Chapter 3. Results

Results of the Literature Search

Our search identified 1,102 articles. Of these 1,102 articles, 291 were references from Broom and colleagues' draft evidence report on obesity treatment ("NHS Report"); 415 were references from the other reviews described in the methods section; our library search identified another 325 articles; and our experts sent an additional 71 articles. Figure 1 displays the flow of the literature review.

We were unable to obtain 11 of the1,102 articles, which were mostly non-English language or very old articles. Our physician obesity specialist rejected another 20 as irrelevant. Eight articles were not received by the cutoff date. This left 1,063 articles to screen.

Of the 1,063 articles screened, 235 articles were either controlled trials of weight loss medication, controlled trials of surgery, or surgery case reports/case series. These articles went on to quality review to assess the applicability for data pooling or narrative synthesis. The other articles were rejected for the following reasons: 113 did not study weight loss; 204 studied diet; 255 others studied an intervention other than weight loss medication or surgery; 30 studied the weight loss drug mazindol, which is rarely used today; 39 studied sibutramine, phentermine, or diethylproprion (for which recent previous meta-analyses of efficacy are summarized in this report); 103 were medication trials with less than six months of followup; 66 were rejected because of study design (descriptive articles, background, reviews, etc.); three were animal studies; three were duplicate articles ordered accidentally; and four articles were published in eastern European languages for which we could not find translators. Ten surgery articles did not include weight loss outcomes but were considered for analysis of adverse events. Two articles compared surgery to diethylproprion and are counted tice in these numbers.

We quality-reviewed 78 medication studies that reported on sertraline (1 article), zonisamide (1 article), orlistat (49), buproprion (5), topirmate (9), and fluoxetine (13). Meta-analysis was performed for all medications except sertraline and zonisamide which are summarized in the text. We quality-reviewed 159 surgery studies reporting on weight loss and considered an additional 8 surgery studies reporting only on complications, for a total of 167 surgery studies. Of these 167 studies, 20 were duplicate publication of an already included study. Of the remaining 147 studies, 89 contributed to the weight loss analysis, 134 contributed to the mortality analysis, and 128 contributed to the complications analysis. Studies could contribute to one or more surgery analyses.

We found no direct comparisons of weight loss medications (key question 2). In addition, we found no RCT evidence regarding the "optimum amount of time to treat" (key question 3). Consequently, our results focused on the efficacy of medications relative to placebo.

Efficacy of Medications

Sibutramine

Our literature search identified a high-quality meta-analysis that was "in press" at the time of our search and has since been published [53]. The authors of this paper agreed to let us incorporate

their results into our evidence report. In their literature search, the authors did not restrict their search to English-language publications and made extensive efforts to identify unpublished and ongoing trials, including contacting representatives of the pharmaceutical industry. Inclusion criteria for the review were that the study was a RCT that assessed sibutramine (10 or 20 mg daily), enrolled adults 18 years of age or older who had a BMI of 25 or more, assessed weight loss, and had a treatment duration of at least eight weeks. The primary outcome was mean change in body weight, and data on blood pressure, heart rate, cholesterol, fasting glucose, and glycosylated hemoglobin were abstracted if reported. Studies were analyzed in three strata, based on duration of the trial: 8 to12 weeks, 16 to 24 weeks, and 44 to 54 weeks. Of 1,245 potentially relevant citations, 432 manuscripts and abstracts were reviewed in more detail, which resulted in 44 trials that were considered for inclusion in their analysis. Ten authors provided additional, unpublished data. The meta-analysis authors identified seven trials of 8 to 12 weeks duration that included a total of 546 participants; 12 trials of 16 to 24 weeks duration that included a total of 1,179 participants; and five trials of 44 to 54 weeks duration that included 2,188 participants. The mean age of enrolled patients ranged from 34 to 54 years of age. Adults with known cardiovascular disease were generally excluded from most primary studies. Dietary interventions were a co-intervention in nearly all primary studies, and exercise and behavior modification were each interventions in about one quarter of the studies. Ultimately, twenty-nine studies met all the authors' criteria for inclusion in the analysis. Of these, 23 (79 percent) had a Jadad score of 3 or greater.

The summary result for weight loss for the seven studies reporting results at 8 to 12 weeks was a mean difference in weight loss (sibutramine compared to placebo) of 2.78 kg (Figure 2). The authors reported that this result changed little in sensitivity analyses that excluded small trials, those with low-quality scores, those reporting data only for subjects who completed the study, or unpublished data.

Among the 12 trials reporting results at 16 to 24 weeks, the authors reported statistical heterogeneity among trials and therefore analyzed the data in three subgroups. Subgroup A included those studies with a greater than 70 percent followup and used the "last observation carried forward" method to impute missing observations (the most recent previous observation is used). This subgroup of studies had a pooled result of 3.43 kg favoring treatment with sibutramine. Studies in subgroup B, which analyzed only participants who completed the entire study, had a summary result of 6.03 kg favoring sibutramine treatment. Studies in subgroup C also used the "last observation carried forward" analysis, had less than 70 percent followup, and had a summary mean difference in weight loss of 6.04 kg in favor of sibutramine treatment. The authors detected statistical evidence of publication bias in these trials (Figure 3).

Among the five studies that assessed outcomes at 44 to 54 weeks duration, the summary mean difference in weight loss was 4.45 kg favoring sibutramine (Figure 4). This result was changed little by the authors' sensitivity analysis, and no evidence of publication bias was detected.

In a dose-ranging study not included in the meta-analysis, 1,047 patients were given instructions on diet, physical activity, and lifestyle changes and then randomized to received placebo or sibutramine at 1 mg, 5 mg, 10 mg, 15 mg, 20 mg, or 30 mg a day. Weight loss at 24 weeks was dose-dependent, with a mean weight loss above placebo equal to 4.9 percent, 6.2 percent, 7.6 percent, and 8.2 percent for the 10 mg, 15 mg, 20 mg, and 30 mg doses,

respectively. Side effects such as dry mouth, insomnia, and nausea also increased in a dose-dependent manner.[54] Of note, sibutramine was not FDA approved in the 20 mg and 30 mg doses.

Regarding other assessed outcomes, the authors did not identify any evidence that sibutramine reduces mortality or morbidity from obesity-associated diseases. Systolic and diastolic blood pressure outcomes were variable, with some studies reporting small decreases and other studies reporting small increases. Fasting blood glucose and hemoglobin A1c fell slightly in sibutramine-treated patients, but no consistent effect was observed on cholesterol or lipid outcomes. Adverse-event analysis identified no studies in which participants died. The analysis showed that in patients who took sibutramine, heart rate was consistently increased by about four beats per minute.

