ICSI

INSTITUTE FOR CLINICAL SYSTEMS IMPROVEMENT

Health Care Guideline:

Prevention and Management of Obesity (Mature Adolescents and Adults)

Fourth Edition
January 2009

The information contained in this ICSI Health Care Guideline is intended primarily for health professionals and the following expert audiences:

- physicians, nurses, and other health care professional and provider organizations;
- health plans, health systems, health care organizations, hospitals and integrated health care delivery systems;
- health care teaching institutions;
- health care information technology departments;
- medical specialty and professional societies;
- researchers;
- federal, state and local government health care policy makers and specialists; and
- employee benefit managers.

This ICSI Health Care Guideline should not be construed as medical advice or medical opinion related to any specific facts or circumstances. If you are not one of the expert audiences listed above you are urged to consult a health care professional regarding your own situation and any specific medical questions you may have. In addition, you should seek assistance from a health care professional in interpreting this ICSI Health Care Guideline and applying it in your individual case.

This ICSI Health Care Guideline is designed to assist clinicians by providing an analytical framework for the evaluation and treatment of patients, and is not intended either to replace a clinician's judgment or to establish a protocol for all patients with a particular condition. An ICSI Health Care Guideline rarely will establish the only approach to a problem.

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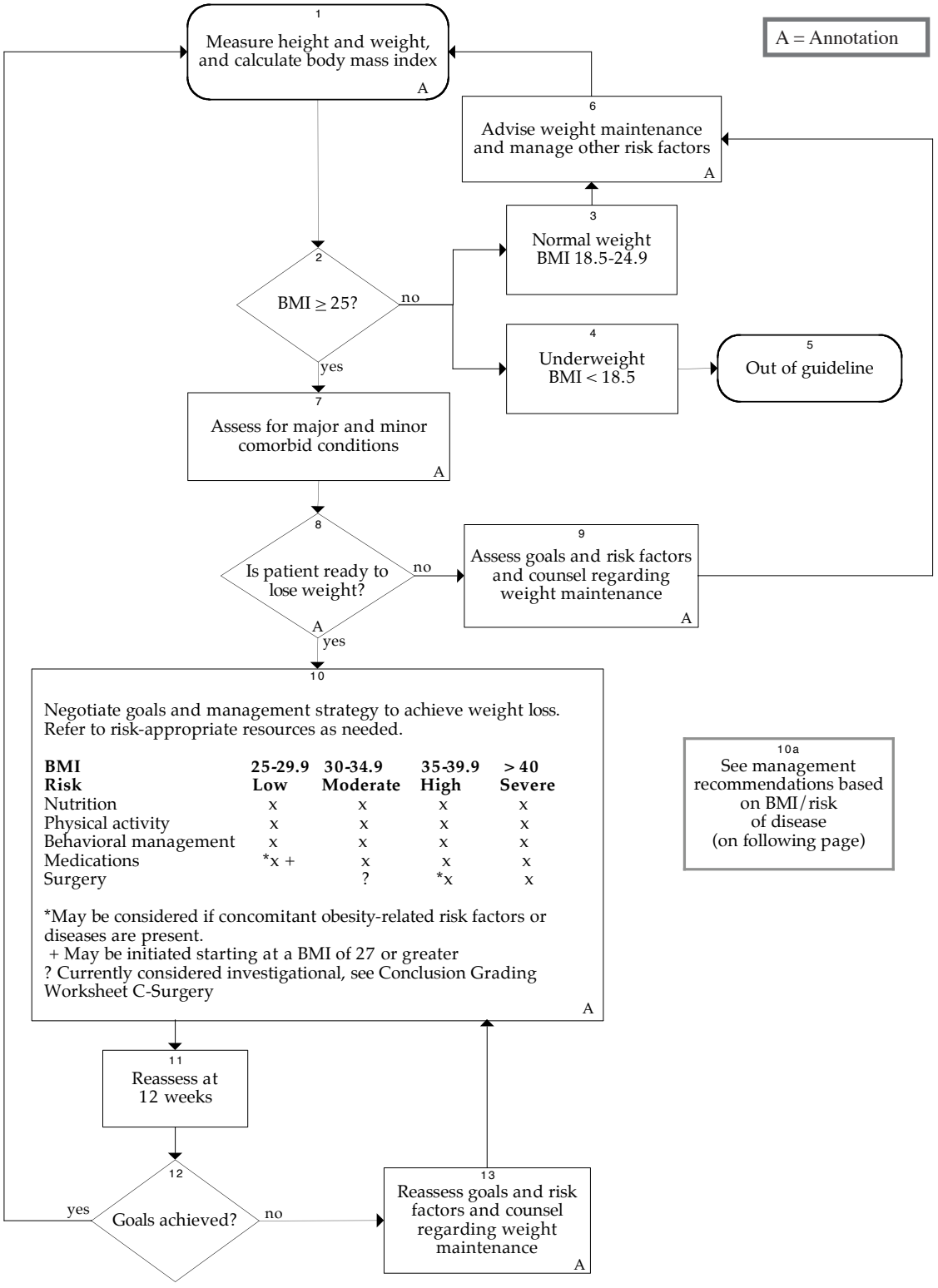
Prevention and Diagnosis Algorithm



Management Recommendations Based on Body Mass Index/Risk of Disease

Nutrition (balanced healthy eating plan or lower calorie balanced eating plan)

- Encourage at least five servings of fruits and vegetables per day, whole grains with a fiber intake of 35 grams or more daily, less than or equal to 30% of calories from fat (7%-10% of calories from saturated fat, less than or equal to 1% from trans fat).
- For weight loss, encourage calorie reduction by evaluating portion sizes and number of servings recommended.
- Provide tips for managing eating in social situations, dining out, take-out foods and food label reading.
- Provide referral to a dietitian, nutritionist or structured medically supervised nutrition program if available.

Physical activity

- Minimally, all patients should be encouraged to do at least 10 minutes of physical activity above what they are already doing each day and gradually increase the amount of time, followed by an increase in intensity.
- Ideally, all patients should meet the current recommendations of 30 to 60 minutes of moderate-intensity activity on most days per week.
- Patients with chronic activity limitations (e.g., arthritis, respiratory dysfunction, neuropathy, morbid obesity) should be evaluated and managed to establish or enhance patient mobility.
- Provide tips for adding small bouts of physical activity to daily activities: for example, taking the stairs, parking farther away, exercising while watching TV. Activity breaks from screens (TV, computer, other media) are also important.

Behavioral management

- Identify behaviors that may lead to increased weight gain: for example, stress, emotional eating, boredom.
- Help patients set specific, measurable, time-limited goals to decrease calorie intake and increase physical activity as appropriate.
- Suggest patients weigh themselves weekly and record on a daily basis the amount and type of food/beverages consumed and physical activity completed.
- Provide support and encourage patients to also seek support from family, friends and support groups in order to assist them with their eating, activity and weight goals.

Medication

- The short-term use of drugs (less than three months) has not generally been found to be effective.
- Pharmacotherapy should be included only in the context of a comprehensive treatment strategy.
- Sibutramine and orlistat are safe for most patients when carefully monitored by a physician; they may be part of a program for weight management or maintenance, which should include nutrition and physical activity changes when indicated.

Surgery

- Bariatric surgery is indicated in carefully selected patients: evidence indicates that patients with preoperative body mass index between 30 and 35 kg/m^2 have comparable initial weight loss results and comorbidity interventions under both surgical and behavioral/pharmaco therapies, but one trial showed that only surgically treated patients continued to lose weight six months later with a body mass index greater than or equal to 40 or with a body mass index of 35-39.9 and who are at a very high absolute risk for increased morbidity or premature mortality (see Annotation #7, Table 5). Patients are to be motivated, well-informed in disease management, psychologically stable and accepting of operative risks.

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Foreword

Introduction

Obesity is a chronic, multifactorial disease with complex psychological, environmental (social and cultural), genetic, physiologic, metabolic and behavioral causes and consequences. The prevalence of overweight and obese people is increasing worldwide at an alarming rate in both developing and developed countries. Environmental and behavioral changes brought about by economic development, modernization and urbanization have been linked to the rise in global obesity. Obesity is increasing in children and adults, and true health consequences may become fully apparent in the near future.

Obesity has become a national epidemic in the United States with 32% of non-institutionalized adults being obese, and 66.3% being overweight or obese. The most recent data suggests that 17% of adolescents age 12-19 years are overweight and an additional 16% are at risk for overweight *(Ogden, 2006 [C])*.

The economic impact of obesity and its related conditions on the U.S. economy is staggering and has been estimated at about $118 billion in the late 1990s, or about 12% of the national health care budget, according to the Worldwatch Institute in 2000.

Obesity is the second leading cause of preventable death in the U.S., with only tobacco use causing more deaths *(Mokdad, 2004 [C])*. More than 110,000 deaths per year are associated with obesity *(Flegal, 2005 [C])*.

The prevalence of various medical conditions increases with overweight and obesity for men and women as shown in Tables 1 and 2.

Note: Some studies show significant ethnic variability *(Hedley, 2004 [C]; Ogden, 2002 [C])*.

Table 1. Prevalence of Medical Conditions by Body Mass Index (BMI) for Men

Medical Condition	Body Mass Index			
	18.5 to 24.9	25 to 29.9	30 to 34.9	≥ 40
	Prevalence Ratio (%)			
Type 2 Diabetes	2.03	4.93	10.10	10.65
Coronary Heart Disease	8.84	9.60	16.01	13.97
High Blood Pressure	23.47	34.16	48.95	64.53
Osteoarthritis	2.59	4.55	4.66	10.04

Table 2. Prevalence of Medical Conditions by Body Mass Index (BMI) for Women

Medical Condition	Body Mass Index			
	18.5 to 24.9	25 to 29.9	30 to 34.9	≥ 40
	Prevalence Ratio (%)			
Type 2 Diabetes	2.38	7.12	7.24	19.89
Coronary Heart Disease	6.87	11.13	12.56	19.22
High Blood Pressure	23.26	38.77	47.95	63.16
Osteoarthritis	5.22	8.51	9.94	17.19

Source: National Health and Nutrition Examination Survey (NHANES) III, 1988-1994.

Scope and Target Population

This guideline will address the prevention, diagnosis and management of obesity in mature adolescent and adult patients, including behavioral approaches, drug treatment and surgery.

This guideline does not include the patient populations of pregnant women or bodybuilders/weight trainers. This guideline does not address investigational therapies or trials, but will review them once approved from the Food and Drug Administration.

While this guideline does not address the pediatric population, the work group acknowledges the importance of addressing this epidemic and is continuing to gather evidence for future guideline expansion. The work group encourages health care systems to take an active role to educate families and children on body mass index measurements, nutrition, physical activity and lifestyle change.

For more information, the work group recommends the following resources:

Appendix A of this guideline, "Body Mass Index-for-Age Percentiles."

Whitlock E, et al. Screening and Interventions for Childhood Overweight: A Summary of Evidence for the U.S. Preventive Services Task Force. *Pediatrics* 2005;116;125-44.

Institute for Clinical Systems Improvement. Treatment of Obesity in Children and Adolescents. (#90, 2005).

Himes JH, et. al. Guidelines for overweight in adolescent preventive services: recommendations from an expert committee. The Expert Committee on Clinical Guidelines for Overweight in Adolescent Preventive Services. *Am J Clin Nutr* 1994;59:307-16.

Clinical Highlights and Recommendations

- Obesity is a chronic disease that is a multifactorial, growing epidemic with complex political, social, psychological, environmental, economic and metabolic causes and consequences. Obesity affects essentially every organ system in the body. Health consequences increase across the body mass index span, not just for the extremely obese. *(Introduction)*
- Calculate the body mass index; classify the individual based on the body mass index categories. Educate patients about their body mass index and their associated risks. *(Annotation #1; Aim #1)*
- Effective weight management strategies are available and include nutrition, physical activity, lifestyle changes, medication and surgery. *(Annotation #6; Aim #2)*
- The physician should follow the 5 A's (Ask, Advise, Assess, Assist, Arrange). Physician intervention can be effective, the physician can have an important influence, and successful weight management is possible. *(Annotation #8, Aim #3)*
- Weight management requires a team approach. Be aware of clinical and community resources. The patient needs to have an ongoing therapeutic relationship and follow-up with a health care team. Weight control is a lifelong commitment, and the health care team can assist with setting specific goals with the patient. *(Annotations #10, 13; Aim #4)*
- Beyond their clinical role, primary care physicians should be aware of their roles as community leaders and public health advocates. *(Annotations #10, 13; Aim #4)*

Priority Aims

1. Increase awareness of body mass index. (*Annotation #1)*
2. Improve the percentage of patients with an elevated body mass index who have received education and counseling regarding weight loss. *(Annotation #10)*
3. Improve the outcome of treatment for obesity. *(Annotations #8, 10)*
4. Improve community (employers, schools) involvement in the prevention and treatment of obesity. *(Annotations #10, 13)*

Key Implementation Recommendations

The following system changes were identified by the guideline work group as key strategies for health care systems to incorporate in support of the implementation of this guideline.

1. Establish a system for using a Patient Readiness Scale. The scale can be used to determine if the patient is ready to talk about weight loss and/or would like information.
2. Establish a system for staff to efficiently calculate body mass index prior to the physician entering the exam room. This action may be considered a vital sign and built into the rooming protocol. A body mass index chart can be placed by each scale in the clinic, if the organization has an electronic medical record, it may have a component for immediate calculation.
3. Develop tracking systems to produce periodic audits for use in developing solutions to identified problems.
4. Establish a system for staff and physician training around skills and knowledge in the areas of motivational interviewing; brief, focused advice on nutrition, physical activity and lifestyle changes; and evaluation of evidence of effectiveness of treatment options.
5. Establish a system for continuing education on evidence-based obesity management for providers, nurses and ancillary clinic staff.
6. Remove barriers to referral programs for weight loss. Know where your resources are and what processes are required: for example, if your organization refers patients to an outside source, what are the criteria for referral?
7. Develop medical record systems to track status of patients under the provider's care with the capability to produce a tickler system for patient follow-up by provider/staff.
8. Use tools such as posters and brochures throughout the facility to promote a healthy lifestyle around nutrition and activity while encouraging patient knowledge of their body mass index.
9. Develop patient-centered education and self-management programs, which may include self-monitoring, self-management and skills such as journaling.
10. Outcomes measurement:
    - Build systems for outcomes measures, as well as ongoing process measures
    - Response rate to various treatments/strategies
    - Improvement rates – the body mass index is stable or has decreased over time

11. Systems to coordinate care ensure continuity and keep providers informed of progress.
    - Build electronic systems or tickler system (if no electronic medical record).
    - Educate patients to foster awareness and knowledge of body mass index for self-monitoring and reporting.
    - Structure follow-up visits with patient per guideline recommendations.

Related ICSI Scientific Documents

Guidelines

- Hypertension Diagnosis and Treatment
- Diagnosis and Management of Type 2 Diabetes Mellitus in Adults
- Lipid Management in Adults
- Major Depression in Adults in Primary Care
- Diagnosis and Treatment of Obstructive Sleep Apnea
- Preventive Services for Adults
- Assessment and Management of Chronic Pain

Technology Assessment Reports

- Pharmacological Approaches to Weight Loss in Adults (#71, 2003)
- Gastric Restrictive Surgery for Clinically Severe Obesity in Adults (#14, 2005)
- Diet Programs for Weight Loss in Adults (#83, 2004)
- Behavioral Therapy Programs for Weight Loss in Adults (#87, 2004)
- Treatment of Obesity in Children and Adolescents (#90, 2005)

Disclosure of Potential Conflict of Interest

ICSI has adopted a policy of transparency, disclosing potential conflict and competing interests of all individuals who participate in the development, revision and approval of ICSI documents (guidelines, order sets and protocols). This applies to all work groups (guidelines, order sets and protocols) and committees (Committee on Evidence-Based Practice, Cardiovascular Steering Committee, Women's Health Steering Committee, Preventive & Health Maintenance Steering Committee and Respiratory Steering Committee).

Participants must disclose any potential conflict and competing interests they or their dependents (spouse, dependent children, or others claimed as dependents) may have with any organization with commercial, proprietary, or political interests relevant to the topics covered by ICSI documents. Such disclosures will be shared with all individuals who prepare, review and approve ICSI documents.

No work group members have potential conflicts of interest to disclose.

Introduction to ICSI Document Development

This document was developed and/or revised by a multidisciplinary work group utilizing a defined process for literature search and review, document development and revision, as well as obtaining input from and responding to ICSI members.

For a description of ICSI's development and revision process, please see the Development and Revision Process for Guidelines, Order Sets and Protocols at http://www.icsi.org.

Evidence Grading System

A. Primary Reports of New Data Collection:

Class A: Randomized, controlled trial

Class B: Cohort study

Class C: Non-randomized trial with concurrent or historical controls
Case-control study
Study of sensitivity and specificity of a diagnostic test
Population-based descriptive study

Class D: Cross-sectional study
Case series
Case report

B. Reports that Synthesize or Reflect Upon Collections of Primary Reports:

Class M: Meta-analysis
Systematic review
Decision analysis
Cost-effectiveness analysis

Class R: Consensus statement
Consensus report
Narrative review

Class X: Medical opinion

Citations are listed in the guideline utilizing the format of *(Author, YYYY [report class])*. A full explanation of ICSI's Evidence Grading System can be found at http://www.icsi.org.

Algorithm Annotations

1. Measure Height and Weight, and Calculate Body Mass Index

Key Points:

- Health consequences exist across the body mass index span, and obesity is a multifactorial, chronic disease.
- Body mass index should be calculated preferably annually for screening and as needed for management.
- Body mass index calculation extends to all age groups. Adolescents less than Tanner stage 5 and children should be evaluated by available growth charts.

1a. Calculate body mass index

Calculate the body mass index at least annually for screening and as needed for management. Classify it based on the body mass index categories. Educate patients about their body mass index and associated risks for them *(McTigue, 2003 [M])*.

Body Mass Index Calculation

$$\frac{\text{weight}}{\text{height squared}} = \frac{\text{kg}}{\text{m}^2} \text{ or } \frac{(\text{lbs} \times 703)}{\text{inches}^2}$$

Table 3: Adult BMI Categories

BMI	Category
Less than 18.5	Underweight
18.5-24.9	Normal weight
25-29.9	Overweight
30-34.9	Obese – class I
35-39.9	Obese – class II
40 or more	Extreme obesity – class III

Mature adolescents

For the purpose of this guideline, physiologic maturity will be considered as skeletal maturity (greater than 95% of adult height) and a minimum Tanner stage of 3. The extension of guideline medication and surgical recommendations to this population is physiologically feasible. However, given the complexity of obesity treatment and psychological issues, the use of medication and surgery in physiologically mature adolescents needs to be addressed within provider community practice standards.

Body mass index in children and adolescents is based on a percentile while the child is still growing in height. These percentiles are defined by National Health and Nutrition Examination Survey (NHANES) data and therefore may not need to be adjusted for different ethnic groups.

Overweight is defined as a body mass index greater than 85%, and obesity is defined as body mass index greater than 95%. Extreme obesity is now defined as a body mass index greater than 99% for age.

See Appendix A, "Body Mass Index-for-Age Percentiles."

A body mass index calculation is worthwhile in the growing patient because it provides a reference point for future comparison. Subsequent observations establish a relative trajectory for this index of obesity. Although there are no standards for rate of change of body mass index per year, a rapid increase or decrease warrants clinical attention. The separation between 50th and 75th percentiles is approximately two to three body mass index units for adolescent girls across ethnic groups. Adolescent boys have approximately two body mass index units difference between these percentiles. An annual increase of greater than three units suggests excessive gain *(Barlow, 1998 [R])*.

The clinical significance of an abnormal or rapidly changing body mass index is assessed with the following in mind:

- Body mass index is not a direct measure of adiposity. It is a derived value that correlates well with total body fat and markers of secondary complications, e.g., hypertension and dyslipidemia *(Barlow, 1998 [R])*.
- An abnormally high body mass index does not address the distribution of body fat: i.e., central vs. peripheral or visceral vs. subcutaneous. Central or visceral fat carry greater risk for morbidity and mortality.
- Waist circumference (as recommended by the National Heart, Lung and Blood Institute: see Annotation #7), provides an additional dimension for assessing visceral adiposity and clinical risk.
- Metabolic assessment is important in the patient at risk, especially if there is a family history of heart disease or type 2 diabetes mellitus.
- Clinical conditions associated with adolescent obesity are found in Table 4: Clinical Conditions Associated with Adolescent Obesity.

Table 4: Clinical Conditions Associated with Adolescent Obesity*

History:	Physical:	Condition:
Developmental delays	Dysmorphic features	Genetic disorders, e.g., Prader-Willi syndrome, Lawrence Moon-Biedl syndrome
Poor linear growth	Short stature	Hypothyroidism, Cushing's, growth hormone deficiency
Nocturnal breathing difficulty	Enlarged tonsils	Sleep apnea, hypoventilation syndrome
Exercise intolerance	Wheezing	Asthma
"Dirty neck"	Acanthosis nigricans	Insulin resistance, type 2 diabetes mellitus
Hip/knee pain	Loss of hip range of motion	Slipped capital femoral epiphysis
Amenorrhea	Hirsutism, Acanthosis nigricans, Insulin resistence	Polycystic ovarian syndrome or HAIRAN syndrome
Headache	Optic disc changes	Pseudotumor cerebri
Abdominal pain	Right upper quadrant tenderness	Gall bladder disease

* Depression, anxiety, eating disorders and sexual abuse are also important clinical associations with adolescent obesity and should be screened by history of dysfunction in mood, school performance, peer relationships and eating patterns.

6. Advise Weight Maintenance and Manage Other Risk Factors

Key Points:

- It is important to address the issue of weight maintenance for those with body mass index in the normal range.
- Weight management includes physical activity, nutrition and behavior management strategies.

Lifetime risk of obesity is high for residents of the United States. Lifetime risk of diabetes is about 30% for men and 35% for women, and lifetime risk for obesity is higher than this *(Narayan, 2003 [C])*.

Therefore, it is important to address the issue of weight maintenance for those with body mass index in the normal range (18.5 to 24.9).

Successful weight management requires a lifestyle approach that integrates physical activity, nutrition, behavioral management and attention to psychosocial needs.

- First, encourage regular physical activity at recommended levels. Regular physical activity is strongly related to maintaining normal weight. In selecting types of physical activity, it is important to consider the age of the patient, musculoskeletal limitations and availability of exercise facilities. For inactive patients, this may include as little as 10 minutes of physical activity a day. Ideally, 30 to 60 minutes of moderate physical activity on most days of the week is recommended. However, for those who have lost a considerable amount of weight, higher amounts of physical activity may be required for weight maintenance. Enjoyment and variety of physical activity are also key features for adherence.
- Second, provide structured lifestyle modification suggestions that include specific nutrition recommendations, educational sessions and frequent contact with health care providers, such as a dietitian. Focus on calorie balancing, using a combination of decreased caloric intake with increased calorie expenditure. Include nutrition education (e.g., interpreting food labels); managing restaurant and social eating situations; making healthy, nutritious food choices; using portion control; and recipe modification.

  There is considerable evidence that individuals consuming low-fat, low-calorie diets are successful at maintaining weight loss for 12 months and longer. Data from the National Weight Control Registry demonstrates that successful weight maintainers consume a low-calorie diet containing ~ 40 g fat (24% of calories), 200 g carbohydrate (56% of calories) and 70 g protein (19% of calories). A low-fat diet (25%-30% calories from fat) is considered the conventional therapy for treating obesity *(Klein, 2004 [R])*.
- Third, encourage behavior management strategies that may include weekly weight checks, food journals and monitoring daily routine that focuses on a balanced lifestyle. Balance includes eating a nutritionally balanced breakfast soon after awakening and eating balanced meals at regular intervals thereafter; incorporating fun physical activity into the day; and scheduling the week to include rest, play and social interactions along with work, school and family responsibilities.

  Specific behavioral strategies to promote behavior change include self-monitoring some aspect of behavior that, in itself, typically results in behavior change; non-food rewards and positive reinforcements; reminders; stimulus control (changing social or environmental cues that trigger eating behavior); stress management and problem solving and helping patients believe they can be successful.

7. Assess for Major and Minor Comorbid Conditions

Key Points:

- It is important to assess for other conditions as treatment decisions and outcomes may be influenced by their presence.
- Waist circumference greater than or equal to 40 inches for males and greater than or equal to 35 inches for females is an additional risk factor for complications related to obesity.
- For depression and eating disorders, brief screenings should be conducted if appropriate.
- Assessment should include a complete medical history to identify medications that may induce weight gain or interfere with weight loss.

Table 5: Comorbid Condition Assessment

Comorbid Condition	BMI			
	25-30	**30-35**	**35-40**	**40 +**
0	Counsel and educate: • Lifestyle changes • Behavioral management	Counsel and educate: • Lifestyle changes • Behavioral management • Medication therapy	Counsel and educate: • Lifestyle changes • Behavioral management • Medication therapy	Counsel and educate: • Lifestyle changes • Behavioral management • Medication therapy • Surgical options
1-2 Minor Comorbid Conditions	Counsel and educate: • Lifestyle changes • Behavioral management	Counsel and educate: • Lifestyle changes • Behavioral management • Medication therapy	Counsel and educate: • Lifestyle changes • Behavioral management • Medication therapy • Surgical options	Counsel and educate: • Lifestyle changes • Behavioral management • Medication therapy • Surgical options
Major Comorbid Conditions OR 3 Minor Comorbid Conditions	Counsel and educate: • Lifestyle changes • Behavioral management • Medication therapy The FDA approves drug therapy only for BMI greater than 27.	Counsel and educate: • Lifestyle changes • Behavioral management • Medication therapy	Counsel and educate: • Lifestyle changes • Behavioral management • Medication therapy • Surgical options	Counsel and educate: • Lifestyle changes • Behavioral management • Medication therapy • Surgical options

Minor Comorbid Conditions

- Cigarette smoking
- Hypertension (BP greater than or equal to 140/90) or current use of antihypertensives†
- LDL cholesterol > 130 mg/dL
- HDL cholesterol < 40 mg/dL for men; less than 50 mg/dL for women†
- Prediabetes*†
- Family history of premature coronary artery disease
- Age ≥ 65 years for males
- Age ≥ 55 years for females or menopausal females

Major Comorbid Conditions

- Waist circumference (males ≥ 40 inches, females ≥ 35 inches) †
- Established coronary artery disease
  - History of myocardial infarction
  - History of angioplasty
  - History of CABG
  - History of acute coronary syndrome
- Peripheral vascular disease
- Abdominal aortic aneurysm
- Symptomatic carotid artery disease
- Type 2 diabetes mellitus
- Obstructive sleep apnea

* The term pre-diabetes has recently been adopted by the American Diabetes Association and others, and refers to those who have a fasting plasma glucose of 100 mg/dL to 125 mg/dL inclusive, as well as those with a two-hour post-75-gram-oral-glucose tolerance test value of greater than or equal to 140 mg/dL to 200 mg/dL.

†The clustering of these symptoms have been described as the metabolic syndrome. Several formal definitions exist *(deFerranti, 2004 [C]; National Heart, Lung and Blood Institute, 2003 [R]; World Health Organization, 2004 [R])*.

Waist Circumferences

Clinicians may use the waist circumference as a measure of central adiposity. Men with waist circumferences greater than or equal to 40 inches (102 cm) and women with a waist circumference greater than or equal to 35 inches (88 cm) are at increased risk for cardiovascular disease and a range of other conditions such as sleep disorders and diabetes *(Lean, 1998 [D])*.

Body mass index conveys information about obesity, but this information may be supplemented by additional information on waist circumference. Body mass index has been shown to be an accurate predictor of future health states, and elevated body mass index elevates risk of cardiovascular events, cardiovascular death, total mortality, type 2 diabetes, sleep disorders, and myriad other clinical conditions *(Balkau, 2007 [D])*. Increased waist circumference also predicts many of these disorders *(Balkau, 2007 [D]; Davidson, 2008 [D])*. There is considerable current debate on whether or not waist circumference adds additional incremental information when measured in addition to body mass index. There is some evidence that for some patient subgroups, waist circumference that is elevated adds additional incremental information on future health states *(Janssen, 2002 [D]; Koster, 2008 [D])*.

