# OBESITY RELATED COMORBIDITIES & MEDICAL EVALUATION OF OBESITY

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INTRODUCTION

Many medical conditions are directly a result of obesity or are worsened by obesity as a result of physiological changes and because of the burden of the weight mass itself. An understanding of the comorbidities frequently associated with overweight and obesity serves as a guide for appropriate medical evaluation. Early treatment of weight-related comorbidities including vigorous weight management is important. A long list of medical and psychological comorbidities of obesity need to be considered when evaluating obese patients. Weight loss is an important part of their medical management.

PATHOGENESIS OF OBESITY COMORBIDITIES

Fat Mass vs. “Sick Fat Mass” or “Adiposopathy” Diseases

Two forms of obesity-related comorbidities can be distinguished based on pathogenesis: Fat Mass and Adiposopathy or “Sick Fat Mass”. Understanding the two types of pathogenesis in obesity comorbidities aids an understanding of their prevention, effective treatments, and inter-relationship with other comorbidities:

- **Fat Mass Diseases:**
  - These diseases come from the impact of the bulky, heavy fat mass itself.
  - **Examples** include congestive heart failure, hypoventilation syndrome, and problems of musculoskeletal functioning and pain.

- **“Adiposopathy” or “Sick Fat Mass” Diseases:**
Resistance to weight loss and chronic physiological changes that help perpetuate obesity and contribute to easier weight regain. The metabolic change often persists even after weight loss.

Metabolic: These diseases come from physiological changes including increased circulating free fatty acids, pathogenic endocrine responses, disordered immune response, fatty infiltration in various organs, and dysfunction of the fat cells themselves.

- **Examples** are thought to include cardiovascular disease, diabetes, increased risk of cancer, and non-alcoholic hepatitis.

Inflammatory: This class of diseases can also be caused by excess nutrients and energy which produce low-grade, chronic inflammation in metabolic tissues including adipose, liver, muscle, pancreas, and brain. The inflammation contributes to insulin resistance and metabolic dysfunction.

- **Examples** This mechanism is thought to contribute to fibromyalgia, rheumatoid arthritis, lupus, psoriasis, pain, and many other conditions.

**Hormonal Mechanisms Associated with Abdominal Fat**

Central adiposity is associated with complex hormonal and neuroendocrine changes:

- Insulin levels and insulin resistance are further increased. The resulting high serum glucose is converted by the liver into more intra-abdominal fat.

- Leptin, which is released by fat cells after a meal, typically calms the appetite. However, in central subcutaneous obesity, there appears to be resistance to leptin, similar to insulin resistance in diabetes. Therefore, despite high levels of circulating leptins, the obese individual does not feel as sated after eating.

**Metabolic Syndrome**

Metabolic Syndrome includes having 3 or more the following risk factors that increase the risk of cardiovascular disease:

- Elevated Waist Circumference/Central obesity
- Abnormal glucose (elevated fasting or being treated for it)
- Elevated blood pressure
- Low HDL
- Elevated triglycerides

Other factors that have been associated with metabolic syndrome include:

- Chronic proinflammatory and prothrombotic states
- Non-alcoholic fatty liver disease
- Sleep apnea

**Sequellae of Metabolic Syndrome**

Metabolic syndrome has been strongly associated with the following:

- Increased diabetes risk.
• Increased risk of coronary heart disease.
• Increased cardiovascular disease mortality and disease including strokes.

CLINICAL TIP
Understanding the likely progression from metabolic syndrome to cardiovascular disease or type 2 diabetes may motivate patients to lose weight and increase their physical activity.

The physiological changes from obesity appear to be mostly permanent. Unfortunately, this makes it easier for patients who were once obese to regain weight. Thus, permanent changes in lifestyle and long-term follow-up are critical after weight loss.

OBESITY-RELATED COMORBIDITIES

Many diseases are comorbid with obesity. An understanding of the comorbidities associated with excess weight can guide a comprehensive medical evaluation and early treatment, including vigorous weight management. Causality can go in either direction or both. Therefore, taking a weight-centered approach to treating many comorbid conditions makes sense. For example, for an obese person with diabetes, choose an antidiabetes medication that would also support weight loss, and start obesity treatment as part of diabetes treatment.