The conclusions of this systematic review and meta-analysis were that sibutramine with lifestyle modification was more effective than placebo with lifestyle modification in promoting weight loss in overweight and obese adults at all time points that were assessed, with an average of 4.5 kg greater weight loss at one year and a 20 to 30 percent greater likelihood of achieving a weight loss of 5 percent or more (compared to placebo). The authors also concluded that treatment with sibutramine is associated with modest increases in heart rate and blood pressure, very small improvements in glycemic control among diabetics, and (based on the longest-duration and best-quality studies) small improvements in HDL cholesterol and triglycerides. Efficacy and safety beyond two years of treatment are unknown. We calculated that, in aggregate, the RCTs of sibutramine contained sufficient numbers of patients to evaluate adverse outcomes that occurred at a rate of 8 per 10,000 or higher; the existence of outcomes at lower rates is untested.

Orlistat

Our literature search identified 28 studies of orlistat eligible for inclusion in a meta-analysis.[55-82] The average age of patients enrolled in these studies was 48 years old; 73 percent were women; and the average BMI was 36.7. In all 28 studies, diet was a co-intervention in all experimental arms; 39 percent of studies included educational, behavioral, or psychosocial co-interventions; and 18 percent of studies included exercise co-interventions. Consistent with the meta-analysis of sibutramine, we stratified the data according to treatment duration for analysis.

We identified 11 studies[56, 63, 65-68, 70, 72, 78, 81, 82] that reported six-month treatment outcomes. The weight loss for individual studies is presented in Table 4 and shown graphically in Figure 5. The pooled random-effects estimate of the mean weight loss for orlistat-treated patients over placebo-treated patients, was 2.51 kg (95% CI, 1.63, 3.4). The total weight lost in the orlistat-treated patients was 5.35 kg. Significant heterogeneity was found among studies ($p = 0.00$). In a sensitivity analysis by study quality, five studies with a Jadad score of 3 or more showed a pooled random-effects estimate of mean weight loss of 2.32 kg (95% CI, 1.0, 3.6) over placebo. No effect of quality score on outcome was detected by meta-regression. No effect of year of publication on outcome was detected. No sensitivity analysis by dose was possible. All studies had followup rates of 80 percent or more, so no sensitivity analysis by followup was performed. No evidence of publication bias was found.

We identified 21 studies[55-58, 60-63, 69-71, 73-77, 79, 80, 82-84] that reported data with 12-month outcomes. The weight loss for individual studies is presented in Table 5 and shown graphically in Figure 6. The pooled random-effects estimate of the mean weight loss for orlistat-treated patients,

compared to placebo-treated patients, was 2.75 kg (95% CI, 2.2, 3.3). The total weight lost in the orlistat-treated patients was 8.10 kg. Significant heterogeneity was observed between studies (p = 0.00). In a sensitivity analysis by study quality, 15 studies with a Jadad score of 3 or more had a pooled random-effects estimate of mean weight loss of 2.58 kg (95% CI, 1.9, 3.3). No effect of quality score on outcome was detected by meta-regression. No effect of year of publication on outcome was detected. No sensitivity analysis by dose was possible. In a sensitivity analysis by followup rate, the pooled random-effects estimate of 15 studies with followup rates of 70 percent or more was a mean weight loss of 2.83 kg (95% CI, 2.0, 3.6) over placebo; using 80 percent as the threshold for successful followup, no effect of completeness of followup on outcome was detected by meta-regression. One test of publication bias was statistically significant (Egger's test p = 0.006), whereas the other test was not (Begg's test p = 0.695).

Table 6 presents the results of our adverse-event analysis for orlistat. In this analysis, all 28 studies were considered for inclusion. Our results indicate an increase in diarrhea, flatulence, and bloating/abdominal pain/dyspepsia in orlistat-treated patients compared to placebo, with RR of 3.4, 3.1, and 1.5, respectively. As described in Chapter 2, adverse-event data are typically reported as the number of adverse events, rather than per patient. Thus, our results may overestimate the number of individuals who reported the adverse events, because we cannot distinguish between one person who reported diarrhea twice and two people who each reported diarrhea once. Five trials reported more incidents of diarrhea than the number of enrolled subjects; for these five (out of 13 trials reporting this complication), we assumed all patients reported this event. Hence, we may overestimate the true risk of diarrhea. Nevertheless, our data suggest significant gastrointestinal side effects from orlistat. We attempted to determine if the proportion of persons reporting adverse events decreased over time, but since our search strategy eliminated studies with a duration of less than 6 months we could assess only whether adverse-event reports differed between 6 and 12 months. No difference was detected. We calculated that in aggregate, the RCTs of orlistat contained a sufficient number of patients to evaluate outcomes occurring at a rate of 2 per 10,000 or higher; the existence of outcomes at lower rates is untested.

Phentermine

Our literature search identified a recent meta-analysis[85] that assessed RCTs of the use of phentermine for weight loss in obese individuals. This review identified nine studies published between 1975 and 1999. Our literature review identified no new RCTs of phentermine since this time; consequently, we rely on the existing meta-analysis for our evidence regarding efficacy of phentermine. In this review, six placebo-controlled RCTs contributed data to the pooled analysis. The duration of treatment with phentermine varied from 2 to 24 weeks. More than 80 percent of enrolled individuals were female, and more than 80 percent of participants also received lifestyle modification treatments as co-interventions. The dose of phentermine ranged from 15 to 30 mg a day. In the authors' pooled analysis, subjects treated with phentermine lost an average of 3.6 additional kg of weight compared to placebo, (95% CI, 0.6 to 6.0). In an analysis assessing the effect on maintenance of weight loss, the authors reported that patients treated with phentermine maintained a "fairly large" weight loss compared to placebo (2.43 kg) after discontinuation of the drug. The authors concluded that phentermine use, in addition to lifestyle interventions, resulted in a statistically significant, but modest, increase in weight loss. In this review, no side-effect or adverse-event data were reported. We identified no systematic reports of adverse events

with phentermine. However, since phentermine is a sympathomimetic amine, side effects consistent with this class of drugs can be expected, e.g. palpitations, tachycardia, elevation of blood pressure, central nervous system effects, and gastrointestinal effects. Case reports of stroke in persons taking phentermine for weight loss have been reported,[86,87] but as with all case-report analyses, a causal relationship cannot be established or assumed. We calculated that in aggregate, the RCTs of phentermine contained sufficient numbers of patients to evaluate outcomes occurring at a rate of 8 per 1,000 or higher; the existence of outcomes at lower rates is untested.

Diethylpropion

Our literature search identified a recent meta-analysis[85] that assessed RCTs of the use of diethylpropion for weight loss in obese individuals. This review identified 13 studies published between 1965 and 1983. Our literature review identified no new RCTs of diethylpropion since this time; consequently, we rely on the existing meta-analysis for our evidence regarding efficacy of diethylpropion. In this review, nine placebo-controlled RCTs contributed data to the pooled analysis. The duration of treatment with diethylpropion varied from 6 to 52 weeks. More than 80 percent of enrolled individuals were female, and 100 percent of participants received lifestyle modification treatments as co-interventions. The dose of diethylpropion was 75 mg a day. In the authors' pooled analysis, subjects treated with diethylpropion lost an average of 3.0 additional kg of weight over placebo (95% CI, -1.6, 11.5). The authors concluded that diethylpropion use, in combination with lifestyle interventions, was associated with a modest increase in weight loss of borderline statistical significance. In this review, no side-effect or adverse-event data were reported. We calculated that, in aggregate, the RCTs of diethylpropion contained sufficient numbers of patients to evaluate outcomes occurring at a rate of 8 per 1,000 or higher; the existence of outcomes at lower rates is untested.

Fluoxetine

Our literature search identified nine studies of fluoxetine treatment that reported weight loss outcomes (fluoxetine is usually indicated for treatment of depression, obsessive compulsive disorder, and bulimia).[44,88-95] Of note is that the doses used for weight loss were higher (60 mg) than those used for depression (20 mg). The average age of patients enrolled in these studies was 48 years old; 69 percent were women; and the average BMI was 35.5. In 78 percent of the studies (7 of 9), diet was a co-intervention; 33 percent of studies included an educational, behavioral, or psychosocial co-intervention; and 12 percent of the studies included exercise as a co-intervention. Consistent with the analyses of sibutramine and orlistat, we stratified the data according to treatment duration for analysis.

We identified seven studies of fluoxetine that reported weight loss outcomes at 6 months. The individual weight loss values for each study are listed in Table 7 and shown graphically in Figure 7. The pooled random-effects estimate of the weight loss in fluoxetine-treated patients, compared to placebo-treated patients, was 4.74 kg (95% CI, 2.8, 6.7). The total weight lost in the fluoxetine-treated patients was 5.81 kg. Significant heterogeneity was found among studies ($p = 0.00$). In sensitivity analyses of study quality, the pooled random-effects estimate for four studies with Jadad scores of 3 or more found a mean weight loss of 5.27 kg (95% CI, 3.0, 7.5). No effect

of quality score on outcome was detected by meta-regression. No effect of year of publication on outcome was detected. In a sensitivity analysis that dropped the one study that used only 20 mg/day of fluoxetine, the pooled estimate of increased weight loss in the remaining six studies was 5.36 kg (95% CI 3.7, 7.0). In a sensitivity analysis by followup rate, four studies with a followup rate of 70 percent or more had a pooled random-effects estimate for mean weight loss of 3.96 kg (95% CI, 1.4, 6.5). Using 80 percent as the threshold for successful followup, no effect of completeness of followup on outcome was detected by meta-regression. We did not detect any evidence of publication bias.

We identified six studies of fluoxetine that reported weight loss outcomes at 12 months.[44,88-92] The individual results for studies are listed in Table 8 and shown graphically in Figure 8. The pooled random-effects estimate of weight loss in fluoxetine-treated patients over placebo-treated patients was 3.15 kg (95% CI, 0.5, 5.8). The total weight lost in the fluoxetine-treated patients was 4.70 kg. There was significant heterogeneity among studies (p = 0.00). In sensitivity analyses by study quality, the pooled random-effects estimate for four studies with Jadad scores of 3 or more was a mean weight loss of 3.28 kg (95% CI, 0.6, 7.2) over placebo. No effect of quality score on outcome was detected by meta-regression. No effect of year of publication on outcome was detected. In a sensitivity analysis that dropped the one study that used only 20 mg/day of fluoxetine, the pooled estimate of increased weight loss in the remaining five studies was 3.9 kg (95% CI 0.9, 6.9) In a sensitivity analysis by followup rate, the pooled random-effects estimate of effect for three studies with followup rates of 70 percent or more was a mean weight loss of 2.60 kg (95% CI, -2.0, 7.2) over placebo. Using 80 percent as the threshold for successful followup, no effect of completeness of followup on outcome was detected by meta-regression. We did not detect any evidence of publication bias.

Table 9 presents the results of our adverse-event analysis, which included all nine studies. Our results indicate an increase in nervousness/sweating/tremors, nausea/vomiting, fatigue/asthenia/ hypersomnia/somnolence, insomnia, and diarrhea in fluoxetine-treated patients compared to placebo-treated patients, RR 6.4, 2.7, 2.4, 2.0, and 1.7, respectively). Our results may overestimate the risk of side effects, because we cannot distinguish between one person who reported nervousness twice, and two people who each reported nervousness once. Nevertheless, the results indicate that certain central nervous system and gastrointestinal adverse events are common with fluoxetine treatment. The literature on the use of fluoxetine for other indications is large, and the results of our analysis are comparable with the adverse events reported in those studies.

Sertraline

Our literature search identified one study of sertraline.[96] This study assessed the effect of sertraline in maintaining weight loss in 53 women (out of a total of 68) who had completed a 26-week weight reduction program that combined a very low calorie diet and behavior therapy. To be eligible for inclusion in the sertraline trial, subjects had to have lost at least 10 percent of their initial weight; they were then randomly assigned to receive sertraline beginning at 50 mg per day, titrating upwards to 200 mg per day, or placebo. All patients also attended a 54-week relapse prevention program that addressed skills required to maintain weight loss. Patients had a mean age of 42 years and a mean BMI of 30, having lost approximately 23 kg in the prior six-month study. At the end of the 54-week period of evaluation, sertraline-treated patients had

regained an average of 17.7 kg, while placebo-treated patients had regained an average of 11.8 kg, a difference the authors did not report as statistically significant. However, in the first 10 weeks of the study, sertraline-treated patients regained significantly less weight than did the placebo-treated patients.

More sertraline-treated patients than placebo-treated patients reported fatigue, nausea, difficulty concentrating, and problems urinating. Three sertraline-treated subjects discontinued the study because of adverse events, compared with no adverse events were associated with the placebo. Of note is that insomnia, headache, nausea, and fatigue were reported by approximately half of all sertraline-treated patients.

