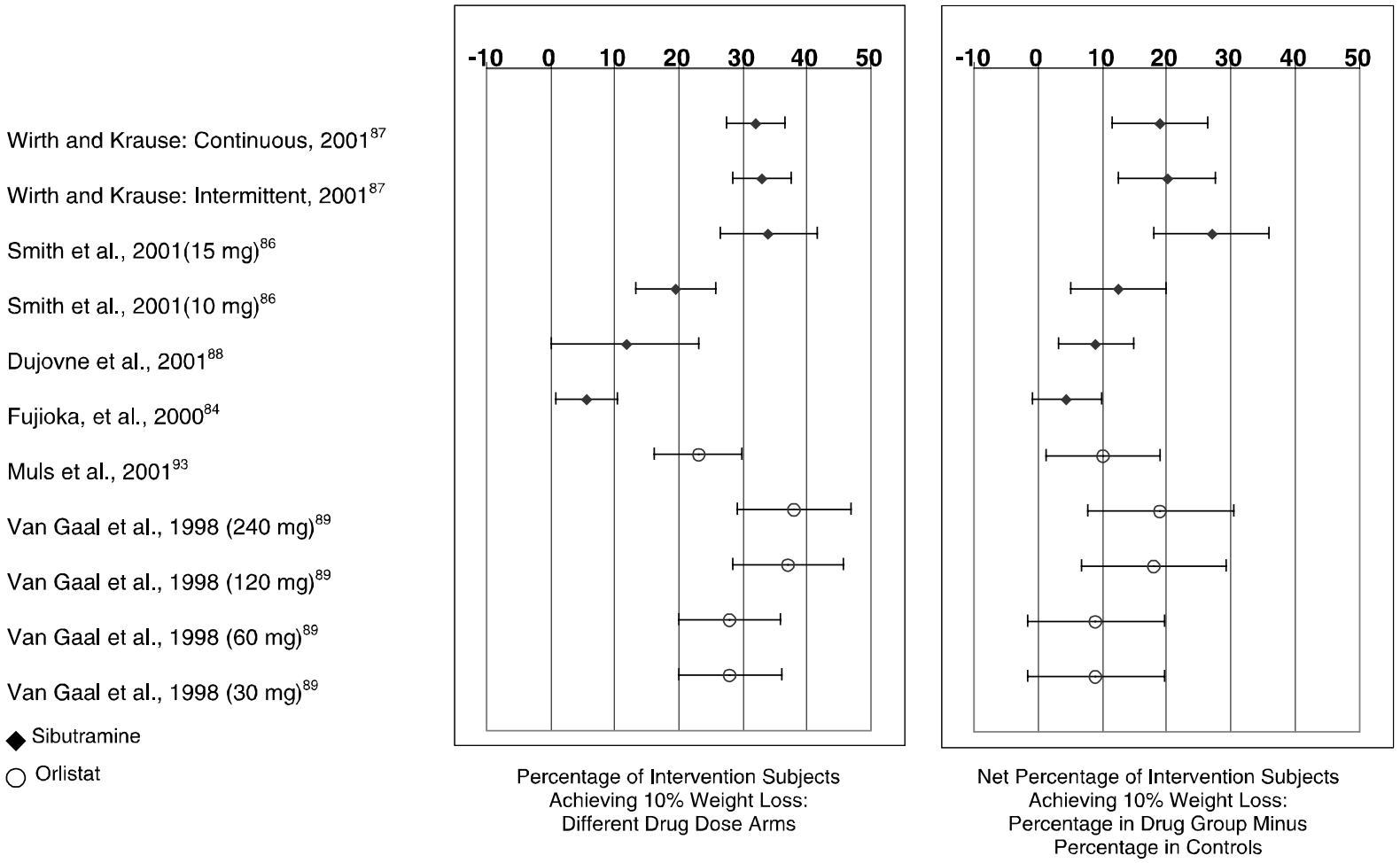
◆ Sibutramine studies

O Orlistat studies

Data points (diamonds, circles, and squares) represent mean weight change in intervention group (kg) – mean weight change in placebo group (kg). Only studies for which this difference can be calculated are included; each arm is represented by a data point. Error bars represent 95% confidence intervals and are presented for studies in which those data are available. Intensity of co-interventions is not assessed as most trials provided insufficient information for evaluation.

* = Statistically significant ($P < 0.05$) but with insufficient data to calculate 95% confidence intervals; QD=daily, BID=twice daily, TID=three times daily, D=diet, E=exercise, B=behavioral therapy.

Figure 8. Frequency of 10% Weight Loss for Pharmacotherapy Interventions (Sibutramine and Orlistat)



4. Discussion

General Conclusions

In this review, we found that obesity and overweight are common, are easy to screen for, can potentially pose a substantial health burden in this country, and can be addressed with a substantial array of therapies. These factors make this a significant clinical condition for clinicians in primary care settings like those addressed by the U.S. Preventive Services Task Force.

Data specific to the overweight population are very limited, but they suggest that counseling interventions may promote modest weight loss in overweight people (those with body mass index [BMI] of 25-29.9). Obese patients can achieve modest but clinically significant weight loss with counseling, for either diet or exercise, or both, with or without additional behavioral interventions to modify motivations, skills, and supports related to dietary or physical activity patterns.

In prior systematic reviews, counseling-based interventions of at least 1 year duration led to weight changes in the range of +1.9 kg to -10.6 kg.[3,46,47] In our updated searches of counseling efficacy, mean weight loss in counseled groups beyond that in control groups was as follows, depending on the intensity of the intervention: high intensity, 0 kg to 5.4 kg; moderate intensity, 0.25 kg to 3.5 kg; and low intensity, 0 kg to 2.7 kg. We defined intensity in terms of numbers of face-to-face encounters in the first 3 months of an intervention; moderate intensity was 3 such encounters and high (or low) was more (or fewer) than that. Importantly, these may

be conservative estimates of counseling-based weight loss, as "control" groups frequently did receive some form of intervention.

Patients can achieve similar levels of weight loss with pharmacotherapy interventions. Prior review has noted that patients treated with either sibutramine or orlistat lose 3 kg to 4 kg beyond those treated with placebo.[51] Limited data suggest that appetite suppressants may be effective in the short term, but they have not been tested or approved for long-term use. In our updated searches for pharmacotherapy efficacy, the mean loss beyond placebo was between 3.2 kg and 5.5 kg. From 5% to 27% more of those treated with drugs (sibutramine or orlistat) achieved 10% weight loss than those treated with placebo, and 19% to 37% more of those with sibutramine achieved at least a 5% weight loss. Again, these figures may be conservative estimates of weight loss achieved with drugs because they do not reflect the effect of diet and exercise. Behavioral interventions should accompany pharmacotherapy use.

Finally, in a select group of patients, surgical options promoted large amounts of average weight loss (9.7-57.9 kg over 1-2 years). Generally, these are patients with extreme body mass index (BMI >40) or marked obesity (BMI >35) with associated health complications and failure to respond to other modalities in the past.

We arrived at all these findings through a variety of sources of evidence. Systematic reviews of primary literature comprising randomized controlled trials (RCTs) found counseling, behavioral, and pharmacotherapy efficacy similar to levels in more recent RCTs of fair to good quality. Our conclusions about surgical therapy are based upon RCTs comparing different types of banding techniques (open vs laparoscopic approaches, and different placements of laparoscopic techniques), a well-conducted nonrandomized comparison study, and dramatic results from cohort studies.

Cross-cutting Findings and Future Research Issues

The literature on which this systematic review is based yielded some insights into more, or less, effective approaches, although some questions remain unanswered. Studies also had a variety of limitations. We note here some important additional conclusions, together with our assessment of significant future research that should be pursued.

Clarifying Benefits Over the Longer Term

Counseling-based interventions involving diet and exercise were consistently more effective in the setting of a behavioral component. Treating patients on an individual basis, as contrasted with using group interventions, appeared to be less important. Of note, many of the interventions evaluated here were not carried out in the health providers' office, and high-intensity programs may be difficult to incorporate into routine clinical practice. One option may be referral to intensive counseling and behavioral therapy programs. Another is to evaluate further the long-term efficacy of combining less intensive office-based counseling approaches with different delivery approaches for behavioral therapy such as video or internet-delivered adjuncts. Although evidence examining the role of behavioral interventions in coordination with pharmacotherapeutical approaches is limited, 1 sibutramine trial suggested that such an approach may provide substantial added benefit.