Not everyone with obesity develops even the most common comorbidities, such as type 2 diabetes or heart disease. Genetic factors, diet quality, and amount of exercise probably all play a role. Some patients who are obese are metabolically normal initially, but eventually, at least some of the many comorbidities are experienced.

CLINICAL TIP
Educate patients about diseases that are highly correlated with obesity, but avoid scare tactics. Patients may not fully understand the risks of obesity. The effects of obesity develop slowly and so may not be noticed.

What Obesity-Related Comorbidities Are Most Likely?
Which comorbid conditions are most likely in obesity?

High Risk
• Type 2 diabetes
• Dyslipidemia
• Obstructive sleep apnea
• Obesity hypoventilation syndrome
• Shortness of breath
• Excessive daytime fatigue
• Fatty liver

Moderate Risk
• Cardiovascular disease (Heart attack and stroke)
• High blood pressure
• Gallstones
• Gout
• Osteoarthritis
• Endometrial cancer
• Overall mortality

Mild Risk
• Cancer (breast, prostate, colon)
• Fertility Problems
• Pregnancy complications
• Asthma
• GERD

DETAILS FOR THE SEVERAL COMMON COMORBIDITIES

1. Cardiovascular Disease
Obesity is especially harmful to the cardiovascular system. It causes direct harm through\textsuperscript{14}:
• Epicardial (outer layer of heart) fat deposition
• Increased intra-myocardial triglyceride deposition
• Lipotoxicity
• Cardiomyocyte apoptosis (a type of cell death) which produces cardiac dysfunction

Obesity also causes an elevation of cardiovascular risk factors\textsuperscript{15}:
• Dyslipidemia
• Hypertension
• Elevated fibrinogen
• Increased plasminogen activator inhibitor-1 (impaired fibrinolysis)

2. Type 2 Diabetes
A high percentage of the population (around 34%) has diabetes, most of which is type 2 diabetes mellitus and another 10 to 15% have prediabetes and the risk is strongly increased by obesity\textsuperscript{16}. this percentage is increasing along with the increase in obesity\textsuperscript{17}. The impact of the associated morbidity is significant.

3. Obstructive Sleep Apnea
Sleep apnea is characterized by pauses in breathing or shallow breaths that bring the individual from deep to light sleep\textsuperscript{18}. Apnea lasts a few seconds to minutes and happens as often as 30 times an hour. The result is daytime sleepiness, unrefreshing sleep, fatigue, insomnia, and snoring. Approximately 70% of patients with obstructive sleep apnea are also obese\textsuperscript{19}. Weight loss is an important treatment. Referral for evaluation in a sleep study with polysomnography is ideal.
4. Obesity Hypoventilation Syndrome (OHS)
Obesity hypoventilation syndrome results in lower oxygen and higher carbon dioxide in the blood. It is believed to be due to excess weight against the chest wall and a defect in the brain’s control of breathing. Symptoms include being chronically tired, daytime sleepiness, depression, and headaches. Obesity hypoventilation syndrome can be reversed with weight loss. Most patients with this syndrome also have sleep apnea.

5. Psychosocial Comorbidities
- Social stigmatization
- Problems with personal hygiene
- Eating disorders
- Mood disorders
- Other psychological disorders

6. Other Comorbidities and Risks
- Pseudotumor cerebri: Neurological symptoms from increased intracranial pressure
- Skin comorbidities: Intertrigo (bacterial and/or fungal), acanthosis nigricans (pigmented thickening of areas of the skin), hirsutism (hairiness), risk for cellulitis (diffuse acute inflammation) and carbuncles (localized acute inflammation)
- Surgical risks: Increased surgical risk and postoperative complications (wound infection, postoperative pneumonia, deep venous thrombosis, and pulmonary embolism)

OBESITY-RELATED MORTALITY
The overall mortality rate is increased 29% for overweight and obesity; the increase goes up almost linearly as BMI increases. The longer an individual is obese, the greater the impact on longevity. The effect is greater for blacks than whites and men than women.
- For non-smoking individuals age 40-49 with a BMI over 40, from 4.7 to 5.4 years of life is lost.