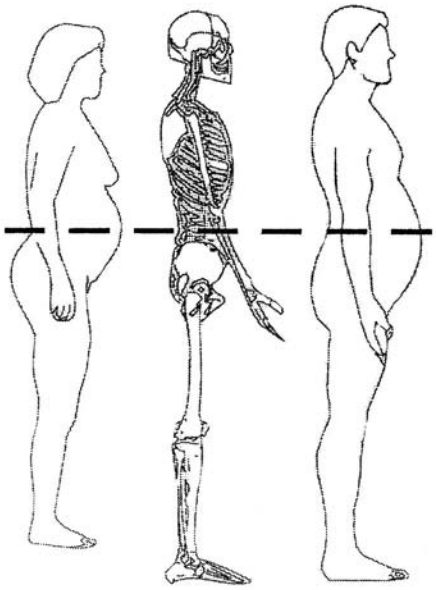
However, there is a cost associated with regular measurement of both body mass index and waist circumference. Body mass index measures require a mathematical calculation based on weight and height. Thus, body mass index can be computed automatically within electronic medical record (EMR) systems. Measurement of waist circumference would add time to primary care and other clinic visits, and measurements may be imprecise or variable in the absence of systematic and ongoing training of clinic staff members who measure waist circumference *(Panoulas, 2008 [C])*.

At this point in time, the data support systematic and periodic assessment of body mass index and use of this information to assess risk and guide interventions to manage elevated body mass index. In the opinion of the work group, measurement of waist circumference is useful in particular clinical circumstances, but is not justified as a routine clinic-based measure until additional data demonstrate how best to use waist circumference data clinically and demonstrate that the additional cost of waist circumference measurement on a routine basis translates into clinical benefits for patients with known elevation of body mass index, or in those with normal body mass index *(Freiberg, 2008 [C]; Klein, 2007 [R])*.

Waist circumference is an additional risk factor for complications related to obesity for males measuring greater than or equal to 40 inches, and females greater than or equal to 35 inches. While the work group acknowledges potential difficulty implementing the measurement of waist circumference, evidence shows the importance of measuring waist circumference because of other risk factors *(Lean, 1998 [D]; Yusuf, 2005 [C])*.

Waist Circumference Measurement

To measure waist circumference, locate the upper hip bone and the top of the right iliac crest. Place a measuring tape in a horizontal plane around the abdomen at the level of the iliac crest. Before reading the tape measure, ensure that the tape is snug, but does not compress the skin, and is parallel to the floor. The measurement is made at the end of a normal expiration.



Measuring-Tape Position for Waist (Abdominal) Circumference in Adults

Source: National Heart, Lung and Blood Institute.

Screening for Depression

The evidence showing the linkage between depression and obesity is mixed *(DiPietro, 1992 [B]; Friedman, 1995 [R]; Jorm, 2003 [D]; Roberts, 2003 [B])*. Higher rates of depression have been found in severely obese people, especially younger women with poor body image *(Dixon, 2003 [C]; Onyike, 2003 [D])*. It is difficult to study whether the depression is secondary to the obesity or to existing comorbid conditions *(Stunkard, 2003 [R])*. Weight loss often leads to improvement of depression scores *(Dixon, 2003 [C])*.

Depression is identified more often in obese women and teenagers and is less likely to be diagnosed in men *(Istvan, 1992 [D]; Jorm, 2003 [D]; Palinkas, 1996 [C]; Stunkard, 2003 [R])*. Depression in the elderly is often associated with weight loss, while depression in younger females can be associated with weight gain *(DiPietro, 1992 [B])*.

Depression has been associated with poor weight-loss outcomes *(Linde, 2004 [C])*. Bariatric surgery patients with poorly managed depression or anxiety are at greater risk for weight regain within the first five postoperative years *(Waters, 1991 [D])*. One explanation for this may be found in a line of research investigating biological pathways that link depressive symptomatology to increased adiposity and weight gain *(Miller, 2003 [C])*. Weight-loss studies have often excluded people with depression *(Linde, 2004 [C])*. More studies to address this issue are warranted.

Screening for depression can include asking the following questions.

Over the past month, have you been bothered by:

- little interest or pleasure in doing things?
- feeling down, depressed or hopeless?

If the patient answers "yes" to either one of the above questions, consider using a questionnaire to further assess whether the patient has sufficient symptoms to warrant a full clinical interview and a diagnosis of clinical major depression. An example of such a questionnaire is the PHQ-9 (Patient Health Questionnaire).

This should not be considered a comprehensive screening for depression, which is beyond the scope of this guideline. See the ICSI Major Depression in Adults in Primary Care guideline for more information.

Screening for an Eating Disorder

Eating disorders, particularly binge eating disorder, may complicate the treatment of obesity.

Screening for eating disorders can include asking the following questions:

- Do you eat a large amount of food in a short period of time – like eating more food than another person may eat in, say, a two-hour period of time?
- Do you ever feel like you can't stop eating even after you feel full?
- When you overeat, what do you do (e.g., Have you ever tried to "get rid of" the extra calories that you've eaten by doing something like: Take laxatives? Take diuretics [or water pills]? Smoke cigarettes? Take street drugs like cocaine or methamphetamine? Make yourself sick [induce vomiting])?

If the patient answers "yes" to any of the above questions, consider further evaluation or a referral to a dietitian or a behavioral health specialist who specializes in eating disorders or in health psychology and working with bariatric patients.

More comprehensive screening tools include the SCOFF Questionnaire or Eating Attitudes Test (EAT-24).

Screening for Medication Use That Contributes to Weight Gain

The assessment of the obese patient should include a complete medication history to identify medications that may induce weight gain or interfere with weight loss. Non-steroidal anti-inflammatory drugs and calcium channel blockers may cause peripheral edema rather than body fat weight gain. HIV protease inhibitors are associated with lipodystrophy (central obesity) that is actually a change in body fat distribution rather than a body fat weight gain. If possible, alternative medications that are weight-neutral or that induce weight loss should be selected *(Ganguli, 1999 [R]; Kushner, 2003b [R]; Vanina, 2002 [R])*. A common belief exists among women and clinicians that there is an association between the use of combination hormonal contraceptives and weight gain. This belief may prevent some women from starting hormonal contraception or cause early discontinuation of medication. A recent review of 42 clinical trials – including three randomized, placebo-controlled trials – did not find evidence to support a causal relationship between the use of combination oral contraceptives and weight gain. The authors of the review concluded that current evidence is not sufficient to determine the effect of combination contraceptives on weight, but no large effect is evident *(Gallo, 2004 [M])*.

See Appendix B, "Medications Associated with Weight Gain."

Antidiabetic medications

Several mechanisms contribute to the weight gain associated with antidiabetic agents, including:

- correction of hyperglycemia leading to elimination of a catabolic state and rebuilding of muscle and fat,
- correction of hyperglycemia leading to elimination of glycosuria and retention of previously lost calories,
- hypoglycemia resulting in appetite stimulation,
- insulin-induced (endogenous and exogenous) inhibition of lipolysis and stimulation of lipogenesis,
- differentiation of adipocytes, and
- retention of fluid and edema.

Insulin

Several short- and long-term studies have associated insulin with weight gain. The Diabetes Control and Complications Trial (DCCT) demonstrated that intensive treatment with insulin caused a significantly greater weight gain than conventional therapy *(The Diabetes Control and Complications Trial Research Group, 1993 [A])*. After five years of therapy, patients in the intensive-therapy group gained an average 4.6 kg more than patients in the conventional therapy group. Weight gain continued in the DCCT cohort on follow-up and many of the patients exhibited features of the metabolic syndrome *(Purnell, 1998 [A]; Williams, 1999 [B])*.

Insulin secretagogues

Weight gain is a well-known side effect of sulfonylurea medications, nateglinide and repaglinde.

Metformin

Metformin is thought to be a drug that induces weight loss. In the long term, however, it may actually be weight-neutral. Metformin may be especially useful in combination with an antidiabetic agent that is associated with weight gain *(Fonseca, 2000b [A])*. The combination of metformin with a thiazolidinedione may lessen the weight gain associated with thiazolidinediones *(Fonseca, 2000b [A]; Gomez-Perez, 2002 [A])*. Metformin combined with insulin results in lower glycosylated hemoglobin (HbA1c) values and causes less weight gain than insulin alone *(Avilés-Santa, 1999 [A]; Yki-Järvinen, 1999 [A])*.

α-Glucosidase inhibitors

The α-glucosidase inhibitors (e.g., acarbose and miglitol) delay the absorption of carbohydrates in the small intestine, resulting in decreased postprandial plasma glucose levels. These agents have not been associated with weight gain.

Thiazolidinediones

Through clinical trials, it has been demonstrated that treatment with thiazolidinediones may be associated with weight gain *(Fonseca, 2003 [R])*. Glycemic control and insulin sensitivity do improve, however, with thiazolidinedione therapy. There is a positive correlation between increases in body weight with thiazolidinedione use and reductions in A1c. Weight gain eventually stabilizes after the initial reductions in HbA1c *(Fonseca, 2003 [R])*. The largest increments of weight gain occur when thiazolidinediones are used in combination with insulin or sulfonylureas and least when used as monotherapy or in combination with metformin *(Fonseca 2000a [D]; Fonseca 2000b [A])*.

Mechanisms of thiazolidinedione-induced weight gain

- Adipogenesis through receptor binding, fat cell differentiation and proliferation, fat redistribution with an increase in subcutaneous adipose tissue and a concomitant decrease in visceral fat content
- Decreased leptin production and increased appetite
- Decreased glycosuria and calorie retention
- Non-adherence with diet
- Fluid retention and edema through stimulation of renal tubular sodium re-absorption, increased sympathetic nervous system activity, and altered interstitial ion transport

Interventions to minimize weight gain associated with the use of thiazolidinediones

- Education about nutrition and physical activity when prescribing the medication
- Calorie restriction in high-risk patients such as the severely obese, those unable to engage in physical activity, and those concurrently using insulin or sulfonylureas
- Low-calorie diets for patients who experience weight gain
- Combination therapy with metformin when indicated

Weight gain does occur with most medication treatments for diabetes. Weight gain is commonly associated with thiazolidinediones and can be controlled with dietary interventions *(Asnani, 2003 [D])*. Although thiazolidinediones may cause weight gain, they also improve insulin sensitivity and promote a favorable redistribution of fat. Combining metformin with a thiazolidinedione does not cause additional weight gain and may have an additive effect on insulin sensitivity *(Fonseca, 2003 [D])*.

Psychotropic drugs associated with weight gain

Several drugs commonly used in the treatment of psychosis, depression and epilepsy can induce significant weight gain. This weight gain can negatively impact patient adherence and may increase the risk of an adverse health outcome. The antipsychotics risperidone, sertindole, olanzapine and clozapine have caused weight gains ranging from 2.1-4.5 kg over a 10-week course of therapy. Ziprasidone has been known to cause only small weight gains (0.04 kg) that have not differed significantly from placebo. The mechanisms responsible for this weight gain are currently unknown *(Allison, 1999 [M])*.

A consensus panel on antipsychotic drugs, obesity and diabetes has recommended monitoring a patient's weight at 4, 8 and 12 weeks after initiating or changing antipsychotic therapy, and quarterly thereafter with routine visits. If a patient gains greater than or equal to 5% of his or her initial weight at any time during therapy, consideration should be given to changing agents *(American Diabetes Association, 2004 [R])*.

The risk for significant weight gain among the antidepressants is highest for the tricyclics, monoamine oxidase inhibitors, and mirtazapine *(Fava, 2000 [R]; Masand, 2000 [R])*. Nefazodone appears to be weight-neutral, and bupropion has been known to produce small weight losses that increase with increasing baseline body weight *(Croft, 2002 [A])*.

The antiepileptics valproate *(Isojärvi, 1996 [C])* and gabapentin *(DeToledo, 1997 [D])* have been known to cause extreme weight gain. Lamotrigine is probably weight-neutral. In a 32-week study, lamotrigine caused a mean weight gain of only 0.6 kg compared to 5.8 kg in subjects on valproate *(Biton, 2001 [A])*. Although further studies are needed, topiramate appears to be a unique antiepileptic that can actually produce weight loss. In an uncontrolled one-year study, obese patients (body mass index greater than 30) who completed

one year of therapy experienced a mean weight loss of 4.2 kg (4.3% of baseline) at 3 months and 10.9 kg (11.0%) at one year *(Ben-Menachem, 2003 [D])*.

Clearly, the choices made among these agents can greatly affect a patient's effort to control weight *(Weigle, 2003 [R])*.

8. Is Patient Ready to Lose Weight?

Key Points:

- Knowing the patient's readiness to change can help the provider understand a patient's level of motivation and how to tailor communication about weight loss.
- Patients need to set realistic, achievable goals and to be held accountable to practice new behaviors that produce and maintain weight loss.

Introduction to Weight Management/Lifestyle Change

Weight management is a skill. Patients need to set realistic, achievable goals and to be held accountable to practicing the new behaviors that produce and maintain weight loss. Recordkeeping or self-monitoring of progress on specific behaviors is key to successful weight management. Strategies to reduce calorie intake are to incorporate more fruits and vegetables into meals and snacks, make lower-calorie, healthy choices at the grocery store and in social settings, and become more aware of portion sizes consumed. Additionally, portion-controlled, calorie-controlled meal replacements may be used. Every effort needs to be made to incorporate more physical activity on a daily basis.

Patients and physicians must realize that the culture we live in continues to make eating less and being more physically active extremely challenging. It is easy for patients to become overwhelmed by the process if they believe all they need is willpower. It is discouraging if they think they have to quit eating all of their favorite foods and/or do hours of grueling exercise. It is even more challenging if they have a high level of stress in their lives.

The physician should follow the 5 A's (Ask, Advise, Assist, Assess, Arrange). Physician intervention can be effective, the physician can have an important influence, and successful management is possible.

- *ASK* about, and measure height and weight. Implement an officewide system to ensure that for every patient, preferably on an annual basis, weight is measured, body mass index is calculated, and that patients are educated about their body mass index and risk status.
- *ADVISE* to lose weight. In a clear, strong but sensitive and personalized manner, urge every overweight or obese patient to lose weight.
- *ASSESS* readiness to lose weight. Ask every overweight or obese patient if he or she is ready to make a weight loss attempt at the time, e.g., within the next 30 days.
- *ASSIST* in weight-loss attempt. Help the patient with a weight-loss plan. Refer to appropriate resources.
- *ARRANGE* follow-up. Schedule follow-up contact, either in person or via telephone.

ASK

See Annotation #1, "Measure Height, Weight and Calculate Body Mass Index."

ADVISE to lose weight

Patients who are in the normal weight range should be encouraged to be physically active and eat a healthy diet to help prevent future weight gain. If a patient is overweight or obese, physicians need to communicate this in a direct but sensitive manner and also make the recommendation to consider losing weight. Research suggests that adults who report that their physician advised them to lose weight are more likely to initiate weight-loss attempts. Obese patients who reported receiving advice to lose weight have been shown to be almost three times as likely to report trying to lose weight compared to those who did not receive advice. *(Abid, 2005 [M])*. The next important step will be to engage the patient in a discussion regarding his/her current level of motivation for losing weight.

ASSESS readiness to change/motivation for weight-loss

Although definitive evidence regarding the prognostic significance of an individual's stage of change is not available, assessment of an individual's readiness to make a weight-loss attempt is a key step in encouraging weight-loss efforts. There is evidence that moving into and/or staying longer in the "action" stage for weight-loss and is associated with better weight outcomes. For example, Prochaska and colleagues found that the more clients progressed into the action stage early in weight-loss therapy, the more successful they were in losing weight by the end of treatment *(Prochaska, 1992 [A])*. A more recent study showed that the elapsed time in action or maintenance for multiple weight-loss-related target behaviors is longitudinally related to weight-loss over a two-year period *(Logue, 2004 [B])*. However, others have found no association between baseline stage of change for weight-loss and short *(Macqueen, 2002 [C])* and long-term (e.g., three years) weight outcomes *(Jeffery, 1999 [C])*. The only published randomized trial specifically evaluating the efficacy of a primary-case based, transtheoretical model, stage-matched weight-loss intervention delivered was associated with weight maintenance, but not weight-loss at one year follow-up *(Logue, 2005 [A])*. The authors note that their intervention (e.g., monthly telephone advice) was not intensive enough to produce clinically significant weight-losses, which is consistent with a large body of evidence suggesting that intervention intensity and frequency of contact are strongly associated with successful outcomes *(Jeffery, 2000 [R])*.

Additional psychological and lifestyle factors clearly have an influence on weight-loss success. For example, research suggests that depression status may adversely affect treatment outcome *(Linde, 2004 [C])* and should be considered when making recommendations for weight-loss to patients. It is recommended that physicians assess patient motivation and support, stressful life events, psychiatric status, time availability and constraints, and appropriateness of goals and expectations to help establish the likelihood of lifestyle change in the area of nutrition and physical activity. Assessing readiness to change involves more than simply asking patients, "Are you ready to lose weight?"

One helpful strategy to begin an assessment is to anchor patients' interest and confidence for change on a numerical scale. Ask patients, "On a scale from 0 to 10, with 0 being not important and 10 being very important, how important is it for you to lose weight at this time?" Follow this by asking, "Also, on a scale from 0 to 10, with 0 being not confident and 10 being very confident, how confident are you that you can lose weight at this time?" Physicians can also ask patients, "On a scale from 0 to 10, with 0 being not interested and 10 being very interested, how interested are you in losing weight at this time?"

To obtain further information about patient readiness to change, a Patient Readiness Checklist can be administered. For example, see the American Medical Association's "Road Maps for Clinical Practice – Assessment and Management of Adult Obesity" (http://www.ama-assn.org/ama/pub/category/10931.html, booklet 3, figure 3.2.). This checklist assesses multiple domains including patient motivation/support for change, stressful life events that may hinder change efforts, psychiatric issues (e.g., depression, binge eating), time availability/constraints, and weight-loss goals/expectations. Figure 3.3 of the AMA guideline is a weight-loss questionnaire that may also be a useful tool.

ASSIST in weight-loss attempt

- **Patient not currently interested/motivated for weight loss?** Patients may fit into this category either because they are unaware that their weight status is a problem, or they are not interested in changing (precontemplator), or they are aware of the problem but are just starting to think about changing (contemplator). Providing information about the health risks of obesity and the potential health benefits of weight loss may be most appropriate for those who are not yet interested in changing. For patients who are just beginning to contemplate change, discussion of ambivalence about change and of barriers to change may be helpful strategies. Patient readiness to lose weight should be reassessed at regular intervals.
- **Patient interested/motivated for weight loss?** Patients who are interested and motivated to lose weight likely need information about appropriate nutrition, activity and behavioral recommendations and support in making these lifestyle changes. The sections below describe in detail recommendations for eating, physical activity and behavioral modification. Physicians need to be aware of resources and appropriate referral sources within their clinics and/or local communities for their patients. See the Support for Implementation section, "Resources Available," for Web sites and further information about weight management.

ARRANGE follow-up

Although physicians may not necessarily be directly involved in weight management counseling, it is recommended that a follow-up appointment to evaluate progress be scheduled approximately three months following initiation of a weight-loss program by a patient and progress should be reassessed at appropriate intervals thereafter.

See Annotation #13, "Reassess Goals and Risk Factors, and Counsel Regarding Weight Maintenance."

9. Assess Goals and Risk Factors, and Counsel Regarding Weight Maintenance

See Annotation #13, "Reassess Goals and Risk Factors, and Counsel Regarding Weight Maintenance," for additional information.

10. Negotiate Goals and Management Strategy to Achieve Weight Loss. Refer to Risk Appropriate Resources as Needed.

- Nutrition recommendations include calorie reduction by evaluating portion size and number of servings recommended in mypyramid.gov.
- The physiological effects of physical activity greatly depend on the frequency, duration and intensity of movement.
- Pharmacotherapy, when used for six months to one year, along with lifestyle modification including nutrition and physical activity, can produce weight loss in obese adults.
- Bariatric surgery is indicated in carefully selected patients with a body mass index greater than or equal to 40 or 35-39.9 who are at a very high absolute risk for increased morbidity or premature mortality (See Annotation #7, Table 5). Patients are to be motivated, well-informed in disease management, psychologically stable and accepting of operative risks.
- Daily, weekly and short-term goals are important.

Nutrition Assessment and Therapy

Appropriate nutrition therapy for weight management will be developed collaboratively with the patient. Assessment and education may require a provider with expertise in nutrition therapy. It is important that physicians understand and support the general principles of nutrition recommendations for weight management.

Diet history or eating pattern history. A food/beverage frequency checklist, three-day food/beverage record and weekly food/beverage diary are common tools used to collect information about dietary habits.

Nutrition assessment. Evaluate the patient's current food and beverage choices and eating and drinking habits. Assessment may include the following:

- Current intake of food and beverage calories and fat
- Portion sizes and inclusion of all food groups
- Underconsumption or overconsumption of nutrients
- Use of supplements
- Use of meal replacements
- Stage of behavior change for specific behaviors, such as fruit and vegetable consumption
- Symptoms of possible eating disorder – triggers for overeating
- Timing/consistency of meals and snacks

For more information, including interactive guidance for evaluating portion sizes and calorie analysis, the work group recommends The Center for Nutrition Policy and Promotion Web site at: http://www.usda.gov/cnpp and mypyramid.gov.

Nutrition recommendations. Select a meal planning approach that the patient is willing and ready to incorporate into present lifestyle. Dietary guidance should be individualized and tailored to food and beverage preferences; it should allow for flexible approaches to reducing calorie intake *(National Heart, Lung and Blood Institute, 2000 [R])*. Recommend:

- Achieving weight loss by a reduction in calorie intake. A moderate decrease in calories (500-1,000 kcal per day) can result in a progressive weight loss of 1-2 pounds per week *(National Heart, Lung and Blood Institute, 2000 [R])*.
- A weight-loss eating plan that supplies at least 1,000-1,200 kcal/day for women and 1,200-1,600 kcal/day for men *(National Heart, Lung and Blood Institute, 1998 [R])*.
- An eating plan that is balanced and consistent with other national dietary guidelines *(Esposito, 2003 [A])*. Encourage at least five servings fruits and vegetables per day. Limit fat intake to 30% of calories from fat, 7%-10% of calories from saturated fat, less than or equal to 1% trans fat. Emphasize whole grains, with a fiber intake of 35 grams or more daily.
- Keep trans fat intake below about 1% of calories. The lower the combined intake of saturated and trans fat and the lower the dietary cholesterol intake, the greater the cardiovascular benefit will be *(USDA, 2005 [R])*. Many products served in restaurants, including fast food, often contain high levels of trans fat and are exempt from labeling regulations. Reduce the amount of trans fat by limiting foods that contain "partially hydrogenated" vegetable oils that are found in some margarines, shortenings, crackers, candies, baked goods, cookies, snack foods, fried foods, salad dressings and other processed foods.

Table 6: *Lower-Calorie Meal Plan for Weight Loss *(NHLBI, 2000; NHLBI 2002)*

Nutrient	Recommended Intake
Calories	500-1,000 kcal/day reduction from usual intake
Total fat	30% or less of total calories
Trans Fat	Less than or equal to 1% of total calories
Saturated fat	7%-10% of total calories
Monounsaturated fat	Up to 15% of total calories
Protein	15% of total calories
† Carbohydrates, complex, from variety of vegetables, fruits and whole grains	55% of total calories
Fiber	Equal to or greater than 25-35 grams

* The macronutrient composition of weight loss diets continues to be controversial and the subject of ongoing research.

† The RDA (recommended daily allowance) for carbohydrates has been established as a minimum of 130 grams per day for adults and children *(Institute of Medicine of the National Academies, 2002 [NA])*.

- All low-calorie diets will produce weight loss in the short term (3 to 12 months) *(Bravata, 2003 [M]; Freedman, 2001 [R]; National Heart, Lung and Blood Institute, 1998 [R])*. More studies are needed to determine long-term efficacy of weight loss and maintenance of low-carbohydrate (less than 100 grams) diets. Low-carbohydrate diets have been found to result in more rapid short-term weight loss than conventional low-calorie diets at three and six months, but the difference was not significant at one year. Over a one-year period, low-carbohydrate diets have been found to result in greater improvements than conventional diets in triglycerides and HDL cholesterol levels but not LDL cholesterol. Long-term safety and effectiveness of low-carbohydrate diets for weight loss and cardiovascular risk factor improvements are not yet known.
- For information on popular diets, see the Resources Available section.
- Weight-loss recommendations that exclude food groups and/or restrict macro nutrients substantially below the dietary reference intakes and RDAs can cause nutrient deficiencies and increase health risks *(Bonow, 2003 [NA]; Freedman, 2001 [R])*. A dietitian can assess food and beverage records using a variety of tools. A quick method is to evaluate portion sizes and number of servings recommended for food groups in the food guide pyramid. There are also food guide pyramid assessment tools available on the USDA Web site that calculate calories and total nutrients from entered food records. See the "Resources Available" section for more information.
- There are reviews of low-cost, moderate-cost and high-cost food plans available at the USDA Web site that evaluate the weekly cost of healthy eating plans. The Web site is http://www.usda.gov/cnpp/FoodPlans/FP2003/FoodPlans2003.pdf.
- Another meal planning approach is utilizing meal replacements. This typically involves using frozen meals, formula shakes or bars or prepackaged meals to control portion sizes and simplify food decisions. Drinks and bars are used to replace two meals and one snack per day. Most meal replacements contain 200-400 calories, and additional servings of fruits and vegetables are recommended. Weight maintenance usually involves replacing one meal per day *(Delahanty, 2002 [R]; Heymsfield, 2003 [M]; Kushner, 2003a [R])*.

- VLCDs (very low calorie diets) should not be used routinely for weight-loss therapy because they require experienced practitioners with specialized monitoring and use of supplements. *(National Heart, Lung and Blood Institute, 2000 [R])*. If VLCDs are used, weight loss can be expected in the first six months (~20 kg); however, there is rapid regain between 6 to 12 months. Weight loss is typically not maintained without ongoing dietary and behavioral support *(Paisey 2002 [C]; Torgerson, 1999 [A])*.
- Several recent studies have demonstrated a low glycemic index diet is not effective for weight-loss or weight maintenance. More studies are needed to determine long-term effect on hunger and satiety *(Ebbeling, 2005 [A]; Thompson, 2005 [A])*.

Nutrition outcomes and goals

- Increasing calorie expenditure by increasing physical activity is necessary for improved weight-loss outcomes and weight maintenance *(Esposito, 2003 [A]; Miller, 1997 [M]; National Heart, Lung and Blood Institute, 2000 [R]; Rejeski, 2002 [A])*.
- Improved outcomes for long-term weight reduction occur when a low calorie intake is combined with increased physical activity and behavior therapy *(Chao, 2000 [A]; Diabetes Prevention Program Research Group, 2002 [A]; Freedman, 2001 [R]; Miller, 1997 [M]; National Heart, Lung and Blood Institute, 2000 [R]; National Heart, Lung and Blood Institute, 1998 [R]; Rejeski, 2002 [A]; Tuomilehto, 2001 [A])*.
- Weight loss requires frequent follow-up with planned education/counseling by health care providers to be most effective (i.e., improve adherence) *(Chao, 2000 [A]; National Heart, Lung and Blood Institute, 2000 [R]; Rejeski, 2002 [A]; Tuomilehto, 2001 [A])*.
- Successful weight-loss maintenance is sustained by a combination of lower calorie intake and increased physical activity *(Franz, 2007 [M]; Freedman, 2001 [R]; McGuire, 1998 [C]; Wing, 2001 [R])*. Analysis of data from the National Weight Control Registry indicates weight-loss maintainers have an average intake of 1,400 kcal/day and get one hour of moderate activity per day, and eat breakfast daily.

Physical Activity

Physical activity refers to all types and intensities of body movement, including activities of daily living. Exercise, physical fitness and training are terms that suggest elevated intensity, a sense of obligation or sports participation. These terms may have negative connotations for some obese patients. Physical activity is a more inclusive, attainable and acceptable term.