Thus, we would advocate for continued development and testing of counseling and behavioral interventions with better, and longer, follow-up, whether independently or as part of a multi-faceted approach that involved medications. Such multi-component studies might also add social components to standard counseling or behavioral therapies. In addition, we emphasize the need for investigators to invoke more conservative intention-to-treat analyses, rather than falling

back on methods involving last-observation-carried-forward approaches. Finally, the efficacy of interventions to alter body fat distribution and clarification of health effects of purposeful reduction of central adiposity deserve more attention.

For non-surgical options, weight loss was evaluated with relatively short-term follow-up (at least 1 year for counseling trials and at least 6 months for drug trials). Longer follow-up seems to be associated with lesser weight loss. Both prolonged counseling- and pharmacotherapy-based interventions do appear to help maintain weight loss. Nonetheless, studies of longer-term interventions (over several years) have not been done. A key area of future research is to institute longer-term follow-up for benefits and harms, particularly for pharmaceutical interventions. In addition, we note that work on weight maintenance interventions (independent of investigations of weight loss) deserve attention (including long-term follow-up as well).

Although evidence does not conclusively show that reducing weight extends life, we can estimate the potential reduction in coronary heart disease (CHD) events from the effect of weight reduction on risk factors. For example, studies of weight loss from counseling and behavioral interventions find a reduction in systolic blood pressure of about 3 mm Hg and a reduction in total cholesterol of about 5% from a 7% reduction in weight.[3] Using the Framingham risk equation, and assuming that these reductions in blood pressure and cholesterol would be maintained for 10 years, we calculated that 1 CHD event would be avoided per 180 to 200 obese people age 50 with mildly elevated blood pressure (140 mm Hg) and total cholesterol (220 mg/dl) who were treated according to the protocol of the Diabetes Prevention Program intervention.[79]

For patients with higher levels of BMI, combinations of interventions may be more effective than a single modality. Studies of long-term outcomes with ongoing counseling, behavioral, and pharmacologic therapies are needed, as already suggested, but some research emphasis needs to be directed at studies of multi-component interventions, especially those that draw on recent conceptualizations of the behavioral elements of such approaches.

In addition, we found very limited data regarding efficacy of treatment options for patients who are overweight but not obese (ie, BMI 25-29.9). In the interest of obesity prevention, this patient population deserves further attention. Among the obese, studies of surgery among patients with BMI levels lower than among patients who have been subjects of recent trials may be warranted.

Clarifying Harms and Risks

All modes of treatment appear to be reasonably safe. We uncovered no evidence documenting harms of the diet and/or exercise counseling or behavioral interventions. With respect to medications, sibutramine is sometimes associated with increased blood pressure (mean increase of up to 3.9 mm Hg), and orlistat causes gastrointestinal distress in 15% to 37% of people taking the drug. However, safety has been assessed in trials lasting, at most, 1 to 2 years; as noted, long-term adverse effects of pharmacotherapy are less well defined and ought to be clarified through studies with longer follow-up periods. Useful future research would entail developing and testing newer drugs that would pose even fewer side effects, especially medications that do not increase blood pressure.

Surgical options clearly involve the highest risk, but current surgical approaches have much lower complication rates than those of the past. Surgical procedures lead to mortality in

less than 1% of patients in pooled samples; in up to 25% of patients, however, re-operation is necessary over 5 years.

Clarifying Benefits and Harms for Specific Populations

We were not able to assess the relative effectiveness of treatment options by sex or ethnicity. Investigations have tended to focus on women; including more men in these studies is desirable. In addition, most studies of health outcomes related to weight and of treatment efficacy have been carried out in people of European origin. Because certain ethnic groups have a disproportionate prevalence of obesity, including black populations, Mexican Americans, American Indians, and Alaska Natives, this area needs further attention. Limited evidence suggests that mortality risk is not as closely linked with body mass in African Americans as in European Americans. However, the prevalence of diabetes, hypertension, and heart disease is clearly disproportionate in black populations, suggesting that the elevated risk for these conditions in the presence of obesity that has been established in white samples is not specific to race. Further evaluation is needed to clarify these links.

Clarifying Costs and Cost-Effectiveness

At the outset of this work, we had intended to examine issues of costs and cost-effectiveness of screening and treatment options, as a means of understanding the financial ramifications of addressing this clinical problem in the face of its demonstrable financial impact on patients, health budgets, and the economy. In the end, constraints of time and resources and the paucity of new relevant literature meant that we did not pursue this question further. Moreover, we doubt the utility of pursuing cost or cost-effectiveness with respect to use of BMI

as the screening tool; it is for all intents and purposes costless and is clearly the screening measure of choice for both clinical and research applications.

We note, however, that significant questions ought to be subjected to economic investigation, which could take several directions. First are questions of documenting better both direct and indirect costs of treatment for specific interventions *within* the 3 broad types of treatments we have dealt with in this review. Such data would enable researchers and policymakers to determine better, for example, the cost-effectiveness of different approaches for providing diet and exercise counseling, whether or not they are coupled with additional behavioral interventions. Obviously, the same is true for pharmaceutical interventions and surgical options. Second, and far more challenging, are questions of costs and relative cost-effectiveness of options *across* these 3 categories. Finally, understanding better the costs and cost-effectiveness of various options directed at special patient populations (eg, only overweight, obese, or extremely obese; populations defined by ethnic and cultural background) will be of important long-term benefit for policymaking at both the clinical and health plan levels.

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Appendix A
Evidence Tables

Glossaries

Codes for Evidence Table 1

Code or Abbreviation	Definition
Intervention Mode: Group	Group-based
Intervention Mode: Individual	Individual-based
Intervention Intensity: Low	<1 encounter/month (first 3 mos)
Intervention Intensity: Moderate	1 encounter/month (first 3 mos)
Intervention Intensity: High	>1 encounter/month (first 3 mos)
Trial Type Loss	Weight loss
Trial Type Main	Maintenance of weight loss
Intervention Type: D	Diet
Intervention Type: E	Exercise
Intervention Type: B	Behavioral

Appendix A. Evidence Tables

Abbreviations for All Evidence Tables and Appendices

Code or Abbreviation	Definition
ASGB	Adjustable silicone gastric banding
approx	approximately
B	Behavior, behavioral therapy
bid	Twice a day
BMI	Body mass index
BP	Blood pressure
BPM	Beats per minute
BT	Behavioral therapy
CA	Cancer
CVD	Cardiovascular disease
D	Diet, dietary intervention
diff	Difference
dL	Deciliter
DM	Diabetes mellitus
dx	Diagnosis
E	Exercise, exercise intervention
Ed	Education
EGP	Esophagogastric placement
ETOH	Excess alcohol use
F	Female
FPG	Fasting plasma glucose
f/u	Follow-up
G	Group
GI	Gastrointestinal
HbA1c	Hemoglobin A1c
I	Individual
Int	Intervention
Kcal/d	Kilocalories/day
kg	Kilogram
L	Loss
LASGB	Laproscopic adjustable silicone gastric banding
lb	Pound
LCD	Low-calorie diet
LDL	Low-density lipoprotein
LOCF	Last observation carried forward analysis
M	Male, maintenance
m^2 (or kg/m^2)	Meters squared
MI	Myocardial infarction
MJ	Megajoule
mm	Millimeters
mmol/l	Millimoles per liter
mo	Month
n	Number
NR	Not reported
NS	Not significant
OASGB	Open adjustable silicone gastric banding
P	P-value
PA	Physical activity
PCP	Primary Care Provider
PE (or PE Ed)	Physical exercise (education)

qd	Once a day
RGP	Retrogastric placement
SES	Socio-economic status
s.e.	Standard error
Signif	Significant
tid	Three times a day
tit	Titrate
tx	Treatment
VLCD	Very-low-calorie diet
vs	Versus
wk	Week
w/o	Without
Wt	Weight
Yr	Year

Appendix A. Evidence Tables

Evidence Table 1. Randomized Controlled Trials of Counseling and Behavioral Interventions

Citation	Intervention Mode/ Intensity	Trial Type	Intervention Type	Baseline Weight
Stevens et al, 2001[69]	Group and individual/ high	Loss and main	D/E/B	Mean BMI: Men: 31 Women: 31
Kuller et al, 2001[65]	Group and individual/ high	Loss and main	D/E/B	Mean BMI: 25
Tuomilehto et al, 2001[66]	Group/ high	Loss	D/E/B	Mean BMI: 31
Fogelholm et al, 2000[74]	Group/ high	Loss and main	D/E/B	Mean BMI: 34
Diabetes Prevention Program, 2000[79]	Group/individual high	Loss and main	D/E/B	Mean BMI: 34
Jakicic et al, 1999[71]	Group/ high (diet individualized)	Loss	D/E/B	Wt: 20%-75% higher than ideal body wt
Jones et al, 1999[68]	Group and individual/ High	Loss	D/B	Mean BMI: 34
Sbrocco et al, 1999[73]	Group/ high	Loss	D/E/B	Mean BMI: 33
Wadden et al, 2001[52]	Group/ high	Loss	D/E/B	BMI: 36-39