WEIGHT LOSS HELPS OBESITY COMORBIDITIES
CONSIDER COMORBIDITIES IN DETERMINING OBESITY TREATMENT
Guidelines for obesity treatment recommend treatments based on the extent of weight-related comorbidities. Lower functional status, symptoms, and risk factors may raise the level of care needed. For patients who are at least moderately overweight or heavier, the following treatments are recommended:
- No Weight-Related Comorbidities: Recommend lifestyle change counseling by an MD or dietitian, consider recommending a weight-loss program.
Basics of Obesity Medicine – for Medical Students

• **Low Severity Comorbidities:** Recommend lifestyle modification counseling by an MD or dietitian, weight-loss support program, or structured, multidisciplinary weight-loss program that includes these interventions.

• **Medium Severity Comorbidities:** Recommend weight-loss medications along with lifestyle modification counseling by an MD or dietitian, weight-loss support program or structured, multidisciplinary weight-loss program that includes these interventions.

• **High Severity Comorbidities and/or High BMI (35 kg/m² or greater):** Recommend surgical therapy along with lifestyle modification by an MD or dietitian, weight-loss support program, and a structured, multidisciplinary weight-loss program.

WEIGHT-LOSS IS A TREATMENT FOR OBESITY-RELATED COMORBIDITIES

Obesity treatment should not be delayed while focusing on the treatment of its comorbid conditions. Obesity should be treated at the same time as associated serious comorbidities because reducing weight is a treatment for many of these comorbidities.

Many illnesses are improved by even a modest intentional loss of weight:

1. **Cardiovascular Disease** – Weight loss improves cardiovascular disease especially if body fat is lost without loss of lean muscle mass.

2. **Type 2 Diabetes Mellitus** – Weight loss helps prevent diabetes and improves the disease for those who already have it.

3. **Non-Alcoholic Fatty Liver Disease**

4. **Osteoarthritis** – Weight loss improves symptoms and functionality and sometimes slows disease progression.

5. **Cancer** – Weight loss decreases some risk, lowers mortality.

6. **Sleep Apnea** – Improves.

7. **Others:** Weight loss improves pancreatitis, cholecystitis, gout, kidney disease, infertility, carpal tunnel syndrome, rheumatoid arthritis, impaired immunity, asthma/reactive airway disease, polycystic ovaries, male hypogonadism, GERD, urinary incontinence, and low back pain.

Details on the Effects of Weight Loss for Several Common Comorbidities

1. **Cardiovascular Risk Factor Improvement from Weight Loss**

   **Serum Lipids**

   Weight loss of as little as 6.6 lbs lowers serum triglyceride and LDL and increases HDL modestly. There is a dose-response relationship between the amount of weight lost and improvement in the patient’s lipid profile.

   **Hypertension Improvement With Weight Loss**

   There is a dose-response relationship between the amount of weight loss achieved for up to 3 years and the lowering of blood pressure.
• Weight loss of 5% results in systolic and diastolic blood pressure reduced by a weighted mean of 3 and 2 mm Hg respectively\(^{41}\).

### Atrial Fibrillation Improvement With Weight Loss

Long-term weight loss of 10% reduces symptoms of atrial fibrillation\(^{43}\). However, fluctuations in weight of 6% or more in a year resulted in worsening of atrial fibrillation\(^{43}\).

### 2. Diabetes and Weight Loss

Weight loss for overweight or obese patients with type 2 diabetes produces improvements in HbA1c and fasting plasma glucose and reduction in need for diabetes medications. Greater weight loss corresponds to greater improvements\(^{41}\). Diabetes medications having modest weight loss or at least weight neutral should be used if possible while still achieving A1C targets.

• Weight loss of 2% – 5% of current weight maintained for at least 1 – 4 years results in HbA1c being lowered 0.2% – 0.3% and fasting plasma glucose reduced modestly\(^{41}\).

### Reduced Progression from Prediabetes to Diabetes

• Weight loss of 5.5 – 12.1 lbs (2.5 – 5.5 kg) maintained for at least 2 years results in the risk of developing diabetes being reduced by 30 – 60%\(^{41}\).

• 10% weight loss is recommended in pre-diabetes\(^{38}\).

### 3. Obstructive Sleep Apnea Improvement With Weight Loss

Sleep apnea is likely to improve with weight loss as part of the treatment. Breaking the cycle between inadequate sleep and obesity is an important part of obesity treatment for many patients\(^{18}\).