Physical activity has long been recognized as an important component of a healthy lifestyle and longevity *(Paffenbarger, 1986 [B])*. Physical inactivity, or sedentary lifestyle, has been previously identified as an independent risk factor for cardiovascular disease by the American Heart Association *(Fletcher, 1992 [R])*. Physical inactivity is currently seen as a key contributor to the obesity problem. With approximately 60% of adults in the United States overweight *(Flegal, 2002 [D])*, it is essential to improve physical activity levels for the prevention and management of obesity.

The translation of physical activity research into improved activity habits for individuals and lowered health risks for the population has proved problematic. There are several clinical guides to help physicians assess and manage obesity:

- National Heart, Lung and Blood Institute, *The Practical Guide: Identification, Evaluation and Treatment of Overweight and Obesity in Adults*. September 1998.
- Kushner RF. *Roadmaps for Clinical Practice: Case Studies in Disease Prevention and Health Promotion – Assessment and Management of Adult Obesity: A Primer for Physicians*. Chicago, Ill: American Medical Association; 2003 (Booklet 5 - Physical Activity Management).

The literature on physical activity in obesity prevention and management is extensive and the overall results are variable. Some of the confusion arises from inherent individual variability in response to exercise *(Skinner, 2001 [C])*. There is also significant interstudy variability, (e.g., self-reported physical activity compared to measured physical activity). There are variable exercise regimens and research designs that confound comparison of results.

Specific roles for physical activity in obesity

Physical activity has several potential roles in obesity: prevention, acute weight loss, long-term weight loss and weight maintenance and metabolic fitness with or without weight loss. A brief review of the literature will be done for each potential role.

Prevention of obesity

There is general consensus that energy expended in physical activity has the potential to affect energy balance and weight regulation. There is some evidence that physical activity can minimize weight gain *(Jakicic, 2002 [R])*. However, physical activity alone cannot be expected to overcome unhealthy eating habits. Both must be balanced to prevent excessive weight gain. The optimum dose of physical activity to prevent weight gain is still being researched. Individual requirements will likely vary, given age, gender, occupational energy expenditure and habitual caloric intake. The current activity recommendation of 30 to 60 minutes of moderate intensity, five days per week, is a reasonable point of departure for an individualized activity prescription *(American College of Sports Medicine, 2001 [R])*. Becoming physically active is recognized as an important component of overall behavioral change in obesity. See "Behavioral Management" further in this section.

Acute weight loss

Without some control of caloric intake, studies suggest difficulty losing weight with exercise alone. There appear to be gender differences in exercise effect while on ad libitum diets. Men were more likely to lose weight while women only prevented weight gain *(Donnelly, 2003 [A])*. In the HERITAGE Family Study, men and women of various ages (16-65), two races (black and white), and variable body composition were given 20 weeks of cycle ergometry endurance training, three days per week. All measures of body fat decreased with training and fat-free mass increased. The magnitude of the changes was judged of limited biological significance. Gender differences in training response were noted *(Wilmore, 1999 [C])*.

Long-term weight maintenance

The literature shows more support for the role of physical activity in preventing weight regain *(Jeffery, 1984 [C]; Pronk, 1994 [R])*. A 16-week randomized control trial with a one year follow-up on 40 obese women found that diet plus lifestyle activity may be a suitable alternative to diet plus structured aerobic activity *(Andersen, 1999 [A])*. Total weight loss was not improved with aerobic exercise or strength training, but regular exercisers regained significantly less weight at the one-year follow-up *(Wadden, 1998 [A])*. Long-term weight maintenance may require as much physical activity as expended during the weight loss phase. As cited previously, data from the National Weight Control Registry indicates that weight-loss maintainers get one hour or more of moderate activity per day.

Metabolic fitness with or without weight loss

The beneficial effects of physical activity extend beyond weight loss. There is very strong evidence that physical activity is important in the prevention and management of cardiovascular disease (and related risk factors) and type 2 diabetes mellitus. The literature supports a role for physical activity in improving metabolic syndrome with 5% to 10% weight loss *(Goldstein, 1992 [R])*. Intermittent exercise, two 15-minute brisk walks five days per week, did not result in weight loss but did significantly improve HDL and insulin levels in moderately obese females *(Donnelly, 2000 [A])*. In men, weight loss induced by increased daily

physical activity without caloric restriction reduced abdominal obesity and insulin resistance. Exercise without weight loss reduced abdominal fat and improved cardiovascular fitness but not insulin levels *(Ross, 2000 [A])*.

Obese men and women with impaired glucose tolerance who received lifestyle intervention and exercise counseling had improved weight loss and significantly reduced progression to diabetes *(Tuomilehto, 2001 [A])*.

There are studies of physical activity that do not show an independent metabolic effect beyond weight loss. In obese women, aerobic exercise and resistance exercise had no additional affect over diet alone on weight loss, change in regional adiposity nor improvement in insulin or lipid levels *(Janssen, 2002 [A])*.

Physical activity prescription

Over 20 years ago it was suggested that physicians write individualized exercise prescriptions *(Gibson, 1983 [R])*. Yet, the assessment and recommendation of individualized physical activity remains generally unfamiliar to the primary physician. The previously introduced National Heart, Lung and Blood Institute and AMA physician guides on obesity management contain sections on physical activity.

Physical activity can be categorized according to occupation or recreation. It can be characterized by the frequency, duration and intensity of movement. The physiologic effects of exercise greatly depend on these dimensions of activity, and each will be briefly discussed.

Frequency

In general, three days per week is a minimum frequency to induce physiologic adaptations. Direct improvements in blood pressure or insulin sensitivity require almost daily exercise. Many current activity regimens recommend five or more days per week to reap exercise benefits. From a behavioral perspective, it is better to start with an attainable frequency goal and progress as exercise capacity improves. Having a variety of activities augments greater frequency without onset of boredom or burnout. Enjoyment of physical activity is also a key feature for adherence.

Duration

The recommended duration of activity **for fitness** effects is variable. The traditional cardiovascular fitness guideline was 30 minutes of continuous exercise at 60%-80% of maximal heart rate for three to five days per week. The current American College of Sports Medicine position is 30 minutes of moderate-intensity activity on most days per week *(American College of Sports Medicine, 2001 [R])*. Multiple short bouts of exercise for 10 minutes duration also achieved cardiovascular improvement and weight loss with better program adherence *(Jakicic, 1995 [A])*.

The Institute of Medicine has recommended 60 minutes a day of total physical activity time t**o control body weight**. Prescribing a weekly energy expenditure of 2,500 kcal (~ 300 cal /day) improved weight loss for overweight men and women compared to the standard 1,000 kcal/week (~150 cal/day) *(Jeffery, 2003 [A])*.

Intensity

The appropriate intensity of activity is difficult to adjust for individual patients. The obese, physically deconditioned patient will have greater effort and perceived exertion at lower levels of exercise. At-risk, obese patients with cardiovascular disease may warrant a treadmill evaluation to benchmark their current exercise tolerance. Appropriate intensity may be estimated by the patient's ability to talk during activity. Inability to converse suggests a fairly rigorous effort that will be difficult to sustain. Excessive intensity of activity increases the risk of injury and likelihood of lost activity time. It is better to start at a sustainable intensity level and progress as tolerated to continue improvement. Varying the intensity level by adding intermittent

hills or stairs will also improve capacity. Slowing the pace to recover breathing and complete the duration of the exercise session is preferable.

Physical activity intensity can be quantified by caloric expenditure per minute or hour. The estimation of calories used depends on weight and intensity of movement. There are extensive reference tables for caloric expenditure by occupation, household activities, recreation and sports *(Katch, 1993 [NA])*. See the following table as an example.

Table 7: Energy Expended in Common Physical Activities

Light (less than 3.0 METs or less than 4 kcal/min)	Moderate (3.0-6.0 METs or 4-7 kcal/min)	Hard/Vigorous (greater than 6.0 METs or greater than 7 kcal/min)
Walking slowly (strolling) (1-2 mph)	Walking briskly (3-4 mph)	Walking briskly uphill or with a load
Cycling, stationary (less than 50 W)	Cycling for pleasure or transportation (less than or equal to 10 mph)	Cycling, fast or racing (greater than 10 mph)
Swimming, slow treading	Swimming, moderate effort	Swimming, fast treading or crawl
Conditioning exercise, light stretching	Conditioning exercise, general calisthenics	Conditioning exercise, stair ergometer, ski machine
—	Racquet sports, table tennis	Racquet sports, single tennis, racquetball
Golf, power cart	Golf, pulling cart or carrying clubs	—
Bowling	—	—
Fishing, sitting	Fishing, standing/casting	Fishing in stream
Boating, power	Canoeing leisurely (2.0-3.9 mph)	Canoeing rapidly (greater than or equal to 4 mph)
Home care, carpet sweeping	Home care, general cleaning	Moving furniture
Mowing lawn, riding mower	Mowing lawn, power mower	Mowing lawn, hand mower
Home repair, carpentry	Home repair, painting	—

Source: Journal of the American Medical Association, 1995 Feb 1; 273(5):404.

As a rule of thumb, sitting at rest or reading consumes ~ 1 kcal/minute. An average-weight person burns approximately 5 kcal/minute walking, 10 kcal/minute jogging a 10-minute mile and 15 kcal/minute running a 7-minute mile. These same activities done by someone weighing 300 lbs. approximately double the energy expenditures.

Another measure of activity intensity is the metabolic equivalency. The metabolic equivalency is defined as the energy expenditure for sitting quietly at rest. For the average adult this is 1 kcal/kg body weight/hour. A compendium of activities with their metabolic equivalency values can be used to estimate total energy expenditure: (metabolic equivalency value for the activity) x (weight in kgs) x (activity time) *(Ainsworth, 1993 [R]; Ainsworth, 2000 [R])*.

The recommended daily goal for physical activity ranges from 150 calories (kcal) to 300 calories. An initial level of physical fitness must be established to sustain the duration of activity at moderate levels that is required for weight loss. A pound of body fat contains 3,500 kcal of energy and can sustain 35 miles of walking for the average-weight person. Energy expenditure by physical activity is easily negated by uncontrolled caloric intake. A moderate level of physical activity (5 kcal/min) for 30 minutes expends 150 kcal. This is equivalent to 15 french fries, 15 snack chips or one 12-ounce can of sugared beverage. Physical activity and nutritional recommendations must be coordinated in any weight-management effort.

Although there is consensus on the value of physical activity in obesity management, there is not a standard format for recommending physical activity. The closest examples in the literature are Project PACE (Physician-based Assessment and Counseling for Exercise) *(Patrick, 1994 [NA])* and the Activity Pyramid developed by Norstrom at Park Nicollet HealthSource *(Park Nicollet Medical Foundation, 1999 [R])*.

Office-based assessment of physical activity was pioneered by Project PACE. The one-page questionnaire determines the patient's level of physical activity and readiness to increase activity. The counseling protocols are designed to tailor the message to different patient needs. The program may be administered by physicians, nurses or other health professionals *(Patrick, 1994 [NA])*.

Written advice to exercise was found to be more effective than just verbal recommendation *(Swinburn, 1998 [A])*. Yet, activity prescriptions seem more difficult to write than drug prescriptions. Individualized activity prescriptions appear to be very context-dependent. They must take into account individual motivation, self-efficacy, type of activity, available resources, potential physical constraints or possible medical contraindications *(CME Resource, 2004 [R])*. The "dosages" must be individualized to current patient capacity and then titrated toward improvement *(Bhaskarabhatla, 2004 [R]; Ward, 1991 [R])*. The time course for expected improvement also varies across patients.

Patient handouts for improving physical activity can be very informative and helpful but often have a target population in mind. Handouts for older patients *(Barry, 1993 [R])*, "Walking Your Way to Feeling Better" and "Getting Stronger by Using Weights," can be extended to obese patients with similar current activity capacity.

A prototype general Physical Activity Prescription is offered in Appendix H. It represents a composite of key features suggested from the literature *(CME Resource, 2004 [R]; Patrick, 1994 [NA])*. It has not been evaluated and is intended only as a suggestion for operationalizing the written physical activity prescription. The ICSI Obesity Guideline work group will continue to search for an evidence-based activity prescription format.

An example of a physical activity questionnaire can be found in the American Medical Association's "Road Maps for Clinical Practice – Assessment and Management of Adult Obesity" at www.ama-assn.org/ama/pub/category/10931.html, booklet 5, figure 5.1.

Behavioral Management

Self-monitoring of weight, nutrition and activity

A key component of successful weight loss and maintenance is regular self-monitoring of energy intake, expenditure and body weight. Participants in weight-loss trials who regularly self-monitor their diet and activity tend to lose more weight compared to those who don't *(Boutelle, 1999 [A]; Boutelle, 1998 [D])*. Regular monitoring of weight is also a predictor of successful weight control. Evidence from the National Weight Control Registry (NWCR), which was created to compile data on individuals who were successful at losing at least 13.6 kg and maintaining that loss for one year or more, shows that over 75% of these successful weight-loss maintainers report weighing themselves at least once a week *(Klem, 1997 [D])*.

Patients should be encouraged to keep track of their dietary intake, physical activity level and body weight. Dietary intake and activity should be recorded on a daily basis and weight should be recorded on a weekly basis. For example, see the American Medical Association's "Road Maps for Clinical Practice – Assessment and Management of Adult Obesity," www.ama-assn.org/ama/pub/category/10931.html, booklet 8, figures 4.2 and 5.7.

Teach life skills

Regardless of how long or why a patient is overweight or obese, the ultimate goal is to get the patient to make enough permanent, long-term lifestyle changes in order to reduce calorie intake and increase the level of physical activity. The number of changes that need to be made will vary with the individual and the amount of weight to be lost. Small changes can have a big impact. For example, switching from two regular 12-ounce sodas to two diet sodas or water each day is a calorie savings of 30 pounds per year.

See also the Support for Implemention "Resources Available" section.

Additional behavioral modification strategies that play a key role in successful weight loss and maintenance include:

Stimulus control: Stimulus control refers to a set of behavioral procedures designed to help people reduce environmental cues associated with eating behavior and inactivity. Individuals should be taught to limit the presence of high-calorie/high-fat foods in the home; to reduce the visibility of unhealthy food choices in the home; to limit where and when they eat; to avoid distractions when eating, such as television watching; and to eat more slowly.

Cognitive restructuring: Negative thinking (i.e., perfectionistic thinking, dichotomous/"all-or-none" thinking, pessimistic thinking and self-doubt) often interferes with behavior change efforts. Individuals need to be taught to identify negative thoughts that interfere with their weight-loss efforts and counter them with positive self-statements that promote adherence to healthy eating and activity patterns.

Goal setting: Individuals need to be taught the importance of setting short-term goals for enhancing motivation; setting daily and weekly goals that are reasonable and attainable for eating, physical activity and weight loss should be encouraged.

Problem solving: Teaching problem-solving strategies to deal with barriers to changing eating and physical activity patterns is an important component of weight-loss intervention. Strategies such as defining the problem, brainstorming solutions, selecting a solution, and evaluating the success of the solution are recommended.

Social support: Spouses, family members, friends and co-workers can serve as both barriers and facilitators of successful weight loss. Individuals need to be able to engage their social support systems in ways that facilitate weight loss, eating and physical activity behavior change. Participants may also benefit from learning how to be assertive in social situations involving eating and physical activity so that they can adhere to their behavior change efforts.

Relapse prevention: Restarts are common in behavior change. Patients who relapse should be encouraged to try again when they are ready. In fact, a permanent cure may never be achieved; willingness to engage in lifelong battle is better for the patient than surrender.

The relapse prevention model (RPM), originally developed to address cognitive and behavioral factors associated with the relapse process for addictive behaviors (e.g., alcohol abuse) *(Marlatt, 1984 [R]),* has been shown to be helpful for long-term weight management *(Baum 1991 [A]; Perri, 1984 [A])*. A key component of relapse prevention model is its distinction between "lapses" and "relapse." Lapses are defined as a "single event, a reemergence of a previous habit, which may or may not lead to the state of relapse," whereas "relapse" refers to a full return to an unhealthy state. An individual's response to a "lapse" is thought to determine the likelihood of relapse. The "abstinence violation effect" is the reaction to a behavioral slip, guilt and perceived loss of control; when this occurs an individual is more likely to experience a full relapse. Alternatively, when framed as a "lapse," people can respond proactively to a slip in behavior, thus avoiding complete relapse. Additional relapse prevention strategies may include helping individuals manage lapses in behavior, identifying high-risk situations for relapse, enhancing skills for coping with these situations and increasing self-efficacy for avoiding relapse *(Larimer, 1999 [R])*.

For more information on effective components of behavioral programs, see ICSI's Technology Assessment Report, "Behavioral Therapy Programs for Weight Loss in Adults" *(Institute for Clinical Systems Improvement, 2005 [R])*.

Pharmacologic Therapy

This work group concurs with several current positions regarding the use of medications for the treatment of obesity *(American Society of Health System Pharmacists Therapeutic Position Statement on the Safe Use of Pharmacotherapy for Obesity Management in Adults, 2001 [R]; National Heart, Lung and Blood Institute, 1998 [R]; National Heart, Lung and Blood Institute, 2000 [R])*.

Behavior therapy, including nutrition and physical activity, for the treatment of obesity has often produced poor long-term results and has led to an increased interest in a drug treatment component. It is thought that the addition of medication to a behavior regimen that includes nutrition and physical activity will produce more successful results in weight loss and weight maintenance. A randomized trial of lifestyle modification and pharmacotherapy for weight loss showed that the combination of sibutramine and an intensive group-based lifestyle modification program resulted in more weight loss than either medication or lifestyle modification alone, underscoring the importance of prescribing weight loss medications in combination with lifestyle modification *(Wadden, 2005 [A])*.

Pharmacotherapy, when used for six months to one year, along with lifestyle modification including nutrition and physical activity, can produce weight loss in obese adults. The average weight loss is 4%-12%.

The drugs that have been used in weight-loss therapy are primarily in the therapeutic categories known as anorexiants and appetite suppressants. The Food and Drug Administration has approved Sibutramine and Orlistat. Sibutramine inhibits the reuptake of norepinephrine and serotonin. Orlistat has a different mechanism of action and is not an appetite suppressant. Orlistat inhibits pancreatic lipase and blocks about one-third of fat absorption.

See Appendix C, "FDA-Approved Medications for the Treatment of Obesity."

Herbal medications have unpredictable amounts of active ingredients and unpredictable, potentially harmful, effects. These preparations should not be included as part of a weight-loss program.

Providers considering pharmacotherapy should obtain complete medication histories on their patients including the use of other prescription, non-prescription or herbal preparations for weight loss before recommending or prescribing prescription weight-loss medications.

Safety and adverse effects

Adverse side effects from the use of weight-loss drugs have been observed in patients. Dose-related minor effects may occur soon after beginning therapy. These effects are often mild and spontaneously resolve over time. Initial adverse effects can be avoided or minimized by:

- adjusting dosage and administration schedules,
- identifying patients at high risk for adverse effects and selecting drug therapy accordingly, and
- providing patient education and monitoring for adverse effects at the beginning of therapy or when making dosage adjustments

Infrequent, but potentially serious, effects can also occur much later in the course of therapy.

See Appendix D, "Adverse Effects of FDA-Approved Medications for the Treatment of Obesity."

Sibutramine

Table 8: Incidence of Adverse Events from Placebo-Controlled Trials

Adverse Effect	Sibutramine	Placebo
Headache	30.3%	18.6%
Dry mouth	17.2%	4.2%
Constipation	11.5%	6.0%
Anorexia	13.0%	3.5%
Insomnia	10.7%	4.5%
Increased blood pressure	2.1%	0.9%

Compared to placebo, sibutramine has been associated with a mean increase in systolic or diastolic blood pressure (1-3 mm Hg) and heart rate (4-5 beats/min) in normotensive patients or patients with controlled hypertension. Since the cardiovascular effects can be serious, sibutramine is contraindicated in patients with uncontrolled or poorly controlled hypertension.

Primary pulmonary hypertension has been identified in relation to the use of several weight-loss drugs, especially when the duration of therapy exceeds three months *(Abenhaim, 1996 [C]; McCann, 1997 [M])*. It is thought that the mechanism for drug-induced primary pulmonary hypertension is related to elevated serotonin levels. Elevated serotonin levels can cause pulmonary vasoconstriction. Sibutramine acts as a serotonin-reuptake inhibitor, rather than a serotonin-releasing agent. This different mechanism of action may reduce the risk of sibutramine causing cardiac valve abnormalities.

Patients who receive long-term therapy should be carefully evaluated for dyspnea, chest pain, syncope and edema. They should be instructed to report any symptoms during therapy and within the first year following cessation of weight-loss drugs. If any of these symptoms emerge and are suspected to be related to drug therapy, the medication should be promptly discontinued.

Orlistat

The adverse events of orlistat are mainly gastrointestinal. Absorption of the drug is minimal.

Table 9: Incidence of Adverse Events Commonly Observed During the First Year of Treatment

Adverse Event	Orlistat	Placebo
Oily spotting	26.6%	1.3%
Flatulence	23.9%	1.4%
Fecal urgency	22.1%	6.7%
Oily stool	20.0%	2.9%
Oily evacuation	11.9%	0.8%
Increased defecation	10.8%	4.1%
Fecal incontinence	7.7%	0.9%

Most common adverse reactions were mild and transient and decreased during the second treatment year. Events usually began within the first three months of therapy. Approximately 50% of all episodes of GI adverse events lasted for less than one week, and most lasted for no more than four weeks.

Adherence with a low-fat diet containing less than 30% of calories derived from fat can lessen or avoid the fat-intake related adverse effects. Since orlistat is useful only if taken with a meal containing some fat, a dose should be skipped when a meal is fat free. Cardiac abnormalities have not been reported in association with the use of orlistat.

The practice of combination drug therapy may increase the frequency of adverse events. There is also a lack of safety data on the use of combination therapy. Until data is available, it would be more prudent to use weight-loss medications as single agents. Using the lowest possible effective dose may also reduce the chance of an adverse event.

None of the weight-loss drugs is approved for use in pregnant or lactating women, and the safe use of these drugs in pregnant or lactating women has still not been determined. The FDA has approved labeling for the use of orlistat in the management of obesity in adolescents ages 12-16. Safety and efficacy of orlistat and sibutramine have not been established in the geriatric (65 years and older) population. Sibutramine is approved for one year and orlistat is approved for two years of therapy. The safe and effective use of these drugs beyond two years has not been established.

Drug interactions

The potential for drug-drug interactions should be assessed before initiating therapy with weight-loss agents.

See Appendix E, "Drug Interactions of FDA-Approved Medications for the Treatment of Obesity."

Sibutramine is not currently approved for use with other weight-loss drugs. The combination of sibutramine with another serotonergic agent may impact the risk of serotonin syndrome due to sibutramine's ability to inhibit serotonin reuptake. Combinations of sibutramine and other serotonergic drugs should be avoided. If such a combination is used, patients should be informed about the signs and symptoms of serotonin syndrome, which include excitement, hypomania, restlessness, loss of consciousness, confusion, disorientation, anxiety, agitation, motor weakness, myoclonus, tremor, hyperreflexia, ataxia, incoordination, hyperthermia, shivering pupillary dilation, diaphoresis, emesis and tachycardia *(Sporer, 1995 [R])*.

Patients should have their cyclosporine levels monitored more frequently if they are receiving concomitant therapy with orlistat. Increased monitoring should also apply to patients taking other medications with a narrow therapeutic index, such as warfarin, that could be affected by fat malabsorption.

Orlistat has also been shown to reduce serum concentrations of fat-soluble vitamins (vitamins A, D, E and K). Although most patients' plasma levels remained within normal ranges during clinical trials, a daily multivitamin supplement containing fat-soluble vitamins at bedtime is recommended.

Efficacy

Medication therapy can result in modest weight reductions (2-10 kg) when combined with nutritional therapy and increased physical activity. Weight is primarily lost during the first six months of therapy. Additional weight loss seldom occurs after six months of pharmacotherapy, but weight can be maintained if medication therapy is continued. Some patients, however, do experience weight gain with continuous drug therapy. Once drug therapy has been discontinued, patients frequently regain weight to pretreatment levels or higher.

Orlistat

Patients taking orlistat as part of a program of nutritional and physical activity changes can expect a weight loss of 3.9 to 10.6 kg after one year of treatment and 4.6 to 7.6 kg after two years of treatment. A weight loss of at least 5% of initial body weight at one year is reported by 30% to 73% (vs. 13% to 45% of patients taking placebo); a weight loss of at least 10% of initial body weight at one year is reported by 10% to 41% (vs. 4% to 21% of patients taking placebo). *[Conclusion Grade I: See Conclusion Grading Worksheet A – Annotation #10 (Orlistat)] (Institute for Clinical Systems Improvement, 2003 [R])*.

Sibutramine

Patients taking sibutramine as part of a program of nutritional and physical activity changes can expect a weight loss of 4.4 to 16.6 kg after 24 to 52 weeks of treatment. A weight loss of at least 5% of initial body weight at up to one year is reported by 39% to 77% of patients taking sibutramine (vs. 11% to 40% of patients taking placebo); a weight loss of at least 10% of initial body weight at up to one year is reported by 14% to 46% of patients taking sibutramine (vs. 0% to 8% of patients taking placebo). *[Conclusion Grade I: See Conclusion Grading Worksheet B – Annotation #10 (Sibutramine)] (Institute for Clinical Systems Improvement, 2003 [R])*.

Summary

- When on sibutramine, blood pressure and pulse rate should be monitored at regular intervals to identify those patients who experience clinically significant increases in blood pressure or pulse rate during treatment.

- When on orlistat, gastrointestinal side effects are common, but the frequency and severity decrease over time (typically after one week) and can be reduced by careful attention to dietary fat content.
- As an adjunct to intensive nutritional and lifestyle changes, both orlistat and sibutramine are associated with greater weight loss than placebo.
- With both drugs, 5%-25% fail to complete the run-in phase of the study; of those who are randomized, 9%-54% of both the active treatment and placebo groups fail to complete the treatment phase of the study. The greatest benefit may be in patients with comorbid conditions such as diabetes.
- Programs in which more than 50% of patients lose greater than 5% of initial body weight and more than 30% of patients lose greater than 10% of initial body weight are characterized by a placebo run-in period that identified individuals willing and able to make changes in their nutritional and activity patterns, information on behavior modification, changing nutritional choices and increasing physical activity, regular monitoring in a clinic setting and exclusion criteria that exclude patients with serious disease, major depression and substance abuse.
- The longest reported follow-up is two years. There is little published evidence to suggest that pharmacotherapy is effective in maintenance of weight loss for longer than two years or in decreasing long-term morbidity or mortality. Possible harms associated with long-term use of orlistat or sibutramine are unknown.

Therapeutics

Weight loss drugs should only be used as part of a comprehensive weight loss regimen that includes a low-calorie diet, increased physical activity and behavior therapy. If a patient has been on a combination regimen that includes nutrition therapy, physical activity and behavior modification and has not lost 1 lb./week, the addition of pharmacotherapy should be considered.

Patients considered for pharmacotherapy should have a body mass index of greater than or equal to 30 or a body mass index of greater than or equal to 27 with concomitant obesity-related risk factors or diseases. The risk factors and diseases that are serious enough to support pharmacotherapy at a body mass index of 27 to 29.9 include hypertension, dyslipidemia, CHD, type 2 diabetes and sleep apnea.

Medication therapy should consist of an initial trial period with a single drug to establish efficacy in a given patient. If a patient does not respond to a drug with reasonable weight loss, the patient should be evaluated to determine adherence with the medication regimen and adjunctive therapies, or to consider the need for a dosage adjustment. If the patient continues to be unresponsive to the medication, or serious adverse effects occur, the medication should likely be discontinued.

