Putting the AACE Obesity Guidelines into Practice

AACE, The Practice of Obesity Medicine
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W. Timothy Garvey, MD, FACE
Professor and Chair
Department of Nutrition Sciences
University of Alabama at Birmingham
Director, UAB Diabetes Research Center
Disclosures

► Consulting Fees/Advisory Boards:

Merck, Astra Zeneca, Eisai, Janssen, Novo Nordisk, Vivus, Takeda, Alexion

► Research:

Merck, Novo Nordisk, Pfizer, Sanofi, Eisai, Astra Zeneca, Lexicon, Weight Watchers, Elcelyx
Obesity is a Disease

- AACE, September 2012 ¹
- AMA, June 2013 ²

“…..the view of obesity as a behavioral decision is debunked by biomedical evidence……..obesity is a primary disease, and the full force of our medical knowledge should be brought to bear on its prevention and treatment……”

Determinants of Body Weight

Genes
- Protective and at risk alleles for weight gain
- Race (ancestral admixture)
- Gene-Gene interactions

Environment
- Food availability
- Food quality
- Built environment
- Socioeconomic status
- Education

Biological factors
- In utero environment
- Birth Weight
- Gender
- Age
- Concurrent diseases

Behavior
- Dietary preferences
- Physical activity
- Psychological factors
- Cultural factors
- Diurnal life patterns
AMA: Essential Criteria of a Disease

1. Characteristic signs or symptoms
2. Impairment in the normal functioning of some aspect of the body
3. Results in harm or morbidity
Regulation of Energy Intake

Peripheral Signals

- GHRELIN
- LEPTIN
- CCK
- GLP-1
- PEPTIDE YY
- AMYLIN
- INSULIN

Hypothalamic Pathways

- Arcuate Nucleus
- PVN, LHA, DMN

- NPY
- AgRP
- LepR
- LepR
- GLPR1
- Y2R
- Y1R
- Y5R
- 5HT2c
- μ-OR
- αMSH

- NTRK2
- GSHR
- LepR

Higher Cortical Centers

- BDNF
- MCH
- MCH1R
- NTRK2
- Garvey WT, 2013.
In Obesity, biology protects against weight loss and maintains a high body weight

- ↑ Ghrelin
- ↓ Leptin, PYY, CCK, Amylin
- ↓ Resting energy expenditure
- ↑ Hunger
- ↑ Calorie-dense food preferences

Increased Appetite
Decreased Energy Out
Increased Energy In

Garvey WT, 2014
Remember the Pathophysiology of Obesity: mechanisms protecting against weight loss

It is difficult for patients to maintain their weight loss over time.

Sacks FS. et al. *NEJM* 2009;360(9) 859-873.
Medical Complications of Obesity

Other Complications
- Depression
- Cancer
- Gallbladder Disease

BioMechanical Complications
- Sleep Apnea
- Osteoarthritis
- Stress
- Incontinence
- GERD
- Dismobility/Disability

Prediabetic States
- Diabetes
- NALFD
- PCOS

Cardiometabolic Disease
- CVD
Problems with the Term, Obesity

• Medical diagnosis based solely on anthropometric measurement (BMI),
• Uncertainty regarding health implications and definition in various racial/ethnic groups,
• Was not an actionable term for health care policy since relationship to health is obscure (AACE First Consensus Conference on Obesity\(^1\)),
• Sigmatization in public domain; derogatory use in social media,
• Engenders guilt and weight bias.

Adiposity-Based Chronic Disease

Abnormalities in Adipose Tissue
- Mass
- Distribution
- Function

- Lifelong disease with complications
- Pathophysiology and natural history c/w three phases of chronic disease prevention

Current Understanding of Obesity as a Disease

Abnormal quantity, distribution, and/or function of adipose tissue associated with adverse health outcomes\(^1\)

Genes, environment, and behavior all contribute\(^2,3\)

Associated with multiple cardiometabolic and biomechanical complications conferring morbidity and mortality\(^3\)

Chronic, relapsing, multifactorial disease that requires regular, long-term follow-up\(^4\)

Adiposity-Based Chronic Disease (ABCD)\(^1\)

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How Do We Use Available Treatment Modalities for Overweight and Obese Patients?

- Balance efficacy, safety, and cost
- Optimize benefit: risk ratio
- Achieve best outcomes
- Cost-effectiveness of care
Recent Treatment Recommendations and Algorithms for Treatment of Adult Obesity

- AACE/ACE⁴ [EBG]: most recent evidence-based guideline provides comprehensive recommendations
- The Endocrine Society² [EBG]: detailed description of pharmacological intervention
- AHA/ACC/TOS³ [EBG]: focus on lifestyle intervention with guidance on referral for surgery
- OMA - Obesity Medicine Association⁴: comprehensive and holistic approach – online

5. https://www.nice.org.uk/guidance/cg189
<table>
<thead>
<tr>
<th>BMI Category</th>
<th>25–26.9</th>
<th>27–29.9</th>
<th>30–34.9</th>
<th>35–39.9</th>
<th>≥40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diet, physical activity, and behavior</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Pharmacotherapy</td>
<td>No</td>
<td>With comorbidities</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Surgery*</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

* Bariatric surgeries require lifestyle medical follow-up.

FDA approved gastric band surgery for patients with BMI ≥30 and one weight related medical condition (February 2011).

LAGB, laparoscopic adjustable gastric banding

AACE/ACE Clinical Practice Guidelines for Comprehensive Medical Care of Patients with Obesity


www.aace.com/publications/guidelines
An evidenced-based care model is needed that is:

(i) Comprehensive: all aspects of diagnosis, evaluation, treatment decisions, and treatment goals

(ii) Practical: applicable to real-world patient care

(iii) Evidence-Based: Considers the totality of the evidence pertinent to all key aspects of patient management

(iv) is designed to optimize benefit and risk based on defined outcomes that reflect impact of treatment on the health of the patient.
What are we Treating?
Q1. Do the 3 phases of chronic disease prevention and treatment—ie, primary, secondary, and tertiary—apply to the disease of obesity?
Q3. What complications are attributable to obesity?
Q4. Does BMI or other measures of adiposity convey full information regarding the impact of excess body weight on the patient’s health?

Why are we Treating it?
Q5. Do patients with excess adiposity and related complications benefit more from weight loss than patients without complications, and, if so, how much weight loss would be required?

How do we Treat it?
Q6. Is lifestyle/behavioral therapy effective?
Q7. Is pharmacotherapy effective?
Q8. How to optimally individualize pharmacotherapy?
Q9. Is bariatric surgery effective?
Obesity and 3 Phases of Chronic Disease Prevention and Treatment

Q1. Do the 3 phases of chronic disease prevention and treatment apply to the disease of obesity?
— i.e., primary, secondary, and tertiary
Chronic Disease Phases and Interventions

**PHASE**
- **Primary Prevention**
- **Secondary Prevention**
- **Tertiary Prevention**

**GOAL**
- **Primary Prevention**
  - Prevent disease from occurring
- **Secondary Prevention**
  - Halt early progression and prevent sequelae (before complications)
- **Tertiary Prevention**
  - Reduce complications and prevent further deterioration (after complications)

**INTERVENTION**
- Prevent complications and worsening of the disease.
- Eliminate risk factors
  - Primordial (population)
  - Primary (high risk)
- Limit adverse consequences of a disease on health
Chronic Disease Model - Obesity
(similar to diabetes, asthma, alcoholism, etc.)