Bupropion

Our literature search identified five articles assessing the efficacy of bupropion for weight loss. Of the five, one article[97] was an abstract that reported the same data as a subsequent full report,[43] so only four articles reported on unique studies. One of those studies was dropped because the duration of treatment and followup was only 8 weeks, which left three studies available for a pooled analysis. In these three studies, the average age of enrolled patients was 42.7; 81 percent were female; and the average weight was 94.3 kg. Patients in one study[98] had major depression and in another[99] had depressive symptoms. Two studies reported results at 6 months,[43,99] and one study reported results at 12 months.[98] Hence, we were unable to do separate analyses by 6-month and 12-month outcomes, and readers should keep in mind that our pooled result for bupropion is a mix of 6- and 12-month outcomes. Two of the three studies included diet as a co-intervention, and one study included exercise. One study reported results for both 300 mg/day and 400 mg/day of bupropion; the other two studies assessed only the 400 mg/day dose. In this analysis, we present results only for 400 mg/day of bupropion compared to placebo. The individual weight loss values for each study are presented in Table 10 and shown graphically in Figure 9. The pooled random-effects estimate of the weight loss in bupropion-treated patients compared to placebo-treated patients was 2.77 kg (95% CI 1.0, 4.5). The total weight loss in the bupropion-treated patients was 4.14 kg. There was significant heterogeneity among studies ($p = 0.000$). There were too few studies to support sensitivity analyses based on study quality, year of publication, or dose. We did not detect any evidence of publication bias.

Table 11 presents the results of our adverse event analysis. Our results indicate an increase in dry mouth (pooled odds ratio = 3.26, RR = 2.99), and nonsignificant increases in diarrhea and constipation. The research literature on the use of bupropion for depression and smoking cessation is extensive: In addition to dry mouth, insomnia is a commonly reported side effect in these studies.

Topiramate

Our literature search identified nine studies that assessed the efficacy of the drug topiramate for weight loss. One study,[100] which did not include a placebo group, is excluded from review. One study[101] was dropped because it duplicated data in another included study.[31] Two articles reported data on the same trial;[102,103] however, one had a larger sample size, so only it was included, leaving six studies for analysis. [31,103-107] These six were judged sufficiently clinically similar to support a pooled analysis. All but one of these studies were published only as abstracts at the time of our

analysis. Of note, all these studies reported their data only as percent weight loss, so the outcome for this analysis was percent weight loss. Many of the studies assessed multiple doses, the most common being 96 mg/day and 192 mg/day. We determined that the higher dose produced significantly more weight loss than the lower dose (by 1.75 percent) over the duration of the study, so we present data only on the higher dose. In these studies, the average age of subjects was 47; 68 percent were female, and the baseline weight was 102 kg. Four of the six studies had as co-interventions diet, exercise, education, and behavioral theraphies.

The individual percent weight loss values for the six studies reporting 6-month weight loss outcomes are listed in Table 12 and graphically in Figure 10. The pooled random-effects estimate of the percent weight loss in topiramate-treated patients, compared to placebo-treated patients, was 6.5 percent (95% CI 4.8 percent to 8.3 percent). The total percent weight lost in the topiramate-treated patients was 8 percent. In a sensitivity analysis of study quality, only one study had a Jadad score of 3 or greater (as studies were assessed based on data in abstracts, this finding may have been the result of the incomplete nature of the report), and its exclusion did not materially alter the pooled result. All studies were recent, so no sensitivity analysis by year of publication could be performed. As previously mentioned, in our dose analysis, we determined that a daily dose of 192 mg/day produces more weight loss than a daily dose of 96 mg/day. Only one study reported a followup rate of less than 80 percent and its exclusion did not materially alter the pooled result. We did not detect any evidence of publication bias.

Table 13 present the results of our adverse event analysis. Paraesthesia and taste perversion were reported much more commonly in topiramate-treated patients than in placebo-treated patients (pooled odds ratios of 20 and 11, respectively; RR of 4.9 and 9.2). Other central nervous system effects and gastrointestinal effects were also reported more commonly in topiramate-treated subjects. Adverse events were more common in patients treated with 192 mg/day of topiramate compared to 96 mg/day. We calculated that, in aggregate, the topiramate studies had enough patients to evaluate outcomes occurring at a rate of 3.2 per 1,000; the existence of outcomes at lower rates is untested.

Zonisamide

Our literature search identified one eligible study that assessed the efficacy of the drug zonisamide for weight loss.[108] This study was a double-blind, RCT that enrolled 60 patients with a mean age of 37 years. Approximately 90 percent were women, and their mean BMI was 36. Patients were randomized to begin receiving placebo or zonisamide at 100 mg per day; daily doses were increased to a maximum of 600 mg per day, based on response. Patients in both groups were also instructed to follow an individualized diet that was devised to reduce their daily energy intakes to 500 kilocalories per day below maintenance level. Increased physical activity was also encouraged for participants in both groups. Patients were followed for 16 weeks in the double-blind portion of the study, with an additional 16-week single-blind extension available. Of the 60 patients, 51 (85 percent) completed the 16-week phase. Using a “last observation carried forward” analysis for dropouts, the researchers found that patients in the zonisamide group lost an average of 6.0 percent of baseline body weight, compared to 1.0 percent for placebo patients ($p < .001$). In the extension phase of the study, 37 patients (20 in the zonisamide group, 17 in the placebo group) continued, and 36 completed the study at week 32. Ten of the 19 zonisamide patients who completed the study had lost at least 10 percent of initial body weight at

week 32 (compared with none of the placebo patients) ($p < .001$). Heart rate decreased by an average of approximately two beats per minute in the overall sample, and there were no differences between groups. The authors reported that systolic and diastolic blood pressure readings did not change over time. The authors also reported that the total numbers of adverse effects over the study period were 2.1 and 1.6, for those assigned to zonisamide and placebo, respectively, a difference that did not reach statistical significance. Among individual adverse effects, the only statistically significant differences observed were in fatigue: ten patients in the zonisamide group reported fatigue, compared with one in the placebo group ($p < .006$ by the Fisher exact test). The mean serum creatinine increased from 0.79 milligrams per deciliter to 0.92 milligrams per deciliter for zonisamide-treated patients and from 0.76 milligrams to 0.79 milligrams per deciliter in placebo-treated patients ($p < .001$).

Summary of Medication Studies

Table 14 presents a short summary of our findings regarding medications. As previously stated, we identified no direct comparisons of weight loss medications. Our summary of the results for each drug (compared to placebo) does not support a hypothesis that any one drug is more effective than the others, as the difference among drugs in placebo-corrected mean weight loss at one year is only about 1 to 2 kg. A further observation is that none of these medications appears to support large weight loss: The mean placebo-corrected weight loss for all drugs was less than 5 kg at one year. Total weight loss at one year was higher, up to 8.0 kg. However, as noted in the introduction, even moderate weight loss (5 percent of body weight) can significantly influence obesity-associated risk factors for poor health outcome (Type II diabetes, hypertension, etc.).