Patients who respond to pharmacotherapy should lose at least 2 kg (4.4 lb.) in the first four weeks after initiating therapy. If a patient has not lost 2 kg (4.4 lb.) in the first four weeks, the chance of a long-term response is low and they may be considered nonresponders. The amount of weight lost in the first four weeks may be used as a guide to subsequent therapy. Medication can be continued in patients meeting the appropriate response criteria. Consideration should be given to stopping medication in those patients who fail to meet the four-week weight-loss guide. Successful therapy is characterized by weight loss in the first six months of therapy or weight maintenance after the initial weight-loss-phase, and consideration should be given to continued use of medication. Drug therapy may be continued as long as there is a clinical response and there are no serious or unmanageable adverse effects. Patients should be monitored for adverse events as long as they continue on a medication regimen.

Patient monitoring

Patient monitoring is important once weight-loss medications have been initiated. A suggested monitoring schedule would include return visits between two and four weeks, then monthly for three months, and then every three months for the first year after starting the medication regimen. The purpose of these visits would be to measure weight, waist circumference, blood pressure, heart rate, to assess any adverse effects, and to conduct laboratory tests and answer questions.

Therapy should be considered successful if, after six months of therapy, a weight loss of greater than or equal to 10% of body weight is achieved and there have been no serious adverse effects from the medication. After six months of drug therapy, the rate of weight loss generally reaches a plateau and weight maintenance should take priority. To achieve additional weight loss, lifestyle modifications to further decrease caloric intake and increase energy expenditure should be implemented.

To be considered successful weight maintenance, weight regain should be less than 3 kg (6.6 lb) in two years and there should be a sustained reduction in waist circumference of at least 4 cm *(National Heart, Lung and Blood Institute/NIH, 1998 [R])*.

Non-Prescription and alternative medicine

Numerous products, touted as weight-loss preparations, are available to patients without a prescription. These products contain a wide range of ingredients either alone or in combination.

Alternative therapy agents have become attractive options for the treatment of obesity. Herbal and dietary supplements are thought to be natural products and perceived to be safer than prescription medications. Also, patients do not perceive a need to seek professional assistance with these products. Obese patients with limited financial resources may find this to be a cheaper solution. Other patients choose alternative therapies after previous failed attempts at weight loss with more conventional treatments.

No long-term data (longer than one year) are available for any of these agents. While there has been a growing popularity and interest in herbal therapies, there is no adequate data to support their use for weight loss. The short- and long-term adverse effects of these agents are largely unknown. Since many herbal products are not standardized, the content of the ingredients can vary substantially from the label and among lots of the same product *(Gurley, 2000 [D])*. Patients who use non-prescription or herbal preparations should be cautioned about adverse effects, drug interactions and the potential impurities of herbal products *(Miller 1998 [R]; Winslow, 1998 [R])*.

Surgical and Endoscopic Procedures

- Studies have consistently found that patients with preoperative body mass index between 30 and 35 kg/m^2 have good weight loss results.
- Additionally, studies have consistently found improvements of comorbidities.
- One randomized controlled trial (80 participants) found comparable results for surgical and behavioral/pharmacotherapy at six months follow-up, but at later follow-ups the non-surgical group regained weight while the surgical group continued to lose weight.
- Findings from case series are consistent with randomized controlled trial findings.

[Conclusion Grade III: See Conclusion Grading Worksheet C – Annotation #10 (Surgery)]

Patient selection

Bariatric surgery is a highly effective last resort for the treatment of morbid obesity *(Torgeson, 2001 [B])*.

Table 11: Patient Selection Criteria for Bariatric Surgery (Either A or B, below)

A. Body mass index greater than or equal to 40

B. Body mass index greater than or equal to 35, plus any *one* of the following comorbid conditions:
- Severe cardiac disease (coronary artery disease, pulmonary hypertension, congestive heart failure, and cardiomyopathy)
- Type 2 diabetes
- Obstructive sleep apnea and other respiratory disease (chronic asthma, obesity hypoventilation syndrome, Pickwickian syndrome)
- End-organ damage
- Pseudo-tumor cerebri
- Gastroesophageal reflux disease
- Hypertension
- Hyperlipidemia
- Severe joint or disc disease if interferes with daily functioning

Surgery should be employed only after all other means have been tried. Those patients that meet the appropriate criteria for surgery should be thoroughly counseled as to the risks and alternatives to the procedure. Patients should be evaluated by a multidisciplinary team prior to surgery. Bariatric surgery needs to be performed in conjunction with a comprehensive follow-up plan consisting of nutritional, behavioral and medical programs.

A candidate is in an optimal position to go forward with surgery when he/she is emotionally stable (with or without psychotropic medication), has a stable home life and is not facing significant life stressors in the near future, is able to utilize adaptive coping skills, and has a stable and meaningful system of social support that he/she is able to effectively access. Data implicate an adaptive coping style and a good sense of self-efficacy as factors contributing to successful outcome (*National Heart, Lung and Blood Institute, 2000 [R]).* The candidate is, moreover, well informed of and prepared for the possible life changes and challenges that may occur after surgery.

Bariatric surgery techniques are rapidly changing. The evaluation of techniques and patient outcomes is an ongoing process.

Bariatric surgery is just a tool for the treatment of obesity. It allows for resumption of a healthy active lifestyle. However, in the absence of exercise and improved food choices, maintenance of weight loss is jeopardized.

The primary care physician is frequently the first person to encounter complications after surgery. Bariatric practices should have a mechanism to facilitate contact with the primary care physician to discuss concerns without significant delay to the patient.

The American Society of Bariatric Surgeons (ASBS) has announced guidelines for the establishment of Centers of Excellence (COE) for bariatric surgery programs (http://www.asbs.org).

Low Body Mass Index Bariatric/Metabolic Surgery

The original 1991 National Institute of Health consensus body mass index was deliberately set at a conservative level, partly due to limitations of data and expert opinion, and partly for the perceived need to avoid controversy in a skeptical, even bigoted medical and social environment. These guidelines have been criticized as scientifically arbitrary, and studies have shown benefit in lower body mass index classes. Experimental work is also being done for procedures with less weight loss that still have antidiabetic effects.

A recent American Society of Metabolic and Bariatric Surgeons statement forwarded their belief that "there are studies which show significant benefit for the surgical treatment of type 2 diabetes mellitus patients with a body mass index greater than or equal to 30" and "a body mass index cutoff of greater than or equal to 35 may be discriminatory for type 2 diabetes mellitus in certain minority groups, such as Asian Americans, who have metabolic syndrome at lower body mass indexes."

As the perioperative risk profile of all bariatric operations improves with evolution of technique and tools, patient selection, preparation and postop intensive care unit capabilities, the "risk/benefit" equation has changed. Now, there is argument that those with less morbid conditions may benefit.

Lower weight individuals, however, still often do have very significant obesity-related risks, especially in Indo-Asian ethnic groups with the onset of diabetes mellitus/metabolic syndrome at a much lower body mass index than the ethnic groups more commonly included in North American Studies. The globalization of caloric excess may have impacts that differ based on genetic susceptibilities that are yet to be characterized.

Even in the largely Caucasian group of 30-34 body mass index study showed significant advantage over maximal medical therapy at two years *(Dixon, 2008 [A])*.

Work in India and Brazil has shown effective remission of diabetes mellitus in those with body mass index less than 25, some with modifications of limb length and pouch size to minimize excessive weight loss.

Contraindications for surgery

The decision to use surgery to manage morbid obesity requires the surgeon to weigh the risks against the sustained benefits of the surgical procedure *(NIH Consensus Statement, 1992 [R])*. On occasion, the risk of not having bariatric surgery may be greater than the risk of a contraindication.

Table 12: Contraindications for Surgery

A. **Strong Contraindications** are medical or psychiatric conditions that significantly increase the risk of surgery.

1. Life-threatening, multisystem organ failure
2. Uncontrolled or metastatic malignancy, or other serious medical illness where caloric restriction may compromise the patient
3. Uncontrolled HIV infection
4. Hypercarbic respiratory failure
5. Active systemic infection
6. Untreated endocrine dysfunction
7. Pregnancy and/or lactation
8. Current abuse of alcohol or other substances
9. Severe or unstable psychiatric illness that would prevent adjustment to the surgical procedure

B. **Relative Contraindications** are medical or psychosocial conditions that may need to be managed or resolved *before* surgery in order to minimize the risk of an adverse outcome.

1. Reversible obstructive sleep apnea (that can be medically optimized before surgery)
2. Presence of severe liver, renal or gastrointestinal disease
3. Current tobacco abuse (nicotine addiction)
4. Binge eating at an average frequency of twice a week for the past six months
5. Problems with impulse control
6. Documented history of non-compliance (either medical or psychosocial)

Indications for surgery include patients with a body mass index greater than or equal to 40 with psychological stability and documented weight loss attempts. In the presence of significant comorbid conditions, the body mass index should be greater than or equal to 35 *(NIH Consensus Statement, 1992 [R])*.

Survival Advantage with Weight Loss Surgery

There is strong evidence that surgery improves health outcomes for patients with morbid obesity compared to non-surgical treatment. There are few randomized studies to support bariatric surgery to non-surgical methods, though cohort studies are compelling.

Significant new reports have come to light since the last guideline update. A large population study compared 7,925 patients at mean 7.1 years from surgery with 7,925 matched controls in the state of Utah showed "significantly reduced (mortality), particularly deaths from diabetes, heart disease, and cancer." This study showed adjusted long-term mortality decreased by 40% *(Adams, 2007 [B])*.

The Swedish Obese Subjects Trial has presented updated data, continuing to show long-term survival benefit, also particularly a significant decrease in both the incidence and lethality of new malignancy with an average of 10.9 years of follow-up *(Sjostrom, 2007 [B])*.

The group from McGill reported a relative mortality risk reduction of 89% when followed for a minimum of five years, and also noted significant reduction in solid-organ malignancy. They noted no difference in hematologic malignancy, and an increase in digestive diagnoses *(Christou, 2004 [B])*.

Review of Procedures

Currently, there are four types of bariatric procedures being performed. The procedures are categorized based on the mechanism of weight loss. These include restrictive procedures, resective procedures, malabsorbtive procedures and a combination of the two. Also see Appendix F, "Weight-Loss Comparison of Surgical Procedures."

There are general complications related to surgery and anesthesia. There are also specific procedure-related complications.

Restrictive Procedures

The mechanism of function of the restrictive procedures is to limit the intake of food by creating a small gastric pouch. The resulting gastric distention creates a sensation of fullness and, in some cases, satiety that will stop the patient from eating. In the case that liquid calories are not ingested, this can be a highly successful approach.

Vertical banded gastroplasty (VBG) (See figure 13)

- The gastroplasty has now been used for over 30 years.
- There is a diminished weight loss in patients who are "sweets eaters," though there is no good way to define this.
- There may be many cases of food intolerance, especially to meat and breads, due to the fixed outlet *(Sugerman, 1996 [NA])*.
- The cause of nutrient deficiencies after the adjustable band and the vertical banded gastroplasty is related to the type and the amount of food consumed.
- Except in the case of complications related to persistent vomiting, there are few nutritional complications that follow the restrictive procedures.
- Technical complications following the vertical banded gastroplasty include outlet obstruction or gastroesophageal reflux.

Laproscopic adjustable gastric band (See figure 16)

- In the adjustable banding procedure, an adjustable band is placed posterior to the esophagus and reflected down on to the cardia of the stomach.
- The band is connected to a reservoir on the abdominal wall fascia that can be adjusted beginning six weeks after surgery.
- Expected weight loss is one to two pounds per week following the adjustment. In the case that the weight loss slows or there is a sense of "less restriction" to the passage of food, the band is readjusted.
- The band can be adjusted under fluoroscopy or in the office.
- Esophageal dilatation was a significant initial concern after placement of the band. The incidence now appears to be quite low.
- The weight loss of this procedure is much more gradual than other procedures. As this device has been Food and Drug Administration approved in the U.S. for less than six years, long-term U.S. data is still forthcoming.
- Some have argued that this is a good option for patients at the extremes of age, primarily because of reversibility *(Dixon, 2003 [C])*.
- Technical complications can occur following laparoscopic adjustable banding; they include:
  - Slippage of the band (1.5%). This can occur after prolonged emesis, or spontaneously, and presents as pain or acute obstruction. Upper GI series is the first test to perform, and further evaluation may be needed based on results.
  - Erosion of the band (0.15%). This presents as pain, rapid regain of weight or infection of the port site.
  - Port and tubing complication (8%). This includes infection and twisting of the port.
- The incidence of mortality is less than 0.2%.

FIGURE 13
VERTICAL BANDED GASTROPLASTY (MASON)

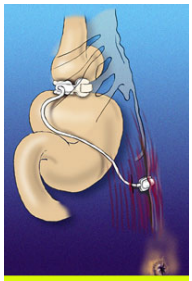


FIGURE 16
ADJUSTABLE GASTRIC BAND "LAP BAND" (KUZMAK)

Source: American Society for Bariatric Surgery

Resective Procedures

Stand-alone sleeve gastrectomy

In Vertical Gastrectomy for Morbid Obesity in 216 Patients: Report of Two-Year Results, *(Lee, 2006 [C])* report a series of planned stand-alone procedures, and found an operative morbidity similar to laparoscopic gastric banding, with weight loss comparable to Roux-en-Y gastric bypass and duodenal switch.

There are several features and potential advantages of stand-alone sleeve gastrectomy, some of which include:

- Patient preference – seen by many as an acceptable compromise to avoid "more invasive" procedures, but with option to revise. Many are self-pay for this procedure, even when they have coverage for band and/or Roux-en-Y gastric bypass.
- No foreign body implanted – many are concerned about erosion or band port problems.
- No need for adjustments, fewer follow-up visits.
- No interruption of bowel continuity
  - Less concern for altered absorption of meds (especially for transplant recipients) *(Butte, 2008 [D]; Takata, 2008 [B])*
  - Less alteration of calcium absorption for those at risk of bone disease
  - Retained endoscopic access to biliary tree
  - No loss of bowel length in those with Crohn's disease
  - Fewer concerns of NSAID use, as no anastomosis
  - No vitamin malabsorption, especially a concern in the less compliant groups, including adolescents *(Baltasar, 2008 [D])*

Though two-year results are not definitive, many researchers postulate that sleeve gastrectomy may be sufficient in a large proportion of cases, especially those who have initial BMI less than 50.

Dr. Himpen's group in Belgium reported five-year results *(Himpens, 2008 [B])*. They have used the sleeve gastrectomy as the "restrictive" procedure of choice since 2001, and 46 patients are beyond five years for analysis. 65% of the cohort had greater than 60% excess weight loss at two years, and 41% of the group had greater than 50% excess weight loss at five years. Those who were immediate and two-year failures were able to attain 60%-81% excess weight loss with a "salvage" duodenal switch second-stage procedure. The results with "salvage" Roux-en-Y gastric bypass were disappointing.

Malabsorbtive Procedures

There are two types of operations that are commonly performed: the biliopancreatic diversion (BPD) and the duodenal switch (duodenal switch). These operations are best used for patients with body mass index greater than 50. These are more invasive procedures.

Biliopancreatic diversion (BPD) (See figure 4)

- This operation includes creation of a 200-500 cc pouch with a distal gastrectomy *(Scopinaro, 1996 [D])*.
- Intestinal continuity is established using a Roux reconstruction.
- The majority of the small bowel has been bypassed to create a common absorptive channel.
- There can be a significant incidence of nutritional complications following the biliopancreatic diversion, including iron deficiency (9%-52%) and B12 deficiency (11%), protein malnutrition and diarrhea.
- Technical complications following this operation include leak, bleeding, stenosis of the duodenoileostomy, and internal hernia formation.

Duodenal Switch (See figure 5)

- This operation was modified from the biliopancreatic diversion to reduce the incidence of marginal ulceration *(Hess, 1998 [D])*.
- The duodenal switch appears to be technically more challenging, especially when performed laparoscopically.
- Some surgeons are performing a staged operation with a sleeve gastrectomy followed several months later with conversion to the duodenal switch in patients with a body mass index greater than 60 *(Gagner, 2002 [D])*.

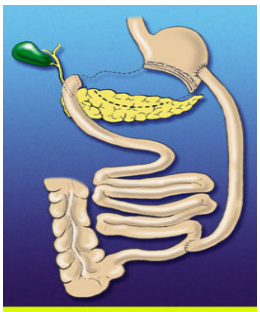


FIGURE 4
BILIOPANCREATIC DIVERSION (BPD) (SCOPINARO)

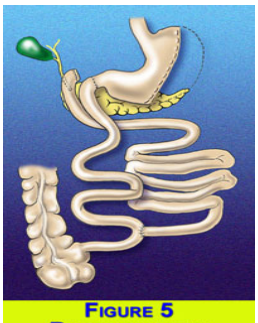


FIGURE 5
BILIOPANCREATIC DIVERSION (BPD) WITH DUODENAL SWITCH (HESS/MARCEAU)

Source: American Society for Bariatric Surgery

Gastric bypass procedures

A compromise of these two types of procedures is the Roux-en-Y gastric bypass.

Roux-en-Y gastric bypass (See figure 10)

- This operation includes creation of a small gastric pouch.
- A variable bypass of the small bowel is possible, based on the patient's body mass index, in order to accentuate weight loss. When the Roux limb portion of the operation is greater than 150 cm, the operation is considered a long limb.
- In the case where the majority of the small bowel has been bypassed and a common channel is created of 75 cm from the ileocecal valve, the procedure is known as a distal bypass. There is evidence to show that lengthening of the Roux limb in this fashion at the expense of the absorbtive area of the bowel can accentuate weight loss *(Brolin, 1992 [A])*.
- This operation has excellent results for patients with type 2 diabetes and is highly effective in the treatment of gastroesophageal reflux disease *(Schauer, 2000 [D])*.
- There are many nutritional considerations with the gastric bypass.
  - The most common considerations include iron, B12 and folate deficiency. Nutritional complications following the gastric bypass are due to restriction of food intake, as well as due to bypass of the gastric fundus, duodenum, jejunum and, in some cases, the proximal ileum (in the case of a more distal gastric bypass). See "Nutritional recommendations" further in this section.
  - Preoperatively and at six months, check complete blood count (CBC), albumin, iron, ferritin, total iron binding capacity (TIBC), vitamin B12, red blood cell (RBC) folate, calcium and 25-hydroxy vitamin D levels.

- Unlike the duodenal switch and the restrictive procedures, there is up to 76% incidence of dumping syndrome characterized by the presence of nausea, lightheadedness, the urge to lie down and palpitations *(Mallory, 1996 [C])*. Dumping syndrome does not equate with diarrhea.
- Unlike dumping following surgery for ulcer disease, this is considered a benefit in those patients who do have it, because it may confer protection against liquid calories and sweets.

- Roux-en-Y bypass is considered by most experts to have the most favorable benefit/risk ratio and accounted for 70% of the bariatric surgery procedures in a 1999 U.S. survey *(Schauer, 2001 [R])*.
- There are a number of technical complications that can follow the gastric bypass. A high index of suspicion should be maintained in patients and prompt bariatric surgical input should be obtained *(Podnos, 2003 [C])*.
  - Leaks (3%) occur early within the first week.
  - Internal bleeding (1%) occurs within the first week and can be in the GI tract.
  - Anastomotic stenosis (2%-20%) occurs most often by three-four weeks.
  - Internal hernia formation (1%-5%) occurs most often beyond six months.
  - Wound infections can occur in up to 6.6% of patients.
- Anastomotic marginal ulceration can be as high as 15%, but the true incidence is likely unknown. Recalcitrant ulcers raise the concern of gastrogastric fistula formation that can be seen even following a divided gastric bypass.
- Severe life-threatening complications appear to be influenced by gender and by weight and age.
  - Overall mortality of the gastric bypass is 0.5% *(Schauer, 2000 [D])*.
  - Livingston et al. found that patients older than 55 years had a threefold higher mortality from surgery than younger patients, although the complication rate (5.8%) was the same in both groups *(Livingston, 2002 [C])*.
  - The risk for severe life-threatening adverse outcomes in women increased from 4% for a 200-lb. female patient to 7.5% for a 600-lb. patient. In males, the risk increased from 7% for a 200-lb. male to 13% for a 600-lb. patient *(Livingston, 2002 [C])*.
  - The waist-to-hip ratio may also correlate with the difficulty of surgery, as it may correlate to increased visceral fat stores and may contribute to possible respiratory difficulty *(Schwartz, 2003 [C])*.
  - The incidence of serious respiratory complications varies from 0% to 4.5% in both laparoscopic and open procedures *(Podnos, 2003 [C])*.
  - Dealing with the excluded limb following the gastric bypass can be a significant issue. Usually concern is warranted to evaluate the excluded stomach in patients with unexplained pain or the presence of a mass. In some cases it becomes useful to access the stomach to perform an ERCP in order to remove common duct stones. The stomach can be accessed using interventional radiologic techniques, laparoscopy or conventional surgery.
  - Pregnancy after the bypass operation is possible. Fertility can be increased following the bypass in some patients. Patients should wait until weight loss has ceased prior to conceiving. Patients should undergo a thorough nutritional evaluation prior to and during pregnancy *(Wittgrove, 1998 [D])*.

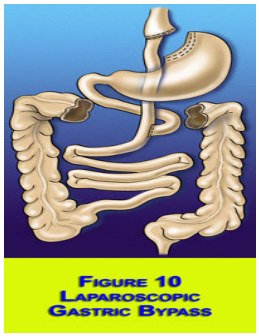


FIGURE 10
LAPAROSCOPIC
GASTRIC BYPASS

Source: American Society for Bariatric Surgery

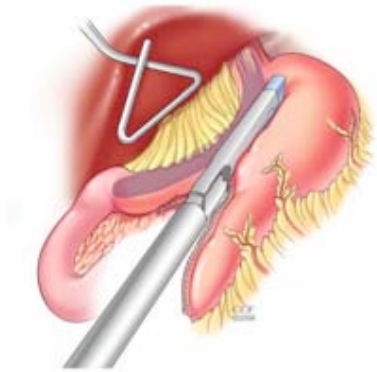
Staged Procedures

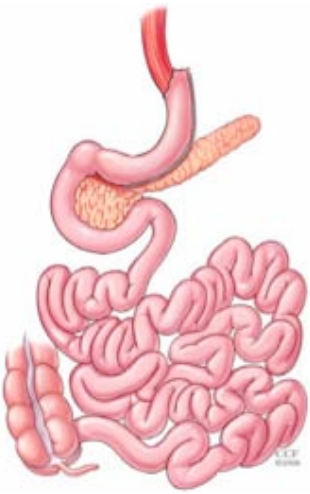
Some patients have a much higher risk profile than average. These include Super Morbid Obesity (body mass index greater than 50), coronary artery disease, heart failure, dysrhythmias, severe sleep apnea, or age greater than 60.

Others have mechanical issues that would interfere with the ability to safely complete surgery, including hepatomegaly or conditions that compromise small bowel mobilization, such as severe adhesions, inflammatory bowel disease, incarcerated ventral hernia malrotation, or previous radiation treatment.

Finally, intraoperative instability or unexpected findings may mandate a choice between doing an interrupted procedure, versus none at all.

Drs. Gagner and Schauer were early proponents of risk modification by splitting definitive treatment into two stages *(Cottam, 2006 [D]; Regan, 2003 [B])*. The first stage is a simple sleeve gastrectomy (see illustration). The sleeve gastrectomy, or vertical gastrectomy, is a resection of 85%-90% of the stomach along the greater curvature, leaving a 80-100 cc tubular pouch, that has a staple line, but no actual anastomosis. A large portion of ghrelin-producing cells are removed with the specimen (largely in the fundus). Since this is qualitatively different from all other described procedures, it has been proposed that this may be a new class of "resective" operation, with features of restriction, but endocrine effects more akin to gastric bypass *(Kotidis, 2006 [C]; Melissas, 2007 [D])*.





Weight loss and satiety have been impressive with the first-stage sleeve gastrectomy (commonly greater than 50% excess weight loss) allowing resolution or significant improvement and measurable risk reduction by ASA class, allowing a "completion" procedure (either Roux-en-Y gastric bypass or duodenal switch) in 6-24 months, or after 100 lbs. weight loss.

In practice in the U.S., many insurance carriers would not authorize the second-stage procedure. As a result, many have only had sleeve gastrectomy, and these patients have been followed as "stand-alone" cases.

Medium term two- and three-year data (which would be categorized as "long-term" in the non-surgical literature) are competitive with established procedures. Weight loss is rapid, similar to Roux-en-Y gastric bypass or duodenal switch, though durability is not expected to match those for all patients. Many patients, however, are reluctant to commit to Roux-en-Y gastric bypass or duodenal switch, and sleeve gastrectomy may be sufficient for many with the option to convert "failures" using a second stage.

Dr. Himpens has reported excellent weight loss (60%-81%) in those converted from an initial sleeve gastrectomy to duodenal switch after either early failure (loss of less than 50 pounds excess weight loss) or late (two-year) recidivism *(Himpens, 2008 [B])*.

Intragastric balloon

The intragastric balloon is a silicone balloon, placed with endoscopy, and filled with saline once in position in the stomach. Its size prevents migration, and it induces satiety by a proposed volume effect.

The intragastric balloon is not Food and Drug Administation approved, but has been reported extensively in South America and Europe, and is approved in Canada and Mexico. Successful six-month weight loss has been shown, with safe outcomes (a significant exception is those with prior gastric surgery, who have shown very high risk of rupture or perforation at previous suture or staple lines). The most common side effect is nausea, which is occasionally (10%-20%) extreme enough to warrant early removal in the first week.

Since it is a non-surgical modality, U.S. practitioners can expect to see some patients who have traveled out of the country to obtain treatment. Practitioners should be familiar with the concept, and be aware that it will likely be immediately a source of interest if Food and Drug Administration approval is obtained.

Endoscopic Treatment of Late Weight Regain

Revisional surgery has been shown to be effective from various primary operations, with best results in those converted from restrictive procedures to Roux-en-Y gastric bypass *(Brolin, 2008 [D])*.

There are several devices in trials for reducing the size of a dilated gastrojejunostomy or dilated gastric pouch. Endoscopic injection sclerotherapy has been shown to reduce stoma size at the dilated G-J, with mixed results, best when the original treated dilation is less than 2 cm (this requires an attempt at formal quantitative measurement, which is not routinely done).

Treatment of dilated gastrojejunostomy with sclerotherapy *(Spaulding, 2003 [D])*. Weight gain after bariatric surgery as a result of a large gastric stoma: endotherapy with sodium morrhuate may prevent need for surgical revision *(Catalano, 2007 [D])*.

Both authors stress the need for additional dietary counseling and behavior change to maximize benefit of the treatment, and most patients require more than two sessions to approach optimal stoma size of 1 cm.

Surgical procedure selection process

Not only is there a choice of procedures, but also a choice of how the procedure is performed, i.e., laparoscopic vs. open. Laparoscopic approaches to the treatment of morbid obesity have been around for almost a decade. All operations can be performed using the laparoscope. Even many revisional procedures can be performed laparoscopically *(Gagner, 2002 [D])*. Potential advantages of laparoscopic surgery include shorter

hospital stay with faster return to work, less pain, decreased abdominal wall hernias and fewer complications related to adhesion formation. Patients with multiple previous abdominal procedures may not be candidates for laparoscopy. The downside is that the learning curve for the procedures is quite steep.

There are no standard or "cookbook" guidelines that determine surgical procedure selection. The surgeon decides which procedure to perform and how it is performed (laparoscopically vs. open) after considering several factors, including:

- body mass index;
- food and eating preferences (e.g., "sweet eaters*," "volume eaters");
- presence of certain comorbid conditions (e.g., type 2 diabetes, metabolic syndrome, gastroesophageal reflux disease);
- presence of intestinal pathology;
- previous abdominal surgeries;
- surgical risks;
- presence of certain behavioral or psychiatric conditions, even though they may be well-managed at the time of surgery (e.g., low stress tolerance or bipolar disorder); and
- patient preference.

*As defined by Sugerman, 1989, "sweet eaters" are those patients who consume more than 15% of total calories from such foods as candy, ice cream, cake or non-dietetic soft drinks.

The best results in terms of short-term complications are directly related to the experience of the surgeon *(Schauer, 2003 [C])*.