- **Primordial Disease Risk**
- **Primary Disease Risk**
- **Obesogenic Environment**
- **Uncomplicated Obesity 2° Prevention**
- **Obesogenic Environment**
- **Weight-Related Complications 3° Prevention**

- **Genetics**
- **Behavior**
- **Genetics**

Diagram showing the Chronic Disease Model of Obesity, highlighting the interplay between genetics, behavior, environment, and disease risk prevention levels.
Obesity and 3 Phases of Chronic Disease Prevention and Treatment

- **Q1.** Do the 3 phases of chronic disease prevention and treatment—ie, primary, secondary, and tertiary—apply to the disease of obesity?

- **R2.** The modality and intensity of obesity interventions should be based on the primary, secondary, and tertiary phases of disease prevention; this 3-phase paradigm for chronic disease aligns with the pathophysiology and natural history of obesity and provides a rational framework for appropriate treatment at each phase of prevention

- (Grade C; BEL 4, upgraded due to high relevance to natural history of the disease).

<table>
<thead>
<tr>
<th>What Are We Treating</th>
<th>Screening</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Disease</strong></td>
<td><strong>Staging</strong></td>
<td><strong>Anthropometric Diagnosis</strong></td>
</tr>
<tr>
<td><strong>Why Are We Treating</strong></td>
<td><strong>Tx Goals</strong></td>
<td><strong>Clinical Diagnosis</strong></td>
</tr>
<tr>
<td><strong>How We Treat</strong></td>
<td><strong>Tx Plan</strong></td>
<td><strong>What Are We Treating</strong></td>
</tr>
</tbody>
</table>

### Treatment Goals

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No complications</td>
</tr>
<tr>
<td>1</td>
<td>One or more mild-to-moderate complications or may be treated effectively with moderate weight loss</td>
</tr>
<tr>
<td>2</td>
<td>At least one severe complication or requires more aggressive weight loss for effective treatment</td>
</tr>
</tbody>
</table>

### Phases of Chronic Disease Prevention and Treatment Goals

**Primary**
- Prevent overweight/obesity

**Secondary**
- Prevent progressive weight gain or achieve weight loss to prevent complications

**Tertiary**
- Achieve weight loss sufficient to ameliorate the complications and prevent further deterioration

### Treatment Based on Clinical Judgment

<table>
<thead>
<tr>
<th>Phase</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary</td>
<td>Healthy meal plan, Physical activity, Health education, Built environment</td>
</tr>
<tr>
<td>Secondary</td>
<td>Lifestyle/behavioral therapy, Consider pharmacotherapy if lifestyle alone not effective</td>
</tr>
<tr>
<td>Tertiary</td>
<td>Lifestyle/behavioral therapy, Add pharmacotherapy (BMI ≥27), Consider bariatric surgery (BMI ≥35)</td>
</tr>
</tbody>
</table>

### Follow-Up

- Once the plateau for weight loss has been achieved, re-evaluate the weight-related complications. If the complications have not been treated to target, then weight loss therapy should be intensified or complication-specific interventions need to be employed.
- Obesity is a chronic disease and the diagnostic categories for obesity may not be static. Therefore, patients require ongoing follow-up, re-evaluation, and long-term treatment.

### Abbreviation:
- BMI = body mass index
Diagnosis: Anthropometric Component

EVIDENCE-BASED SCREENING AND DIAGNOSIS FOR EXCESS ADIPOSITY IN CLINICAL SETTINGS

Screening → Annual BMI

Diagnosis (Anthropometric Component)

- BMI ≥ 25 kg/m²
- BMI ≥ 23 kg/m² for some ethnicities

Clinical Component of Diagnosis

1. Clinical interpretation of BMI: Ensure elevated BMI is indicative of excess adiposity by assessing: age, gender, muscularity, hydration status, edema, third space fluid collection, large tumors, sarcopenia
2. Waist circumference if BMI < 35 kg/m²: Adds information pertaining to cardiometabolic disease risk; use gender- and ethnicity-specific cut-off values
3. Can consider body composition technologies: eg, bioelectrical impedance, air/water displacement plethysmography, or dual-energy x-ray absorptiometry scan

Abbreviation: BMI = body mass index
### Diagnosis: Clinical Component

#### Evaluate for a Checklist of Weight-Related Complications

<table>
<thead>
<tr>
<th>Patients Present with Overweight or Obesity (Anthropometric Component)</th>
<th>Candidates for Weight Loss Therapy</th>
<th>Patients Present with Weight-Related Disease or Complication (Clinical Component)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients present with BMI $\geq 25$ kg/m², or $\geq 23$ kg/m² in certain ethnicities, and excess adiposity</td>
<td>Evaluate for weight-related complications</td>
<td>Prediabetes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Metabolic Syndrome</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Type 2 Diabetes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dyslipidemia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hypertension</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cardiovascular Disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nonalcoholic Fatty Liver Disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Polycystic Ovary Syndrome</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Female Infertility</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Male Hypogonadism</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Obstructive Sleep Apnea</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Asthma/Reactive Airway Disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Osteoarthritis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Urinary Stress Incontinence</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gastroesophageal Reflux Disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Depression</td>
</tr>
</tbody>
</table>
### Advanced Framework for a New Diagnosis of Obesity as a Chronic Disease

<table>
<thead>
<tr>
<th>DIAGNOSIS</th>
<th>ANTHROPOMETRIC COMPONENT</th>
<th>CLINICAL COMPONENT</th>
<th>Prevention/Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>BMI &lt; 25</td>
<td></td>
<td>Primary</td>
</tr>
<tr>
<td>Overweight Stage 0</td>
<td>BMI 25-29.9</td>
<td>No obesity-related complications</td>
<td>Secondary</td>
</tr>
<tr>
<td>Obesity Stage 0</td>
<td>BMI ≥ 30</td>
<td>No obesity-related complications</td>
<td></td>
</tr>
<tr>
<td>Obesity Stage 1</td>
<td>BMI ≥ 25</td>
<td>Presence of 1 or more mild-to-moderate obesity-related complications</td>
<td>Tertiary</td>
</tr>
<tr>
<td>Obesity Stage 2</td>
<td>BMI ≥ 25</td>
<td>Presence of 1 or more severe obesity-related complications</td>
<td></td>
</tr>
</tbody>
</table>