Evidence Table 1. Randomized Controlled Trials of Counseling and Behavioral Interventions (cont)

Time Interval	Delta (Vs Control Unless Noted)	*P* Value	Loss to Follow-up	Quality Comments
18 mos 36 mos	-2.7 kg -2.0 kg	*P* ≤ 0.001	8% at 36 mos	Good
54 mos	-5.4 lb	*P* ≤ 0.001	Overall, 5% loss at 54 mos	Good
1 yr 2 yrs 1 yr	-3.4 kg -2.7 kg -30% with at least 5% wt reduction	*P* ≤ 0.001 *P* ≤ 0.001 *P* = 0.001	8% loss	Good
1 yr (12 wks L, 40 wks M) 2 yrs	1st PA program: -2.7 kg 2nd PA program: -2.6 kg 1st PA program: -3.8 kg 2nd PA program: -0.5 kg	*P* = 0.06 (group diff) *P* = 0.07 (group diff)	Overall 10% loss	Fair
2.8 yrs	-2.1 kg (metformin) -5.6 kg (lifestyle) -0.1 kg (placebo)	*P* ≤ 0.001	Overall 7.5% dropout	Good minorities over-represented
18 mos	-3.7 kg (BT and short bouts of PA with (vs w/o) home equipment lost more wt)	*P* ≤ 0.05 NS difference other PA groups	22% dropout overall (13%-29% each group)	Fair High dropout
6 mos 12, 18, 24, 30 mos	-1.4 kg not reported	*P* = 0.05 NS	Overall 9% dropout	Fair
12 mos	-5.76 kg (behavioral choice tx led to more wt loss than traditional BT)	*P* ≤ 0.01	17% loss (n = 2)	Fair
1 yr 1 yr	-7.3 kg: addition of lifestyle intervention to sibutramine -12.8 kg: addition of lifestyle intervention + diet to sibutramine	*P* ≤ 0.05 *P* ≤ 0.05	32% dropout (6/19)	Fair

Evidence Table 1. Randomized Controlled Trials of Counseling and Behavioral Interventions (cont)

Citation	Intervention Mode/ Intensity	Trial Type	Intervention Type	Baseline Weight
Ashley et al, 2001[80]	Group and individual/ high	Loss	D/E/B	BMI: 25-35
Wing and Anglin, 1996[76]	Group/ high	Loss	D/E/B	Mean BMI: Black: 37 White: 38
Lindholm et al, 1995[77]	Group/ moderate	Loss	D/E	Mean BMI: Int M: 27 Int F: 30 Control M: 27 Control F: 29
Swinburn et al, 1999[70]	Group/ moderate	Loss	B/E	Intervention: 84 kg Control: 85 kg
Jeffery and French, 1997[75]	Group/ low	Loss	D/E	Mean BMI: Men: 28 Women: 26-28

Evidence Table 1. Randomized Controlled Trials of Counseling and Behavioral Interventions (cont)

Time Interval	Delta (Vs Control Unless Noted)	*P* Value	Loss to Follow-up	Quality Comments
1 yr	-3.7 kg: Addition of meal replacements	$P \leq 0.05$	38% dropout (14/37)	Fair
	-0.1 kg: Addition of meal replacements and intervention not taking place at primary care physicians office	Not reported	32% dropout (12/38) 34% dropout (13/38)	Less than 100 per group
1 yr	Black (approx): -2 kg (BT + VLCD instead of LCD)	Not reported	19% dropout (19/93)	Fair
	White (approx): -4 kg (BT + VLCD instead of LCD)	Not reported		Results reported by race, not by intervention (graph only no variance data)
18 mos	-0.09 kg/m^2	NS	6% dropout	Good
18 mos	-0.25 kg	NS		
12 mos	-3.5 kg	$P \leq 0.001$	38% without full data	Fair, high dropout
12 mos	<u>Men:</u> Diet & PA Education: -1.22 lb Diet & PA Ed + lottery: -1.73 lb <u>Women:</u> High-SES: Diet & PA Education: -0.35 lb Diet & PE Ed.+ lottery: -0.87 lb Low-SES: Diet & PA Education: 0.81 lb Diet & PE Ed + lottery: 1.93 lb	<u>Men:</u> Both tx NS vs control <u>Women:</u> High-SES: Both tx NS vs control Low-SES: Both tx NS vs control	14% dropout	Good

Evidence Table 1. Randomized Controlled Trials of Counseling and Behavioral Interventions (cont)

Citation	Intervention Mode/ Intensity	Trial Type	Intervention Type	Baseline Weight
Bemelmans et al, 2000[81]	Group/ low	Loss	D	Mean BMI: 30
Leermakers et al, 1999[72]	Group/ high	Main	D/E/B	Mean BMI: 31
Rothacker et al, 2001[67]	Individual/ low	Main	D	Mean BMI: 25 Meal replacement: 75 kg Traditional food: 78 kg
OXCHECK Study Group, 1995[78]	Individual/ low	Loss	D	Not reported

Evidence Table 1. Randomized Controlled Trials of Counseling and Behavioral Interventions (cont)

Time Interval	Delta (Vs Control Unless Noted)	*P* Value	Loss to Follow-up	Quality Comments
52 wks	Men: 0.1kg/m^2 Women: 0 kg/m^2	NS NS	Overall 8% dropout	Fair (but, non-randomized) Netherlands population
18 mos	-2.1 kg (less wt regain with wt-focused vs PA-focused program)	$P \leq 0.05$	15% loss 1st 6 mos 28% did not complete 18 mos	Fair ITT used conservance assumptions that all dropouts returned to their baseline wt
18 mos	-36% (extra portion of wt loss maintained with wt-focused vs PA-focused program)	$P \leq 0.01$		
1 yr	-5 kg	$P \leq 0.001$	17% loss	Fair
3 yrs	At f/u: those with health checks were 0.38 kg/m^2 less than control patients	$P \leq 0.05$	25% dropout	Fair

*B, behavior; BMI, body mass index; BT, behavioral therapy; D, diet; E, exercise; F, female; f/u, follow-up; Int, Intervention; L, loss; LCD, low-calorie diet; M, maintenance, male; m2, meters squared; NS, not significant; PA, physical activity; PE (or PE Ed), physical exercise (education); SES, socio-economic status; tx, treatment; VLCD, very-low-calorie diet; w/o, without; HbA1C, Hemoglobin A1c.

Appendix A. Evidence Tables

Evidence Table 2. Randomized Controlled Trials of Pharmacotherapy for Weight Loss: Sibutramine

Citation	Participants		Intervention Drug, Frequency, Time
	Number, Demographics	How Recruited	
Fujioka, et al, 2000[84]	N: 175 Sibutramine: 89 Placebo: 86 <u>Female:</u> Sibutramine: 38 Placebo: 44 <u>Male:</u> Sibutramine: 51 Placebo: 42 <u>Age:</u> Sibutramine: 53.5 yrs Placebo: 55 yrs <u>BMI:</u> Sibutramine: 34.1 (mean) Placebo: 33.8 (mean)	Multi-center (16 centers in U.S.) Recruitment method: unspecified <u>Included:</u> Age: ≥ 18 BMI: ≥ 27-40 At least 1 unsuccessful attempt to lose wt by dieting Diabetes, with stable treatment by diet or a single oral agent <u>Excluded:</u> Patients with: serious cardiovascular disease, metabolic disease, history of drug or alcohol abuse, in need of anti-depressant agents Patients receiving medications to influence body wt	Sibutramine: tit up to 20 qd placebo 24 wks <u>Co-interventions:</u> 250-500 kcal/d caloric deficit diet Individual dietary counseling Interval clinical assessments and measurements of FPG performed

Evidence Table 2. Randomized Controlled Trials of Pharmacotherapy for Weight Loss: Sibutramine (cont)