Efficacy of Surgery for Weight Loss

Our literature search identified a Cochrane review of the literature on surgery for obesity,[38] current as of February 2003. Inclusion criteria for the review were randomized controlled trials (RCTs) and non-randomized controlled trials comparing surgery with nonsurgical management for morbid obesity, and RCTs comparing alternative surgical procedures. The review was restricted to adults age 18 years or older with morbid obesity, defined as BMI greater than 40 or BMI greater than 35 with serious comorbid disease. Studies had to report at least 12 months duration of followup. Because of heterogeneity, the authors did not feel that meta-analysis was justified and summarized their data narratively. The authors identified 2,707 citations, of which they retrieved 99 for detailed examination. Eighteen trials (reported in 33 publications) met their inclusion criteria. The results of their review are summarized in Table 15. The authors concluded that there is limited evidence supporting greater long-term weight loss (maintained at least to eight years) with surgery than with conventional treatments for severe obesity, but that surgery is associated with adverse effects and the possibility of postoperative mortality. In addition, they reported that the data are too limited to draw any conclusions regarding differences in efficacy or safety among surgical procedures. However, the Cochrane review's conclusions were based primarily upon the reports of Andersen and colleagues that compared diet alone to a horizontal, unbanded gastroplasty, which has subsequently been shown to be an ineffective surgical procedure for weight loss and has not been frequently used for over 20 years.

In our review, we went beyond the Cochrane report by including case series articles (those reporting on at least ten cases) in addition to RCTs and also by assessing benefits in terms of weight loss and improvement in comorbidities and risks in terms of adverse events. A total of 142 studies were considered for our analysis. One, a Swedish Obese Subjects (SOS) study,[109-116] was an observational study and will be discussed individually below. We identified 28 RCT/CCTs of surgery[117-148] (all but two of which compared one surgical procedure with another) and 113 case series.[109-116,149-226]

Benefits

Weight loss and maintenance. We identified two RCTs that compared bariatric surgery to a nonsurgically treated control group. The first is the RCT that compared horizontal gastroplasty and diet to diet alone[120,134] and was analyzed in the Cochrane Review. This RCT generated two articles that reported net weight loss at 6 months[121] and 24 months[120] followup. At 6 months, weight loss was not different between the two groups, but at 24 months followup, the net weight change from baseline greatly favored surgical therapy (net weight change of 30.5 kg versus 8.0 kg for surgical and nonsurgical therapy, respectively), although only about half the original patients contributed data at 24 months. We also identified another randomized trial that compared jejunoileal bypass to "medical treatment" (not otherwise specified) in 186 patients. Again at 24 months followup, the mean difference in weight loss greatly favored surgical therapy (mean difference = 37 kg). Of note, these studies were conducted more than 20 years ago, and the surgical procedures assessed are not considered relevant to modern bariatric surgery, in that improvements in procedures and technique have been associated with significantly greater long-term weight loss, as compared to horizontal gastroplasty, and fewer major complications as compared to the jejunoileal bypass.

In addition to the two RCTs, we identified numerous reports from an observational study, the Swedish Obese Subjects (SOS) study.[109-116] In the intervention portion of this study (a cross-sectional registry portion was also included), obese adults (BMI ≥ 34 for men and ≥ 38 for women) were assessed in two groups: those who voluntarily underwent bariatric surgery (most of whom were treated with vertical banded gastroplasty) and a group of matched controls treated medically. Matching was done on 18 variables, including gender, age, height, and weight. The average age of enrolled subjects was 47, about two-thirds were women, and average BMI at baseline was about 41. At eight years of followup, among 251 surgically treated patients, the average weight loss was 20 kg (or 16 percent of body weight), whereas among 232 medically treated patients, the average weight did not change. Patients treated with RYGB lost more weight than those treated with vertical banded gastroplasty or banding procedures.[110] Based on this latter finding and on RCT evidence summarized in the text to follow, had all patients in the SOS trial been treated with RYGB the difference in weight loss between surgical and medical therapy would likely have been even greater—probably on the order of 10 kg more. Even though the SOS study was not randomized, patients were well matched in both groups, and the magnitude of the observed differences is so large that it is very unlikely that unmeasured variables could account for these differences. Thus, we believe this study provides conclusive evidence of the superiority of surgical treatment for the patients enrolled in the study (middle-aged adults with a BMI of about 41). Also contributing to the strength of this study is the extended duration of followup, documenting sustained weight loss and improved health up to eight years after

treatment. The SOS study recently reported sustained improvements in weight loss at 10 years followup, compared to controls (J. Torgerson, presentation at the 2003 annual meeting of the American Society for Bariatric Surgery).

Comorbidities. As mentioned, bariatric surgery is recommended to help control the morbidities associated with excess weight. A series of reports from the SOS study support the superiority of obesity surgery compared to medical therapy in ameliorating or preventing the comorbidities of obesity. At 24 months after surgery, among 845 surgically treated patients and 845 matched controls (two-thirds women, average age of 48, average BMI about 41), the incidence of hypertension, diabetes, and lipid abnormalities was markedly lower in the surgically treated patients (adjusted odds ratios of 0.02 to 0.38, depending on condition).[116] At eight years of followup, the effect of surgery on the reduction in diabetes risk was still dramatic (odds ratio = 0.16), while the effect on reduction in risk for hypertension did not persist (odds ratio = 1.01).[110] However, significant decreases in both systolic (8.3 mm Hg) and diastolic (6.7 mm Hg) blood pressure persisted in the small (6 percent) subset of patients who underwent a gastric bypass and lost significantly more weight than the 94 percent of patients who underwent a vertical banded gastroplasty or gastric banding.[72] Additional reports from the SOS study support a substantial benefit of surgery in reducing sleep apnea,[111] symptoms of dyspnea and chest pain,[111] and improving quality of life.[114] The latter study assessed health-related quality of life in four domains: health perception, mental well being/mood disorders, psychosocial functioning, and self-assessment of eating behavior. The researchers matched 487 surgically-treated patients to an equivalent number of control patients; at two years followup, data were available for 98 percent of surgical patients and 82 percent of control patients. Improvements in all domains in surgical patients compared to control patients were greatest at 6 months after surgery and diminished slightly at 24 months. Differences between groups were substantial in nearly all domains: in general, one-half to two-thirds of an effect size. The differences were related to the degree of weight loss, meaning that patients who lost a greater amount of weight had greater improvements in quality of life. The SOS study is the only one we identified that compares comorbidities between surgically treated patients and a concurrent control group receiving nonsurgical treatment.

We assessed reports of surgery case series for data on the control of four comorbidities: diabetes, hypertension, sleep apnea, and hyperlipidemia. Of the 114 case series publications, 21 papers reported quantitative information on the control of diabetes. The proportion of patients with preoperative diabetes who showed improvement or resolution of their diabetes after surgery ranged from 69 percent to 100 percent, with a median reported value of 100 percent. For control of hypertension, 18 papers reported results that ranged from 25 percent to 100 percent of patients showing improvement or resolution of hypertension following surgery and a median reported improvement of 89 percent. Fourteen studies reported results for sleep apnea: the range of improvement was 95 percent to 100 percent of patients, with a median of 100 percent of patients reporting improvement or resolution of sleep apnea. Ten studies reported on hyperlipidemia following surgery, with 60 percent to 100 percent of patients reporting improvement or resolution of hyperlipidemia following surgery with a median of 88 percent. These reported improvements in comorbidities are substantial and suggest that bariatric surgery is helping to relieve the burden of these comorbidities in severely obese individuals. However, a cause-and-effect relationship cannot be conclusively proven from case series data alone. Still, these results are consistent with the statistically significant improvement reported by the SOS study for

diabetes, hypertension (in the RYGB subset), and sleep apnea, although the magnitude of benefit reported in SOS was smaller than that reported in the case series.

Although not assessed in this report, improvements in cardiac dysfunction,[152,227-231] gastroesophageal reflux,[232-239] pseudotumor cerebri,[240,241] polycystic ovary syndrome,[242] complications of pregnancy,[243-247] stress urinary incontinence,[248] degenerative joint disease,[249-252] nonalcoholic steatohepatitis,[253] severe venous stasis disease,[254-257] and overall quality of life[137, 180, 216,258-267] have been reported in some case series of obesity surgery. As mentioned above, a cause-and-effect relationship cannot be conclusively proven from case series data alone.

Comparing methods. We also identified a large number of RCTs as well as case series that compared weight loss outcomes between or among surgical procedures. Results at 12 months of followup are summarized in Table 16, and results at 36 months (or longer) are summarized in Table 17.

Five RCTs were identified that compared surgical procedures and reported data sufficient for pooling; that is, the studies compared similar surgical procedures and reported weight loss data in sufficient detail. In two studies comparing RYGB procedures to VBG,[128,129] including 231 patients in total, pooled weight loss outcomes for both procedures were substantial (at least 30 kg at 36 months for both) and favored RYGB at both 12 and 36 months (8-9 kg more weight loss from RYGB). These results are supported by the pooled results from all studies combined (both RCTs and case series), which report data on approximately 2,000 patients for each procedure. These combined data show that RYGB patients reported about 10 kg more weight loss than patients treated with VBG, at both 12 and 36 months.

Several additional randomized trials compared RYGB and other gastric bypass procedures with VBG or other gastric partitioning procedures,[125,130,131,140-142] but the results could not be included in our pooled analysis because either they did not report their results in terms of kilograms of weight lost or they did not report the results in sufficient statistical detail. Nevertheless, the results of all these studies support the conclusion that gastric bypass produces superior weight loss to gastroplasty procedures

In two RCTs, the weight lost using VGB, compared to laparoscopic adjustable gastric banding, was 14 kg more at 12 months followup but only about 3 kg more at 36 months followup. No difference in net weight loss was seen in the pooled results from all studies combined.

Finally, one RCT compared open RYGB with that performed laparoscopically.[139] Again, the weight loss for both approaches was substantial, but no significant differences between the two were found (greater than 30 kg for both at 12 months); a result that was supported by the “all studies” pooled analysis at both 12 months and out to 36 months. Because the final anatomic reconfiguration is the same for laparoscopic and open RYGB, weight loss and comorbidity outcomes should be identical. However, these procedures involve very different technical approaches that result in different types and rates of complications.

Summary of Benefit Data

The data we identified support that surgical treatment results in greater weight loss than does medical treatment in obese individuals (BMI ≥ 40), resulting in 20 to 30 kg of weight loss, maintained up to eight years, that is accompanied by significant improvements in several comorbidities. For patients with a BMI between 35 and 40, the data strongly support the

superiority of surgical therapy but cannot be considered conclusive in the absence of a study with a concurrent comparison group. Similarly, the evidence supports but does not prove an effect of surgical treatment for obesity on improvement in a large number of weight-related comorbidities for this population.

Further supporting the superiority of surgical therapy in patients with a BMI of 40 or greater is the observation that the weight loss reported in surgical studies is an order of magnitude greater than weight loss reported in pharmaceutical or diet studies of obesity (weight losses of 20-40 kg at one or two years in surgical studies versus 2 to5 kg in pharmaceutical studies), although direct comparisons cannot be made across studies because the patient populations are clearly different: The surgical studies enrolled only patients who are severely obese, whereas the average BMI in the medical weight loss studies was about 33. Additionally, many surgical studies report sustained weight loss (i.e. at 24 months or longer), whereas studies of medical weight loss therapies that report data beyond 12 months are rare, and those that do tend to report regain of most initial weight loss.

Both RCT data and observational data demonstrate clearly that RYGB results in greater weight loss than vertical banded gastroplasty. All three procedures for which we found data—RYGB; VBG; and laparoscopic adjustable band procedures—report substantial long-term weight loss.

Risks

We divided the risks of surgery or adverse events associated with it, into mortality and morbidity and further divided morbidity risks into four primary and six secondary categories, based on research findings. Our analyses were stratified by study design: Randomized trials have strong internal validity but are frequently of small sample size and limited generalizability; case series frequently contain data on many more patients, but comparisons of outcomes across procedures in different publications may not be warranted. Randomized and controlled clinical trials (CCTs) were considered to have sufficient internal validity for statistical comparisons of outcomes between groups within individual studies to be made, and—where the number of studies comparing the same surgical procedures was sufficient (two or more)—we pooled the results. Data from case series were used (along with data from RCTs/CCTs) to calculate the simple proportion of outcomes by procedure, but no statistical comparisons were made between proportions across different procedures, as we did not judge these comparisons to have sufficient internal validity to justify such comparisons: Patient selection and other factors may vary greatly across studies. Nevertheless, we present these findings alongside our findings from RCTs and CCTs, to allow the reader to compare and contrast the findings from the two study designs.

Our findings for mortality are presented in Table 18. Surgical procedures are divided into four categories: RYGB, biliopancreatic diversion (BPD), adjustable band procedures, and VBG. “Early” deaths were those occurring 30 days or less after the procedure or those self-defined as “early” in the original report. “Late” deaths were those occurring more than 30 days from the procedure or self-defined as “late” in the original report. We included “postoperative” deaths as “early” deaths when the time was not specified. Three observations are worth making from Table 18. First, no clear pattern of differential mortality between the various procedures emerges; second, no clear pattern emerges in terms of higher or lower early death rates in randomized

trials compared with case series. Third, in these reports, early mortality following bariatric surgery is less than 1 percent.

These data on mortality came from selected patient populations, that is, a specific clinic or surgeon performing the procedures on patients enrolled in a research study. The first assessment of 30-day mortality in unselected patients was reported by Dr. David Flum at the 2003 Clinical Congress of the American College of Surgeons.[268] Among more than 62,000 procedures performed in the state of Washington between 1987 and 2001, the 30-day mortality as assessed using administrative data was 1.9 percent. Furthermore, a strong association was observed between a surgeon's experience and mortality: Surgeons who had performed 20 or fewer procedures during the period of the study had an almost 5 percent rate of 30-day mortality.

With regard to adverse events other than mortality, reports vary among the studies. We aggregated these reports by using clinical judgment to create the categories in Tables 3, as described in Chapter 2. Table 19 presents the comparisons among three different procedures: RYGB versus VBG; RYGB versus banding procedures; and VBG versus banding procedures. Data are summarized from RCTs/CCTs (and pooled results calculated, as appropriate) and for case series plus single arms from RCTs/CCTs ("All Studies"). We caution readers when drawing conclusions from these data: *In our judgment, these data support but do not prove any hypothesis.* Still, a few observations are worth noting.

First, we note that most of the RCT/CCT data cells include at most one study. Only four trials were identified, and three of these trials compared RYGB to VBG. In most cases, only a few hundred patients have been studied in each comparison. Second, none of the comparisons of complications between these surgical procedures show statistically significant differences, and the 95% confidence intervals are very wide, that is, we can neither conclude nor exclude that clinically important differences exist. For example, the proportion of patients with reported anastomotic or stomal stenosis was about 5 percent higher (absolute percentage) in the VBG group than in the RYGB group, but these differences are not significant. Third, the absolute rates of some complications are substantial, although many may be minor in their degree of severity. For example, the proportion of subjects receiving VBG who have gastrointestinal complications is 15.2 percent in the RCT/CCT data and 17.8 percent in the case series data; the proportion of subjects receiving RYGB who experience nutritional deficiencies is 26.8 percent in the case series data (many of these nutritional deficiencies were mild); and the proportion of subjects receiving a banding procedure who require reoperation is 7.3 percent in the case series data. Fourth, some differences between procedures in the proportions of subjects with different complications or adverse events are compatible with the anatomic changes caused by the procedure. Thus, for example, gastrointestinal symptoms are reported by almost 18 percent of patients treated with VBG but reported by fewer than half that number of patients treated with banding procedures, although this difference was not statistically significant. At a minimum, these data indicate that the proportion of patients with adverse events or complications may be on the order of 10 percent to 20 percent (although the majority of these may be mild and respond to conservative treatment) and that the occurrence of these complications may differ among procedures in ways that are clinically important.

Table 20 presents our comparisons of adverse events and complications for all bariatric procedures performed with either an open or laparoscopic approach. Again, data are summarized separately for controlled trials and for all studies. While more controlled trials are shown in Table 20 than in Table 19, we note that the number of controlled trials is still relatively small.

Thus, similar caveats apply to the interpretation of these data as applied to the interpretation of the data in Table 20. In contrast to the data presented in Table 19, Table 20 includes several comparisons of RCT/CCT data that have a statistically significant or prima facie difference between procedures: the complications of wound, all; wound infection, major; wound infection, minor; and incisional hernia. Interestingly, for some complications, such as respiratory complications, no data were found to support the beliefs regarding a lower occurrence in laparoscopically treated patients. In summary, the data support a reduced occurrence of wound and incisional hernia complications in patients treated laparoscopically compared to open procedures; however, data are insufficient to reach conclusions about differences in other complications.

Use of Obesity Medication and Bariatric Surgery in the Adolescent and Pediatric Population

As part of our literature search and appraisal process, we attempted to identify studies that reported data specific to adolescent (defined by our technical expert panel as ages 13 to 17) and pediatric (defined by our technical expert panel as age 12 and under) populations. Too few studies were identified to permit quantitative analysis. The following represents a narrative summary of our findings regarding adolescents.

Efficacy and Safety of Weight Loss Medication

We identified three controlled trials of medication that reported data specific to adolescents. One study (described in two reports) assessed mazindol, which was not an included drug for this review.[269,270] A second study assessed the use of a caffeine/ephedrine mixture, which was also not an included drug for this review.[271] Elimination of that study left one study for our review.[272] This study, which examined the efficacy of sibutramine, was conducted in two six-month phases. Phase I was a double-blind RCT; in Phase II, all participants received the drug. The study enrolled boys and girls ages 13 to 17 years who had a BMI of 32 to 44. Subjects were randomized to receive sibutramine (beginning at 5 mg per day and increasing to 15 mg per day) or matched placebo. All participants received the same comprehensive family-based behavioral weight loss program, which included regular group sessions led by dieticians and psychologists or psychiatrists. Participants in both groups were instructed to consume a 1200- to 1500 Kcal-per-day diet of conventional foods with approximately 30 percent of calories from fat, 15 percent from protein, and the remainder from carbohydrate. Exercise of approximately 120 minutes per week or more was also prescribed. Overall, 82 subjects were enrolled, with a mean age of 14 and a mean BMI of 38. Approximately two-thirds of subjects were female. At 6 months, subjects treated with sibutramine lost a mean of 7.8 kg, which was equal to an 8.5 percent reduction in initial BMI, whereas placebo-treated patients had a significantly smaller, 3.2 kg, weight loss, which was equal to a 5.4 percent reduction in BMI. More than twice as many sibutramine-treated patients achieved a 5 percent to 10 percent reduction in initial BMI than did placebo-treated patients. During Phase II, the patients who had switched from placebo treatment to sibutramine lost an additional 1.3 kg of weight, while those who continued on sibutramine gained 0.8 kg.

Sibutramine-treated subjects had an average increase in heart rate of five to six beats per minute compared to placebo-treated subjects, whereas blood pressure changed minimally between groups. With respect to other adverse events, three of the patients treated with sibutramine experienced a “marked and sustained” increase in blood pressure of greater than or equal to 10mm Hg, which required discontinuation of the medication; no such events were reported in the placebo group. No other differences in adverse events were reported between groups.

Efficacy of Bariatric Surgery

Our literature search identified twelve papers that reported weight loss after bariatric surgery in adolescents. Three of these papers[196-198] reported results following jejunoileal bypass and will not be considered here. Two papers[273,274] reported case series results from the same institution; only the latter paper is included to avoid potentially double counting patients.