## Clinical Diagnosis: Screening for Complications that Improve with Weight Loss

<table>
<thead>
<tr>
<th>Condition</th>
<th>Tests/Examinations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolic Syndrome</td>
<td>Waist, BP, HDL, TG, FPG</td>
</tr>
<tr>
<td>Prediabetes</td>
<td>FPG</td>
</tr>
<tr>
<td>Type 2 Diabetes</td>
<td>FPG</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>Lipid panel</td>
</tr>
<tr>
<td>Hypertension</td>
<td>BP</td>
</tr>
<tr>
<td>NAFLD</td>
<td>Exam, LFTs</td>
</tr>
<tr>
<td>PCOS</td>
<td>Exam, ROS</td>
</tr>
<tr>
<td>Sleep Apnea</td>
<td>Exam, ROS</td>
</tr>
<tr>
<td>osteoarthritis</td>
<td>Exam, ROS</td>
</tr>
<tr>
<td>GERD</td>
<td>Exam, ROS</td>
</tr>
<tr>
<td>Disability/Immobility</td>
<td>Exam, ROS</td>
</tr>
<tr>
<td>Psychological Disorder</td>
<td>Exam, ROS</td>
</tr>
<tr>
<td>Secondary: genetic syndromes, hormonal disease, iatrogenic</td>
<td>Exam, ROS, med review, family hx</td>
</tr>
</tbody>
</table>
Goals of Therapy

- To improve the health of the patient
- To prevent or treat weight-related complications

<table>
<thead>
<tr>
<th>NORMAL WEIGHT</th>
<th>STAGE 0</th>
<th>STAGE 1</th>
<th>STAGE 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>No obesity</td>
<td>No complications</td>
<td>One or more mild-to-moderate complications or may be treated effectively with moderate weight loss</td>
<td>At least one severe complication or requires more aggressive weight loss for effective treatment</td>
</tr>
<tr>
<td>BMI &lt;25</td>
<td>BMI 25–29.9</td>
<td>BMI ≥30</td>
<td>BMI ≥25</td>
</tr>
<tr>
<td>&lt;23 in certain ethnicities</td>
<td>OVERWEIGHT</td>
<td>OBESITY</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PRIMARY</th>
<th>SECONDARY</th>
<th>TERTIARY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevent overweight / obesity</td>
<td>Prevent progressive weight gain or achieve weight loss to prevent complications</td>
<td>Achieve weight loss sufficient to ameliorate the complications and prevent further deterioration</td>
</tr>
<tr>
<td>OBESITY COMPILATION</td>
<td>% weight loss required for therapeutic benefit</td>
<td>Notes</td>
</tr>
<tr>
<td>---------------------</td>
<td>-----------------------------------------------</td>
<td>-------</td>
</tr>
<tr>
<td>Diabetes Prevention</td>
<td>3% to 10%</td>
<td>Maximum benefit 10%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>5% to &gt;15%</td>
<td>BP still decreasing &gt;15%</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>3% to &gt;15%</td>
<td>TG still decreasing at &gt;15%</td>
</tr>
<tr>
<td>HbA1c</td>
<td>3% to &gt;15%</td>
<td>HbA1c still decreasing at &gt;15%</td>
</tr>
<tr>
<td>NAFLD</td>
<td>10%</td>
<td>Improves steatosis, inflammation, mild fibrosis</td>
</tr>
<tr>
<td>Sleep Apnea (AHI)</td>
<td>10%</td>
<td>Little benefit at ≤ 5%</td>
</tr>
<tr>
<td>Osteoarthritis</td>
<td>5-10%</td>
<td>Improves symptoms and joint stress mechanics</td>
</tr>
<tr>
<td>Stress Incontinence</td>
<td>5-10%</td>
<td></td>
</tr>
<tr>
<td>GERD</td>
<td>5-10% women 10% men</td>
<td></td>
</tr>
</tbody>
</table>
# TREATMENT GOALS BASED ON DIAGNOSIS IN THE MEDICAL MANAGEMENT OF PATIENTS WITH OBESITY

<table>
<thead>
<tr>
<th>DIAGNOSIS</th>
<th>TREATMENT GOALS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anthropometric Component</strong></td>
<td><strong>Clinical Component</strong></td>
</tr>
</tbody>
</table>
| Primordial Prevention | BMI ≤25 (≤23 in certain ethnicities) | Obesogenic environment | Public education  
- Built environment  
- Access to healthy foods | Decreased incidence of overweight/obesity in populations |
| Primary Prevention | BMI ≤25 (≤23 in certain ethnicities) | High-risk individuals or subgroups based on individual or cultural behaviors, ethnicity, family history, biomarkers, or genetics | Annual BMI screening  
- Healthy meal plan  
- Increased physical activity | Decreased incidence of overweight/obesity in high-risk individuals or identifiable subgroups |

## PRIMARY PREVENTION

## SECONDARY PREVENTION

| Overweight | BMI 25–29.9 (BMI 23–24.9 in certain ethnicities) | No clinically significant or detectable weight-related complications | Prevent progressive weight gain or weight loss | Prevent progression to obesity  
- Prevent the development of weight-related complications |
| Obesity | BMI ≥30 (≥25 in certain ethnicities) | No clinically significant or detectable weight-related complications | Weight loss or Prevent progressive weight gain | Prevent the development of weight-related complications |

## TERTIARY PREVENTION

| Overweight or Obesity | BMI ≥25 (≥23 in certain ethnicities) | Metabolic syndrome | 10% | Prevention of T2DM  
- Reduction in A1C  
- Reduction in number and/or doses of glucose lowering medications  
- Diabetes remission especially when diabetes duration is short |
|                         | Prediabetes | 10% | Prevention of T2DM |
|                         | T2DM | 5% to ≥15% | Prevention of T2DM  
- Lower triglycerides  
- Raise HDL-c  
- Lower non-HDL-c |
|                         | Dyslipidemia | 5% to ≥15% | Prevention of T2DM  
- Lower triglycerides  
- Raise HDL-c  
- Lower non-HDL-c |
<table>
<thead>
<tr>
<th>Overweight or Obesity</th>
<th>TERTIARY PREVENTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI ≥25 (≥23 in certain ethnicities)</td>
<td>Hypertension 5% to ≥15% • Lower systolic and diastolic BP • Reductions in number and/or doses of antihypertensive medications</td>
</tr>
<tr>
<td>Nonalcoholic fatty liver disease</td>
<td>Steatosis 5% or more • Reduction in intrahepatocellular lipid</td>
</tr>
<tr>
<td></td>
<td>Steatohepatitis 10% to 40% • Reduction in inflammation and fibrosis</td>
</tr>
<tr>
<td>Polycystic ovary syndrome</td>
<td>5% to 15% or more • Ovulation • Regularization of menses • Reduced hirsuitism • Enhanced insulin sensitivity • Reduced serum androgen levels</td>
</tr>
<tr>
<td>Female infertility</td>
<td>10% or more • Ovulation • Pregnancy and live birth</td>
</tr>
<tr>
<td>Male hypogonadism</td>
<td>5% to 10% or more • Increase in serum testosterone</td>
</tr>
<tr>
<td>Obstructive sleep apnea</td>
<td>7% to 11% or more • Improved symptomatology • Decreased apnea-hypopnea index</td>
</tr>
<tr>
<td>Asthma/reactive airway disease</td>
<td>7% to 8% or more • Improvement in forced expiratory volume at 1 second • Improved symptomatology</td>
</tr>
<tr>
<td>Osteoarthritis</td>
<td>≥10% • 5% to 10% or more when coupled with exercise • Improvement in symptomatology • Increased function</td>
</tr>
<tr>
<td>Urinary stress incontinence</td>
<td>5% to 10% or more • Reduced frequency of incontinence episodes</td>
</tr>
<tr>
<td>Gastroesophageal reflux disease</td>
<td>10% or more • Reduced symptom frequency and severity</td>
</tr>
<tr>
<td>Depression</td>
<td>Uncertain • Reduction in depression symptomatology • Improvement in depression scores</td>
</tr>
</tbody>
</table>

Abbreviations: A1C = hemoglobin A1c; BMI = body mass index; BP = blood pressure; HDL-c = high-density lipoprotein cholesterol; T2DM = type 2 diabetes mellitus.
How Do We Treat?