There are some unique effects of bariatric surgery, compared with dieting, that should be kept in mind in considering obesity surgery. It is important to note that the decrease in metabolic rate and diminished energy consumption seen after dieting *(Leibel, 1995 [C])* may not be seen after the obesity surgery, which may put patients at an advantage to lose weight *(Flancbaum, 1997 [C])*.

Further, some exciting biochemical studies suggest that there may be an advantage to bypass of the proximal small bowel:

- In obese subjects, the "hunger hormone" ghrelin is lower after the gastric bypass, while it is markedly elevated after dieting *(Cummings, 2002 [C])*.
- Glucagon-like peptide-1 (GLP-1) may have a profound effect on type 2 diabetes independent of weight loss or caloric intake. GLP-1, for example, is known to increase insulin sensitivity, decrease hepatic gluconeogenesis, block pancreatic glucagons secretion and decrease gastric emptying *(Greenway, 2002 [R])*.
- The best choices for patients with a body mass index greater than or equal to 40 or those with diabetes are probably the gastric bypass or the biliopancreatic diversion.
- The gastric bypass procedure involves creation of a tiny gastric pouch with diversion of bile, and therefore this is a better selection for patients who present with gastroesophageal reflux disease. In patients who may have gastric pathology, it may not be suitable to perform the gastric bypass (unless plans are made to remove the distal stomach).

Resolution of comorbidities

Data from the Swedish Obesity Subjects intervention show that hypertension, diabetes mellitus and hyperlipidemia are improved following surgery, but not all to the same degree *(Torgerson, 2001 [B])*.

- Torgerson et al. reported that at two years the surgery group had an incidence of diabetes that was 30-fold lower than usual care (0.2% vs. 6.3%, $p < 0.001$) *(Torgerson, 2001 [B])*.
- The incidence of hypertriglyceridemia is 10-fold lower than usual care (0.8% vs.7.7%, $p < 0.001$).
- The incidence of hypertension was reduced to a lesser degree, with a 2.5-fold reduction in incidence (5.4% vs. 13.6%, $p < 0.001$).
- Changes in comorbidities following the gastric bypass are noted in Table 13.

Table 13: Impact of Gastric Bypass in Obesity Related Comorbidities

Comorbidity	#	%Aggravated	%Unchanged	%Improved	%Resolved
Osteoarthritis/degenerative joint disease	64	2	10	47	41
Hypercholesterolemia	62	0	4	33	63
Gastroesophageal reflux disease	58	0	4	24	72
Hypertension	57	0	12	18	70
Obstructive sleep apnea	44	2	5	19	74
Hypertriglyceridemia	43	0	14	29	57
Depression	36	8	37	47	8
Peripheral edema	31	0	4	55	41
Urinary incontinence	18	0	11	39	44
Asthma	18	6	12	69	13
Diabetes	18	0	0	18	82

Adapted from Schauer PR, Burguera B, Ikramuddin S, Cottam D, Gourash W, Hamad G, Eid GM, Mattar S, Ramanathan R, Barinas-Mitchel E, Rao RH, Kuller L, Kelley D. Effect of laparoscopic Roux-en-Y gastric bypass on type 2 diabetes mellitus. Ann Surg. 2003 Oct;238(4):467-84; discussion 84-5.

Measurement of success and failure

Bariatric surgery, though effective, can fail in up to 21% of patients by five years *(Fox, 1996 [D])*. There are many definitions of success in these patients. Some have defined success as percent excess weight loss greater than 30%. Others have used resolution of comorbid conditions as a marker of success.

There is some evidence to suggest that certain maladaptive eating behaviors predispose to failure after certain operations such as the vertical banded gastroplasty.

- The vertical banded gastroplasty, for example, is notoriously susceptible to failure in patients who are "sweets eaters," i.e., those patients who consume more than 15% of their total caloric intake in the form of sweet foods such as candy, ice cream, cake or non-dietetic soft drinks *(Sugerman, 1989 [C])*.
- Maladaptive eating does appear to be a problem following the vertical banded gastroplasty for some patients, as bread and meat can be poorly tolerated. Patients may use high-caloric liquids as a primary source of food in this case. Additionally, patients should have a thorough dietary evaluation. If the vertical banded gastroplasty ring is too tight, the procedure can be revised.

Failure of the adjustable band can occur in up to 20% of patients *(Favretti, 2002 [D])*. In the case of the compliant patient, alternatives include removal of the band and conversion to a bypass or malabsorbtive procedure within the first three years.

Different patterns of failure follow the gastric bypass.

- If the stomach had not been previously divided, it is possible that the failure is due to gastro-gastric fistula development.
- Stomal enlargement and pouch dilatation can also contribute to failure and are best identified with endoscopy and radiographic evaluation of the GI tract.

Cost effectiveness

A new case-controlled study of 3,651 patients using payer data showed downstream savings to offset initial costs within two years for laparoscopic surgery, and four years for open surgery *(Cremieux, 2008 [M])*. A comparison of cost effectiveness per quality adjusted life-year (QALY) showed that both Roux-en-Y gastric bypass and laparoscopic adjustable gastric band are cost effective at less than $25,000/QALY, with an incremental advantage in most scenarios to laparoscopic adjustable gastric band *(Salem, 2008 [M])*.

Adolescent bariatric surgery

- In adolescents, preliminary work shows equal or better effectiveness to that shown in adults. These reports are from experienced multidisciplinary programs that have very strict criteria for comorbidities, as well as skeletal and psychological maturity. Encouraging results have been shown in both Roux-en-Y gastric bypass and laproscopic adjustable gastric band centers *(Dillard, 2007 [D]; Dolan, 2003 [D]; Inge, 2004 [D]; Lawson, 2006 [C])*.
- Morbidity appears comparable to the adult population. Resolution of certain comorbid conditions appears to be excellent.
- Randomized studies do not exist. However, in certain cases such as end-stage pseudotumor cerebri or sleep apnea, there may not be a reasonable alternative to surgery.
- Some adolescents may experience problems with body image postoperatively. As with the adult patients, there may be a need for plastic surgery *(Capella, 2003 [D])*.
- Procedures should be performed at a regional center that enjoys the benefits of a multidisciplinary program, including child psychology *(Garcia, 2003 [R])*.

The patient process

The primary care physician plays the key role in preoperative preparation of the patient. Consideration for bariatric surgery involves first identifying patients with a body mass index greater than 40, or body mass index greater than 35 with significant comorbid disease (diabetes, hypertension, obstructive sleep apnea, GERD, degenerative joint disease, coronary artery disease).

Documentation of weight-loss attempts is essential prior to referral. Many insurance companies require a patient to be medically followed for one year prior to authorizing payment for surgery. The time period of medically supervised or managed weight loss varies per payor; therefore, it is useful to know their specific requirements.

A psychological health and behavior assessment process is completed preoperatively by a specially trained behavioral health provider. This assessment is designed to prepare the patient, from a behavioral and psychosocial perspective, to adhere to self-management guidelines and to adjust to the various changes and challenges that may occur after surgery. It includes education and skills building, as needed. In addition, the

assessment identifies treatable psychopathology and behavioral problems that may interfere with treatment adherence and/or to surgical outcome. Various indices are used to gather information, including behavioral observation, clinical interview, collateral information, and standardized psychological tests. Multiscale inventories – such as the Minnesota Multiphasic Personality Inventory, second edition (MMPI-2) and the Personality Assessment Inventory (PAI) – are most commonly used in the assessment of bariatric surgery patients.

Specific questions addressed in the assessment include the patient's:

- motivation to learn and ability to adhere to self-management behaviors for overall health improvement;
- understanding of and ability to manage the widespread changes that are associated with having a bariatric surgical procedure;
- level of sophistication and scope of psychological resources, resilience and coping skills;
- degree of social isolation and ability to access and accept social support;
- self-confidence and sense of self-efficacy in lifelong implementation of the behavioral guidelines for managing obesity;
- psychological stability;
- personality structure and evidence of long-standing characterological problems that may ultimately affect patient safety and the delivery of health care.

A candidate is in an optimal position to go forward with surgery when he/she is emotionally stable (with or without psychotropic medication), has a stable home life and is not facing significant life stressors in the near future, is able to utilize adaptive coping skills and has a stable and meaningful system of social support that he/she is able to effectively access. Data implicate an adaptive coping style and a good sense of self-efficacy as factors contributing to successful outcome *(National Heart, Lung and Blood Institute, 2000 [R])*. The candidate is, moreover, well informed of and prepared for the possible life changes and challenges that may occur after surgery.

Medical evaluation

Medical evaluation should follow the American College of Physicians Position Paper for Perioperative Assessment and Management of Risk from Coronary Artery Disease.

Unrecognized sleep apnea can cause significant problems in postoperative management. The likelihood that the patient has significant related comorbid conditions such as sleep apnea can approach 50% *(Frey, 2003 [D])*.

- In some cases patients with untreated obesity hypoventilation syndrome, the administration of narcotics postoperatively can result in respiratory arrest.
- It is important that patients who have been prescribed CPAP be comfortable in the use of this device preoperatively so that they can use it safely postoperatively.

Cholelithiasis is a common problem following any kind of massive weight loss. Up to one-third of patients following bariatric surgery will develop gallstones. The risk of development of symptomatic gallstones can be decreased to 2% with use of actigall postoperatively *(Sugerman, 1995 [A])*. There are a number of surgeons who will obtain a gallbladder ultrasound preoperatively. In the presence of stones, the gallbladder can be removed concomitantly *(Hamad, 2003 [C])*. One advantage of obtaining a preoperative ultrasound is that the "giant liver" can be identified. This may be an argument for further weight loss.

Preoperative weight loss is an unclear issue. Recommendations vary among different surgical practices. The rationale is to decrease perioperative morbidity, thereby making the actual procedure safer. Except in cases of extreme central obesity and in cases of revisional bariatric surgery, 10 to 30 pounds of preoperative weight loss is encouraged to decrease the size of the liver *(Scheen, 2002 [R])*.

Postoperative care

- Lap Band: Begin band adjustments at six weeks postoperatively. Readjust if weight loss drops below one-two pounds per week. If band is too tight, fluid must be withdrawn. Weight loss typically continues until three years postop.
- Bypass: Follow-up at 1 week, 4 weeks, 3 months, 6 months, 9 months, 1 year, 18 months, 2 years and then annually. Weight loss typically peaks at 18 months postop. This procedure is not considered successful until at least five years of follow-up.

Nutrition recommendations

Although there are limited evidence-based nutrition recommendations for postoperative gastric bypass, several consensus-based reports have been published. This is especially true for the progression of foods. In general, most consensus-based reports indicate that practitioners vary in how quickly or slowly they choose to advance the diet. Of course, this depends on the patient's adherence and readiness to advance *(Elliot, 2003 [R])*.

The diet following gastric bypass is always started with liquids only *(Elliot, 2003 [R])*. The progression after liquids tends to rely on "best practice" guidelines. Some practices choose to advance the diet utilizing some or all of the phases listed below.

- Clear liquids
- Full liquids
- Pureed foods
- Soft-textured foods
- Small portions of normal foods

The final phase introduces the lifelong way of eating for patients. Patients should focus on eating protein first as they add solid foods back into their diet. Tougher foods like fruits, vegetables and whole grains should be introduced more slowly. These foods, unless chewed well, have a tendency to plug the outlet from the stomach pouch. Patients should be advised to introduce new foods at separate times to assess for tolerance.

To maintain success with weight management, patients need to do the following:

- Drink fluids 30 minutes before and/or 30 minutes after meals, *not* during the meal.
- Eat lean sources of protein first, followed by fruits, vegetables and whole grains.
- Aim for a minimum of 50 to 60 grams of protein per day.
- Avoid high-fat or high-sugar foods.
- Drink at least six to eight cups of non-calorie fluids daily (choose water most often).
- Drink two glasses skim or 1% milk daily in addition to water (between meals).
- Limit fluids with calories to skim or 1% milk (two cups daily).

- Eat three meals a day.
- Take multivitamins and supplements daily.

Protein. The newly formed anatomy of the stomach reduces availability of rennin, pepsin and hydrochloric acid, consequently limiting protein digestion. These alterations in anatomy, coupled with a significantly reduced intake of food, make it difficult to meet the requirements for protein and prevent catabolism immediately following surgery. Protein supplements should be considered, especially in the early postoperative phase, to prevent excess loss of lean tissue *(Moize, 2003 [D])*.

Counseling patients on adequate protein intake is pertinent both before and after surgery. Many patients cannot tolerate high-protein foods, which may jeopardize their ability to take in recommended amounts. These intolerances may be long term, particularly with red meat *(Avinoah, 1992 [D]; Kushner, 2000 [D])*. Supplements are often used until adequate protein intake through solid foods can be maintained, usually about six months after surgery *(Deitel, 2002 [R]; Moize, 2003 [D])*.

Nutrient deficiencies. Because gastric bypass surgery excludes critical portions of the gastrointestinal tract, including the fundus, duodenum and upper portion of the jejunum, nutrient deficiencies are predictable and should be proactively treated. Patients should be advised to take a multivitamin or prenatal vitamin in addition to the nutrients discussed below.

Calcium and vitamin D. Calcium deficiency is difficult to detect because a normal blood calcium level can be maintained despite poor intake. Several factors affect calcium intake following surgery, including reduced dairy intake as a result of decreased stomach capacity or as a result of lactose intolerance, food dislikes and patient adherence with the meal plan. Since the primary absorption pathway for calcium has been removed with gastric bypass, supplementation is vital to bone health *(Elliot, 2003 [R])*. Calcium citrate with added vitamin D would be the preferable source, since it does not rely on stomach acidity for absorption *(Elliot, 2003 [R]; Kushner, 2000 [D])*.

Iron. Iron deficiency post gastric bypass occurs in 33% to 50% of patients *(Deitel, 2002 [R])*. Deficiency may be due to several factors, including possible food intolerance (patients may not be taking in sufficient heme iron), bypassed absorption site (duodenum and upper jejunum) and reduced stomach acidity. Iron should be supplemented to prevent deficiency *(Avinoah, 1992 [D]; Elliot, 2003 [R])*, with special attention to premenopausal women *(Klein, 2002 [R])*. In addition, the iron may need to be administered either by intravenous or intramuscular methods due to absorption change. Ferritin levels may need to be monitored annually as the levels can decline for up to seven years post bypass *(Buchwald, 2004 [M])*.

Vitamin B12. B12 deficiency occurs in greater than 30% of patients with gastric bypass *(Kushner, 2000 [D])*, and the American Gastroenterological Association reports it may reach greater than 50% if supplemental B12 is not used *(Klein, 2002 [D])*. Of note, most multivitamins do not have enough B12 to return post-gastric bypass patients to their normal plasma levels *(Buchwald, 2004 [M])*. Vitamin B12 has a complex method of absorption, which is greatly impaired by gastric bypass surgery. Additionally, patients may have difficulty tolerating foods rich in B12 (meat, eggs and milk) and consume very little, if any, of these. Supplemental B12 greater than the recommended daily intake has been found to maintain normal plasma cobalamin levels *(Elliot, 2003 [R]; Kushner, 2000 [D])*.

Medications

Extended-release medications may be problematic in some patients since the mechanism by which delayed absorption occurs might be affected. Drugs with narrow therapeutic windows should be monitored especially closely. For example, warfarin dosing may need to be monitored due to alterations in dietary intake post-procedure or due to any possible changes in absorption. Until more research is done in this area there are no standard rules for adjustments of medications following bariatric surgery. Patients taking any medications should be closely monitored for both toxicity and increased side effects. Also drugs with weight require-

ments for dosing should be re-evaluated frequently as patients experience weight loss. Since many drugs are monitored for a therapeutic outcome, the dose can be titrated to this outcome *(Buchwald, 2004 [M])*.

Factors Influencing Patient Choices

The role of the primary care provider is paramount to most patients (after direct family experience). It is particularly concerning, then, that only 6% thought that obesity was best controlled surgically, even though 88% believed obesity was difficult to control with diet and exercise alone *(Perlman, 2007 [D])*.

Adolescents

Initial experience with adjustable gastric band in morbidly obese U.S. adolescents and recommendations need further investigation *(Dillard, 2007 [D])*.

13. Reassess Goals and Risk Factors, and Counsel Regarding Weight Maintenance

Key Points

- Follow-up and long-term management of weight loss are crucial.
- The primary care physician also may serve as a community leader and a public health advocate.

Patients need regular follow-up for obesity, which is a lifelong problem in most cases. Regular follow-up conveys the message that the condition is important to the patient, and it affords the opportunity for monitoring body mass index, as well as evaluation and management of any of the common complications that are often associated with obesity.

A general recommendation of visits every three months is based on expert opinion and may be varied to meet the particular needs of individual patients.

Patients on pharmacotherapy for obesity need ongoing evaluation for blood pressure, adequacy of nutrition, and surveillance for specific nutrient deficiencies such as low levels of fat-soluble vitamins in those on orlistat.

Patients who have had bariatric surgery may also need procedure-specific follow-up. For example, those with gastric bypass are at risk for iron deficiency and for vitamin B12 deficiency, as well as other types of nutritional imbalances or deficiencies.

Ongoing reinforcement of important behavior strategies may include provision of new information on obesity management, control of local food environment, strategies to cope with restaurant eating, strategies to limit perimeal snacking and high-calorie beverages, and strategies for achieving regular physical activity.

See Annotation #6, "Advise Weight Maintenance and Manage Other Risk Factors."

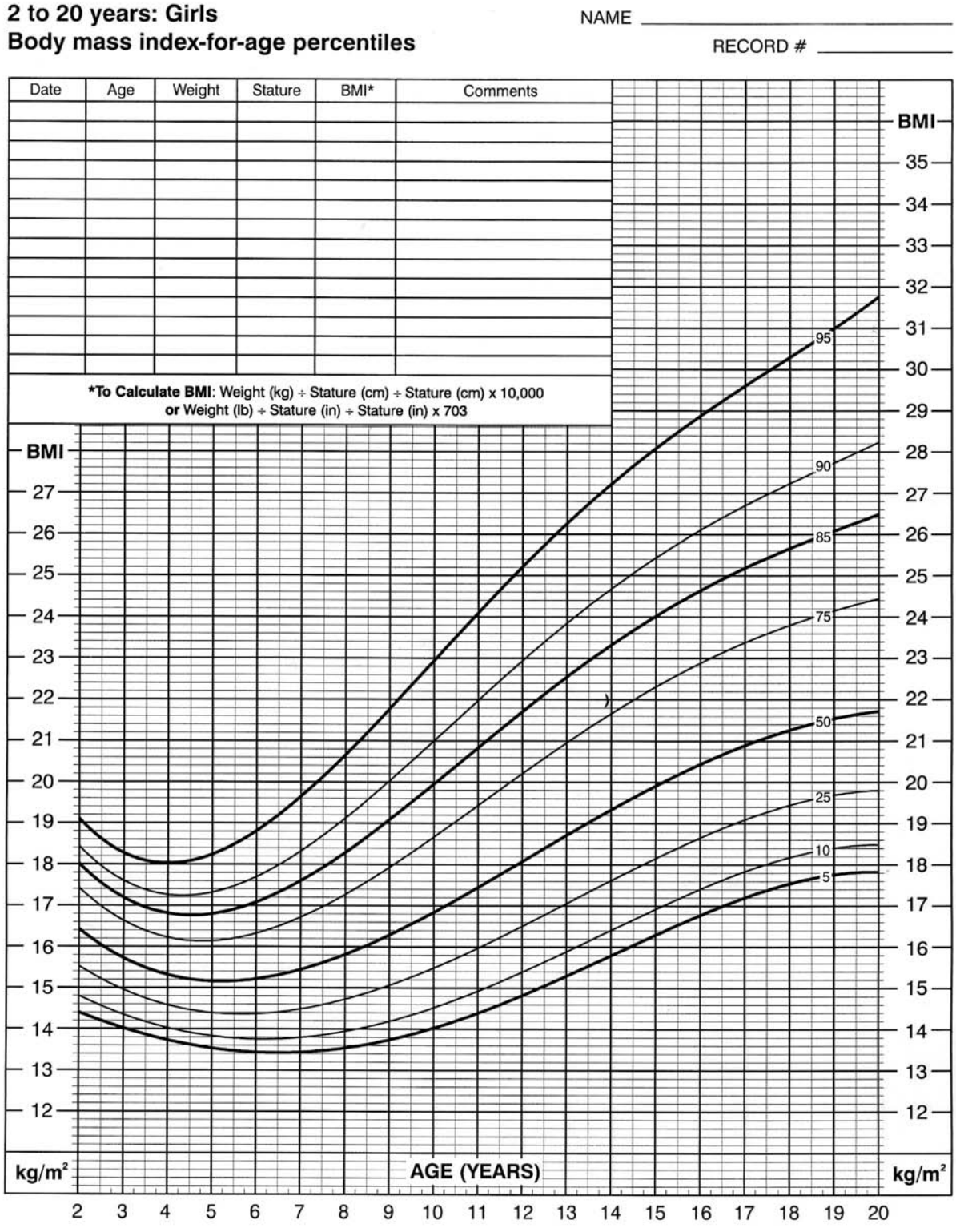
The primary care physician also may serve as community leader and public health advocate. Such advocacy may occur in a variety of forms and settings:

Schools: Priorities for school activities that limit risk of obesity include control of the food environment, enhancement of regular physical activity, including lifelong forms of physical activity as a regular part of the school curriculum and education of students on advantages and practical approaches for healthy eating and regular physical activity.

Work sites: Advocate for healthy food choices at worksites, including both healthy food choices in cafeterias and healthy food choices in vending machines. Especially consider limiting availability of sweetened carbonated beverages and high-calorie, high-fat snacks in vending machines.

Other community settings: There are opportunities for political advocacy and community health education that emphasize the importance of healthy lifestyle. Issues such as availability of sidewalks, pedestrian access to commercial establishments, and availability of public affordable exercise facilities of different sorts are among the issues that may be relevant.

Appendix A – Body Mass Index-for-Age Percentiles



Source: Developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease and Health Promotion (2000). http://www.cdc.gov.growthcharts

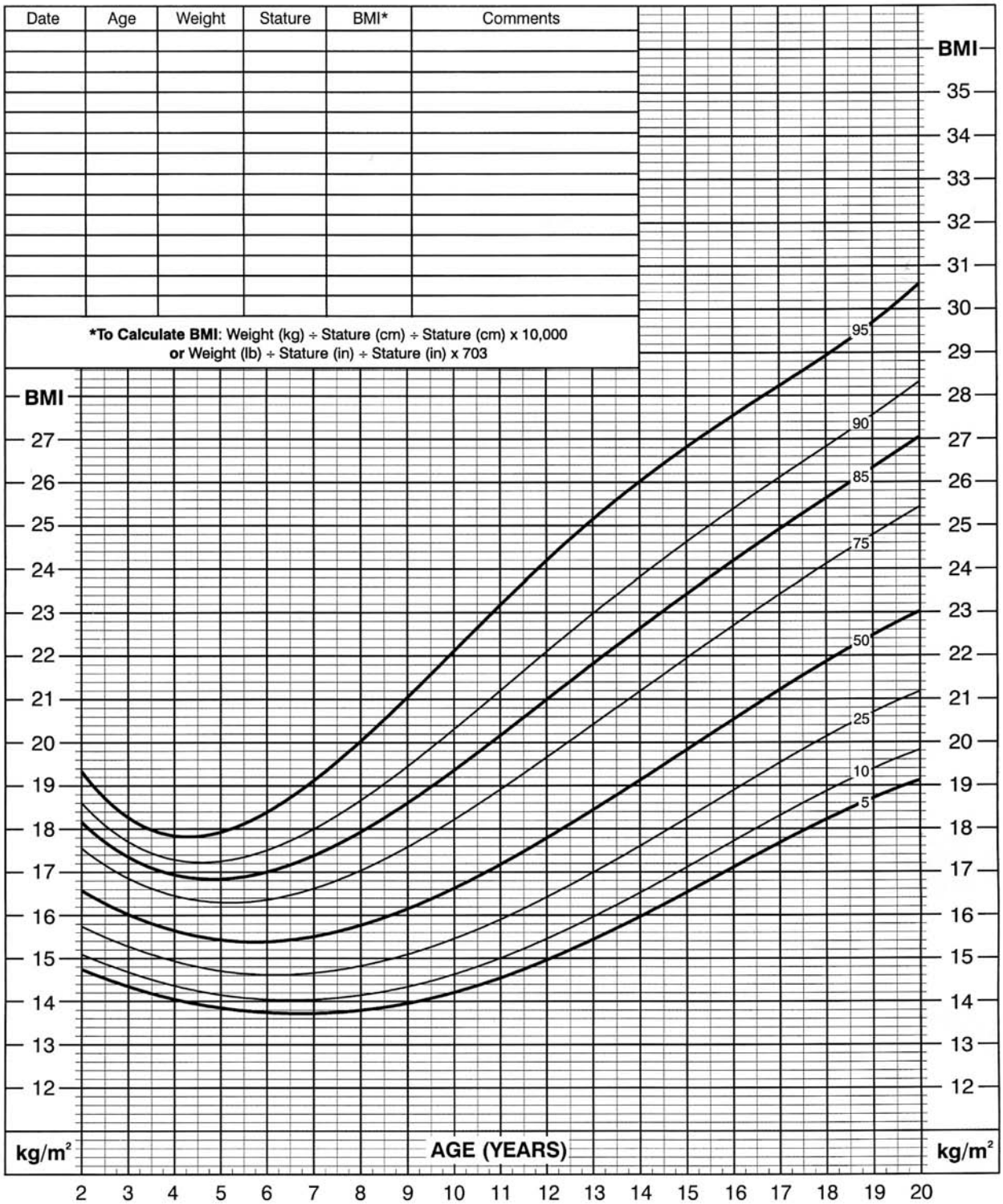
2 to 20 years: Boys
Body mass index-for-age percentiles

NAME _____

RECORD # _____

Date	Age	Weight	Stature	BMI*	Comments

***To Calculate BMI**: Weight (kg) ÷ Stature (cm) ÷ Stature (cm) x 10,000
or Weight (lb) ÷ Stature (in) ÷ Stature (in) x 703



Source: Developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease and Health Promotion (2000). http://www.cdc.gov.growthcharts

Appendix B – Medications Associated with Weight Gain

Medication Class	Alternatives
Antipsychotics ***(Aronne, 2003 [R]):*** • Phenothiazines • Atypical antipsychotics: Clozapine > olanzapine > risperidone = quetiapine	Ziprasidone, Aripiprazole
Mood Stabilizers: • Lithium	
Antidepressants: • Sedating tricyclics *(Masand, 2000 [R]):* Amitriptyline > imipramine • Monoamine oxidase inhibitors (non-selective): Isocarboxazid, Phenelzine, tranylcypromine • Selective serotonin reuptake inhibitors *(Sussman, 2001 [M]):* Paroxetine > citalopram, fluvoxamine, sertraline • Mirtazapine	Nefazodone, Bupropion, Venlafaxine
Antiepileptics: Gabapentin, Valproate, Carbamazepine, Pregabalin	Lamotrigine, Topiramate
Antiepileptics/antipsychotics used in bipolar disorder ***(Nemeroff, 2003 [R]):*** Valproate, Carbamzepine, Clozapine, Olanzapine, Risperidone	Lamotrigine, Topiramate, Ziprasidone
Steroid hormones: • Hormonal contraceptives • Corticosteroids	Yasmin (ethinyl estradiol [EE] 30 mcg and drospirenone 3 mg) Barrier methods NSAIDs
Progestational steroids: • Megestrol acetate	Weight loss, Aromatase inhibitors
Antidiabetes agents: • Insulin • Sulfonylureas • Thiazolidinediones	Metformin, Acarbose, Exenatide injection (Byetta)
Antihypertensives: • Beta and alpha-1 adrenergic blocking agents	ACE inhibitors, ARBs, diuretics, calcium channel blocker
Antihistamines: • Cyproheptadine	Diphenhydramine, decongestants, inhalers

(Adapted from Greenway, 2003 [R]; Kushner, 2003b [R]; Weigle, 2003 [R])

Appendix C – FDA-Approved Medications for the Treatment of Obesity

Generic Name	Brand Name	Mechanism of Action	Indication
Benzphetamine	Didrex CIII®	Sympathomimetic amine; causes central nervous system stimulation and acts as an anorectic.	Indicated for management of exogenous obesity as a short-term adjunct (a few weeks) in a weight-reduction regimen based on caloric restriction.
Diethylpropion	Tenuate CIV® Tenuate® Dospan CIV®	Sympathomimetic amine; causes central nervous system stimulation and acts as an anorectic.	Indicated for management of exogenous obesity as a short-term adjunct (a few weeks) in a weight-reduction regimen based on caloric restriction.
Methamphetamine	Desoxyn CII®	Sympathomimetic amine; causes central nervous system stimulation and acts as an anorectic.	Indicated for management of exogenous obesity as a short-term adjunct (a few weeks) in a weight-reduction regimen based on caloric restriction.
Phendimetrazine	Bontril CIII® Bontril Slow-release CIII®	Sympathomimetic amine; causes central nervous system stimulation and acts as an anorectic.	Indicated for management of exogenous obesity as a short-term adjunct (a few weeks) in a weight-reduction regimen based on caloric restriction.
Phentermine	Adipex-P CIV®	Sympathomimetic amine; causes central nervous system stimulation and acts as an anorectic.	Indicated for management of exogenous obesity as a short-term adjunct (a few weeks) in a weight-reduction regimen based on caloric restriction.
Phentermine resin complex	Ionamin CIV® Fastin CIV®	Sympathomimetic amine; causes central nervous system stimulation and acts as an anorectic.	Indicated for management of exogenous obesity as a short-term adjunct (a few weeks) in a weight-reduction regimen based on caloric restriction.
Sibutramine	Meridia CIV®	Therapeutic effects are produced by norepinephrine, serotonin and dopamine reuptake inhibition. Sibutramine and its major pharmacologically active metabolites (M_1 and M_2) do not act via release of monoamines; result is an enhanced feeling of satiety.	Indicated for the management of obesity, including weight loss and maintenance of weight loss; should be used in conjunction with a reduced-calorie diet.
Orlistat	Xenical® *Orlistat 60	Reversible inhibitor of lipases; exerts its therapeutic activity in the lumen of the stomach and small intestine by forming a covalent bond with gastric and pancreatic lipases and a subsequent reduction in triglyceride hydrolysis and absorption of dietary fat, including cholesterol.	Indicated for obesity management including weight loss and weight maintenance when used in conjunction with a reduced-calorie diet; also indicated to reduce the risk for weight regain after prior weight loss.