### 4. Non-Alcoholic Fatty Liver Disease and Weight Loss

A modest weight loss has a dose-dependent improvement in nonalcoholic fatty liver (aka steatosis), but up to 40% weight loss may be needed to reduce inflammation\(^{38}\). Mediterranean diet, calorie restriction, moderate to vigorous physical activity, and weight loss medications may also be helpful\(^{33}\).

### WEIGHT-LOSS GOAL FOR TREATING COMORBIDITIES

Help patients set goals that are realistic and achievable while also considering medical goals.

The overall goal for initial weight-loss therapy is a weight reduction of approximately 5-10% of body weight\(^{29}\).

A sustained moderate level of weight loss can significantly decrease the severity of many obesity-related comorbidities. A moderate pace of 1 to 2 lbs per week is often recommended\(^{29}\). More rapid weight loss is almost always followed by regain of weight – often more weight than was lost, with negative mental and physical health consequences\(^{41}\). However, in very high BMI or morbid obesity, rapid weight loss is often important in order to achieve functioning and reduce medical risk rapidly.

Health benefits are realized if the weight loss is sustained; a life-long reduction in caloric intake is needed. It is important to support the patient in maintaining each incremental weight loss. The promise of even more health benefits with further weight loss can help motivate patients to continue their weight-loss efforts. With
sustained additional weight loss **beyond an initial 5% weight loss**, patients are likely to experience further improvement in serum lipids, blood pressure, diabetes risk, and fasting plasma glucose.  

**QUIZ: OBESITY COMORBIDITIES SECTION**

**Question:** Which of the following are comorbidities of obesity that are improved by weight loss? (Choose all that apply)

- **Choice 1:** Cardiovascular disease  
- **Choice 2:** Symptoms of osteoarthritis  
- **Choice 3:** Functioning in osteoarthritis  
- **Choice 4:** Non-alcoholic fatty liver disease

**Feedback for Choice 1:**  
Correct. Weight loss improves cardiovascular disease especially if body fat is lost without loss of lean muscle mass.

**Feedback for Choice 2:**  
Correct. Weight loss improves osteoarthritis symptoms and functionality and sometimes slows disease progression.

**Feedback for Choice 3:**  
Correct. Weight loss improves osteoarthritis symptoms and functionality and sometimes slows disease progression.

**Feedback for Choice 4:**  
Correct. A modest weight loss has a dose-dependent improvement in nonalcoholic fatty liver disease, but up to 40% weight loss may be needed to reduce inflammation

**MEDICAL EVALUATION OF OBESITY**

Because of a high rate of comorbidities associated with obesity, extensive medical assessment is often needed, including:

- Physical examination, laboratory and other tests for comorbidities of obesity
- Medications and medical conditions that contribute to weight gain.
- Evaluation for psychological disorders including eating disorders and psychosocial factors contributing to weight

**1. Check for Medications Causing Weight Gain**

A number of medications increase weight or distribution of body fat (lipodystrophy). Those that clearly cause weight gain should be avoided in overweight or obese patient if there is a suitable alternative. Entire classes of medications may cause weight gain or just some medications within a class. The amount of weight gained varies but can be significant.  

**Medications That May Cause Weight Gain:**

- Antidiabetics
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- Psychotropic medications:
  - Antipsychotics
  - Mood stabilizers
  - Antidepressants
  - Antiepileptics
  - Antihypertensives

Medications That Cause Weight Gain and Lipodystrophy:
- Antiretroviral
- Glucocorticoids
- Hypolipidemics

Other possible medications:
- Contraceptives
- Sedating antihistamines

2. Smoking Cessation and Weight Gain
Smoking cessation is often associated with weight gain. In a 10-year study, obese smokers who quit smoking gained an average of 7.1 kg more than those who did not quit. Some smoking cessation pharmacotherapies and antidepressants appear to limit weight gain in the short-term. Exercise appears to be effective in the long-term.

3. Psychological and Psychosocial Problems and Weight Gain
Patients having obesity should be screened and counseled for depression and other psychological disorders. Other issues contributing to weight gain or that are affected by excess weight include low self-esteem, body-image dissatisfaction, ability to work, and ability for sexual intimacy.