- Modality and intensity determined by disease stage

**Primary**
- Prevent overweight / obesity

**Secondary**
- Prevent progressive weight gain or achieve weight loss to prevent complications

**Tertiary**
- Achieve weight loss sufficient to ameliorate the complications and prevent further deterioration

- Healthy meal plan
- Physical activity
- Health education
- Built environment

- Lifestyle/behavioral therapy
- Consider pharmacotherapy if lifestyle alone not effective

- Lifestyle/behavioral therapy
- Consider pharmacotherapy (BMI ≥27)

- Lifestyle/behavioral therapy
- Add pharmacotherapy (BMI ≥27)
- Consider bariatric surgery (BMI ≥35)

**Follow-Up**
- Once the plateau for weight loss has been achieved, re-evaluate the weight-related complications. If the complications have not been treated to target, then weight loss therapy should be intensified or complication-specific interventions need to be employed.
- Obesity is a chronic disease and the diagnostic categories for obesity may not be static. Therefore, patients require ongoing follow-up, re-evaluation, and long-term treatment.
# Comprehensive Lifestyle Management Is the Foundation of Obesity Treatment

<table>
<thead>
<tr>
<th>Meal Plan</th>
<th>Physical Activity</th>
<th>Behavior</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Reduced-calorie healthy meal plan</td>
<td>• Aerobic activity</td>
<td>• Intervenational package of behavioral methods</td>
</tr>
<tr>
<td>• ≈ 500-750 kcal daily deficit</td>
<td>– Goal: &gt; 150 min/wk</td>
<td>• Self-monitoring; goal setting; education; problem-solving; stimulus control; stress reduction; psychological evaluation and treatment; cognitive restructuring; motivational interviewing; social support structures</td>
</tr>
<tr>
<td>• Many healthy meal plan options※</td>
<td>– 3-5 days/wk</td>
<td>Team member/expertise: health educator, behaviorist, clinical psychologist, psychiatrist</td>
</tr>
<tr>
<td>• Meal replacements</td>
<td>• Resistance exercise</td>
<td></td>
</tr>
<tr>
<td>• Very-low–calorie diet is an option for selected patients—requires supervision</td>
<td>– Major muscle groups</td>
<td></td>
</tr>
<tr>
<td></td>
<td>– 2-3 times/wk</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Reduce sedentary behavior</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Individualized (e.g., preferences, limitations)</td>
<td></td>
</tr>
<tr>
<td>*Team member/expertise: dietitian, health educator</td>
<td>*Team member/expertise: exercise trainer, physical activity coach, physical/ occupational therapist</td>
<td></td>
</tr>
</tbody>
</table>

※ AACE/ACE guideline lists: Mediterranean, DASH, low-carb, low-fat, volumetric, high protein, vegetarian.

# Obesity Pharmacotherapy

<table>
<thead>
<tr>
<th>Agents</th>
<th>Action</th>
<th>Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Previously available</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phentermine</td>
<td>• Sympathomimetic</td>
<td>• 1959</td>
</tr>
<tr>
<td>Orlistat</td>
<td>• GI lipase inhibitor</td>
<td>• 1997</td>
</tr>
<tr>
<td><strong>Recently Approved</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phentermine/Topiramate ER</td>
<td>• Sympathomimetic/Anticonvulsant (GABA receptor modulation?)</td>
<td>• Approved, Summer 2012</td>
</tr>
<tr>
<td>Lorcaserin</td>
<td>• 5-HT$_{2C}$ serotonin receptor agonist</td>
<td>• Approved, Summer 2012</td>
</tr>
<tr>
<td>Naltrexone ER/Bupropion ER</td>
<td>• Dopamine/noradrenaline reuptake inhibitor/Opioid receptor antagonist</td>
<td>• Approved, September 2014</td>
</tr>
<tr>
<td>Liraglutide 3 mg</td>
<td>• GLP-1 receptor agonist</td>
<td>• Approved December 2014</td>
</tr>
</tbody>
</table>

**Treatment Based on Clinical Judgment**

**When to Initiate Weight-Loss Medications in Patients with Overweight/Obesity**

**Initiate Lifestyle Therapy**

1. **No Complications.**
   - Patients with overweight or obesity who have no clinically significant weight-related complications (secondary prevention)

2. **Mild to Moderate Complications.**
   - Patients with mild to moderate weight-related complications when lifestyle therapy is anticipated to achieve sufficient weight loss to ameliorate the complication (tertiary prevention)
   - Note: weight loss medications may also be indicated based on clinical judgment

**Initiate Weight Loss Medication as an Adjunct to Lifestyle Therapy**

1. **Failure on Lifestyle Therapy.**
   - Add medication for patients who have progressive weight gain or who have not achieved clinical improvement in weight-related complications on lifestyle therapy alone.

2. **Weight Regain on Lifestyle Therapy.**
   - Add medication for patients with overweight (BMI 27–29.9 kg/m²) or obesity who are experiencing weight regain following initial success on lifestyle therapy alone.

3. **Presence of Weight-Related Complications.**
   - Initiate medication concurrent with lifestyle therapy for patients with overweight (BMI 27–29.9 kg/m²) or obesity who have weight-related complications, particularly if severe, in order to achieve sufficient weight loss to ameliorate the complication (tertiary prevention).
Consideration in Individualizing Pharmacotherapy in Patients with Obesity

- Patient Factors
- Biological Factors
- Pharmacotherapy Factors
Individualizing Pharmacotherapy in Obesity: Patient Factors

- **Motivation** (readiness for change)
- **Reasons for weight loss** (harmonization of treatment goals with health care professional)
- **Intensity of Lifestyle Therapy** (availability, adherence, cultural and personal preferences)
- **Family structure and social support systems**
- **Psychological** (Binge eating disorder, night eating disorder, stress/anxiety, depression, food addictions, body image)
- **Weight history** (responses to previous interventions)
- **Lifestyle** (habits, cultural, sleep hygiene, night-shift, smoking, built environment, life events)
- **Built environment**
Individualizing Pharmacotherapy in Obesity: Biological Factors

- **Demographic**
  1. Race – ethnicities lose less weight
  2. Age – in elderly have clear health related benefits in mind, assess for sarcopenia, osteoporosis
  3. Gender – differences in body composition

- **Genetic factors**

- **Biological** (menopause, low thermogenesis)

- **Concomitant medications** (insulin, anti-psychotics, anti-depressants)