*Orlistat 60, TN Alli, available for over-the-counter use.

Sources:

The Medical Letter. Treatment Guidelines from The Medical Letter. Vol 1 (Issue 16). December 2003.

Weigle duodenal switch. Cardiovascular Endocrinology: Special Features. Pharmacological Therapy of Obesity: Past, Present, and Future. *Journal of Clinical Endocrinology and Metabolism*. Volume 88. Number 6. June 2003.

Dickerson LM, Carek PJ. Drug Therapy for Obesity. *American Family Physician*. April 1, 2000.

Moyers SB. Medications as Adjunct Therapy for Weight Loss: Approved and Off-Label Agents in Use. *Journal of the American Dietetic Association*. June 2005.

DeWald T, Khaodhiar L, Donahue M, et al. Pharmacological and surgical treatments for obesity. *American Heart Journal*. March 2006.

Appendix D – Adverse Effects of FDA-Approved Medications for the Treatment of Obesity

Brand Name	Generic Name	Adverse Effects	Warnings and Contraindications
Didrex CIII®	Benzphetamine	Headache, insomnia, nervousness, irritability, tachycardia, hypertension, and palpitations.	Advanced arteriosclerosis, moderate to severe hypertension, hyperthyroidism, and glaucoma; tolerance may develop.
Tenuate CIV® Tenuate Dospan® CIV®	Diethylpropion	Central nervous system stimulation, dizziness, headache, constipation, dry mouth, nausea, vomiting insomnia, restlessness, mild increases in blood pressure, palpitations/mild tachycardia.	Advanced arteriosclerosis, agitated states, during or within 14 days of MAO inhibitors, glaucoma, history of drug abuse, hypersensitivity or idiosyncrasy to sympathomimetic amines, hyperthyroidism, severe hypertension; tolerance may develop.
Desoxyn CII®	Methamphetamine	Central nervous system stimulation, dizziness, headache, constipation, dry mouth, nausea, vomiting insomnia, restlessness, mild increases in blood pressure, palpitations/mild tachycardia.	Glaucoma, advanced arteriosclerosis, symptomatic cardiovascular disease, hypertension, hyperthyroidism, within 14 days of MAO inhibitors tolerance may develop.
Bontril CIII® Bontril Slow-release CIII®	Phendimetrazine	Central nervous system stimulation, dizziness, headache, constipation, dry mouth, nausea, vomiting insomnia, restlessness, mild increases in blood pressure, palpitations/mild tachycardia.	Advanced arteriosclerosis, symptomatic cardiovascular disease, moderate and severe hypertension, hyperthyroidism, glaucoma, other CNS stimulants including monoamine oxidase inhibitors; tolerance may develop.
Adipex-P CIV®	Phentermine	Primary pulmonary hypertension and/or regurgitant cardiac valvular disease, palpitation, tachycardia, elevation of blood pressure, overstimulation, restlessness, dizziness, insomnia, euphoria, dysphoria, tremor, headache.	Advanced arteriosclerosis, cardiovascular disease, moderate to severe hypertension, hyperthyroidism, glaucoma, within 14 days following the administration of MAO inhibitors; tolerance may develop.
Ionamin CIV® Fastin CIV®	Phentermine resin complex	Primary pulmonary hypertension and/or regurgitant cardiac valvular disease, palpitation, tachycardia, elevation of blood pressure, overstimulation, restlessness, dizziness, insomnia, euphoria, dysphoria, tremor, headache.	Advanced arteriosclerosis, cardiovascular disease, moderate to severe hypertension, hyperthyroidism, glaucoma, within 14 days following the administration of MAO inhibitors; tolerance may develop.
Meridia CIV®	Sibutramine	Abnormal ECG, hypertension, palpitations, tachycardia, dry mouth (17%), headache (30%), insomnia (10%), anorexia (13%), constipation (11.5%).	Anorexia nervosa, concomitant MAO inhibitor use, concomitant use of centrally acting appetite suppressants, use of other serotonergic drugs, coronary heart disease, congestive heart failure, stroke, arrhythmia, uncontrolled hypertension, history of substance abuse, pregnancy or lactation, bulimia nervosa, concomitant medications that affect hemostasis or platelet function, gallstones, liver impairment, narrow angle glaucoma, pulmonary hypertension, renal impairment and seizure history.
Xenical®	Orlistat	Abdominal pain/discomfort, fatty/oily stools, fecal urgency, increased defecation.	Cholestasis, chronic malabsorption syndrome, clinically significant GI disease, patients at risk for fat-soluble vitamin deficiency.

Sources:

The Medical Letter. Treatment Guidelines from the Medical Letter. Vol 1 (Issue 16). December 2003.

Weigle duodenal switch. Cardiovascular Endocrinology: Special Features. Pharmacological Therapy of Obesity: Past, Present, and Future. *Journal of Clinical Endocrinology and Metabolism*. Volume 88. Number 6. June 2003.

Dickerson LM, Carek PJ. Drug Therapy for Obesity. *American Family Physician*. April 1, 2000.

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DeWald T, Khaodhiar L, Donahue M, et al. Pharmacological and surgical treatments for obesity. *American Heart Journal*. March 2006.

Appendix E – Drug Interactions of FDA-Approved Medications for the Treatment of Obesity

Generic Name	Brand Name	Drug Interactions
Benzphetamine	Didrex®	CNS stimulants MAO inhibitors Tricyclic antidepressants Antihypertensives
Diethylpropion	Tenuate®	Guanethidine MAO inhibitors Sibutramine Thioridazine
Methamphetamine	Desoxyn®	Insulin Guanethidine MAO inhibitors Phenothiazines Tricyclic antidepressants Amphetamine
Phendimetrazine	Bontril®	MAO inhibitors Sibutramine
Phentermine resin complex	Ionamin®	Ephedra MAO inhibitors Sibutramine St. John's wort
Sibutramine	Meridia®	Centrally acting appetite suppressants Dextromethorphan Dihydroergotamine Droperidol Ephedra Ergotamine Fentanyl Lithium Meperidine MAO inhibitors Pentazocine SSRIs Serotonin agonists St. John's wort Tryptophan Yohimbine
Orlistat	Xenical®	Cyclosporine Warfarin

Sources:

The Medical Letter. Treatment Guidelines from The Medical Letter. Vol 1 (Issue 16). December 2003.

Weigle duodenal switch. Cardiovascular Endocrinology: Special Features. Pharmacological Therapy of Obesity: Past, Present, and Future. *Journal of Clinical Endocrinology and Metabolism*. Volume 88. Number 6. June 2003.

Dickerson LM, Carek PJ. Drug Therapy for Obesity. *American Family Physician*. April 1, 2000.

Moyers SB. Medications as Adjunct Therapy for Weight Loss: Approved and Off-Label Agents in Use. *Journal of the American Dietetic Association*. June 2005.

DeWald T, Khaodhiar L, Donahue M, et al. Pharmacological and surgical treatments for obesity. *American Heart Journal*. March 2006.

Appendix F – Weight-Loss Comparison of Surgical Procedures

Weight-Loss Comparison of Surgical Procedures

All procedures have excellent midterm (more than five-year) weight loss and remission of comorbidities. One report shows success for Roux-en-Y gastric bypass as far as 16 years after operation.

All procedures work best in coordination with lifestyle changes that include daily activity, improved food choices, peer support and program support.

Vertical banded gastroplasty has been replaced with newer techniques and is rarely performed due to failure in up to 79% of patients at 10 years *(Balsiger, 2000 [D])*.

Procedure	Advantages	Particular Risks
Roux-en-Y Gastric bypass	Very well defined long-term success Most common U.S. procedure "Dumping" symptoms, although uncomfortable, can be beneficial in food choice	Marginal ulcers with NSAID use or smoking Internal hernia risk Vitamin/mineral malabsorption Loss of endoscopic access
Adjustable band	No division or anastomosis of stomach or bowel Adjustability Extremely low mortality No nutrient malabsorption	Higher rate of nonfatal complications Slip requires surgical repair (2%-5%) Erosion/foreign body (less than 1/1,000) Port site infection may require removal and subsequent replacement
Malabsorptive: BPD/duodenal switch	"Normal" intake volumes (can continue to overeat)	Severe malnutrition risk – may require TPN or surgical revision Chronic diarrhea in many Most complex procedure without additional health benefit

(Dixon, 2003 [C]; Gagner, 2002 [D]; Hess, 1998 [D]; Parikh, 2005 [D])

Emergencies

Pulmonary Embolus is the most common fatal complication from weight loss surgery, and the risk extends more than 90 days from surgery in the high-risk group. The patient may present to primary care or a remote emergency room.

Gastric gypass procedure or malabsorptive procedures

Closed loop bowel obstruction with Roux-en-Y may present with subtle or no findings beyond symptoms. CT is unreliable for diagnosis, and diagnostic laparoscopy may be required. Early consultation with a surgeon who is familiar with these issues can avoid catastrophe.

Anastomotic leak or perforation of marginal ulcer may present with equivocal symptoms and subtle findings. Any sustained tachycardia greater than 120 mandates bariatric surgical consultation prior to or concurrent with cardiac workup. A patient's sense of "impending doom" should be taken very seriously.

Neuropathy/encephalopathy – usually in setting of intractable vomiting and noncompliance with supplemental vitamins (after Roux-en-Y gastric bypass or BPD/duodenal switch).

Laproscopic adjustable band

Slip or erosion often presents as nightime reflux or abdominal pain. Peritioneal signs are usually absent. Port site infection also requires surgical care.

Note: Many bariatric programs participate in outcome registries, and many third-party payors, including Medicare, require participation, including guidelines for program structure and process (pathways). While data is pending regarding efficacy of these programs, the evolution of validated databases and coordination of standardized care is to be supported.

See the Surgical Management section in Annotation #10, "Negotiate Goals and Management Strategy to Achieve Weight Loss. Refer to Risk-Appropriate Resources as Needed."

Appendix G – Physical Activity Prescription

Name _____
Date _____
Follow-up interval _____

Health Status for Physical Activity:

Current Diagnoses (see contraindications):
1. _____
2. _____
3. _____

Current Medications:
1. _____
2. _____
3. _____

Assessment:
_____ OK for a self-monitored activity program
_____ OK for a supervised activity program (referral)
_____ Needs exercise tolerance testing (referral)

Activity Planner: Season(s) of Year _____

Indoors - Alone

1. Activity _____
   Resources
   a._____
   b. _____
   c. _____

2. Activity _____
   Resources
   a._____
   b. _____
   c. _____

Indoors - with Others

1. Activity _____
   Resources
   a._____
   b. _____
   c. _____

2. Activity _____
   Resources
   a._____
   b. _____
   c. _____

Outdoors – Alone

1. Activity _____
   Resources
   a. _____
   b. _____
   c. _____

2. Activity _____
   Resources
   a._____
   b. _____
   c. _____

Outdoors – with Others

1. Activity _____
   Resources
   a. _____
   b. _____
   c. _____

2. Activity _____
   Resources
   a. _____
   b. _____
   c. _____

Activity Ideas:

- Walking
- Swimming
- Biking
- Gardening
- Tennis
- Mowing lawn
- Golf
- Yoga
- Hiking
- Rollerblading
- Pilates
- Soccer
- Aerobics

Patient should identify at least two possible *activities* under each circumstance to achieve variety.

For each selected activity, identify key *resources* needed to make it happen. Resources include both physical (e.g., equipment, coach, time) and psychological (e.g., social support, goals).

Goals are to adjust activity plans for seasons and weather, minimize boredom, develop social support and personalize activity selection, given resources.

Dimensions for Physical Activity Improvement:
Frequency – recommended number of days per week to perform selected activities.

1. Cardiovascular – Start at 3x/week and advance to most days per week.
2. Strength – Start at 2-3 x/week and advance to every other day for a given muscle group.
3. Flexibility – Start at every other day and advance to most days per week; especially stretch after aerobic or resistance activities during the cool-down phase.

Duration – recommended amount of time or total work per activity session. Frequency and duration are more important for total caloric expenditure and weight management. They should be increased *before* intensity.

Intensity – recommended speed of movement (walking pace) or amount of weight to be lifted for each repetition. Increasing intensity creates continued improvement after physiologic adaptation to a given frequency and duration of activity. Intensity can be monitored with the Borg Perceived Exertion Scale. Typical target intensity on the Borg 6-20 scale is: 10-12 Fairly Light to 13-14 Somewhat Hard.

Also, the "talk test" indicates need to decrease intensity if difficulty in talking during aerobic activity.

Activity Prescription: Record prescribed activity and amount of time for each day of the week.

Week 1

	Sun.	Mon.	Tues.	Wed.	Thurs.	Fri.	Sat.
Indoors: (Activity)	_____	_____	_____	_____	_____	_____	_____
(Activity)	_____	_____	_____	_____	_____	_____	_____
Outdoors: (Activity)	_____	_____	_____	_____	_____	_____	_____
(Activity)	_____	_____	_____	_____	_____	_____	_____

Week 2

	Sun.	Mon.	Tues.	Wed.	Thurs.	Fri.	Sat.
Indoors: (Activity)	_____	_____	_____	_____	_____	_____	_____
(Activity)	_____	_____	_____	_____	_____	_____	_____
Outdoors: (Activity)	_____	_____	_____	_____	_____	_____	_____
(Activity)	_____	_____	_____	_____	_____	_____	_____

Work up to _____ minutes for (activity) in ____ weeks. Work up to _____lbs. for (activity) in ____ weeks.

I agree to this activity prescription and to keep an activity log on my calendar from _____to _____.

Patient's Signature _____ Provider's Signature _____

Appendix H – Sample Routine Labs for Gastric Bypass Patients

PREOP labs – need to assess for evidence of metabolic bone disease, iron deficiency, renal insufficiency, anemia, active infection, lipid disorders, vitamin deficiencies for B group and D (also hypercoagubility if indicated by personal or family history)

CBC, CMP, thiamine/folate/B12/vitamin D, iron panel, PTH, Hgb A1c, lipids, homocysteine (consider hypercoag panel, thyroid panel)

POSTOP:

- 3 months – CBC, CMP (complete metabolic panel – includes electrolytes, BUN/creatinine, glucose, calcium, liver profile, albumin), vitamin B12/folate, phosphorus
- 6 months – CBC, CMP, vitamin B12/folate, phosphorus
- 9 months – CBC, BMP or CMP, vitamin B12/folate, phosphorus
- 12 months – CBC, CMP, vitamin B12/folate, phosphorus. Iron, ferritin, PTH, homocysteine, vitamin D, thiamin, lipid panel
- 18 months – CBC, BMP or CMP, vitamin B12/folate, phosphorus
- 2 years and annually-CBC, CMP, vitamin B12/folate, phosphorus. Iron, ferritin, PTH, homocysteine, vitamin D, thiamin

Hgb A1C and lipids also as dictated by preoperative comorbidities

"Emergency Panel" for abdominal pain usually includes smoking/NSAID assessment, CBC, CMP, CRP, CT of Abd/pelvis with 50 cc of contrast orally 20 minutes prior, and 30-50 cc orally when patient is actually on CT table.

(EGD endoscopy, and laparoscopy are also useful additional evaluation techniques.)

THIS IS ONLY AN EXAMPLE – BEST TO FOLLOW PROTOCOL FROM PATIENT'S OWN SURGICAL PROGRAM IF POSSIBLE (ESPECIALLY IF BPD OR DUODENAL SWITCH OPERATION.)

Supporting Evidence:

Prevention and Management of Obesity (Mature Adolescents and Adults)

Document Drafted
Dec 2003 – May 2004

Critical Review
Jun 2004

First Edition
Dec 2004

Second Edition
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Third Edition
Dec 2006

Fourth Edition
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Availability of references

References cited are available to ICSI participating member groups on request from the ICSI office. Please fill out the reference request sheet included with your guideline and send it to ICSI.

Contact ICSI at:
8009 34th Avenue South, Suite 1200; Bloomington, MN 55425; (952) 814-7060; (952) 858-9675 (fax)
Online at http://www.ICSI.org

Brief Description of Evidence Grading

Individual research reports are assigned a letter indicating the class of report based on design type: A, B, C, D, M, R, X.

A full explanation of these designators is found in the Foreword of the guideline.

II. CONCLUSION GRADES

Key conclusions (as determined by the work group) are supported by a conclusion grading worksheet that summarizes the important studies pertaining to the conclusion. Individual studies are classed according to the system defined in the Foreword and are assigned a designator of +, -, or ø to reflect the study quality. Conclusion grades are determined by the work group based on the following definitions:

Grade I: The evidence consists of results from studies of strong design for answering the question addressed. The results are both clinically important and consistent with minor exceptions at most. The results are free of any significant doubts about generalizability, bias, and flaws in research design. Studies with negative results have sufficiently large samples to have adequate statistical power.

Grade II: The evidence consists of results from studies of strong design for answering the question addressed, but there is some uncertainty attached to the conclusion because of inconsistencies among the results from the studies or because of minor doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from weaker designs for the question addressed, but the results have been confirmed in separate studies and are consistent with minor exceptions at most.

Grade III: The evidence consists of results from studies of strong design for answering the question addressed, but there is substantial uncertainty attached to the conclusion because of inconsistencies among the results from different studies or because of serious doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from a limited number of studies of weak design for answering the question addressed.

Grade Not Assignable: There is no evidence available that directly supports or refutes the conclusion.

The symbols **+**, **–**, **ø**, and **N/A** found on the conclusion grading worksheets are used to designate the quality of the primary research reports and systematic reviews:

+ indicates that the report or review has clearly addressed issues of inclusion/exclusion, bias, generalizability, and data collection and analysis;

– indicates that these issues have not been adequately addressed;

ø indicates that the report or review is neither exceptionally strong or exceptionally weak;

N/A indicates that the report is not a primary reference or a systematic review and therefore the quality has not been assessed.

References

Abenhaim L, Moride Y, Brenot F, et al. Appetite suppressant drugs and the risk of primary pulmonary hypertension. *N Engl J Med* 1996;335:609-16. (Class C)

Abid O, Galuska D, Khal KL, et al. Are health care professionals advising obese patients to lose weight? A trend analysis. *Medscape Gen Med* 2005;7:3-12. (Class M)

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Conclusion Grading Worksheet A – Annotation #10 (Orlistat)

Work Group's Conclusion: Patients taking orlistat as part of a program of nutritional and physical activity changes can expect a weight loss of 3.9 to 10.6 kg after one year of treatment and 4.6 to 7.6 kg after two years of treatment. A weight loss of at least 5% of initial body weight at one year is reported by 30% to 73% (vs. 13% to 45% of patients taking placebo); a weight loss of at least 10% of initial body weight at one year is reported by 10% to 41% (vs. 4% to 21% of patients taking placebo).

Conclusion Grade: I

Author/Year	Design Type	Class	Quality +, –, 0	Population Studied/Sample Size	Primary Outcome Measure(s)/Results (e.g., p-value, confidence interval, relative risk, odds ratio, likelihood ratio, number needed to treat)	Authors' Conclusions/ *Work Group's Comments (italicized)*
Sjöström et al., 1998	RCT	A	0	-Obese (BMI 28-47 kg/m^2) men and women; ages 18+ years -Excluded: serious diseases (including uncontrolled hypertension and treated diabetes); wt loss >4 kg in past 3 mos; surgery for wt reduction; history of post-surgical adhesions; bulimia, or laxative abuse; use of any drug that might effect body wt or plasma lipids in month before entry; drug/alcohol abuse -4 wk placebo lead-in; if >75% compliance then randomized to orlistat (120 mg) or placebo 3 times/day with meals for 52 wks with hypocaloric diet -After 52 wks those with >75% compliance reassigned to same tx or the alternative tx with wt-maintenance diet (see NOTES)	-Groups did not differ at time of randomization *-Decrease in body wt at 56 wks (lead-in plus 1 yr tx): 10.2% (10.3 kg) with orlistat, 6.1% (6.1 kg) with placebo ($p<0.001$)* -During year 2: former placebo patients taking orlistat in yr 2 reduced wt (0.9 kg) vs. wt regain if taking placebo (2.5 kg); former orlistat patients had smaller weight regain if taking orlistat vs. placebo ($p<0.001$) -After 2 yrs continuous orlistat: 57.1% maintained weight loss >5% (vs. 37.4% continuous placebo) -At 1 yr, orlistat group had greater decreases in total cholesterol, LDL cholesterol, LDL/HDL ratio, and fasting blood glucose; also greater decreases in systolic and diastolic blood pressure (all $p<0.05$) -At 2 yrs, orlistat group also had greater decrease in fasting plasma insulin ($p<0.01$) but blood pressure differences were not significantly different -Overall adverse events in yr 1: 94% (orlistat), 82% (placebo); most not related to treatment; more gastrointestinal adverse events in orlistat group -Adverse events in yr 2: 73% (placebo/placebo), 79% (orlistat/placebo), 87% (placebo/orlistat), 77% (orlistat/orlistat)	-Orlistat taken with an appropriate diet promotes clinically significant weight loss and reduces weight regain in obese patients over a 2-year period. The use of orlistat beyond 3 years needs careful monitoring with respect to efficacy and adverse events. NOTES: study conducted at 15 European centers; 937 screened, 743 entered lead-in phase, 688 randomized (345 to orlistat, 343 to placebo); intention-to-treat analysis at 1 yr included 683 (544 who completed treatment; 260 in orlistat group & 284 in placebo group); 273 former orlistat and 253 former placebo patients were reassigned after 1 yr; intention-to-treat analysis at yr 2 included 519 (435 who completed treatment); more premature withdrawals in placebo group in yr 1 (83 vs. 61)

Author/Year	Design Type	Class	Quality +, –, Ø	Population Studied/Sample Size	Primary Outcome Measure(s)/Results (e.g., p-value, confidence interval, relative risk, odds ratio, likelihood ratio, number needed to treat)	Authors' Conclusions/ *Work Group's Comments (italicized)*
Hauptman et al., 2000	RCT	A	Ø	-Men and women; >18 yrs; BMI 30-44 kg/m^2 -Excluded: pregnancy; wt loss >4 kg in past 3 mos; history of significant cardiac, renal, hepatic, or GI disorders; uncontrolled hypertension; gastrointestinal surgery for wt loss; substance abuse; abnormal lab results; changes in smoking habits in past 6 mos; any drug that could influence food intake or obesity -4 wk placebo lead-in; if ≥75% compliance randomized to placebo, 60 mg orlistat, or 120 mg orlistat for 52 weeks; reduced energy diet -Same treatment for 2nd year with maintenance diet	-212 randomized to placebo, 213 to 60mg orlistat, 210 to 120mg orlistat; no differences at baseline *-Weight loss (intention-to-treat) at 56 wks (lead-in plus 52 wk tx): 4.1 kg (placebo), 7.1 kg (60 mg orlistat), 7.9 kg (120 mg orlistat) (both orlistat groups p= 0.001 vs. placebo)* *-Weight loss (intention-to-treat) at 2 yrs: 1.7 kg (placebo), 4.5 kg (60 mg orlistat), 5.0 kg (120 mg orlistat) (both orlistat groups p= 0.001 vs. placebo)* -Weight loss (completers) at 56 wks: 4.3 kg (placebo), 8.0 kg (60 mg), 8.8 kg (120 mg) (both orlistat groups p=0.001 vs. placebo) -Weight loss (completers) at 2 yrs: 1.5 kg (placebo),4.6 kg (60 mg), 5.2 kg (120 mg) (both orlistat groups p≤0.02 vs. placebo) -Weight loss ≥5% (at 56 wks): 31% (placebo), 49% (60 mg), 51% (120 mg); at 2 yrs: 24% (placebo), 34% (60 mg), 34% (120 mg) -Weight loss ≥10% (at 56 wks): 11% (placebo), 24% (60 mg), 29% (120 mg); at 2 yrs: 7% (placebo), 15% (60 mg), 19% (120 mg) - LDL cholesterol lower at 1 yr and 2 yrs in orlistat groups vs. placebo (p<0.05); total cholesterol lower in 60 mg group at 1 yr and 2 yrs; -Adverse events generally transient; mild or moderate intensity; similar in all groups except more GI events in orlistat group (p<0.01)	-This long-term study indicates that orlistat is an effective adjunct to dietary intervention in the treatment of obesity in primary care settings. NOTES: 17 study centers; 796 eligible; 635 (80%) randomized after lead-in period; 427 completed first year (122 [57%] placebo, 154 [72%] 60 mg orlistat, 151 [71%] 120 mg orlistat); 327 completed 2 yrs (91 [43%] placebo, 120 [56%] 60 mg orlistat, 117 [56%] 120 mg orlistat); 4 behavior modification videos in yr 1; 4 wt. maintenance pamphlets in yr 2; dietary records at 10 points during study; encouraged to increase physical activity