Results/Outcomes		Quality Comments
Weight Loss	**Adverse Effects**	
Mean kg Change: Sibutramine: -3.7 kg Placebo: -0.4 kg *P* < 0.5 Freq 5% wt loss: Sibutramine: 26% *P* < 0.001 Freq 10% wt loss: Sibutramine: 4.8% *P* < 0.12	Sibutramine: Dropout rate: 29/89 Dropout rate due to adverse event: 9/89 Placebo: Dropout rate: 25/86 Dropout rate due to adverse event: 10/86	Fair Very select population, high loss to f/u, adherence not reported

Evidence Table 2. Randomized Controlled Trials of Pharmacotherapy for Weight Loss: Sibutramine (cont)

Citation	Participants		Intervention Drug, Frequency, Time
	Number, Demographics	How Recruited	
Gokcel et al, 2001[85]	N: 60 Gender: Female Age: Sibutramine: 46.93±1.62 Placebo: 49.28±1.34 BMI: Sibutramine: 39.3 (mean) Placebo: 37.4 (mean)	Baskent University Endocrinology and Metabolism Clinic Recruitment method: referred due to poor glucose control Included: Patients with Type II Diabetes and HbA1c > 8, with maximum doses of metformin and sulfonylureas Excluded: Pregnancy, uncontrolled hypertension, glaucoma Patients receiving medications that may influence body wt	Sibutramine: 10 bid placebo 24 wks Co-interventions Monthly clinic visits Physical exam at each visit Initial dietary counseling maintenance diet

Evidence Table 2. Randomized Controlled Trials of Pharmacotherapy for Weight Loss: Sibutramine (cont)

Results/Outcomes		Quality Comments
Weight Loss	**Adverse Effects**	
Mean kg change: Sibutramine: -3.9 kg Placebo: 0.36 kg *P* < 0.0001	Sibutramine: Dropout rate: 1/30 Dropout rate due to adverse event: 1/30 Placebo: Dropout rate: 5/30 Dropout due to adverse event: not reported	Fair Group change only Incomplete side-effect or adherence information Small study set in Turkey

Evidence Table 2. Randomized Controlled Trials of Pharmacotherapy for Weight Loss: Sibutramine (cont)

Citation	Participants		Intervention Drug, Frequency, Time
	Number, Demographics	How Recruited	
James et al, 2000[83]	N: 467 Sibutramine: 352 Placebo: 115 Female: Sibutramine: 294 Placebo: 96 Male: Sibutramine: 58 Placebo: 19 Age: 17-65 yr Sibutramine: 40.7 (mean) Placebo: 40.4 (mean) BMI: Sibutramine: 36.5 (mean) Placebo: 36.6 (mean)	8 European centers Recruitment method: not given Included: BMI of 30-45 Excluded: Recent wt change Many specified diseases including diabetes and hypertension Drugs: anorectic; B-blockers; B-agonists	Sibutramine: 10-20 qd placebo 80 wks Co-interventions: 600 kcal deficit diet (individualized)

Evidence Table 2. Randomized Controlled Trials of Pharmacotherapy for Weight Loss: Sibutramine (cont)

Results/Outcomes		Quality Comments
Weight Loss	**Adverse Effects**	
Mean kg change: Sibutramine: -4 kg *P* < 0.001	Sibutramine: Dropout rate: 148/352 Dropout rate due to adverse event: 48/352 Adverse event rate: not reported per person Placebo: Dropout rate: 58/115 Dropout rate due to adverse event: 6/115 Adverse event rate: not reported per person	Fair No dose titration, high dropout, many exclusion criteria

Evidence Table 2. Randomized Controlled Trials of Pharmacotherapy for Weight Loss: Sibutramine (cont)

Citation	Participants		Intervention Drug, Frequency, Time
	Number, Demographics	How Recruited	
Smith and Goulder, 2001[86]	N: 485 Female: Sibutramine 10 mg: 128 Sibutramine 15 mg: 131 Placebo: 131 Male: Sibutramine 10 mg: 33 Sibutramine 15 mg: 30 Placebo: 32 Age: 18-65 yr Sibutramine 10 mg: 41.0 (mean) Sibutramine 15 mg: 42.7 (mean) Placebo: 41.9 (mean) BMI: Sibutramine 10 mg: 32.9 (mean) Sibutramine 15 mg: 32.7 (mean) Placebo: 32.4 (mean)	Primary care setting Recruitment Method: via PCPs Included: Healthy people Age 18-65 BMI of 25-44 Excluded: Wt loss ≥ 3 kg last 3 mos Obesity of endocrine origin Diabetes mellitus Vital sign Abnormalities Patients receiving drugs altering body wt Inability to follow dietary advice	Sibutramine: 10 qd Sibutramine: 15 qd lacebo 52 wks Co-interventions: Dietary advice

Evidence Table 2. Randomized Controlled Trials of Pharmacotherapy for Weight Loss: Sibutramine (cont)

Results/Outcomes		Quality Comments
Weight Loss	**Adverse Effects**	
Mean kg change: Sibutramine: 10 qd: -4.4 kg Placebo: -1.6 kg Sibutramine: 15 qd: -6.4 kg Placebo: -1.6 kg *P* < 0.01 Freq 5% wt loss: Sibutramine 10 qd: 19% Sibutramine 15 qd: 37% *P* < 0.01 Freq 10% wt loss: Sibutramine 10 qd: 12% Sibutramine 15 qd: 27% *P* < 0.01	Sibutramine 10 mg: Dropout rate: 67/161 Dropout rate due to adverse event: 2/161 Adverse event rate: 20/161 Sibutramine 15 mg: Dropout rate: 79/161 Dropout rate due to adverse event: 2/161 Adverse event rate: 18/161 Placebo: Dropout rate: 83/163 Dropout rate due to adverse event: 4/163 Adverse event rate: 24/163	Fair Very high attrition, generally healthy group, LOCF

Evidence Table 2. Randomized Controlled Trials of Pharmacotherapy for Weight Loss: Sibutramine (cont)

Citation	Participants		Intervention Drug, Frequency, Time
	Number, Demographics	How Recruited	
Wirth and Krause, 2001[87]	N: 1,001 Sibutramine (continuous): 405 Sibutramine (intermittent): 395 Placebo: 201 Female: Sibutramine (continuous): 302 Sibutramine (intermittent): 311 Placebo: 155 Male: Sibutramine (continuous): 103 Sibutramine (intermittent): 84 Placebo: 46 Age: Sibutramine (continuous): 43.1 Sibutramine (intermittent): 42.6 Placebo: 44.0 BMI: Sibutramine (continuous): 34.7 (mean) Sibutramine (intermittent): 34.9 (mean) Placebo: 35.0 (mean)	108 private practices and 3 hospital outpatient departments in Germany Recruitment method: unspecified Included: Age: 18-65 yrs. BMI: 30-40 At least 1 unsuccessful attempt to lose wt by dieting Excluded: Patients with: serious cardiovascular disease, metabolic disease, history of drug or alcohol abuse, in need of anti-depressant agents Patients receiving medications to influence body wt	Sibutramine: 15 qd (continuous) Sibutramine: 15 qd (intermittent) placebo 44 wks Co-interventions: Physician counseling for wt loss Written dietary information Physical exams during interval visits

Evidence Table 2. Randomized Controlled Trials of Pharmacotherapy for Weight Loss: Sibutramine (cont)

Results/Outcomes		Quality Comments
Weight Loss	**Adverse Effects**	
Mean kg change: Sibutramine (continuous): -3.8 kg Placebo: -0.2 kg. Sibutramine (intermittent): -3.3 kg Placebo: -0.2 kg. *P* < 0.001 Freq 5% wt loss: Sibutramine (continuous): 30% Sibutramine (intermittent): 28% *P* < 0.001 Freq 10% wt loss: Sibutramine (continuous): 19% Sibutramine (intermittent): 20% *P* < 0.001	Sibutramine (continuous): Dropout rate: 79/405 Dropout rate due to adverse event: 25/405 Adverse event rate: 303/405 Sibutramine (intermittent): Dropout rate: 80/395 Dropout rate due to adverse event: 13/395 Adverse event rate: 283/395 Placebo: Dropout rate: 55/201 Dropout rate due to adverse event: 9/201 Adverse event rate: 151/201	Good

Evidence Table 2. Randomized Controlled Trials of Pharmacotherapy for Weight Loss: Sibutramine (cont)