- **Co-Morbidities** (T2DM, sleep apnea, hypothyroidism, hypercortisolism, psychological disorders)

- **Complications** (weight-related)
Individualizing Pharmacotherapy in Obesity:

**Pharmacotherapy Factors**

- Effectiveness (Mean weight loss, Categorical weight loss: odds of losing 5% or 10% of body weight)
- Side effects/tolerability profile
- Warnings and Contraindications
- Drug-drug interactions
- Goals of therapy regarding specific health benefits and the presence and severity of weight related complications
- Cost and Availability
<table>
<thead>
<tr>
<th>DRUG</th>
<th>Adverse Events</th>
<th>Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orlistat</td>
<td>GI symptoms, Fat soluble vitamins</td>
<td>Malabsorption syndrome, Cholestasis</td>
</tr>
<tr>
<td>Lorcaserin</td>
<td>Depression and SSRIs, Serotonin Syndrome, Headache, Psychiatric, Moderate prolactin elevation</td>
<td></td>
</tr>
<tr>
<td>Phentermine/topiramate ER</td>
<td>Insomnia, Dry mouth Paresthesia, Dysgeusia, Regular pregnancy testing</td>
<td>Glaucoma, Hyperthyroidism, MAOIs (14 days), Fetal clefts (topiramate)</td>
</tr>
<tr>
<td>Naltrexone ER/Bupropion ER</td>
<td>Nausea, Worsening depression</td>
<td>Uncontrolled HTN, Seizure disorders and risk, Opioid use, MAOIs (14 days)</td>
</tr>
<tr>
<td>Liraglutide 3 mg</td>
<td>Nausea, Cholelithiasis</td>
<td>MTC and MEN II, Acute pancreatitis</td>
</tr>
</tbody>
</table>

Note: all drugs contraindicated in pregnancy; avoid if breast feeding; hypoglycemia

US FDA. Drugs@FDA
AACE Clinical Practice Guidelines for Medical Care of Patients with Obesity, 2016
Direct Meta-Analysis: Likelihood of Discontinuation Due to Adverse Events

Common Adverse Events\(^1\)

- **LIRA 3.0 mg**: hypoglycemia, GI AEs, headache
- **N/B**: GI AEs, headache
- **P/T**: parasthesia, dizziness, distorted taste, insomnia, constipation, dry mouth
- **LOR BID**: hypoglycemia, headache, fatigue
- **ORL**: abdominal pain/discomfort, oily spotting/stool, fecal urgency

\(^1\) Selected common (defined as incidence > 5%) AEs are noted; refer to medication package inserts and cited references for complete information.

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2. Drugs@FDA: FDA approved drug products. [http://www.accessdata.fda.gov/Scripts/cder/DrugsatFDA](http://www.accessdata.fda.gov/Scripts/cder/DrugsatFDA);
<table>
<thead>
<tr>
<th>Anti-obesity Medication (Trade Name) Year of FDA Approval</th>
<th>Mechanism of Action, Study Name, Study Duration: % TBWL Greater Than Placebo</th>
<th>Dose</th>
<th>Common Side Effects</th>
<th>Contraindications, Cautions, and Safety Concerns</th>
<th>Monitoring and Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orlistat (Xenical™ (Alli™) - OTC 1999)</td>
<td>Lipase inhibitor XENDOS 1 yr: 4.0% 4 yr: 2.6%</td>
<td>120 mg PO TID (before meals) OTC: 60 mg PO TID (before meals)</td>
<td>- Steatorrhea - Fecal urgency - Incontinence - Flatulence - Oily spotting - Frequent bowel movements - Abdominal pain - Headache</td>
<td>- Pregnancy and breastfeeding - Chronic malabsorption syndrome - Cholestasis - Oxalate nephrolithiasis - Rare severe liver injury - Cholelithiasis - Malabsorption of fat-soluble vitamins - Effects on other medications:</td>
<td>- Cholelithiasis - Nephrolithiasis - Recommend standard multivitamin (to include vitamins A, D, E, and K) at bedtime or 2 hours after orlistat dose - Eating &gt;30% kcal from fat results in greater GI side effects - FDA-approved for children ≥ 12 years old - Administer levothryoxine and orlistat 4 hours apart</td>
</tr>
<tr>
<td>Lorcaner (Belviq™) 2012</td>
<td>Serotonin (5HT2c) receptor agonist BLOSSOM BLOOM 1 yr: 3.0%-3.6% 2 yr: 3.1%</td>
<td>10 mg PO BID</td>
<td>- Headache - Nausea - Dizziness - Fatigue - Xerostomia - Dry eye - Constipation - Diarrhea - Back pain - Nasopharyngitis - Hyperprolactinemia</td>
<td>- Pregnancy and breastfeeding - Serotonin syndrome or neuroleptic malignant syndrome - Safety data lacking in patients who have depression - Concomitant use of SSRI, SNRI, MAOI, bupropion, St. John's wort as may increase risk of developing serotonin syndrome - Uncontrolled mood disorder - Cognitive impairment - Avoid in patients with severe liver injury or renal insufficiency - Caution with patients with bradycardia, heart block, or heart failure - Unproven concern for potential cardiac valvulopathy - Leukopenia</td>
<td>- Symptoms of cardiac valve disease - Bradycardia - Serotonin syndrome - Neuroleptic malignant syndrome - Depression - Severe mood alteration, euphoria, dissociative state - Confusion/somnolence - Priapism - Leukopenia - Euphoria at high doses could predispose to abuse - Hyponoglycemia in patients having T2DM treated with insulin and/or sulfonylureas</td>
</tr>
<tr>
<td>Phentermine/Topiramate ER (Qsymia™) 2012</td>
<td>NE-releasing agent (phentermine) GABA receptor modulation (topiramate) EQUIP CONQUER SEQUEL 1 yr: 8.6%-9.3% on high dose; 6.6% on treatment dose</td>
<td>Starting dose: 3.75/23 mg PO QD for 2 weeks Recommended dose: 7.5/46 mg PO QD Escalation dose: 11.25/69 mg PO QD Maximum dose: 15/92 mg PO QD</td>
<td>- Headache - Paresthesia - Insomnia - Decreased bicarbonate - Xerostomia - Constipation - Nasopharyngitis - Anxiety - Depression - Cognitive impairment (concentration and memory) - Nausea - Næsa - Dysgeusia</td>
<td>- Pregnancy and breastfeeding (topiramate teratogenicity) - Hypothyroidism - Acute angle-closure glaucoma - Concomitant MAOI use (within 14 days) - Tachyarrhythmias - Decreased cognition - Seizure disorder - Anxiety and panic attacks - Nephrolithiasis - Hyperchloremic metabolic acidosis - Dose adjustment with hepatic and renal impairment - Concern for abuse potential - Combined use with alcohol or depressant drugs can worsen cognitive impairment</td>
<td>- Increased heart rate - Depressive symptomatology or worsening depression especially on maximum dose - Hypokalemia (especially with HCTZ or furosemide) - Acute myopia and/or ocular pain - Acute kidney stone formation - Hyponoglycemia in patients having T2DM treated with insulin and/or sulfonylureas - Potential for lactic acidosis (hyperchloremic non-anion gap) in combination with metformin - MAOI (allow ≥14 days between discontinuation) - 15 mg/92 mg dose should not be discontinued abruptly (increased risk of seizure): taper over at least 1 week - Health care professional should check BUN/Cr before initiating, followed by monthly self-testing at home - Monitor electrolytes and creatinine before and during treatment - Can cause menstrual spotting in women taking birth control pills due to altered metabolism of estrogen and progestins</td>
</tr>
<tr>
<td>Anti-obesity Medication (Trade Name)</td>
<td>Mechanism of Action, Study Name, Study Duration; % TBWL Greater Than Placebo</td>
<td>Dose</td>
<td>Common Side Effects</td>
<td>Contraindications, Cautions, and Safety Concerns</td>
<td>Monitoring and Comments</td>
</tr>
<tr>
<td>-------------------------------------</td>
<td>---------------------------------------------------------------------------</td>
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<td>------------------------</td>
</tr>
<tr>
<td>Naltrexone ER/ Bupropion ER (Contrave®) 2014</td>
<td>Opiate antagonist (naltrexone) Reuptake inhibitor of DA and NE (bupropion) COR-I COR-II COR-BMOD 1 yr: 4.2%-5.2%</td>
<td>Titrate dose: Week 1: 1 tab (8/90 mg) PO QAM Week 2: 1 tab (8/90 mg) PO BID Week 3: 2 tabs (total 16/180 mg) PO QAM and 1 tab (8/90 mg) PO QHS Week 4: 2 tabs (total 16/180 mg) PO QHS</td>
<td>Nausea Headache Insomnia Vomiting Constipation Diarrhea Dizziness Anxiety Xerostomia</td>
<td>Pregnancy and breastfeeding Uncontrolled hypertension Seizure disorder Anorexia nervosa Bulimia nervosa Severe depression Drug or alcohol withdrawal Comorbidities MAOI (within 14 days) Chronic opioid use Cardiac arrhythmia Dose adjustment for liver and kidney impairment Narrow-angle glaucoma Uncontrolled migraine disorder Generalized anxiety disorder Bipolar disorder Safety data lacking in patients who have depression Seizures (bupropion lowers seizure threshold)</td>
<td>Monitor for: Increased heart rate and blood pressure Worsening depression and suicidal ideation Worsening of migraines Liver injury (naltrexone) Hypoglycemia in patients having T2DM treated with insulin and/or sulfonylureas Seizures (bupropion lowers seizure threshold) MAOI (allow ≥14 days between discontinuation) Dose adjustment for patients with renal and hepatic impairment Avoid taking medication with a high-fat meal Can cause hyperthyroidism T2DM and I2DM Hyperglycemia and hypoglycemia in patients taking T2DM with insulin and/or sulfonylureas Dose adjustment for liver and kidney impairment Seizures (bupropion lowers seizure threshold)</td>
</tr>
<tr>
<td>Liraglutide 3 mg (Saxenda®) 2014</td>
<td>GLP-1 analog SCALE Obesity &amp; Prediabetes 1 yr: 5.6%</td>
<td>Titrate dose weekly by 0.6 mg as tolerated by patient (side effects): 0.6 mg SC QD 1.2 mg SC QD 1.8 mg SC QD 2.4 mg SC QD 3.0 mg SC QD</td>
<td>Nausea Vomiting Diarrhea Constipation Headache Dyspepsia Increased heart rate</td>
<td>Pregnancy and breastfeeding Personal or family history of medullary thyroid cancer or MEN2 Pancreatitis Acute interstitial nephritis Gastroesophagitis Severe renal impairment can result from vomiting and dehydration Use caution in patients with history of pancreatitis Use caution in patients with cholelithiasis Suicidal ideation and behavior Injection site reactions</td>
<td>Monitor for: Pancreatitis Cholelithiasis and Cholecystitis Hypoglycemia in patients having T2DM treated with insulin and/or sulfonylureas Increased heart rate Dehydration from nausea/vomiting Injection site reactions Titrate dose based on tolerability (nausea and GI side effects)</td>
</tr>
</tbody>
</table>