Author/Year	Design Type	Class	Quality +, –, Ø	Population Studied/Sample Size	Primary Outcome Measure(s)/Results (e.g., p-value, confidence interval, relative risk, odds ratio, likelihood ratio, number needed to treat)	Authors' Conclusions/ *Work Group's Comments (italicized)*
Rössner et al., 2000	RCT	A	Ø	-Men and women; ≥18 years; BMI 28-43 kg/m^2 -Excluded: pregnant or lactating, any clinically significant condition except obesity; wt loss >4 kg in past 3 mos; smoking stopped in past 6 mos; GI surgery for wt reduction; history of bulimia or laxative use; use of any drug affecting body wt or lipids in past 8 wks; uncontrolled hypertension; drug-treated diabetes mellitus; history or presence of cholelithiasis -4 wk placebo run-in with 600 kcal/day energy deficit; if ≥75% compliance then stratified on wt lost and randomized to 60mg or 120mg orlistat or placebo 3X/day for 52 weeks with same diet; diet adjusted during year 2 based on wt lost during wks 40-52	-243 randomized to placebo; 242 to 60mg, 244 to 120mg; 11 had no follow-up assessments and were excluded from safety analyses; 2 additional patients excluded from intention-to-treat analysis (no efficacy assessment); groups comparable at baseline *-Weight loss from initial weight (intention-to-treat):* *Year 1* *Year 2* *placebo* *6.6%[a] (6.4 kg)* *4.5%[a] (4.3 kg)* *60mg orlistat* *8.6%[a,b] (8.5 kg)* *6.8%[a,b] (6.6 kg)* *120mg orlistat* *9.7%[a,b] (9.4 kg)* *7.6%[a,b] (7.4 kg)* *[a]p<0.05 (vs. baseline)* *[b]p<0.05 (vs. placebo)* -Weight loss >5%: higher percentage in 120mg orlistat group vs. placebo (year 1 & 2; p<0.001) -Weight loss >10%: Year 1 Year 2 placebo 19% 19% 60mg orlistat 31%[a] 29%[a] 120mg orlistat 38%[a] 28%[a] [a]p<0.05 (vs. placebo) -Total cholesterol, LDL, and LDL/HDL ratio decreased during both years of treatment in orlistat groups (all p<0.002) but not placebo; orlistat groups had decreased fasting glucose at groups at year 1 and decreased fasting insulin at year 2 (all p<0.05) -Overall satisfaction with treatment greater for orlistat groups at year 1 and 2 (all p<0.05) -Adverse events similar in all groups except more GI events in orlistat groups; most events mild to moderate, resolved spontaneously; 49 severe GI events (8 placebo, 16 60mg, 25 120mg); 38 in first year -No differences between groups in blood pressure except diastolic pressure in 120mg group at year 1 different from placebo (p<0.05)	-Orlistat administered for 2 years promotes weight loss and minimizes weight regain. Orlistat therapy improves lipid profile, blood pressure, and quality of life. NOTES: study was conducted in 14 centers in Europe; 783 enrolled in run-in; 54 dropped out leaving 729 randomized; for year 2 those who lost ≥3kg during wks 40-52 had caloric intake of estimated total daily expenditure minus 10% kcal/day; those who lost <3 kg were considered weight stable with no adjustment; patients discontinued taking vitamin supplements before taking part in the study; 65% of placebo, 75% of 60mg, and 74% of 120mg group completed year 1, 56%, 58%, and 65%, respectively, completed year 2

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Rissanen et al., 2003	Meta-analysis	M	N/A	-Pooled data from two 2-yr multicenter RCTs (similar design) -M/F; BMI 28-43 kg/m^2; ≥18 yrs -4 wk lead-in with placebo and hypocaloric diet (30% of energy as fat; 500 kcal daily deficit) -If lead-in completed, randomized to orlistat (120 mg 3X/day) or placebo for 2 yrs; hypocaloric diet continued for 1st yr; weight maintenance diet for 2nd yr	-Analysis included only completers of 2-year program (n=220) *-4-week lead-in:* 118 (54%) lost ≥2.5 kg, 102 (46%) lost <2.5 kg; *At 12 wks:* 104 (47%) lost ≥5% of body wt, 116 (53%) did not; *At 6 months:* 47 (21%) lost ≥10% of body wt, 173 (79%) did not; no differences in demographic characteristics of those who achieved criteria -If 4-wk wt loss ≥2.5 kg, loss at 2 yrs=9.4%; if 4-wk loss <2.5 kg, loss at 2 yrs=6.6% *-If 12-wk wt loss ≥5%, loss at 2 yrs=11.9%; if 12-wk loss <5%; loss at 2 yrs=4.7% (p=0.0001)* -Risk factors: wt loss ≥ 5% at 12 wks associated with greater improvement in total cholesterol; LDL cholesterol, triglycerides, fasting glucose, fasting insulin, systolic BP and diastolic BP (all p<0.05)	-A weight loss of 5% or more after 12 wks of treatment with orlistat is a useful predictor of weight loss, 2-year weight maintenance, and risk factor reduction even in those who do not appear to respond immediately to short-term dietary intervention or do not sustain a rapid rate of weight loss from 3 to 6 months of diet plus drug therapy. NOTES: 2-yr treatment phase was double-blind; data are from Sjöström et al. (1998) and Rössner et al. (2000) *Work Group's Comments: analysis was not by intention-to-treat*
Torgerson et al., 2004 (XENDOS)	RCT	A	0	-3,305 patients from 22 Swedish medical centers -Included: ages 30-60 yrs; BMI>30 kg/m^2; non-diabetic glucose tolerance test -Excluded: diabetes; ongoing and active cardiovascular and gastrointestinal disease -Randomized to placebo or orlistat (120 mg 3X/day) and hypocaloric diet (800 kcal/day deficit) with 30% of calories from fat and ≤300 mg cholesterol/day; energy intake adjusted every 6 mos; 4-year study -Dietary counseling every 2 wks for first 6 mos, then monthly -Encouraged to walk 1 km/day in addition to usual activity	-1,650 in orlistat group; 1,655 in placebo; 3,304 were treated; ITT population was 1,640 in orlistat group and 1,637 in placebo group; no differences at baseline -Caloric deficit (-674 kcal/day orlistat, -744 kcal/day placebo), additional walking (9.5 km/wk orlistat, 9.9 km/wk placebo), and drug compliance (93.3% orlistat, 92.8% placebo) were similar *-Progression to type 2 diabetes: cumulative incidence at 4 yrs of 6.2% (orlistat) and 9.0% (placebo) (p=0.003); hazard ratio 0.63 (95%CI 0.46-0.86)* *-Weight loss at 1 yr: 10.6 kg (orlistat), 6.2 kg (placebo) (p<0.001); 73% of orlistat and 45% of placebo patients lost ≥5%; 41% of orlistat and 21% of placebo lost ≥10% (both p<0.001)* *-Weight loss at 4 yrs: 5.8 kg (orlistat), 3.0 kg (placebo) (p<0.001)* -For 4 year completers, 53% (orlistat) and 37% (placebo) lost ≥5%; 26% (orlistat) and 16% (placebo) lost ≥10% (both p<0.001) -Risk factors: at 1 yr greater changes in blood pressure, all cholesterol measures, triglycerides, waist circumference, blood glucose, and insulin (all p<0.05); at 4 years same except no difference in triglycerides -Adverse events: most events mild to moderate and during early phase of treatment; 4% of placebo and 8% of orlistat group withdrew due to adverse events	-Compared with lifestyle changes alone, orlistat plus lifestyle changes resulted in a greater reduction in the incidence of type 2 diabetes over 4 years and produced greater weight loss in a clinically representative obese population. NOTES: study was blinded; did sample size estimate for power of 90% to detect difference in development of type 2 diabetes; 52% of orlistat group and 34% of placebo group completed treatment (p<0.0001); most drop-outs due to refusal of treatment or insufficient therapeutic response; intention-to-treat analysis

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Orlistat for Patients with Type 2 Diabetes Mellitus						
Hollander et al., 1998	RCT	A	0	-Men & women, >18 yrs, BMI 28-40 kg/m^2; oral hypoglycemic therapy for ≥6 mos; stable plasma glucose on 2nd gen. sulfonylurea agent as only hypoglycemic agent -Excluded: pregnant or lactating, clinically relevant condition that might affect outcome; significant complications associated with diabetes; wt loss >4 kg in past 3 mos; history or recurrent nephrolithiasis or symptomatic cholelithiasis; prior GI surgery for wt reduction; history of bulimia or laxative abuse; use of drugs that might influence wt or lipids in 8 wks prior -5-wk placebo lead-in with mildly hypocaloric diet; if ≥70% compliance, HbA_{1c} 6.5-10%, fasting plasma glucose 5.6-12.2 mmol/l at 4 wks, & blood levels of fat soluble vitamins > lower limit of normal then randomized to 120mg orlistat or placebo 3X/day for 52 wks with mildly hypocaloric diet (500kcal/day deficit)	-162 randomized to orlistat, 159 to placebo; no differences at baseline -*Wt loss at 57 wks: 6.2% (6.2 kg) of initial wt (orlistat), 4.3% (4.3 kg) (placebo) ($p<0.001$)* -Wt loss ≥5%: 49% (orlistat), 23% (placebo) ($p<0.001$) -Wt loss ≥10%: 18% (orlistat), 9% (placebo) ($p=0.02$) -After randomization: mean fasting plasma glucose and HbA_{1c} decreased in orlistat group, increased in placebo group (both $p<0.001$) -Average dose of oral sulfonylureas decreased more in orlistat group ($p<0.01$) -After randomization: orlistat group had significant improvement in total cholesterol, LDL cholesterol, LDL/HDL radio, triglycerides, & apolipoprotein B (all $p<0.05$) -Adverse events similar except GI events higher in orlistat group (79% vs. 59% of placebo patients)	-Orlistat is an effective treatment modality in obese patients with type 2 diabetes with respect to clinically meaningful weight loss and maintenance of weight loss, improved glycemic control, and improved lipid profile. NOTES: study was conducted at 12 centers in the US; 391 enrolled, 322 completed 5 wk lead-in and randomized; 254 completed study (73% of placebo and 85% of orlistat groups)

Author/Year	Design Type	Class	Quality +, –, 0	Population Studied/Sample Size	Primary Outcome Measure(s)/Results (e.g., p-value, confidence interval, relative risk, odds ratio, likelihood ratio, number needed to treat)	Authors' Conclusions/ *Work Group's Comments (italicized)*
Kelley et al., 2002	RCT	A	0	-Men & women; ages 40-65 yrs; BMI 28-43 kg/m^2; stable wt (<3kg change) for past 3 mos; stable insulin daily insulin dose for past 6 wks; HbA_{1c} of 7.5-12% -Excluded: treatment with thiazolidinediones or if diabetes medication changed in past 12 wks; renal, hepatic, or endocrine disorders that could affect study results; previous bariatric surgery; use of wt reduction medications or treatments; malabsorption syndrome; bulimia or laxative abuse -2-wk screening phase; 52-wk treatment phase; randomized to reduced calorie diet plus either 120mg orlistat or placebo (3x/day); multivitamin at least 2 hrs before or after evening dose	-269 in placebo group, 266 in orlistat group; similar at baseline *-Wt loss at 52 wks: 3.76% or 3.89kg (orlistat); 1.22% or 1.27kg (placebo) (p< 0.001)* -Wt loss ≥5% of baseline: 33% (orlistat); 13% (placebo) (p<0.0001) -Wt loss ≥10% of baseline: 10% (orlistat); 4% (placebo) (p<0.001) -Decrease in fasting glucose greater in orlistat group (1.63 vs 1.08 mmol/l; p=0.02) -Decrease in serum HbA_{1c} greater in orlistat group (0.62 vs. 0.27; p=0.002); greater proportion with reduction ≥0.5% and ≥1.0% in orlistat group (both p<0.05) -Greater reduction in insulin dose in orlistat group (8.1 vs. 1.6 units/day; p=0.007); overall more orlistat patients decreased dose or discontinued ≥1 medication (41% vs. 31%) and fewer increased dose or added ≥1 medication (15% vs. 32%, p<0.0001) -Greater decreases in total and LDL cholesterol and LDL/HDL ratio in orlistat group (all p<0.05) -No differences in blood pressure changes -GI events more frequent in orlistat group (80% vs. 62%; p<0.05); most had single episode; most mild or moderate	Orlistat therapy produces clinically significant weight loss, with improvements in glycemic control and cardiovascular disease risk factors, in overweight or obese patients with type 2 diabetes who have suboptimal metabolic control with insulin therapy. NOTES: study was done in 43 centers in the U.S.; criteria for changes in diabetes medication doses standardized across study centers; 550 enrolled and randomized; 535 in intention-to-treat analysis (at least 1 dose of medication, had wt or HbA_{1c} assessments); 52% of orlistat group and 48% of placebo group completed treatment; changes in medication due to HbA_{1c} levels may have diminished differences in HbA_{1c} concentration between groups.

Author/Year	Design Type	Class	Quality +, –, ø	Population Studied/Sample Size	Primary Outcome Measure(s)/Results (e.g., p-value, confidence interval, relative risk, odds ratio, likelihood ratio, number needed to treat)	Authors' Conclusions/ *Work Group's Comments (italicized)*
Miles et al., 2002	RCT	A	ø	-Men & women; ages 40-65 years; BMI 28-43 kg/m^2; stable weight ≥3 mos, $HbA_{1c}$of 7.5-12%; metformin treatment of 1,000-2,550 mg/day for ≥6 wks; could take sulfonylurea with metformin if dose stable for ≥12 wks prior -Excluded: patients receiving insulin, thiazolidinediones, or alpha-glucosidase inhibitors; clinical condition that might affect outcomes (renal, hepatic, endocrine, poorly controlled hypertension, active gastrointestinal disease, bariatric surgery; history of bulimia, substance abuse, or use of wt loss medications; pregnant, lactation) -2-wk screening phase; 52-wk treatment phase (120mg orlistat or placebo), 3X/day; reduced calorie diet for all patients; multivitamin	-504 of 516 randomized had at least 1 follow-up visit (254 placebo, 250 orlistat); groups similar at baseline *-Wt loss at 1 yr: 4.6% or 4.7 kg (orlistat) vs. 1.7% or 1.8 kg (placebo) (p<0.001)* -Wt loss ≥5% of baseline: 39% (orlistat); 16% (placebo) (p=0.008) -Wt loss ≥10% of baseline: 14% (orlistat); 4% (placebo) (p=0.003) -Orlistat associated with reductions in daily metformin dose and relative sulfonylurea dose (both p<0.05); more orlistat patients reduced or discontinues ≥1 medication (8% vs. 17%) while more placebo patients required additional doses or medications (22% vs. 12%) (both p<0.001) -More patients treated with orlistat had reductions in HbA_{1c} of ≥0.5% or ≥1.0% (both p<0.01); both orlistat and placebo patients decreased HbA_{1c} from baseline levels (both p<0.05); difference between groups significant when adjusted for changes in medication -Orlistat group: greater improvement in total cholesterol, LDL cholesterol, & LDL/HDL ratio; greater decrease in systolic blood pressure (all p<0.05) -Adverse events similar except more GI events in orlistat group (83% of patients vs. 62%); most mild, transient, early in treatment -Hypoglycemic events: 10% (orlistat), 4% (placebo)	-Orlistat is a useful adjunctive treatment for producing weight loss and improving glycemic control, serum lipid levels, and blood pressure in obese patients with type 2 diabetes who are being treated with metformin. NOTES: study conducted at 34 centers in U.S. and 6 in Canada; 516 enrolled and randomized; 311 completed 1 yr; 44% of placebo and 35% of orlistat withdrew early (p<0.05)

Conclusion Grading Worksheet B – Annotation #10 (Sibutramine)

Work Group's Conclusion: Patients taking sibutramine as part of a program of nutritional and physical activity changes can expect a weight loss of 4.4 to 16.6 kg after 24 to 52 weeks of treatment. A weight loss of at least 5% of initial body weight at up to one year is reported by 39% to 77% of patients taking sibutramine (vs. 11% to 40% of patients taking placebo); a weight loss of at least 10% of initial body weight at up to one year is reported by 14% to 46% of patients taking sibutramine (vs. 0% to 8% of patients taking placebo).

Conclusion Grade: I

Author/Year	Design Type	Class	Quality +,–,0	Population Studied/Sample Size	Primary Outcome Measure(s)/Results (e.g., p-value, confidence interval, relative risk, odds ratio, likelihood ratio, number needed to treat)	Authors' Conclusions/ *Work Group's Comments (italicized)*
Bray et al., 1999	RCT	A	0	-Men and women; ages 18-65 years; BMI 30-40 kg/m^2 -Excluded: pregnancy, hypertension, cardiovascular disease, diabetes, immunological disease, depression, panic disorder, anorexia or bulimia nervosa, history of substance abuse in past 2 yrs, use of drugs that affect appetite or weight in past 14 days, regular use of laxatives -2-wk lead-in; randomized to 1, 5, 10, 15, 20, or 30 mg sibutramine or placebo for 24 wks -One counseling visit (dietitian); recommended exercise program, instruction in behavioral change -Dose reduction if adverse event	-n=145 to 152 per group (randomized); 59% to 71% completed -Groups similar at baseline except for BMI (range of 34.0-34.9; p=0.04) *-Outcomes (at 24 wks):* *Dose %Wt Loss* %Wt Loss^ ≥5% ≥10%* *Placebo 0.9 1.2 (1.3 kg) 20% 0%* *1 mg 1.9 2.7 (2.4 kg) 25% 11%~* *5 mg 3.1 3.9 (3.7 kg)~ 37%~ 12%~* *10 mg 4.7 6.1 (5.7 kg)~ 60%~ 17%~* *15 mg 5.8 7.4 (7.0 kg)~ 67%~ 35%~* *20 mg 6.6 8.8 (8.2 kg)~ 72%~ 39%~* *30 mg 7.7 9.4 (9.0 kg)~ 77%~ 46%~* **intention-to-treat, ^completers (all changes from baseline); ~p<0.05 vs. placebo* -Significant changes in triglycerides, total cholesterol, LDL cholesterol, uric acid, and serum glucose (all p<0.05) vs. placebo with greater changes in those with greater weight loss -Pulse rate increased relative to placebo (p<0.05 for 10 mg sibutramine and higher doses) (see NOTES) -Most common treatment-related adverse events were dry mouth (>20% in 15, 20, and 30 mg groups), anorexia (>20% in 1, 15, 20, and 30 mg groups), insomnia (>10% in 1, 15, 20, and 30 mg groups); and appetite increase (>10% in all sibutramine groups); 11% discontinued due to adverse events	-Sibutramine administered once daily for 24 weeks in the weight loss phase of treatment for uncomplicated obesity produced dose-related weight loss and was well tolerated. Improvements in serum lipids and uric acid accompany weight loss. NOTES: study conducted at 7 centers; 1047 randomized, 683 (65%) completed study; >10% of 10 mg, 15 mg, 20 mg, and 30 mg patients had dose reduced; mean systolic blood pressure increased by 0.3 to 4.0 mmHg in sibutramine groups (range of changes was -20 to +38 mmHg); mean diastolic blood pressure increased by 1.2 to 5.0 mmHg in sibutramine groups (range of change was -26 to +41 mmHg); mean pulse rate increased by 0.3 to 7.0 bpm (range of change was -18 to +31 bpm)

Author/Year	Design Type	Class	Quality +, –, 0	Population Studied/Sample Size	Primary Outcome Measure(s)/Results (e.g., p-value, confidence interval, relative risk, odds ratio, likelihood ratio, number needed to treat)	Authors' Conclusions/ *Work Group's Comments (italicized)*
James et al., 2000 Hansen et al., 2001 van Baak et al., 2003 (STORM)	RCT	A	0	-Men and women; ages 17-65 yrs; BMI 30-45kg/m^2 Excluded: recent weight changes or specified diseases (including diabetes, eating disorders, hepatic or renal dysfunction, cardiovascular disease, unstable hypertension) -6-mo weight-loss phase: 10 mg sibutramine; hypocaloric diet prescribed; increased activity advised -18-mo weight-maintenance phase: if >5% weight loss with <2 kg weight gain from month 4 to 6 of wt-loss phase then randomized to sibutramine or placebo (3:1 ratio)	-Weight-loss phase: mean of 11.3 kg lost *-Weight-maintenance phase (intention-to-treat analysis excluding 3 who withdrew early): sibutramine group gained 2.8 kg from month 6 to endpoint for net loss of 9.3 kg; placebo group gained 6.2 kg for net loss of 5.3 kg* -Weight-maintenance phase (completers): sibutramine group gained 2.6 kg for net loss of 10.4 kg; placebo group gained 7.2 kg for net loss of 5.2 kg (p<0.001) -Of 350 in sibutramine group, 145 (41%) successfully maintained ≥80% of original 6 month weight loss (vs. 16 of 114 or 14% of placebo) (p<0.001) -Predictors of weight maintenance: treatment group (sibutramine or placebo), percentage of initial weight lost, leisure-time physical activity index	-This individualized management program achieved weight loss in 77% of obese patients and sustained weight loss in most patients continuing therapy for 2 years. NOTES: study included 8 European centers; during weight-maintenance phase sibutramine dose increased up to 20 mg if >1 kg wt regain after month 6; 605 enrolled, 505 completed wt-loss phase; 467 eligible for randomization (352 sibutramine, 115 placebo); 204 sibutramine and 57 placebo completed trial *Work Group's Comments: numbers of patients in each phase differ between the two publications*
Smith et al., 2001	RCT	A	0	-Men and women; ages 18-65 yrs; BMI 27-40 kg/m^2 -Excluded: lost > 3 kg in past 3 mos; obesity of endocrine origin; diabetes; seated pulse rate >100 bpm; seated diastolic BP >100 mmHg; uncontrolled hypertension; laxative, anorectic, or diuretic use; bulking agents, antidepressants -Assessed success complying with dietary advice -2-wk placebo run-in then 12 months treatment; randomized to placebo or 10 mg or 15 mg sibutramine	-Randomized 163 to placebo, 161 to 10 mg and 15mg; groups similar at baseline -*Outcome (at 12 mos)* *Placebo (n=157)** *10mg (n=154)** *15mg (n=153)** *Wt change* *-1.6 kg* *-4.4 kg[a]* *-6.4 kg[b]* *≥5% loss* *20%* *39%[b]* *57%[b]* *≥10% loss* *7%* *19%[a]* *34%[b]* **excluded protocol violators;* [a]*p<0.01 vs. placebo;* [b]*p<0.001 vs. placebo* -Significant decreases in triglycerides (15mg only, p<0.05 vs. baseline) and uric acid (10mg and 15mg, p<0.05 vs. baseline and vs. placebo) -No significant differences in blood pressure or pulse rate (vs. baseline or vs. placebo) -Occurrence of dry mouth significantly greater in sibutramine groups vs. placebo (p<0.001); 2 of 8 serious adverse events considered possibly related to sibutramine	-Sibutramine (10 mg or 15 mg daily) given with dietary advice produces and maintains statistically and clinically significantly greater weight loss than dietary advice alone (placebo) throughout a 12-month treatment period, and is safe and well tolerated. NOTES: study included a few patients with BMI in 25 to 44 kg/m^2 range; 510 entered run-in; 485 randomized; 80 (49%) of placebo, 82 (51%) of 15 mg, and 94 (58%) of 10 mg completed study

Author/Year	Design Type	Class	Quality +, –, 0	Population Studied/Sample Size	Primary Outcome Measure(s)/Results (e.g., p-value, confidence interval, relative risk, odds ratio, likelihood ratio, number needed to treat)	Authors' Conclusions/ *Work Group's Comments (italicized)*
Fanghänel et al., 2000, 2001	RCT	A	0	-Men and women; ages 16-65 yrs; BMI >30 kg/m^2 -Excluded: endocrine disease other than type 2 diabetes; uncontrolled hypertension; autoimmune diseases; ischemic heart disease or arrhythmia; pregnant or lactating; psychosis; requiring drugs acting on CNS, cathartics, thyroid replacement, or diuretics -Randomized to 10 mg sibutramine or placebo for 6 mos -Treatment crossed-over after 6 mos and trial continued (double-blind) 6 more mos (Groups designated as S/P [sibutramine then placebo] or P/S)	-109 started trial (55 sibutramine, 54 placebo); groups comparable at baseline *-Weight loss (LOCF analysis) at 6 mos: 7.5 kg or 8.7% (sibutramine), 3.6 kg or 4.2% (placebo) (both p<0.05 vs. baseline)* -% with weight loss ≥5% at 6 mos: 73% (sibutramine), 40% (placebo) -% with weight loss ≥10% at 6 mos: 37% (sibutramine), 8% (placebo) -31 sibutramine patients had 45 adverse events (14 dry mouth; 5 significant increase in blood pressure; 5 significant increase in heart rate) at 6 mos -23 placebo patients had 29 adverse events (10 dry mouth, 11 significant increase in blood pressure, 1 significant increase in heart rate) at 6 mos -No treatment effect for blood pressure; heart rate decreased over time (p<0.05, both groups) at 6 mos -40 in S/P group and 42 in P/S group started 2nd 6 mos (one P/S patient withdrew - adverse event) -Weight change (LOCF) from 6 to 12 mos: +3.2 kg or +4.1% (S/P), -1.62 kg or -2.0% (P/S) (both p<0.005 vs. baseline) -From 6 to 12 mos 85% of S/P group increased wt, 78% of P/S group decreased wt (59% lost <5%, 20% lost 5-10%); after 12 mos, 53% of S/P group lost ≥5% vs. 61% of P/S group -S/P group: no changes in blood pressure, heart rate decreased (p<0.05); P/S group: increased systolic blood pressure; heart rate increased (both p<0.05) -4 in S/P group had significant increase in blood pressure (vs. 4 in P/S group); 2 in P/S group had transient increase in heart rate	-Sibutramine induces significant loss of body weight but does not significantly affect cardiovascular function. Sibutramine was well tolerated by most of the patients. After sibutramine discontinuation patients had weight gain but did not reach baseline weight. In patients given sibutramine after placebo the weight plateau was broken. NOTES: 110 entered trial; 1 ineligible; 40 sibutramine (73%) and 44 placebo (81%) completed trial; significant increase in blood pressure defined as systolic ≥140 and/or diastolic ≥90 mmHg; significant increase in heart rate defined as ≥90 bpm

Author/Year	Design Type	Class	Quality +, –, ø	Population Studied/Sample Size	Primary Outcome Measure(s)/Results (e.g., p-value, confidence interval, relative risk, odds ratio, likelihood ratio, number needed to treat)	Authors' Conclusions/ *Work Group's Comments (italicized)*
Sibutramine for Patients with Type 2 Diabetes Mellitus						
Serrano-Rios et al., 2001	RCT	A	ø	-Men and women; ages 25 to 70 yrs; BMI >27 kg/m^2; type 2 diabetes adequately stabilized with sulfonylurea monotherapy (glucose and HbA_{1c} levels for ≥3 mos and ≤24 mos) -Excluded: ECG abnormalities; seated pulse >100 bpm; diastolic BP >95 mmHg; fasting total cholesterol >7.8 mmol/l, triglycerides >5.6 mmol/l; nephropathy; pregnant or lactating; other conditions (neurological, psychological, cardiovascular, malignancy, hepatic, renal) that might affect outcome; wt loss >3 kg in past 3 mos; medications that might alter body weight or interfere with metabolism (past 3 mos) -Randomized to 15 mg sibutramine or placebo for 24 wks; all received dietary advice	-134 randomized (69 sibutramine, 65 placebo); groups comparable at baseline *-Weight loss at 6 mos: 4.5 kg (sibutramine), 1.7 kg (placebo) (p<0.001)* -Weight loss >5% at 6 mos: 49% (sibutramine), 29% (placebo) (NS) -Weight loss ≥10% at 6 mos: 16% (sibutramine), 6% (placebo) (NS) -HbA_{1c} decreased for both groups; sibutramine patients with >10% weight loss had decrease in HbA_{1c} relative to placebo (-1.79% vs. -0.73%, p=0.05) -Similar pattern for fasting serum glucose (-2.4 mmol/l vs. -0.6 mmol/l, p<0.01) -Adverse events: 61% of sibutramine patients (101 events) and 52% of placebo patients (84 events); 2 patients withdrew from sibutramine due to palpitations; all other withdrawals were non-serious event, unrelated to treatment, or protocol violations -No significant changes in blood pressure or pulse rate	-Sibutramine, in conjunction with moderate caloric restriction, enhances weight loss in overweight and obese type 2 diabetic patients receiving sulfonylurea therapy. This is associated with additional improvements in glycemic control in a limited number of patients losing ≥10% of baseline body weight. NOTES: 77% of sibutramine patients and 88% of placebo patients completed the study

Author/Year	Design Type	Class	Quality +,–,0	Population Studied/Sample Size	Primary Outcome Measure(s)/Results (e.g., p-value, confidence interval, relative risk, odds ratio, likelihood ratio, number needed to treat)	Authors' Conclusions/ *Work Group's Comments (italicized)*
McNulty et al., 2003	RCT	A	0	-195 patients from 21 sites -Included: type 2 diabetes (no ketonuria, rapid preceding weight loss or need for insulin) for >6 mos; BMI≥27 kg/m^2; metformin tx for 3 mos to 2 yrs; fasting serum glucose 7.0-15.0 mmol/l; age 25-70 yrs -Excluded: current or previous ischemic heart disease, heart failure, or stroke; seated pulse >100 bpm; diastolic >95 mmHg; total cholesterol >7.8 mmol/l; triglycerides >5.6 mmol/l; creatine >120 µmol/l; liver enzymes or bilirubin exceeding twice upper limit of normal; wt change >3 kg in past 3 mos; malignancy; significant neurological or psychiatric disturbance; women who were pregnant, lactating, or with inadequate contraception precautions; plus list of excluded drugs -Randomized to 15 or 20 mg/day sibutramine or placebo for 12 mos	-85 men (44%), 109 women (56%); 70 (36%) were hypertensive -68 in 15 mg/day group; 62 in 20 mg/day group, 64 in placebo group; groups similar at baseline -50 withdrew prematurely (19 in 15 mg group; 13 in 20 mg group, 18 in placebo group) *-Weight loss: placebo group weight was stable (88% gained or lost <5%); 15 mg group lost 5.3 kg (6%) at 6 mos and then maintained; 20 mg group lost 8 kg (8%) at 8 mos and then maintained* *-46% of 15 mg group and 65% of 20 mg group lost ≥5% of initial weight; 14% of 15 mg group and 27% of 20 mg group lost ≥10%* -Waist circumference decreased 4.7 cm with 15 mg and 6.6 cm with 20 mg (both p<0.001); no change for placebo -HbA_{1c} decreased significantly only in those who lost >5% of body weight (p<0.03); change in HbA_{1c} correlated with weight lost in sibutramine groups -Metformin dose reduced in 7% of patients in 15 mg group, 10% of those in 20 mg group, and 2% of placebo group -LDL and total cholesterol unchanged; HDL increased 0.1 mmol/l with 15 or 20 mg sibutramine; triglycerides decreased in 20 mg group -Individual blood pressure responses varied; changes influenced by weight change -Pulse rate increased more in sibutramine groups (p<0.01)	-Sibutramine can be an effective adjunct to metformin treatment in selected obese type 2 diabetic subjects and improves metabolic control in individuals who lose weight. NOTES: did sample size estimation for 90% power at 0.05 level; required 60 per group

Conclusion Grading Worksheet C – Annotation #10 (Surgery)

Work Group's Conclusion:

- Studies have consistently found that patients with preoperative body mass index between 30 and 35 kg/m^2 have good weight loss results.
- Additionally, studies have consistently found improvements of comorbidities.
- One randomized controlled trial (80 participants) found comparable results for surgical and behavioral/pharmacotherapy at six months follow-up, but at later follow-ups the non-surgical group regained weight while the surgical group continued to lose weight.
- Findings from case series are consistent with randomized controlled trial findings.