Citation	Participants		Intervention Drug, Frequency, Time
	Number, Demographics	How Recruited	
Dujovne et al, 2001[88]	N: 222 Sibutramine: 162 Placebo: 160 Gender: Female Sibutramine: 56% Placebo: 51% Age: Sibutramine: 45 Placebo: 46 BMI: Sibutramine: 35.1 Placebo: 35.5	13 study centers Included: BMI ≥ 27 TG ≥ 250 or ≤ 1000 mg/dL HDL ≤ 45 women ≤ 40 men Only those with ≥ 75% compliance during run-in were enrolled Excluded: Recent wt loss, ETOH, uncontrolled hypertension, h/o of medical condition affecting major organ system including DM, CVD, CA, signif psycho dysfunction, recent substance addiction	Sibutramine: 20 mg qd placebo 24 wks Co-interventions: Female: 1500 kcal/d Male: 1800 kcal/d

Evidence Table 2. Randomized Controlled Trials of Pharmacotherapy for Weight Loss: Sibutramine (cont)

Results/Outcomes		Quality Comments
Weight Loss	**Adverse Effects**	
Mean kg change: Sibutramine: -4.9 Placebo: -0.6 *P* ≤ 0.05 BMI change: Sibutramine: -1.7 Placebo: -0.2 *P* = not reported Freq 5% wt loss: Sibutramine: 42% Placebo: 8% *P* ≤ 0.05 Freq 10% wt loss: Sibutramine: 12% Placebo: 3% *P* ≤ 0.05	Sibutramine Dropout rate: 29.6% Dropout rate due to adverse event: 9.9% Dropout rate for hypertension: 0.6% Change in systolic blood pressure: +4 mm Change in diastolic blood pressure: 3.6 mm Change in pulse: +6.8 bpm Placebo: Dropout rate: 33.8% Dropout rate due to adverse event: 6.9% Dropout rate for hypertension: 1.9% Change in systolic blood pressure: +2 mm (NS different vs drug arm) Change in diastolic blood pressure: +1.0 mm (*P* ≤ 0.05 vs drug arm) Change in pulse: +0.1 bpm (*P* < 0.05 vs drug arm)	Fair LOCF 30% dropout

*BMI, body mass index; bid, twice a day; bpm, beats per minute; CA, cancer; CVD, cardiovascular disease; dL, deciliter; DM, diabetes mellitus; ETOH, excess alcohol use; FPG, fasting plasma glucose; f/u, follow-up; HbA1c, Hemoglobin A1c; h/o, history of; Kcal/d, kilocalories/day; LOCF, Last observation carried forward analysis; mm, millimeters; N, number; PCP, primary care provider; qd, once a day; signif, significant; tit, titrate.

Evidence Table 3. Randomized Controlled Trials of Pharmacotherapy for Weight Loss: Orlistat

Citation Design	Participants		Intervention Drug, Frequency, Time
	Number, Demographics	How Recruited	
Hill et al, 1999[90]	N: 729 Orlistat 30 mg: 187 Orlistat 60 mg: 173 Orlistat 120 mg: 181 Placebo: 188 Age: Orlistat 30 mg: 46.8±0.8 Orlistat 60 mg: 46.1±0.7 Orlistat 120 mg: 45.9±0.7 Placebo: 46.4±0.7 BMI: Orlistat 30 mg: 32.6 (mean) Orlistat 60 mg: 32.9 (mean) Orlistat 120 mg: 32.8 (mean) Placebo: 32.8±0.2 (mean)	17 clinical research centers in the U.S. Recruitment method: via PCPs Included: Age: ≥ 18 yrs BMI: 28-43 Obese subjects with ≥ 8% loss of body wt in 6-mo lead-in Excluded: Significant medical disorders including hypertension and diabetes Patients receiving medications that may influence body wt	Orlistat: 30 mg tid Orlistat: 60 mg tid Orlistat: 120 mg tid placebo 52 wks Co-interventions: Clinic visits every 2 wks Maintenance diet Dietary counseling Encouraged to increase activity Multi-vitamin 4-session behavioral modification program in lead-in
Muls et al, 2001[91]	N: 294 Orlistat: 147 Placebo: 147 (but 3 withdrew early) Gender: Female Orlistat: 82% Placebo: 78% Mean age: (range 18-70) Orlistat: 50 Placebo: 48 Mean BMI: (range 27-40) Orlistat: 33 Placebo: 33	19 centers in Belgium	Orlistat: 120 mg tid placebo 24 wks Co-intervention: Hypocalorie diet

Evidence Table 3. Randomized Controlled Trials of Pharmacotherapy for Weight Loss: Orlistat (cont)

Results/Outcomes		Quality Comments
Weight Loss	**Adverse Effects**	
Mean kg change: Orlistat 30 mg: +0.5 kg Orlistat 60 mg: -0.6 kg Orlistat 120 mg: -1.8 kg *P* < 0.001	Orlistat 30 mg: Dropout rate: 47/187 Dropout rate due to adverse event: 17/187 Orlistat 60 mg: Dropout rate: 40/173 Dropout rate due to adverse event: 17/173 Orlistat 120 mg: Dro-out rate: 55/181 Dropout rate due to adverse event: 27/181 Placebo: Dropout rate: 50/188 Dropout rate due to adverse event: 5/188	Fair Gender differential not quantified Very select patient population Race/ethnicity distributions differ among the 3 dosing regiments
Mean kg change: Orlistat: -4.66 Placebo: -1.88 *P* ≤ 0.001 Mean % wt change: (Not including run-in) Orlistat: -5.3 Placebo: -2.3 *P* ≤ 0.001 Freq 5% wt loss: Orlistat: 64% Placebo: 39% *P* = not reported Freq 10% wt Loss: Orlistat: 23% Placebo: 13% *P* = not reported	Orlistat: Dropout rate: 19/147 Adverse event rate: 80% (*P* = 0.016 vs placebo) Placebo: Dropout rate: 20/147 Adverse event rate: 67%	Good

Evidence Table 3. Randomized Controlled Trials of Pharmacotherapy for Weight Loss: Orlistat (cont)

Citation	Participants		Intervention Drug, Frequency, Time
	Number, Demographics	How Recruited	
Rissanen et al, 2001[96]	N: 55 Orlistat: 25 Placebo: 26 Only 51 completed trial Gender: Female Mean age: 44 (s.e. = 0.7) Mean BMI: 36.2 (s.e. = 0.5	Healthy Finnish women	Orlistat: 120 mg tid placebo 12 mos Co-intervention: 600 Kcal deficit diet adjusted for actual body wt and daily activities
Karhunen et al, 2000[91]	N: 72 (59 women, 13 men) Age: 43.4±6.0 y BMI: 35.9±3.9 kg/m^2	2 centers (Kuopio and Helsinki) in Finland Recruitment method: Occupational health care systems Included: BMI of 30-43 Age ≥ 18 Excluded: Many specified diseases including diabetes and uncontrolled hypertension Eating disorders	Orlistat: 120 mg tid placebo (rerandomized after 1 yr) Interventions: Dietary advice 0-52 wks (loss phase of 104 wk trial)

Evidence Table 3. Randomized Controlled Trials of Pharmacotherapy for Weight Loss: Orlistat (cont)

Results/Outcomes		Quality Comments
Weight Loss, BP, Lipids	**Adverse Effects**	
Mean kg change: Orlistat: -13 Placebo: -7.2 *P* = NS	Dropout rate: 4/55 Dropout and adverse event rates not reported by intervention status	Fair
Mean kg change: Orlistat: -13.1 kg Placebo: -8.6 kg *P* = 0.007	No data	Fair Group change only No data on adverse effects No gender-breakdown by group

Evidence Table 3. Randomized Controlled Trials of Pharmacotherapy for Weight Loss: Orlistat (cont)

Citation Design	Participants		Intervention Drug, Frequency, Time
	Number, Demographics	How Recruited	
Micic et al, 1999[92]	N: 119 Orlistat 120 mg: 60 Placebo: 59 Age: 18-75 (range) BMI: Orlistat: 34.8 (mean) Placebo: 35.2 (mean)	Referent Yugoslav endocrinology centers Recruitment method: not mentioned Included: BMI ≥ 30 kg/m^2 Serum LDL cholesterol ≥ 4.2 mmol/l If female, use of adequate contraception Excluded: Total serum triglyccrides > 4.5 mmol/l Many specified diseases including diabetes Patients receiving drugs altering body wt	Orlistat: 120 tid placebo 24 wks Co-interventions: Hypocaloric diet with dietary advice Monthly MD visits

Evidence Table 3. Randomized Controlled Trials of Pharmacotherapy for Weight Loss: Orlistat (cont)

Results/Outcomes		
Weight Loss	**Adverse Effects**	**Quality Comments**
Mean kg change: Orlistat: -10.75 kg Placebo: -7.34 kg *P* = 0.001	Orlistat: Dropout rate: 10/60 Dropout rate due to adverse event: 1/60 Adverse event rate: 18/60 Placebo: Dropout rate: 10/59 Dropout rate due to adverse event: not reported Adverse event rate: 7/59	Fair Individual-based wt results only in terms of “gain” or “loss” Yugoslavian population Small study

Evidence Table 3. Randomized Controlled Trials of Pharmacotherapy for Weight Loss: Orlistat (cont)

Citation Design	Participants		Intervention Drug, Frequency, Time
	Number, Demographics	How Recruited	
Van Gaal et al, 1998[89]	N: 613 Orlistat 30 mg: 122 Orlistat 60 mg: 123 Orlistat 120 mg: 120 Orlistat 240 mg: 117 Placebo: 123 Mean age: 40-44 Mean BMI: 34-35 kg/m^{-2}	14 centers in Austria, Belgium, Brazil, Finland, Germany, Italy, Sweden, Switzerland, United Kingdom Recruitment method: not specified Included: BMI of 28-43 Good compliance in run-in Excluded: Wt loss > 4 kg last 3 mos Many specified diseases including diabetes and hypertension Patients receiving drugs altering body wt Pregnancy/lactation	Orlistat: 30 tid Orlistat: 60 tid Orlistat: 120 tid Orlistat: 240 tid placebo 52 wks Co-interventions: Hypocaloric diet Dietary advice from dietician

Evidence Table 3. Randomized Controlled Trials of Pharmacotherapy for Weight Loss: Orlistat (cont)

Results/Outcomes		Quality Comments
Weight Loss	**Adverse Effects**	
Mean kg change: Orlistat 30: -2% Orlistat 60: -2.3% Orlistat 120: -3.3% Orlistat 240: -2.8% *P* ≤ 0.001 Frequency of 10% wt loss: Orlistat 30: 9% Orlistat 60: 9% Orlistat 120: 18% Orlistat 240: 19% *P* = not reported	Orlistat 30 mg: Dropout rate: 29/122 Dropout rate due to adverse event: 7/122 Adverse event rate: 79% Orlistat 60 mg: Dropout rate: 29/124 Dropout rate due to adverse event: 6/124 Adverse event rate: 83% Orlistat 120 mg: Dropout rate: 23/122 Dropout rate due to adverse event: 2/122 Adverse event rate: 84% Orlistat 240 mg: Dropout rate: 20/120 Dropout rate due to adverse event: 3/120 Adverse event rate: 87% Placebo: Dropout rate: 27/125 Dropout rate due to adverse event 3/125 Adverse event rate: 69%	Fair Multiple countries, adequate outcomes, but very select population, no race data

*BMI, body mass index; BP, blood pressure; Kcal, kilocalories; kg/m2, meters squared; mmol/l, millimoles per liter; N, number; *P*, P-value; PCP, primary care provider; s.e., standard error; tid, three times daily.

Appendix A. Evidence Tables

Evidence Table 4. Randomized Controlled Trials of Pharmacotherapy for Weight Loss: Metformin

Citation Design	Participants		Intervention Drug, Frequency, Time
	Number, Demographics	How Recruited	
Giugliano et al, 1993[95]	N: 50 Metformin: 27 Placebo: 23 Female: Metformin: 17 Placebo: 14 Male: Metformin: 10 Placebo: 9 Age: Metformin: 60 (mean) Placebo: 60.8 (mean) BMI: Metformin: 33 (mean) Placebo: 32.7 (mean)	17 Clinical research centers in the U.S. Recruitment method: not reported Included: DM on insulin, dx after age 40 DM > 3 yrs Inadequate glucose control despite therapy oral > 1 yr Excluded: Age > 70 Creatinine > 1.2 Ischemic or wasting disease Acute severe disease	Metformin: 850 bid placebo 6 mos Co-interventions: Patients seen on outpatient basis 1 mo interval visits Body wt and BP

Evidence Table 4. Randomized Controlled Trials of Pharmacotherapy for Weight Loss: Metformin (cont)

Results/Outcomes		
Weight Loss	**Adverse Effects**	**Quality Comments**
Data in graph form P = NS	Not reported	Fair/good No information on the population involved BMI results graphed, without actual numbers Small sample size

*bid, twice a day; BP, blood pressure; DM, diabetes mellitus; dx, diagnosis, N, number; NS, not significant; *P*, P-value.

Appendix A. Evidence Tables

Evidence Table 5. Randomized Controlled Trials of Surgical Therapies for Obesity

Citation Design	Participants		Intervention Time, Surgical Procedure
	Number, Demographics	How Recruited	
de Wit et al, 1999[97] Open vs Laparoscopic Adjustable Silicone Gastric Banding (ASGB)	N: 50 Laparoscopic ASGB: 25 Open ASGB: 25 Sex ratio: (M/F) Laparoscopic ASGB: 8/17 Open ASGB: 8/17 Age: 18-55 yrs. Mean BMI: Laparoscopic ASGB: 51 Open ASGB: 50	Recruitment method: Gastroenterology Outpatient Clinic Included: Obesity > 5 yrs with documented prior wt loss attempts BMI > 40 kg/m^2 Excluded: Previous gastric surgeries Large hiatal hernias Alcohol abuse Pregnancy Psychiatric disease/treatment Hormonal or genetic obesity-related diseases	18 mos Laparoscopic ASGB Open ASGB
Weiner et al, 2001[98] Open vs Laparoscopic Adjustable Silicone Gastric Banding (ASGB)	N: 101 RGP: 51 EGP: 50 Sex: (Female/Male) RGP: 42/8 EGP: 44/7 Mean Age: RGP: 35 (18-54) EGP: 35 (19-52) Mean BMI: (kg/m_2) RGP: 50 EGP: 49	Nordwest Hospital, Frankfurt, Germany Included: Patients who underwent a laproscopic ASGB between May 1996 and August 1999 at the Nordwest hospital	18 mos Retrogastric placement Esophagogastric placement

Evidence Table 5. Randomized Controlled Trials of Surgical Therapies for Obesity (cont)

Results/Outcomes		Quality Comments
Weight Loss	**Adverse Effects**	
Mean wt loss: Laparoscopic ASGB: 35 kg Open ASGB: 34 kg NS difference between groups, significant change ($P < 0.05$) both groups over time	Readmissions: LASGB: 6 OASGB : 15 (NS) Surgical complications: LASBG: 1 OASGB : 8 (NS)	Fair Group-data only No co-morbidity information No co-intervention information
Mean wt loss: RGP: > 43 kg EGP: > 46 kg	Intra-operative complications: RGP: 0 EGP: 0 Post-operative complications: RGP: 0 EGP: 3 Deaths: 0 Hunger at 18 mo: RGP: 3 EGP: 1 GI esophagitis at 18 mo: RGP: 1 EGP: 1	Fair No individual-based outcome data No co-morbidity data No co-interventions specified

*ASGP, Adjustable Silicone Gastric Banding; BMI, body mass index; EGP, Esophagogastric placement; F, female; kg/m2, meters squared; LASGB, laproscopic adjustable silicone gastric banding; M, male; N, number; OASGB , open adjustable silicone gastric banding; PCP, Primary care provider; RGP, retrogastric placement.