Abbreviations: BID = twice daily; DA = dopamine; FDA = US Food and Drug Administration; GI = gastrointestinal; HCTZ = hydrochlorothiazide; MAOI = monoamine oxidase inhibitor; MEN2 = multiple endocrine neoplasia type 2; NE = norepinephrine; OTC = over-the-counter medication; % TBWL = percent total body weight loss from baseline over that observed in the placebo group; PO = oral; QAM = every morning; QD = daily; QHS = every bedtime; SC = subcutaneous; SNRI = serotonin-norepinephrine reuptake inhibitor; TID = 3 times a day; T2DM = type 2 diabetes mellitus.

FDA indication for all medications: BMI ≥ 30 kg/m² or BMI ≥ 27 kg/m² with significant comorbidity.

After 3 to 4 months of treatment with antiobesity medication:
- For naltrexone ER/bupropion ER andlorlistat:
  - If the patient has not lost at least 5% of their baseline body weight at 12 weeks on the maintenance dose, the medication should be discontinued.
- For phentermine/topiramate ER:
  - If the patient has not lost >5% body weight after 12 weeks on recommended dose (7.5 mg/42 mg); if the patient has not lost at least 3% of body weight after being on the recommended dose for 12 weeks then the medication should be discontinued, or the patient can be transitioned to maximum dose (15 mg/92 mg); if patient has not lost at least 5% after 12 additional weeks on the maximum dose, the medication should be discontinued.

For liraglutide 3 mg:
- If the patient has not lost at least 4% of body weight 16 weeks after initiation, the medication should be discontinued.

References:
# Preferred Weight-Loss Medications: Individualization of Therapy

<table>
<thead>
<tr>
<th>Clinical Characteristics or Coexisting Diseases</th>
<th>Orlistat</th>
<th>Lorcaserin</th>
<th>Phentermine/topiramate ER</th>
<th>Naltrexone ER/bupropion ER</th>
<th>Liraglutide 3 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes Prevention (metabolic syndrome, prediabetes)</td>
<td>Insufficient data for T2DM prevention</td>
<td>Monitor heart rate, rhythm</td>
<td>Monitor heart rate, BP, rhythm</td>
<td>Monitor heart rate</td>
<td>Monitor heart rate</td>
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<tr>
<td>Type 2 Diabetes Mellitus</td>
<td>Monitor heart rate</td>
<td>Monitor heart rate, rhythm</td>
<td>Monitor heart rate, BP, rhythm</td>
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<td>Monitor heart rate, BP, rhythm</td>
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<td>Chronic Kidney Disease</td>
<td>Do not exceed 7.5 mg/46 mg per day</td>
<td>Do not exceed 8 mg/90 mg bid</td>
<td>Urinary clearance of drug</td>
<td>Avoid vomiting and volume depletion</td>
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<tr>
<td>Mild (50–79 mL/min)</td>
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<td>Moderate (30–49 mL/min)</td>
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<td>Severe (&lt;30 mL/min)</td>
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<td>Nephrolithiasis</td>
<td>Calcium oxalate stones</td>
<td>Calcium phosphate stones</td>
<td>Calcium phosphate stones</td>
<td>Calcium phosphate stones</td>
<td>Calcium phosphate stones</td>
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<tr>
<td>Hepatic Impairment</td>
<td>Watch for cholelithiasis</td>
<td>Hepatic metabolism of drug</td>
<td>Do not exceed 7.5 mg/46 mg per day</td>
<td>Do not exceed 8 mg/90 mg in AM</td>
<td>Watch for cholelithiasis</td>
</tr>
<tr>
<td>Mild-Moderate (Child-Pugh 5–9)</td>
<td>Do not exceed 8 mg/90 mg in AM</td>
<td>Not recommended</td>
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<tr>
<td>Severe (Child-Pugh &gt;9)</td>
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<td>Depression</td>
<td>Insufficient safety data</td>
<td>Avoid maximum dose 15 mg/92 mg per day</td>
<td>Insufficient safety data</td>
<td>Avoid in adolescents and young adults</td>
<td>Insufficient safety data</td>
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<tr>
<td>CLINICAL CHARACTERISTICS OR COEXISTING DISEASES</td>
<td>MEDICATIONS FOR CHRONIC WEIGHT MANAGEMENT</td>
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<tr>
<td></td>
<td>Orlistat</td>
<td>Lorcanerin</td>
<td>Phentermine/topiramate ER</td>
<td>Naltrexone ER/bupropion ER</td>
<td>Liraglutide 3 mg</td>
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<td>Anxiety</td>
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<td>Psychoses</td>
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<td>Binge Eating Disorder</td>
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<td>Glaucoma</td>
<td>Contraindicated, may trigger angle closure</td>
<td>May trigger angle closure</td>
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<tr>
<td>Seizure Disorder</td>
<td>If discontinue at dose of 15 mg/92 mg, taper slowly</td>
<td>Bupropion lowers seizure threshold</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Pancreatitis</td>
<td>Monitor for symptoms</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Opioid Use</td>
<td>Will antagonize opioids and opiates</td>
<td></td>
<td></td>
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<tr>
<td>Women of Reproductive Potential</td>
<td>Use contraception and discontinue orlistat should pregnancy occur</td>
<td>Use contraception and discontinue lorcanerin should pregnancy occur</td>
<td>Use contraception and discontinue phentermine/topiramate should pregnancy occur (perform monthly pregnancy checks to identify early pregnancy)</td>
<td>Use contraception and discontinue naltrexone ER/bupropion ER should pregnancy occur</td>
<td>Use contraception and discontinue liraglutide 3mg should pregnancy occur</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>Not recommended</td>
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<td>Not recommended</td>
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<tr>
<td>Breast-feeding</td>
<td>Not recommended</td>
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<td>Age ≥65 years *</td>
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<td>Limited data available</td>
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</tr>
<tr>
<td>Alcoholism/Addiction</td>
<td>Might have abuse potential due to euphoria at high doses</td>
<td>Insufficient data</td>
<td>Avoid due to seizure risk and lower seizure threshold on bupropion</td>
<td></td>
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<tr>
<td>Post-Bariatric Surgery</td>
<td>Insufficient data</td>
<td>Insufficient data</td>
<td>Limited data available</td>
<td>Insufficient data</td>
<td>Data available at 1.8 – 3.0 mg/day</td>
</tr>
</tbody>
</table>

* Use medications only with clear health-related goals in mind; assess patient for osteoporosis and sarcopenia.

Abbreviations: BP = blood pressure; CAD = coronary artery disease; CHF = congestive heart failure; HTN = hypertension; T2DM = Type 2 Diabetes Mellitus.
Q7.4. Are there differences in weight-loss drug efficacy and safety?

- **R80.** In selecting the optimal weight-loss medication for each patient, clinicians should consider differences in efficacy, side effects, cautions, and warnings that characterize medications approved for chronic management of obesity, as well as the presence of weight-related complications and medical history; these factors are the basis for individualized weight-loss pharmacotherapy; a generalizable hierarchical algorithm for medication preferences that would be applicable to all patients cannot currently be scientifically justified (Grade A; BEL 1).

- **R81.** Clinicians and their patients with obesity should have available access to all approved medications to allow for the safe and effective individualization of appropriate pharmacotherapy (Grade D).
DIAGNOSIS AND MEDICAL MANAGEMENT OF OBESITY

a. All patients with BMI ≥ 25 have either overweight stage 0, obesity stage 0, obesity stage 1, or obesity stage 2, depending on the initial clinical evaluation for presence and severity of complications. These patients should be followed over time and evaluated for changes in both anthropometric and clinical diagnostic components. The diagnoses of overweight/obesity stage 0, obesity stage 1, and obesity stage 2 are not static, and disease progression may warrant more aggressive weight-loss therapy in the future. BMI values ≥ 25 have been clinically confirmed to represent excess adiposity after evaluation for muscularity, edema, sarcopenia, etc.
b. Stages are determined using criteria specific to each obesity-related complication; stage 0 = no complications; stage 1 = mild-to-moderate; stage 2 = severe.
c. Treatment plans should be individualized; suggested interventions are appropriate for obtaining the sufficient degree of weight loss generally required to treat the obesity-related complication(s) at the specified stage of severity.
d. BMI ≥ 27 is consistent with the prescribing information mandated by the US Food and Drug Administration for weight-loss medications.

Abbreviation: BMI = body mass index.
George: Routine Follow-Up and Weight Concerns

<table>
<thead>
<tr>
<th>History</th>
<th>Lifestyle/ Psychosocial</th>
<th>Current Medications</th>
</tr>
</thead>
</table>
| • White man (aged 57 yr)  
• Referred for evaluation of possible hypogonadism  
• CC: low energy, fatigue, feels weak  
• Hx: HTN, dyslipidemia, depression  
• Stent 18 mo ago; no symptoms of angina  
• States that he would like help in losing weight | • US Postal Service employee  
• Divorced (2 y)  
• 2 adult children and 1 grandchild  
• Has tried Atkins diet with initial weight loss but regained weight within a year  
• Membership to YMCA and works out 1x/wk (elliptical, Nautilus) | • Losartan/HCTZ: 100 mg/25 mg once daily  
• Atorvastatin: 40 mg once daily  
• Aspirin: 81 mg once daily  
• Duloxetine: 60 mg once daily |

DSME, diabetes self-management education.
# George: Clinical data

## Physical Examination

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Height</td>
<td>70 in (178 cm)</td>
</tr>
<tr>
<td>Weight</td>
<td>245 lb (111 kg); waist (43 in)</td>
</tr>
<tr>
<td>BMI</td>
<td>35.2 kg/m(^2) (confirm excess adiposity)</td>
</tr>
<tr>
<td>BP</td>
<td>146/88 mm Hg</td>
</tr>
</tbody>
</table>

## Laboratory Evaluation

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Fasting blood glucose</td>
<td>98 mg/dL</td>
</tr>
<tr>
<td>Lipids</td>
<td>LDL 106, HDL 38, TG 155 mg/dL</td>
</tr>
<tr>
<td>TSH</td>
<td>1.145 mIU/L</td>
</tr>
<tr>
<td>Testosterone</td>
<td>Total T 285 ng/dl, free T 17, SHBG 30 nmol/L</td>
</tr>
<tr>
<td>LFTs</td>
<td>AST 44 U/L   ALT 112 U/L   GGT and bili WNL</td>
</tr>
<tr>
<td>CBC, electrolytes</td>
<td>normal</td>
</tr>
<tr>
<td>eGFR</td>
<td>(\geq 92) mL/min/1.73 m(^2)</td>
</tr>
</tbody>
</table>
George: Initial Summary

• Adiposity Based Chronic Disease (ABCD)
  – Anthropometric BMI 35 with excess adiposity
  – Clinical, Stage 1 (mild-moderate weight-related complications)

• Metabolic Syndrome

• Hypertension, suboptimal control on 2 drugs

• Elevated LFTs, R/O NAFLD

• CVD, S/P stent, asymptomatic

• LDL-c not at target

• Fatigue, etiology not clear

You exclude diagnosis of hypogonadism based on symptoms, exam, and hormonal testing
What is your initial treatment plan for George?