Relationship of Stress and Weight:
Prolonged chronic stress can lead to a cyclical pattern of stress hormones, leading to obesity, and then chronic obesity itself contributing stressors, such as chronic pain, social effects, and limited mobility, which, in turn, leads to release of more stress hormones and more obesity.

Mood Disorders and Obesity:
Mood disorders and obesity have a high level of co-occurrence. They share clinical, neurobiological, genetic, and environmental factors.

- Depression: The association between obesity and depression is clear and strong, especially in women. The relationship between excess weight and depression appears to be reciprocal. Having depression increases the risk of later development of obesity. Having obesity increases the risk for developing depression.
- Bipolar Disorder: Individuals with bipolar disorder have a higher rate of metabolic syndrome than the overall population. A high BMI in Bipolar disorder is a risk factor for suicide.
- Anxiety Disorders and Obesity: Being overweight or obese was associated with lifetime diagnosis of anxiety in women. The association does not appear to be as strong as for depression.

Suicide Risk: Suicide risk increases with BMI for women but may even be a little decreased with increase BMI in men.
4. Eating Disorders and Obesity

- **Binge eating disorder (BED)** is the most common eating disorder among people who are obese, affecting between 15% and 50% of obese patients. It is characterized by:
  - Recurring episodes of eating significantly more food in a short period of time than most people would without purging
  - Related feelings of lack of control and marked distress
  - May eat too quickly, even when not hungry
  - May have feelings of guilt, embarrassment, or disgust and may hide binging behaviors
  - Occurs, on average, at least once a week over three months

- **Bulimia Nervosa**: Bulimia is characterized by binge eating plus recurrent inappropriate compensatory behavior in order to prevent weight gain, such as self-induced vomiting, misuse of laxatives, diuretics, enemas, fasting, or excessive exercise. Most individuals with bulimia are normal weight or even below, but some are overweight or obese.

- **Night Eating Syndrome**: Characterized by a combination of eating disorder, sleep disorder, and mood disorder characterized by consuming 25-50% of daily calories, typically high in carbohydrates, after the evening meal.

- **Anorexia Nervosa**: The onset of anorexia, which is characterized by pathological fear of gaining weight, restrained eating, insufficient body weight, and distorted body image, is often preceded by dieting. However, given that dieting to lose weight is very common and the incidence of anorexia is low, the rate of transition from dieting to anorexia is very low. Screen for this eating disorder in vulnerable patients. Patients who develop anorexia or who have a history of anorexia should have healthy lifestyle emphasized over dieting options.

**PHYSICAL EXAM FOR OBESITY**

An algorithm for the physical examination of overweight/obesity should include the following:

- Height
- Weight
- Blood pressure
- Body composition analysis
- Waist measurement
- Neck circumference
- Complete physical – Include a check for common comorbidities and mobility problems.

**Assess Mobility**

Impaired mobility is a common problem in chronic obesity. The severity increases with increased BMI, years of obesity, osteoarthritis, and history of injuries.
A baseline evaluation of functioning and tracking changes over time is part of a complete physical evaluation of obesity. Mobility assessments can be used in:

- Deciding on more aggressive treatments, such as bariatric surgery or very low-calorie diets.
- Determining what, if any, equipment is needed (e.g. canes, walkers, wheelchairs).
- Tracking improvements in response to obesity treatment.

Patients are assessed on their ability to sit and stand, walk forward and backward, and turn. Other movements used in evaluations include stair climbing, chair rise time, and time to get up and go. Slower walking and movement speeds and shorter stride lengths are evidence of decreased mobility. Patients can be questioned on pain, stiffness, activities of daily living, indoor mobility, housework, outdoor activities, occupational activities, and social life. A classification system can be used to accurately describe and track the severity of the problem.

An examination by a physical therapist can identify movement and posture impairments. Very few obese patients seek physical therapy for obesity, but do see PT for pain, likely caused or worsened by obesity, such as for sprains/strains, osteoarthritis, or disc herniation.

### Diagnostic Tests Often Indicated

Diagnostic tests in overweight and obesity should be individualized. However, the following tests are often part of a comprehensive evaluation:

1. **Electrocardiogram in Obesity**
   Obesity is associated with multiple hemodynamic effects and cardiovascular adaptations including increased intravascular blood volume, stroke volume, heart rate, cardiac output, systemic vascular resistance, blood pressure, pulmonary artery systolic pressure, filling pressures in the left and right heart cavities.