Conclusion Grade: III

Author/Year	Design Type	Class	Quality +,–,ø	Population Studied/Sample Size	Primary Outcome Measure(s)/Results (e.g., p-value, confidence interval, relative risk, odds ratio, likelihood ratio, number needed to treat)	Authors' Conclusions/ *Work Group's Comments (italicized)*
Michaelson et al, 2008	Case series	D	-	118 patients (108 women and 10 men) with BMI between 30 and 35, mean BMI of 33.2 kg/m^2 and mean excess body weight of 22.7 kg followed for 6 months after surgery	Primary outcome was mean weight loss at 6 months post laparoscopic adjustable gastric banding surgery. Mean (SD) weight loss at 6 months was 15.0 kg (7.2), mean excess body weight lost was 63.7% (36.6). Secondary outcomes were reported improvement or resolution of comorbidities including sleep apnea, diabetes mellitus, insulin resistance, hypertension, hyperlipidemia, reflux, joint pain, low back pain, incontinence, asthma, depression, polycystic ovarian syndrome.	The authors conclude that the lap band is an effective tool for weight loss and improvement of obesity-related comorbidities in an obese population no currently considered candidates for surgical intervention. There were 8 complications – 2 port revisions for slipped ports, 2 port replacements for leaks, and 4 slipped bands that were repositioned laparoscopically. *[This is a meeting abstract, so there are no details of study design, data collection, loss to follow-up, or study limitations.]*
Kakoudlidis et al, 2008	Case series	D	-	23 patients (21 women and 2 men) with BMI between 30-35 kg/m^2 who underwent sleeve gastrectomy and were followed for 6 months. At baseline, median BMI was 33.8 kg/m^2.	Primary outcome was excess body weight lost at 6 months. Median excess BMI lost (%) was: 1 month: 37.3 3 month: 66.8 6 month: 100 On average, the patients lost 100% of the excess BMI (excess BMI defined as body mass in excess of 25 kg/m^2) and BMI at 6 months had decreased to 25 kg/m^2 Most comorbidities resolved at 6 months as well (diabetes mellitus, hypertension, dyslipidemia, osteoarthritis, infertility, sleep apnea, GERD)	The authors conclude that sleeve gastrectomy results in promising early weight loss and quality of life improvements. *[There are some serious limitations with this study. 1) 79 patients underwent surgery, but only 23 were followed for 6 months. It's possible and likely that those who were not followed up for 6 months were non-compliant patients and potentially had less favorable outcomes, which suggests that the results presented in the paper are biased away from the null. 2) The authors claim that there were quality-of-life improvements, but they only report quality-of-life measures at follow-up, not at baseline, so there is no comparison. While this study provides some information regarding surgical interventions for class I obesity (BMI 30-35 kg/m^2), the important limitations should be considered.]*

Author/Year	Design Type	Class	Quality +,–,ø	Population Studied/Sample Size	Primary Outcome Measure(s)/Results (e.g., p-value, confidence interval, relative risk, odds ratio, likelihood ratio, number needed to treat)	Authors' Conclusions/ *Work Group's Comments (italicized)*
Cohen et al, 2006	Case series	D	Ø	37 patients (30 women and 7 men) with BMI between 32 and 35 kg/m^2 were enrolled. Mean BMI was 32.5 kg/m^2. Patients were followed between 6 and 48 months post laparoscopic roux-en-Y gastric bypass surgery.	Primary outcome was mean excess weight lost. At 6 months follow-up the mean excess weight lost was 44% (excess weight defined using Metropolitan Life Foundation height and weight tables). 33 patients were followed for 12 months and lost 71.6% of excess weight, 9 patients were followed for 48 months and lost 81% of excess weight. 36 of 37 patients had total remission of their comorbidities (diabetes, hypertension, dyslipidemia, GERD and sleep apnea).	The authors conclude that gastric bypass surgery in the selected patients was associated with no morbidity or mortality. They also report that the short-term weight loss was slightly better than that observed in patients with BMI > 35kg/m^2. The authors acknowledge limitations related to selection bias and study design limitations. [*In the abstract, the authors report that patients lost 81% of excess weight; however, only the 9 patients followed for 48 months account for that number. There was substantial loss-to-follow-up.*]
Parikh et al, 2006	Case series	D	Ø	93 patients (76 women and 17 men) with BMI between 30-35 kg/m^2 who underwent adjustable gastric bandings surgery (LAP-BAND) and followed for up to 3 years. Mean BMI preoperative was 32.7 kg/m^2.	The primary outcome was excess weight lost (excess weight defined as weight in excess of ideal weight based on Metropolitan Life height and weight tables). 72 patients were followed for one year, percent excess weight lost was 58% and mean (SD) BMI at 1 year was 27 kg/m^2 (2). 70 patients were followed for 2 years with 57% excess weight lost and mean BMI at 2 years was 27 kg/m^2 (3). At 3 years postoperative, 67 patients were retained and had 54% excess weight lost, mean BMI of 27 kg/m^2 (3).	In this series of low BMI patients who underwent LAP-BAND surgical interventions, there was good weight loss, minimal complications, and comorbidities were partially or wholly resolved. The discussion section of the paper mentions that the advantages of bariatric surgery over other interventions include good compliance and weight loss is maintained, thus ensuring resolution of comorbidities compared to behavioral interventions and pharmacotherapy, which both have poor compliance and relatively modest weight losses.

Author/ Year	Design Type	Class	Qual -ity +,–,ø	Population Studied/Sample Size	Primary Outcome Measure(s)/Results (e.g., p-value, confidence interval, relative risk, odds ratio, likelihood ratio, number needed to treat)	Authors' Conclusions / *Work Group's Comments (italicized)*
O'Brien et al, 2006	Randomized controlled trial	A	+	80 adults with BMI between 30-35 kg/m^2 randomly assigned to either program of very low calories diets, pharmacotherapy, and lifestyle change for 24 months (non-surgical group) or to placement of a laparoscopic gastric band (LAP-BAND) and followed for 24 months.	Primary outcomes measured were weight change and excess weight lost (excess weight defined as weight in excess of BMI of 25 kg/m^2). Adjusted for age, sex and baseline weight, mixed effect models were run to estimate changes in weight, BMI and excess weight lost at 6, 12 and 24 months follow-up. At 6 months follow-up there were no statistically significant differences between treatment groups with regard to weight change or excess weight lost (p=0.99 and 0.98 respectively). At 12 months follow-up there were statistically significant differences between treatment groups – the surgical group lost 76.3 kg and non-surgical group lost 85.3 kg (p <0.0001), the surgical group lost 78.6% and the non-surgical group lost 41.1% of excess weight (p <0.0001). At 24 months follow-up, the surgical group had lost 74.5 kg and the non-surgical group lost 89.5 kg (p <0.0001), and the surgical group had 87.2% and non-surgical group had 21.8% excess weight lost (p <0.0001). Secondary outcomes included resolution of comorbidities and changes in quality of life. At 2 years follow-up, the resolution of metabolic syndrome between the two groups differed significantly: at baseline metabolic syndrome was present in 15% of each group and at 24 month follow-up present in 2.7% in surgical group and 24% in the medical group (p = 0.006). There were no baseline differences in quality of life scores from SF-36. At 24 months follow-up, both groups had statistically significant improvements in quality of life on all 8 domains of the SF-36.	In this randomized, controlled trial of surgical and non-surgical obesity interventions, both groups showed improvement in weight, health and quality of life. Patients in the surgical group had statistically significant better outcomes in each area compared to the non-surgical group. The extent of weight loss was similar for both groups at 6 months follow-up, but the non-surgical group regained weight at 24 months, whereas the surgical group continued to lose weight throughout follow-up period. There were minimal adverse events in the surgical group – 4 patients required repositioning of LAP-BAND. In the non-surgical group, 4 patients required cholecystetomy, possibly linked to the very low calorie diet. The authors acknowledge several limitations to this study. This study was not powered to determine if the treatment groups were equally safe. *[This study is among very few studies that have compared surgical and non-surgical therapies for obesity, especially in this group with relatively "low BMI" (30-35 kg/m^2).* *The authors did use intention-to-treat analytic principles for the primary outcome analysis, but not for the secondary outcomes.]*

Author/Year	Design Type	Class	Qual -ity +,–,ø	Population Studied/Sample Size	Primary Outcome Measure(s)/Results (e.g., p-value, confidence interval, relative risk, odds ratio, likelihood ratio, number needed to treat)	Authors' Conclusions / *Work Group's Comments (italicized)*
Angrisani et al, 2004	Case series	D	Ø	210 patients (34 males, 176 females) with BMI ≤ 35 kg/m^2 were included in this retrospective study using data collected from 27 Italian surgical team sites. Mean BMI preoperative was 33.9 kg/m^2 and mean excess weight was 29.6 kg.	Primary outcomes in this study were change in BMI and excess weight lost. At 6 months follow-up, mean (SD) BMI was 31.1 kg/m^2 (2.15) and mean (SD) excess weight lost was 28.1% (20.7). At later follow-ups, patients were lost to follow-up. At 12 months, 182 patients had a mean (SD) BMI of 29.7 kg/m^2 (2.19) and mean (SD) excess weight loss of 52.5% (13.2). At 36 months follow-up, 119 patients had a mean BMI 28.7 kg/m^2 (3.8) and mean excess weight lost of 61.3% (14.7). At 48 months follow-up, 75 patients had a mean BMI of 27.9 kg/m^2 (3.2) and mean excess weight loss of 68.8% (15.3). And at 60 months follow-up, 75 patients had mean BMI of 28.2 kg/m^2 (0.9) and mean excess weight loss of 71.9% (10.7).	In this study of the LAP-BAND, all but one patient achieved normal weight and most experienced resolution of all their comorbidities. The authors suggest that low BMI (30-35 kg/m^2) patients are good candidates because they have more underlying comorbid conditions that apparent and they pose fewer risks and have fewer surgical complications. They further suggest that indications of this procedure should be carefully evaluated by internist and surgeon in each individual case. *[This study has a fair amount of loss-to-follow-up but is among those with the longest follow-up time. They do not report what standard they are using to define excess weight.]*
Nadler et al, 2008	Case series	D	+	53 adolescents (54 female and 19 male) aged 13 to 17 years who have undergone laparoscopic adjustable gastric banding. Mean preoperative weight was 298 lb with mean BMI of 48 kg/m^2.	At 6 months follow-up, 53 patients had a mean (SD) weight of 247 lb (53), mean (SD) BMI of 39.8 kg/m^2 (7.0), and excess weight loss of 35.1 % (16.2). At 1 year follow-up, 47 patients had mean weight of 214 lb (59), mean BMI of 34.3 kg/m^2 (23.0), and excess weight loss of 56.7% (23.0). At 2 years follow-up, 16 patients had a mean weight of 204 lb (41), mean BMI of 32.1 kg/m^2 (6.4), and mean excess weight loss of 60.9% (26.5). At 1 year of follow-up, 70% of comorbid conditions were resolved (among 21 patients with comorbid conditions preoperatively). No patients experienced intraoperative complications. 27 patients experienced non-surgical complications including hair loss, iron deficiency, band slip, and vitamin D deficiency. Two patients required post-operative band removal because of slippage.	The authors advocate the use of laparoscopic gastric banding in morbidly obese pediatric populations.

Author/Year	Design Type	Class	Qual-ity +,–,ø	Population Studied/Sample Size	Primary Outcome Measure(s)/Results (e.g., p-value, confidence interval, relative risk, odds ratio, likelihood ratio, number needed to treat)	Authors' Conclusions/ *Work Group's Comments (italicized)*
Pinheiro et al, 2007	Case series	D	-	13 patients with BMI between 30-35 kg/m^2 with low quality of life results and without serious comorbidity underwent gastric sleeve gastraectomy procedure.	Excess weight loss was 30% at 6 months, 45% at 12 months (4 patients), 56% at 24 months (3 patients). BMI was under 27 kg/m^2 in all patients. At 12 months, patients presented with higher scores in labor and self-esteem compared to previous questionnaires.	These initial results suggest that sleeve gastrectomy might be an option for improving quality of life in class I obese patients. *[This report is from a meeting abstract, so there is little information with regard to study design and limitations. It is not clear how many patients completed the quality-of-life questionnaire at 12 months follow-up. If only 3 were measured, it is possible that there was considerable bias away from the null as those who were lost to follow-up may be more likely to have poor quality of life.]*
Dixon et al, 2008	RCT	A	+	60 obese patients (BMI >30 and <40, mean BMI 37 kg/m) with type 2 diabetes diagnosed within last 2 years. Patients were randomized to conventional diabetes therapy with a focus on lifestyle change or laparoscopic adjustable gastric banding with conventional diabetes care.	The primary outcome of this study was remission of type 2 diabetes. The secondary outcomes were weight and components of the metabolic syndrome. Of the 60 patients enrolled, 55 completed the 2-year follow-up. Remission of diabetes was achieved by 22 in the surgical group and 4 in the conventional-therapy-alone group. The surgical group lost a mean (SD) of 20.7% (8.6%) and 1.7% (5.2%) of weight, respectively, at 2 years. At baseline, the metabolic syndrome was present in 97% of each treatment group. At 2 years follow-up, 70% of surgically treated and 13% of conventionally treatment patients did not meet NCEP criteria for metabolic syndrome.	The authors conclude that participants randomized to surgical treatment were more likely to achieve remission of type 2 diabetes through greater weight loss. Additionally, these results need to be confirmed in a larger, more diverse population with longer follow-up to assess long-term efficacy and relapse. Study limitations: caution is required in interpreting results in metabolic syndrome outcomes as the study was not powered to assess multiple outcome measures; study was restricted to recent diabetes diagnoses, these results may not apply to those with longer history of disease; study was not powered to detect differences in safety, mortality or cardiovascular events. *[This study was not powered to assess safety, which is a concern related to weight-loss surgery in the low BMI group. It should also be noted that the mean BMI for study participants was 37 kg/m^2, and they did not present any results stratified by BMI below and above 35 kg/m^2, so it is difficult to make a conclusion regarding low BMI patients.]*

Support for Implementation:

Prevention and Management of Obesity (Mature Adolescents and Adults)

This section provides resources, strategies and measurement specifications for use in closing the gap between current clinical practice and the recommendations set forth in the guideline.

The subdivisions of this section are:

- Priority Aims and Suggested Measures
  - Measurement Specifications
- Key Implementation Recommendations
- Knowledge Resources
- Resources Available

Priority Aims and Suggested Measures

1. Increase awareness of body mass index. *(Annotation #1)*

   Possible measures for accomplishing this aim:

   a. Percentage of patients who have a screening body mass index calculated and documented in the medical record during the last 12 months. *(2009 HEDIS Measure)*

   b. Percentage of patients with documentation in the medical record indicating they were made aware of their body mass index during the last 12 months.

2. Improve the percentage of patients with an elevated body mass index who have received education and counseling regarding weight loss. *(Annotation #10)*

   Possible measures for accomplishing this aim:

   a. Percentage of patients with a documented elevated body mass index who receive education and counseling for weight loss strategies that include nutrition, physical activity, lifestyle changes, medication therapy and/or surgery:

      - BMI 25-30: Lifestyle changes and behavioral management.
      - BMI 30-35: Lifestyle changes, behavioral management and medication therapy.
      - BMI 35-40: Lifestyle changes, behavioral management and medication therapy.
      - BMI 40+: Lifestyle changes, behavioral management, medication therapy and surgical options.

   b. Percentage of patients with a documented body mass index equal to or greater than 25 with comorbidities who received diagnosis appropriate education and counseling.

3. Improve the outcome of treatment for obesity. *(Annotations #8, 10)*

   Possible measures for accomplishing this aim:

   a. Percentage of patients with a body mass index equal to or greater than 25 with documentation in the medical record indicating they have a stable body mass index or a reduction in body mass index during the last 12 months.

   b. Percentage of patients with documentation in the medical record of physical activity of 30 minutes five times per week. *(Annotation #10)*

   c. Percentage of patients who set an individualized goal along with target date for reduction in body mass index.

   d. Percentage of patients who reach their goal body mass index by the set target date.

4. Improve community (employers, schools) involvement in the prevention and treatment of obesity. *(Annotations #10, 13)*

   Possible measures for accomplishing this aim:

   a. Number of employers or schools that offer or support weight-management programs.

   b. Number of employers or schools that offer healthy food choices.

   c. Number of employers or schools that facilitate/support physical activity to degree possible at work site or community sites.

Measurement Specifications

Possible Success Measurement #2a

Percentage of patients with a documented elevated body mass index who receive education and counseling for weight loss strategies, which include nutrition, physical activity, lifestyle changes, medication therapy and/or surgery.

Population Definition

Patients with an elevated body mass index in the following range:

- 25-30
- 30-35
- 35-40
- 40+

Numerator/Denominator Definitions

Numerator:	# of patients with an elevated body mass index who receive education and counseling for weight loss, which include nutrition, physical activity, lifestyle changes, medication therapy and/or surgery in appropriate patients (See Annotation #10)
Denominator:	Patients with an elevated body mass index.

Method/Source of Data Collection:

No electronic medical record:

Select 20 patients who have been seen within the last month and who have an elevated body mass index. If the body mass index is not documented, use the following calculation: weight (lbs.) x 703 divided by height (inches) squared.

Or

Refer to a body mass index chart or wheel.

The medical record will be reviewed to determine if one or more of the weight management strategies have been documented. The presence of narrative comments or flow sheets reflecting discussion of one or more of the following weight-management strategies is acceptable evidence for this measure: nutrition, physical activity, lifestyle changes, medication therapy and/or surgery.

Electronic medical record available:

Query data for patients seen in the last month with an elevated body mass index (assuming this is a field in the electronic medical record).

The medical record will be reviewed to determine if one or more of the weight-management strategies have been documented. The presence of narrative comments or flow sheets reflecting discussion of one or more of the following weight-management strategies is acceptable evidence for this measure: nutrition, physical activity, lifestyle changes, medication therapy and/or surgery.

Time Frame Pertaining to Data Collection

The suggested time period is advice over a 12-month period.

Key Implementation Recommendations

The following system changes were identified by the guideline work group as key strategies for health care systems to incorporate in support of the implementation of this guideline.

1. Establish a system for using a Patient Readiness Scale. The scale can be used to determine if the patient is ready to talk about weight loss and/or would like information.
2. Establish a system for staff to efficiently calculate body mass index prior to the physician entering the exam room. This action may be considered a vital sign and built into the rooming protocol. A body mass index chart can be placed by each scale in the clinic, if the organization has an electronic medical record, it may have a component for immediate calculation.
3. Develop tracking systems to produce periodic audits for use in developing solutions to identified problems.
4. Establish a system for staff and physician training around skills and knowledge in the areas of motivational interviewing; brief, focused advice on nutrition, physical activity and lifestyle changes; and evaluation of evidence of effectiveness of treatment options.
5. Establish a system for continuing education on evidence-based obesity management for providers, nurses and ancillary clinic staff.
6. Remove barriers to referral programs for weight loss. Know where your resources are and what processes are required: for example, if your organization refers patients to an outside source, what are the criteria for referral?
7. Develop medical record systems to track status of patients under the provider's care with the capability to produce a tickler system for patient follow-up by provider/staff.
8. Use tools such as posters and brochures throughout the facility to promote a healthy lifestyle around nutrition and activity while encouraging patient knowledge of their body mass index.
9. Develop patient-centered education and self-management programs, which may include self-monitoring, self-management and skills such as journaling.
10. Outcomes measurement:
    - Build systems for outcomes measures, as well as ongoing process measures
    - Response rate to various treatments/strategies
    - Improvement rates – the body mass index is stable or has decreased over time
11. Systems to coordinate care ensure continuity and keep providers informed of progress.
    - Build electronic systems or tickler system (if no electronic medical record).
    - Educate patients to foster awareness and knowledge of body mass index for self-monitoring and reporting.
    - Structure follow-up visits with patient per guideline recommendations.

Knowledge Resources

Criteria for Selecting Resources

The following resources were selected by the Prevention and Management of Obesity (Mature Adolescents and Adults) guideline work group as additional resources for providers and/or patients. The following criteria were considered in selecting these resources.

- The site contains information specific to the topic of the guideline.
- The content is supported by evidence-based research.
- The content includes the source/author and contact information.
- The content clearly states revision dates or the date the information was published.
- The content is clear about potential biases, noting conflict of interest and/or disclaimers as appropriate.

Resources Available to ICSI Members Only

ICSI has a wide variety of knowledge resources that are ***only*** available to ICSI members (these are indicated with an asterisk in far left-hand column of the Resources Available table). In addition to the resources listed in the table, ICSI members have access to a broad range of materials including tool kits on CQI processes and Rapid Cycling that can be helpful. To obtain copies of these or other Knowledge Resources, go to http://www.icsi.org/improvement_resources. To access these materials on the Web site, you must be logged in as an ICSI member.

The resources in the table on the next page that are not reserved for ICSI members are available to the public free-of-charge.

Resources Available

*	Author/Organization	Title/Description	Audience	Web sites/Order Information
	America On the Move	**America On the Move (AOM):** Challenges you, your family and your community to take small steps and make small changes to a healthier way of life. Get involved!	Patients and Families	http://aom.americaonthemove.org/site/c.krLXJ3PJKuG/b.1524889/
	American Academy of Family Physicians	**American Family Physician:** Patient education article, "Exercise: How to Get Started"	Patients and Families	http://www.aafp.org/afp/20030115/367ph.html
	American Dietetic Association	**American Dietetic Association:** Provides information on nutrition and current research	Patients and Families; Health Care Professionals	http://www.eatright.org
	Calorie King	**Calorie King:** Provides a review of the most popular diets	Patients and Families	http://www.calorieking.com/library/article.php?path=13,17&art_id=485
	Centers for Disease Control (CDC)	**Overweight and Obesity:** an overview. Includes a body mass index calculator.	Patients and Families; Health Care Professionals	http://www.cdc.gov/nccdphp/dnpa/obesity/contributing_factors.htm
	Department of Food Science and Human Nutrition, University of Illinois at Urbana-Champaign	**NAT (Nutritional Assessment Tools for Good Health):** Provides a free Web-based program that allows one to perform a nutritional analysis of one's diet	Patients and Families	http://www.nat.uiuc.edu
	Department of Health and Human Services	**President's Council on Physical Fitness and Sports:** Online pamphlet providing information on physical fitness fundamentals	Patients and Families	http://www.fitness.gov/fitness.html
	Dole Company	**Dole Super Kids:** Provides basic nutrition education for kids and classroom ideas for teachers	Patients and Families	http://www.dole5aday.com
*	Institute for Clinical Systems Improvement	**Prevention and Management of Obesity Guideline Pilot Summary:** Affiliated Community Medical Centers and St. Mary's/Duluth Clinic Health System participated in a guideline pilot from mid-2005 to early 2006. This summary will tell their story and provide information around strategies for implementation, measurement/outcomes and overall improvement in processes.	Health Care Professionals	http://www.icsi.org

* Available to ICSI members only.

*	Author/Organization	Title/Description	Audience	Web sites/Order Information
	Institute for Research and Education - PNC	More Flavor, Less Fat – Easy Low Fat Cooking; Nutrition pamphlet	Patients and Families	http://www.healthsource.org or 800-372-7776
	Institute for Research and Education - PNC	**Simple Strategies for Meal Planning:** Nutrition pamphlet	Patients and Families	http://www.healthsource.org or 800-372-7776
	Institute for Research and Education - PNC	**Simple Strategies for Eating Out:** Nutrition pamphlet	Patients and Families	http://www.healthsource.org or 800-372-7776
	Institute for Research and Education - PNC	**Simple Strategies for Weight Management:** Nutrition pamphlet	Patients and Families	http://www.healthsource.org or 800-372-7776
	Krames - Health and Safety Education	**Understanding Bariatric Surgery:** Your Surgical Options for Weight Loss; Surgery pamphlet	Patients and Families	Call 1-800-333-3032
	Mayo Clinic	**Mayo Clinic:** Provides a wide variety of information on nutrition, programs and a food pyramid placing fruits and vegetables at the bottom vs. carbohydrates.	Patients and Families	http://www.mayoclinic.com
	National Heart, Lung and Blood Institute	**Aim for a Healthy Weight:** provides key recommendations from the National Heart, Lung and Blood Institute national guidelines, how to get started, and links to other publications.	Patients and Families	http://www.nhlbi.nih.gov/health/public/heart/obesity/lose_wt/index.htm
	National Institute of Health	**The National Institute of Diabetes and Digestive and Kidney Diseases:** Provides science-based information on obesity, weight management and nutrition.	Patients and Families; Health Care Professionals	http://www.niddk.nih.gov/index.htm
	OptumHealth	**Health A to Z:** Provides information on nutrition and fitness, as well as self-assessment tools.	Patients and Families	http://www.healthatoz.com
	Shape Up America	**Shape Up America:** Provides information on an interactive personalized weight-loss program with links to a support center, recipes and fitness information.	Patients and Families	http://www.shapeup.org
	The Discovery Health Channel	**Discovery Health:** Provides information on nutrition, fitness and weight management.	Patients and Families	http://www.health.discovery.com
	U.S. Department of Agriculture	**My Pyramid:** Use the pyramid as an interactive nutrition education tool. Create a personalized dietary and activity guide to achieve a healthy lifestyle.	Patients and Families; Health Care Professionals	http://www.mypyramid.gov

* Available to ICSI members only.