1. Recommend that he re-initiate Atkins diet based on previous success, and recruit a friend to join him in increasing his physical activity at the YMCA.

2. Add a calcium channel blocker, increase atorvastatin to 80 mg/day, recommend that he work out at the YMCA at least 3x/week

3. Participate in a structured commercial or community-based program of comprehensive lifestyle management including a reduced calorie diet

4. Participate in a commercial or community-based program of comprehensive lifestyle management and add a weight loss medication

5. Schedule bariatric surgery consult
You elect to start George on a structured lifestyle intervention: low-carb diet, 1800 kcal/day and 3 times/week aerobic + resistance exercise at the YMCA.

1. After 2 months he has lost 5 lbs but having a hard time losing more. His blood pressure is better at 140/80.

2. You order an imaging study of the liver which shows hepatic steatosis.

3. Because you suspect sleep apnea may be contributing to his fatigue, you obtain a polysomnographic study which shows AHI value of 42.

As a result of the additional data, you alter his obesity diagnosis to ABCD Stage 2 (severe complications).
You now add a weight loss medication to his structured lifestyle intervention. Which medication for long-term weight management would be best for George given his clinical profile?

1. Lorcaserin
2. Naltrexone ER/bupropion ER
3. Liraglutide 3 mg
4. Orlistat
5. Phentermine/topiramate ER
How much weigh loss do you need to treat George’s ABCD complications (Stage 2)?

– HTN
– NAFLD
– Obstructive Sleep Apnea
Presence and Severity of Sleep Apnea in Patients with Obesity and T2DM

Mean BMI = 36.7
Mean HbA1c = 7.2%


AHI=apnea-hypopnea index
Obstructive Sleep Apnea

Psychology/Behavior
- Fatigue, irritability
- Depression
- Poor cognitive function
- Decreased libido/ED
- Depression
- Auto accidents

Cardiovascular
- MI
- Stroke
- Sudden death
- Cardiac arrhythmias
- HTN
- CHF
- Pulmonary HTN

Metabolic
- Insulin resistance
- Metabolic Syndrome
- Diabetes
- PCOS
- Obesity

Sleep Apnea Consequences and Associations
Staging the Severity of Obstructive Sleep Apnea

Apnea Hypopneea Index

<5  No Sleep Apnea

5-14  Mild Sleep Apnea

15-29  Moderate Sleep Apnea

≥ 30  Severe Sleep Apnea

Ruehland WR et al, Sleep 32:150-157, 2009
Changes in weight and AHI by treatment group

DSE = Diabetes support and education
ILI = Intensive lifestyle intervention

AHI = apnea-hypopnea index

Stable (±5 kg)

Gain (≥5 kg)

Loss (5-9.9 kg)

Loss (≥10 kg)

P < 0.001

ILI = Intensive lifestyle intervention
DSE = Diabetes support and education
AHI = apnea-hypopnea index

Effects of Phentermine/Topiramate ER-Induced Weight Loss in Patients with Sleep Apnea

Winslow DH et al, Sleep 35:1529-1539, 2012

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Placebo (n = 23)</th>
<th>Topiramate 92 mg (n = 22)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AHI, events/h (SD)</td>
<td>45.2 (34.25)</td>
<td>44.2 (22.40)</td>
</tr>
<tr>
<td>RDI, events/h (SD)</td>
<td>60.7 (31.78)</td>
<td>58.8 (21.24)</td>
</tr>
<tr>
<td>Mean overnight oxygen saturation, % (SD)</td>
<td>93.9 (2.39)</td>
<td>93.4 (1.99)</td>
</tr>
<tr>
<td>Minimum overnight oxygen saturation, % (SD)</td>
<td>76.3 (13.88)</td>
<td>77.1 (13.59)</td>
</tr>
<tr>
<td>Arousal index, arousals/h (SD)</td>
<td>63.5 (30.49)</td>
<td>61.5 (20.27)</td>
</tr>
<tr>
<td>Apnea index, events/h (SD)</td>
<td>16.1 (24.23)</td>
<td>9.4 (15.95)</td>
</tr>
<tr>
<td>Hypopnea index, events/h (SD)</td>
<td>29.1 (18.78)</td>
<td>34.8 (18.76)</td>
</tr>
</tbody>
</table>
Improvements in Sleep Apnea with Phentermine/Topiramate ER Therapy

Change in Apnea/Hypopnea Index

Change in Body Weight

Winslow DH et al, Sleep, 35:1529, 2012
Recommendations pertaining to pharmacological therapy in patients with obesity and obstructive sleep apnea; cardiovascular disease

- R55. Patients with overweight or obesity and obstructive sleep apnea should be treated with weight-loss therapy including lifestyle interventions and additional modalities as needed, including phentermine/topiramate ER or bariatric surgery; the weight-loss goal should be at least 7% to 11% or more.

- R94. In patients with established cardiovascular disease, orlistat and lorcaserin are preferred weight-loss medications (Grade A; BEL 1). Liraglutide 3 mg, phentermine/topiramate ER, and naltrexone ER/bupropion ER are reasonable to use with caution .... with careful monitoring of heart rate and blood pressure (Grade A; BEL 1). Cardiovascular outcome trials are planned or ongoing for all weight-loss medications except orlistat.
In Summary

• AACE Obesity Guidelines constitute an evidenced based model for patient care that encompasses screening, diagnosis, staging, treatment decisions, goals of therapy, and follow-up.

• Establishes a diagnostic approach that incorporates both an assessment of adiposity and the impact of excess adiposity on health as manifest by weight-related complications.

• Guides treatment modality and intensity based on the phases of chronic disease prevention and treatment, and the risk, presence, and severity of weight-related complications.

• Establishes desired outcomes and goals of therapy that do not simply reflect the amount of weight lost but the improvements in patient health.

• Emphasizes a patient-centric approach for individualization of therapy to optimize effectiveness, patient safety, and the benefit/risk ratio.

• A model that can be rationally adopted by health care systems with integration into overall portfolios of patient care.
Thank You

Hippocrates

“Corpulence is not only a disease itself, but the harbinger of others.”