Appendix A. Evidence Tables

Appendix B
Counseling Intervention Descriptions

Appendix B: Counseling Intervention Descriptions

Author	Population Description	Intervention Description
Stevens et al, 2001[69]	N: 1191 79% white, 18% black 66% male	3 yr program for control vs intervention. Intervention: group meetings and individual counseling focused on dietary change, physical activity, and social support.
Jakicic et al, 1999[71]	N: 148 Race NR 100% female	3 treatment arms with varying exercise regimens. All participants were prescribed the same amount of exercise, and instructed to reduce daily energy and fat intake. All groups with weekly group meetings in mos 1-6, biweekly in mos 7-12, and monthly in mos 13-18 focusing on behavioral strategies for modifying diet and exercise. LB: Long-bout exercise 5 d/wk: initially 20 min, up to 40 min/session by wk 9. SB: Short-Bout exercise 5 d/wk: same daily duration but divided into 10 min bouts. SBEQ: SB as above, but participants were provided with motorized treadmills.
Kuller et al, 2001[65]	N: 535 92% white 100% female	5 yr cognitive-behavioral program: intervention vs control. Intensive group program x 6 mos then individual and group sessions from 6-54 mos. Intervention participants were asked to lower dietary fat intake, saturated fat intake, and dietary cholesterol, for a modest wt loss goal of 5-15 lb, and to increase physical activity to 1000-1500 kcal/wk.
Bemelmans et al, 2000[81]	N: 42 Race NR Intervention group, 37% male; Control group 49% male	Intensive group education on the Mediterranean diet vs distribution of leaflet with Dutch nutritional guidelines. Intervention: 3 2 hr group meetings within the 1st 2-mos of the study, with a focus on education, establishment of a positive attitude, and improved skills in the preparation of Mediterranean diet food. Follow-up with an individualized letter about their adherence to Mediterranean nutritional guidelines.
Fogelholm et al, 2000[74]	N: 82 Race NR 100% female	Diet alone vs diet plus 1 of 2 40-wk moderate-intensity walking training programs. Dietary component was a low-energy diet with weekly small-group meetings focusing on wt loss and maintenance strategies. All participants had weekly small group meetings throughout the maintenance programs. 1st PA Regimen: targeted to expend 4.2 MJ/wk. 2nd PA Regimen: targeted to expend 8.4 MJ/wk.
Jones et al, 1999[68]	N: 102 Intervention group: 63% white, 37% black; Control group: 57% white, 43% black Intervention group: 45% male; Control group 51% male	Intervention vs control. Intervention: dietary counseling regarding food selection, preparation, and goals. No exercise advice. Counseling repeated once in 2-4 wks. Also twice monthly group support sessions x 3 mos then every 3-6 mos. Control: advised to lose wt -- no formal dietary counseling or group support.

Appendix B: Counseling Intervention Descriptions (cont)

Author	Population Description	Intervention Description
Sbrocco et al, 1999[73]	N: 24 Race NR 100% female	Behavioral Choice Treatment (BCT) vs Traditional Behavioral Therapy (TBT). All participants attended 13 weekly 1.5 hour group sessions, then group sessions at 3 and 6 mos. All participants were given 2-wk meal plans (BCT = 1800 kcal/day, TBT = 1200 kcal/day) and recipe booklets, and encouraged to walk 30 mins, 3 days a wk.
Swinburn et al, 1999[70]	N: 176 Intervention group: 69% European, 12% Maori, 14% Pacific Islander, 4% other; Control group: 75% European, 7% Maori, 14% Pacific Islander, 3% other Intervention group: 65% male; Control group 79% female	Monthly small-group meetings aimed at identifying and reducing dietary fat, with counseling included goal setting, self-monitoring, and evaluation. Control group received standard dietary information for healthy eating (comorbidity-specific).
Jeffery and French, 1997[75]	N: 822 (228 men, 594 women) Men were 94% white 27.7% male	Education alone, education plus a lottery incentive or control. Education included monthly newsletters and semi-annual classes on nutrition and exercise. Focus included weekly self-weighing, adequate fruit and vegetable intake, reduced intake of high-fat foods, moderate walking.
Lindholm et al, 1995[77]	N: 681 Race NR 85% male	Usual health advice vs usual advice plus 6 group sessions with a health care professional that included 5 videos of MI risk factors and discussion, practical advice for buying and cooking recommended foods, and information regarding local exercise facilities. The first 3 sessions were 90 mins and monthly. The 4th session lasted all day. 5th session at mo 12. 6th session 3-6 mos later. Usual health advice included instruction to reduce dietary fat, lose wt if necessary, exercise daily, stop smoking if appropriate. It was reinforced with a small pamphlet.
Imperial Cancer Research Fund OXCHECK Study Group, 1995[78]	N: 4121 Race NR 53% male	General-practice-based nurse-run health check vs no check. Check included medical history, lifestyle questionnaire, dietary assessment, height, wt, blood pressure, cholesterol measurement, with scheduled follow-up for patients with multiple risk factors.
Tuomilehto et al, 2001[66]	N: 522 Race NR 33% male	Diet plus physical activity counseling with behavioral therapy vs control. Intervention: 7 visits in 1st yr, then 4 times per yr (4 yr total). Control included basic counseling once a yr.

Appendix B: Counseling Intervention Descriptions (cont)

Author	Population Description	Intervention Description
Wadden et al, 2001[52]	N: 53 Race NR 100% female	Participants randomized to counseling adjuncts with sibutramine therapy, vs sibutramine therapy alone. Sibutramine plus lifestyle intervention: weekly groups for 20 wks with daily record-keeping. Sibutramine plus lifestyle intervention plus portion-controlled low-calorie diet.
Rothacker et al, 2001[67]	N: 75 Race NR 100% female	Participants randomized to 1 of 2 1200 kcal/day diets: Low-calorie liquid supplement to replace at least 1 meal/day vs low energy-low-fat food diet. Both plans with similar carbohydrate, fat, and protein composition.
Wing and Anglin, 1996[76]	N: 93 80% white, 17% black, 2% other white: 25% male; black 34% male	Two different diets delivered with behavioral therapy. Behavioral therapy included weekly sessions led by a multidisciplinary team, with discussions of nutrition, behavioral techniques, and exercise. 1st diet: low-calorie (1000-1200 kcal/day) 2nd diet: alternating low-calorie diet and very-low-calorie diet VLCD (VLCD: 500 kcal/day in wks 1-12 and 24-36).
Leermakers et al, 1999[72]	N: 66 94% white 20% male	Participants randomized to 1 of 2 maintenance programs following 6 mos of wt loss. Maintenance program was either exercise-focused or wt-focused. Exercise-focused maintenance program: 6 mos of biweekly group sessions: supervised exercise, payment for meeting exercise goals, competitions and prizes, training in relapse prevention. Wt-focused maintenance program: 6 mos of biweekly group sessions with therapist-led discussion on the maintenance of wt loss, including factors that represented an obstacle to maintaining wt loss. All participants kept track of diet and physical activity.
Knowler et al, 2002[79] (DPP)	N: 3234 55% white 32% male	Participants randomized to 1 of 3 groups, receiving metformin therapy (850 mg bid), lifestyle modification, or placebo. Lifestyle modification group received high intensity counseling for diet and exercise, as well as behavioral therapy.
Ashley et al, 2001[80]	N: 113 Race NR 100% female	Participants randomized to 1of 3 groups, Group A participated in 26 1-hr dietician-led group interventions over the course of 1 yr; Group B participated in 26 1-hr dietician-led group interventions over 1 yr and were given meal replacement; Group C received a 1 yr, 26 session (lasting 10-15 mins) program based in a primary care office, including a 1200 calorie diet incorporating meal replacements and walking.

*BCT, Behavioral Choice Treatment; Kcal/wk, kilocalories/week; MI, myocardial infarction; MJ, megajoule; N, number; NR, not reported; PA, physical activity; TBT, Traditional Behavioral Therapy; VLCD, very-low-calorie diet.

Appendix C
Descriptions of Intensive Counseling and Behavioral Intervention Studies

Appendix C: Descriptions of Intensive Counseling and Behavioral Intervention Studies

Study	Intervention	Intervention Setting	Intervention Delivery	Counseling and Behavioral Description
Stevens et al, 2001[69]	Control	Not noted	Not noted	Usual care (details not noted)
	Wt loss only	Not noted	Dieticians or health educators	One individual counseling session, then 14 weekly group meetings, then 6 biweekly group meetings, then monthly group meetings. After 18 mos, alternative options were offered, including individual counseling and special group sessions focused on selected wt 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 wt loss goals of no more than 0.9 kg per wk. Physical activity goal was for gradually increased activity to moderate-intensity activity (40%-55% of heart rate reserve) 30-45 mins per day, 4-5 days per wk. The primary exercise was brisk walking.
Diabetes Prevention Program, 2002[79]	Standard lifestyle + placebo:	Not noted	Not noted	Written information and an annual 20-30 min individual session emphasizing importance of healthy lifestyles. Advice included encouragement to follow the Food Guide pyramid and the equivalent of a National Cholesterol Education Program Step I diet, reduce wt, and increase physical activity.
	Intensive lifestyle:	Not noted	Case managers	16 session curriculum covering diet, exercise and behavior modification taught by case managers on a 1:1 basis in the first 24 wks. Flexible, culturally sensitive, and individualized. Subsequent individual (typically monthly) and group sessions with case managers to reinforce behavioral change.

Appendix C: Descriptions of Intensive Counseling and Behavioral Intervention Studies (cont)

Study	Intervention	Intervention Setting	Intervention Delivery	Counseling and Behavioral Description
Kuller et al, 2001[65]	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 rises in LDL cholesterol and wt gain, and increasing leisure-time activity. Intensive group program in the first 6 mos, then follow-up individual and group sessions from mos 6-54. Wt loss goal was 5-15 lbs, depending on baseline wt. Participants were asked to lower dietary fat intake and daily caloric intake. Lifestyle approach to increasing physical activity to 1000-1500 kcal expenditure weekly.

Appendix C: Descriptions of Intensive Counseling and Behavioral Intervention Studies (cont)

Study	Intervention	Intervention Setting	Intervention Delivery	Counseling and Behavioral Description
Tuomilehto et al, 2001[66]	Control	Not noted	Not noted	General oral and written information about diet and exercise at baseline and at subsequent annual visits. 3-day food diary at baseline and at each annual visit.
	Intervention	Not noted	Nutritionist	Detailed advice about how to achieve their wt loss, diet, and exercise goals. Participants met with the nutritionist 7 times over the 1st yr, then every 3 mos. Dietary advice was tailored to each subject based on quarterly food diaries, and included behavioral modification tips. Also, participants received individual guidance on increasing their 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.
Fogelholm et al, 2000[74]	Control (40 wk follow-up after 12-wk wt reduction program)	Not noted	Nutritionist (wt loss phase)	12-wk wt reduction program (wk 1: low energy diet based on meal-exchange; wks 2-9 VLCD; wks 10-12: low energy diets), with weekly small groups (5-12 participants) instructing on diet, wt 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 wt reduction program	Not noted	Nutritionist (wt loss phase) exercise instructor (maintenance phase)	12-wk wt 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 subjects 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.

Appendix C: Descriptions of Intensive Counseling and Behavioral Intervention Studies (cont)

Study	Intervention	Intervention Setting	Intervention Delivery	Counseling and Behavioral Description
Fogelholm et al, 2000[74] continued	Walking program (8.4 MJ/wk target expenditure) following 12-wk wt reduction program.	Not noted	Nutritionist (wt loss phase) exercise instructor (maintenance phase)	12 wk wt reduction program, then 40 wk walking wt maintenance program as described in the 4.2 MJ program above; only difference was increased targeted energy expenditure.
Jakicic et al, 1999[71]	Short-bout exercise	Not noted	Nutritionists, exercise physiologists, behavioral therapists	Behavioral wt loss program: group treatment meetings of diminishing frequency (weekly in mos 1-6, biweekly in mos 7-12, monthly in wks 13-18). 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 wt, with goal of 0.45-0.9 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 days/wk: initially 20 mins/day (wks 1 -4), increasing to 40 mins/day 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, behavioral therapists	Behavioral wt loss program as in the short-bout exercise arm. Exercise: daily total exercise amounts as described in the short-bout Exercise arm. Exercise was to be performed in one long-bout.
	Short-bout exercise with equipment	Not noted	Nutritionists, exercise physiologists, behavioral therapists	Behavioral wt loss program as in the short-bout exercise arm. Exercise: daily total exercise amounts as described in the short-bout exercise arm. Participants were provided with motorized home treadmills.

Appendix C: Descriptions of Intensive Counseling and Behavioral Intervention Studies (cont)

Study	Intervention	Intervention Setting	Intervention Delivery	Counseling and Behavioral Description
Jones et al, 1999[68]	Control	Not noted	Study nurse	Participants were told that they should lose wt, but received no formal diet counseling or group support.
	Wt loss	Not noted	Registered dietician	Patients individually counseled within 10 days of randomization, and 2-4 wks later. Content focused on food selection and preparation, and wt reduction goals were established. No exercise advice. They also met in groups twice monthly for 3 mos, then every 3-6 mos.
Sbrocco et al, 1999[73]	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 hr group sessions with 5-7 members per group. Participants received 2-wk meal plans and recipe booklets for a low fat (25%) diet: 1800 kcal/day. Diaries 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 encouraged to eat at a constant calorie level. Self-monitoring phased out before acute treatment ended. Participants were encouraged to complete a walking program 30 mins/day, 3 days/wk in a single bout. No formal exercise groups, but daily exercise logs. State purpose: to stop dieting and to view eating as a choice; to expect slower wt 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 wt, rather than focusing on how quickly wt can be lost.

Appendix C: Descriptions of Intensive Counseling and Behavioral Intervention Studies (cont)

Study	Intervention	Intervention Setting	Intervention Delivery	Counseling and Behavioral Description
Sbrocco et al, 1999[73], continued	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 (psych) were co-leaders	Weekly group sessions, meal plans, recipes, food diaries, and exercise as above, but with 1200 kcal/day diet. Stated purpose: to promote a substantial wt loss and to help develop habits and strategies to maintain this loss. Standard behavioral wt management techniques (eg self-monitoring, stimulus control, and behavioral substitution) were taught. Participants were encouraged to avoid eating and purchasing high-calorie foods, to lose wt 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[80]	Dietician-led lifestyle intervention	Not noted	Registered dietician	26 1-hr sessions over 1 yr. Participants received instruction manuals that included lessons based on an established wt control program (LEARN). Diet included a low-calorie diet (1200 kcal/day, 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 per day, measured by a supplied pedometer. Self-monitoring of food intake and energy expenditure in diaries. Specific to this group, participants attended small (8-10) people classes led by a registered dietician. Classes were weekly for 3 mos, then biweekly for 3 mos then monthly for 4 mos. Diet was made up of conventional food items.
	Dietician-led lifestyle intervention with meal replacements	Not noted	Registered dietician	As in the traditional group above, instruction manuals for dieting, 1200 kcal/day diet, and exercise instructions with pedometer use and self-monitoring. Sessions with registered dietician 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).

Appendix C: Descriptions of Intensive Counseling and Behavioral Intervention Studies (cont)

Study	Intervention	Intervention Setting	Intervention Delivery	Counseling and Behavioral Description
Ashley et al, 2001[80], continued	Primary care office intervention with meal replacements	Physician office	Primary care physician (2/3 of visits) or Registered Nurse (1/3 of visits)	26 biweekly 10-15 min individual sessions over 1 yr, with a focus of helping patients lose wt (although other related medical problems were also discussed). Diet prescription with meal replacements as in the "Dietician-led with meal replacement" plan above. During each visit, diet, behavior modification, and physical activity habits were reviewed, and questions answered about the diet instructions.
Wadden et al, 2001[52]	Sibutramine alone	Not noted	Physician	Baseline meeting with a physician who described medication use and the importance of lifestyle modification. A balanced diet (1200-1500 kcal/day) was prescribed. Gradual increased exercise (typically walking) to 4-5 sessions per wk, each of 30-40 mins duration. Literature supporting these instructions was disseminated. Over the trial, patients had 10 brief (5-10 min) follow-up visits with the physician (wks 2, 4, 8, 12, 16, 20, 24, 32, 40, 52). No lifestyle counseling or instruction for self-monitoring of lifestyle change.
	Sibutramine plus lifestyle	Not noted	Physician (outcomes monitoring) doctoral-level psychologists (counseling)	Physician visits on same schedule as sibutramine alone group. Additionally, in the first 20 wks, 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 asked to self-monitor food intake and physical activity for at least 16 wks. Behavioral topics discussed at weekly sessions included stimulus control, slowed rate of eating, social support and cognitive restructuring. During wks 24-52, sessions focused on skills for maintenance of wt loss.
	Sibutramine plus lifestyle plus 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 wks prescription of a 1000 kcal/day portion-controlled diet (4 servings/day of a liquid nutritional supplement with an evening balanced meal). After wk 16, gradual decreased consumption of liquid supplement, with 1200-1500 kcal/day diet of conventional food diet by wk 20 (similar to the patients in the other 2 arms).

Appendix C: Descriptions of Intensive Counseling and Behavioral Intervention Studies (cont)

Study	Intervention	Intervention Setting	Intervention Delivery	Counseling and Behavioral Description
Wing and Anglin, 1996[76]	Behavior therapy with a LCD	Not noted	Multidisciplinary team (all white)	1 yr 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 encouraged to gradually increase activity until walking 2 miles/day, 5 days/wk. LCD (1000-1200 kcal/day), with <30% calories as 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 wks 1-12 and 24-36. During VLCD intervals, goal consumption of approximately 500 kcal/day, either as liquid formula or lean meat, fish, or fowl. After each VLCD, other foods gradually reintroduced until consumption of 1000-1200 kcal/day was reached.

*Information source: primarily published articles. In selected cases (Tuomilehto et al, Kuller et al) [65] additional information was obtained from study staff.
†Kcal/day, kilocalories/day; LCD, Low calorie diet; LDL, low-density lipoprotein; MJ/wk, megajoules per weekVLCD, Very low calorie diet.