The first study was a case series of ten adolescents who underwent RYGB surgery.[275] These patients ranged in age from 15 to 17 years, 7 of the 10 were female, and their BMIs ranged from 41.4 to 70.5. Most patients had comorbidities, including sleep apnea, hypertension, and vertebral compression fractures. The authors reported no early postoperative complications. Weight loss in excess of 30 kg was observed in 9 of the 10 patients at postsurgical followup times of 8 months to 156 months. The “most serious complication” reported was protein calorie malnutrition and micronutrient deficiency, which developed in one patient approximately one year after the bypass. This patient’s recovery was “uneventful” after total parental nutrition was instituted. Two other patients had symptomatic cholelithiasis that required cholecystectomy. A fourth patient experienced small bowel obstruction ten years after gastric bypass surgery, and a fifth patient required repair of an incisional hernia. Iron deficiency anemia occurred in five of the seven girls, and transient folic acid deficiency occurred in three patients.

The second study reviewed the 20-year experience of one bariatric surgery center with adolescents ages 13 to 17.[276] Thirty-three subjects received surgery between 1981 and 2001. Of these 33, 19 were female and 14 were male. The mean preoperative BMI was 52, and the mean age was 16 years. Preoperative comorbid illnesses included one case of Type II diabetes, 10 cases of hypertension, 6 cases of sleep apnea, 5 cases of gastroesophageal reflux, and 10 cases of degenerative joint disease. One patient underwent horizontal gastroplasty, two had vertical banded gastroplasties, 17 had standard gastric bypass procedures, 10 had long limb gastric bypass, and three had distal gastric bypass. The authors reported no operative deaths or anastomotic leaks. They reported one case of pulmonary embolism, one major wound infection, four minor wound infections, three stomal stenoses treated with laparoscopic dilation, and four marginal ulcers treated medically. The authors report initial weight loss in all patients, but five patients had regained all or most of their lost weight at five or ten years after surgery. For the other 28 patients, the authors report an average of 77 percent of excess weight lost and a BMI of 29 at five postoperative years, with slight increases over longer durations (to a BMI of 30 and 31 at ten years and 14 years, respectively). Two late deaths were judged unrelated to surgery. Comorbid conditions were resolved in all but two patients with hypertension, two patients with gastroesophageal reflux disease, and 7 patients with joint pain.

The third study[277] reported the results of one surgeon’s experience performing the procedures on 22 severely obese children between 1983 and 1995 (9 males and 13 females; 3 patients were

under the age of 12). During the first 5 years of the study period, VBG was performed; then the procedure was changed to RYGB and BPD. The author stratified his analysis by the diagnosis of preoperative sleep apnea. Among patients without the diagnosis, the BMI fell postoperatively from 56.4 to 35.5, whereas among those with the diagnosis, the BMI fell from 70.3 to 46.5. Of the nine sleep apnea patients who had long-term followup, all had resolution of their sleep apnea. Postoperative complications included one case each of vitamin A and D deficiency, folic acid deficiency, gallstone development, kidney stone, laryngeal edema, and incisional hernia, and three cases of protein deficiency. One patient was found to have a brain stem tumor at the time of operation and subsequently died. The author reported two late deaths, the one just mentioned and one in an eighteen-year-old female who was found dead at home 3.5 years postoperatively.

The fourth study[274] reports the results of gastric bypass surgery in 41 children and adolescents, including 11 with Prader-Willi syndrome (a type of developmental disability that is characterized in part by insatiable appetite and resultant weight gain), who were all under age 20 years. Most patients underwent gastric bypass; however, eight patients had gastroplasty. Results reported here are for the 30 patients without Prader-Willi syndrome only. The average preoperative weight was 238 percent of ideal body weight. At three years post-op, average weight decreased to 171 percent of ideal body weight, and at five years post-op, it was 187 percent of ideal body weight. Eleven major complications occurred in the early postoperative period : three wound infections, two of which occurred in conjunction with dehiscence; two cases of stomal obstruction (one which required revision); three cases of atelectasis; two cases of pneumonia; and one case of subphrenic abscess. Two deaths occurred. One death occurred on the third postoperative day, ostensibly due to a suture line leak and overwhelming sepsis or massive pulmonary embolus, although no postmortem was performed. The second death was sudden and unexpected at 36 months postoperatively. Four of the patients ultimately underwent revisions for failure to lose weight satisfactorily.

Two studies reported results for patients who were treated with laparoscopic gastric banding. The first of these[278] studies reported on 17 patients under the age of 20 who were operated on by a single surgeon; of these patients, 7 were between the ages of 12 and 17. Among the larger group of 17 patients, the median preoperative BMI was 44.7 which fell postoperatively to 36.1 at 6 months, 32.6 at 12 months, and 30.2 at 24 months. The authors reported no effect on growth or development at followup in patients who underwent the procedure. They also reported complications in two patients, one with band slippage at 11 months, which was corrected laparoscopically, and another that required replacement of a leaking port. The second study[279] reported on 11 patients between the ages of 11 and 17 years (8 girls), all of whom received laparoscopic adjustable gastric bands. The mean preoperative BMI was 46.6. One patient had heart failure and pulmonary hypertension, two patients had amenorrhea, and another had gallstones. The author reported no perioperative complications and no late complications. After a mean of 23 months of followup, the mean BMI had fallen to 32.1 with improvement in all comorbid conditions.

The last two studies involved surveys of patients who had undergone bariatric surgery as adolescents. The first of these contacted 14 of 18 patients who had been less than 21 years of age at the time of surgery (performed between 1982 and 1994). These patients (11 females and 3 males) had all undergone VBG. The preoperative BMIs were 45 and 59, respectively, which fell postoperatively, and at the time of the interview were 33 and 35, respectively. The authors reported that one male patient with preoperative sleep apnea had “complete clinical resolution”

following weight loss. The second study consisted of an interview of 34 out of 39 patients who had undergone RYGB or VBG between 1979 and 1990. The patients (27 females and 7 males) were all between the ages of 11 and 19 at the time of the surgery. Preoperative BMI averaged 47 and at followup was 32. Complications included a staple line failure in one patient, which was also "suspected in other patients with large weight regains." The authors reported no major postoperative complications. Five revision procedures and four subsequent cholecystectomy procedures were scheduled or performed.

In summary, a handful of case reports of bariatric surgery in adolescents have appeared, reporting on a total of 172 subjects. These reports document benefits in terms of weight loss and resolution of complications as well as harms in terms of surgical complications. No studies have compared these benefits and harms to those of similar patients who received nonsurgical therapies such as diet or medication.