2. **Sleep Study**
   History-taking for possible sleep apnea should include questions on fatigue, sleepiness, witnessed breathing cessation. The neck circumference measurement associated with sleep apnea risk is >17” for men, > 16” for women.

3. **Secondary Studies Commonly Needed in Obesity**
   The following secondary studies may be needed if indicated by the primary exam:
   - **GERD** – endoscopy, esophageal motility
   - **Conditions causing secondary obesity** including polycystic ovary syndrome, hormonal or genetic causes, may require genetic or hormonal testing.
   - **Non-alcoholic fatty liver disease** – Liver inspection and function, secondary imaging, biopsy if needed
   - **Osteoarthritis** – secondary radiographic imaging
   - **Urinary Stress Incontinence** – secondary urine culture, urodynamic testing

Additional possible weight-related comorbidities include asthma/reactive airway disease, hypogonadism, infertility in females, polycystic ovary syndrome (premenopausal females with overweight/obesity and/or metabolic syndrome).
OTHER MEDICAL CONDITIONS CAUSING WEIGHT GAIN:

- Growth hormone imbalance
- Hypercortisolism (Cushing’s disease)
- Hyperphagia (e.g. associated with injury to the hypothalamus)
- Hypothyroidism
- Insulinoma
- Smoking cessation

21,46,74,75

Rare Genetic Conditions and Excess Weight
Genetics is commonly a contributing factor in obesity, affecting satiety and hunger, but simple genetic causes for obesity are rare. Examples include the uncommon autosomal dominant Prader-Willi Syndrome or the autosomal recessive Bardet Biedl Syndrome.

MODULE SUMMARY

Health Effects of Obesity and Benefits of Weight Loss
The following six diseases/conditions are most likely to co-occur with obesity76–78:

- Cardiovascular Disease
- Type 2 Diabetes Mellitus/Prediabetes
- Hypertension
- Dyslipidemia
- Sleep Apnea
- Cancer: Breast, Cervical, Ovarian, Endometrial, Prostate, Thyroid, Colon, Rectal, Pancreatic, Biliary Tract, Gallbladder

Many comorbidities and risks are improved significantly by as little as a 3 to 5% weight loss and further weight loss often produces even more health benefits.

Medical Evaluation of Obesity
It is important to rule out other potential causes of weight gain, including medications, medical conditions, eating disorders, and other psychological disorders.

Conditions that can cause weight gain include:

- Hypothyroidism
- Sleep apnea/reduced sleep
Genetics
Smoking cessation

Medications that can cause weight gain include:
- Anticonvulsants
- Antidepressants (Both tricyclic & MAOI's)
- Antihypertensives
- Antidiabetics

RESOURCES AVAILABLE THROUGH THIS MODULE:
- Article: The questionnaire on eating and weight patterns-5 (QEWP) The QEWP-5 is a revised version of the QEWP-R, updated to reflect Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition criteria for Binge Eating Disorder
- Directory of Diplomates, American Board of Obesity Medicine Search a Directory of Diplomates to find specialists in Obesity Medicine, by name or location
- National Diabetes Prevention Programs. Find One in Your Area The National Diabetes Prevention Program is a national partnership, community-based intervention designed to prevent or delay the onset of type 2 diabetes through evidenced-based lifestyle changes. (From the website.)
- NHLBI Lifestyle Interventions to Reduce Cardiovascular Risk An evidence review from the Lifestyle Work Group on lifestyle interventions to reduce cardiovascular risk
- PAR-Q & You The PAR-Q will tell you if you should check with your doctor before you start.
- PARmed-X The PARmed-X is a physical activity-specific checklist to be used by a physician with patients who have had positive responses to the Physical Activity Readiness Questionnaire (PAR-Q).
- Screening Form – Questionnaire on Eating and Weight Patterns Form used to evaluate for binge eating disorder
- VA/DoD clinical practice guideline for screening and management of overweight and obesity Guidelines for screening and treatment of obesity by the VA/DOD
- Weight-Related Comorbidities These are the risk levels of common weight-related comorbidities

REFERENCES USED IN THIS MODULE:


