Obesity Management in Primary Care

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Which of these best characterizes your beliefs about obesity treatment?

A. Obesity is a medical condition; it is the healthcare provider’s responsibility to ensure that patients are counseled and receive treatment for obesity

B. Obesity is a personal issue; it is the patient’s responsibility to ensure that he/she gets the help they need

C. Obesity is both a medical and personal issue; the responsibility for addressing obesity is shared between healthcare providers and patients

D. Obesity is an issue of personal responsibility and willpower; patients should take better care of themselves and not burden the healthcare system
An Obesity Paradox

Whose responsibility is it to ensure that a patient is counseled about obesity? (% Responding, single mention)

- Both patient and provider responsibility: 66% PCPs (N=1000), 61% OB-GYNs (N=250), 66% NPs (N=251)
- It is my responsibility: 31% PCPs, 36% OB-GYNs, 33% NPs
- It is the patient’s responsibility: 2% PCPs, 1% OB-GYNs, 0% NPs
- Responsibility of other provider or referral: 1% PCPs, 2% OB-GYNs, 1% NPs

An Obesity Paradox

When HCPs Talk to Patients About Weight...

- 6-8x increased likelihood of correctly perceiving excess weight status
- 2-3x increased likelihood of having obesity management plan in place
- 3-4x increased likelihood of attempting weight loss
- 2x increased likelihood of losing >5% body weight
- Improved weight loss, weight loss maintenance, weight-related behaviors, weight-related comorbidities

Kahan, Petrin 2017 (submitted); Post 2011; Jackson 2013; Rose 2013; Bardia 2007; Pool 2014; McTigue 2003; Moyer 2012; Digenio 2009.
Current Practice: (Under-whelming)

• Under-diagnosis
  – BMI 30-35: 10.2% diagnosed
  – BMI >50: 56.8%

• Under-documentation
  – 34% of 33,718 patients with severe obesity

• Under-discussion
  – 54% with BMI >25 told of excess weight
  – 2% of PCPs discussed recorded BMI with patients

• Under-counseling
  – 67% with severe obesity receive weight loss advice
  – Weight discussions last as little as 55 seconds

Current Practice: Under-Treatment

Today

• Obesity epidemiology and background
• Why is it so hard to lose/maintain weight?
• Key clinical guidelines for obesity management
• Evidence-based treatment options for obesity
Prevalence of Obesity in US Adults

CDC/NCHS, NHANES 2007-2010.
320,000 Deaths/Year Attributable to Obesity

Obesity Strongly Impairs Quality of Life

Why Is It So Hard To Manage Weight?

Effect of Weight Loss on Satiety

Before Meal
- Baseline Weight
- Weight-10%

After Meal
- How full?
- How much eaten?
Hormone Changes and Hunger Persistently Oppose Weight Loss

Effect of Weight Loss on EE

CDC Framework for Addressing Obesity

- Home & Family
- School
- Community
- Work Site
- Healthcare

- Genetics
- Psychosocial
- Other Personal Factors

- Food and Beverage Industry
- Agriculture
- Education
- Media
- Government
- Public Health Systems
- Healthcare Industry
- Business and Workers
- Land Use and Transportation
- Leisure and Recreation

Social Norms and Values
Sectors of Influence
Behavioral Settings
Individual Factors

Food and Beverage Intake
Physical Activity

Energy Intake
Energy Expenditure
Energy Balance
Key Obesity Guidelines

AHA/ACC/TOS Guidelines for Managing Overweight and Obesity in Adults

Pharmacologic Management of Obesity: An Endocrine Society Clinical Practice Guideline

“Modest, sustained weight loss of 3-5% produce clinically meaningful health benefits, and greater weight loss produces greater benefits”

Adults with Obesity and Pre-Diabetes (n=3234)

Behavioral Therapy (1079)  Metformin (1073)  Placebo (1082)

Modest Weight Loss Improves Health and Health Risks

- Placebo
- Metformin
- Lifestyle intervention

Modest Weight Loss Improves Health and Health Risks

Modest Weight Loss Improves Health and Health Risks

Benefits of 5–10% weight loss

- Reduced risk of T2DM
- Reduced CV risk factors
- Improved lipid profile
- Improved blood pressure
- Improved sleep apnea
- Improved quality of life

Modest Weight Loss Improves Health and Health Risks

<table>
<thead>
<tr>
<th>OBESITY COMPLICATION</th>
<th>% wt loss for Rx benefit</th>
<th>Notes</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>T2DM Prevention</td>
<td>3-10%</td>
<td>Maximum benefit at 10%</td>
<td>DPP (Lancet, 2009) SEQUEL (Garvey et al, 2013)</td>
</tr>
<tr>
<td>T2DM (HbA1c)</td>
<td>3-15%</td>
<td>HA1c still decreasing at &gt;15%</td>
<td>Look AHEAD (Wing, 2011)</td>
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<tr>
<td>Dyslipidemia (TG/HDL)</td>
<td>3-15%</td>
<td>TG still decreasing at &gt;15%</td>
<td>Look AHEAD (Wing, 2011)</td>
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<tr>
<td>HTN</td>
<td>5-15%</td>
<td>BP still decreasing at &gt;15%</td>
<td>Look AHEAD (Wing, 2011)</td>
</tr>
<tr>
<td>NAFLD</td>
<td>10%</td>
<td>Improved steatosis, inflammation, mild fibrosis</td>
<td>Assy et al, 2007; Dixon et al, 2004; Anish et al, 2009</td>
</tr>
<tr>
<td>Sleep Apnea</td>
<td>10%</td>
<td>Little benefit at ≤ 5%</td>
<td>SleepAHEAD (Foster, 2009) Winslow et al, 2012</td>
</tr>
<tr>
<td>Osteoarthritis</td>
<td>5-10%</td>
<td>Improved symptoms and joint stress mechanics</td>
<td>Christensen et al, 2007 Felson et al, 1992; Aaboe et al, 2011</td>
</tr>
<tr>
<td>Stress Incontinence</td>
<td>5-10%</td>
<td></td>
<td>Burgio et al, 2007 Leslee et al, 2009</td>
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<tr>
<td>GERD</td>
<td>5-10% (F) 10% (M)</td>
<td></td>
<td>Singh et al, 2013 Tutujiyan R, 2011</td>
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</tbody>
</table>
Clinical Obesity Treatment Modalities

• Self-directed management
• Intensive behavioral therapy
• Structured or medically monitored diets
• Pharmacotherapy
• Medical devices
• Surgical therapy
Clinical Obesity Treatment Modalities

- Self-directed management
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- Medical devices
- Surgical therapy
Guidelines For Behavioral Therapy

• Patients who need to lose weight should receive a comprehensive behavior management program of at least 6 mo (Level A)
• Gold standard is on-site, high-intensity (14+ sessions during initial 6 mo) comprehensive intervention, either individually or in a group setting, delivered by trained interventionist and persisting for at least 1 year (Level A)
• Low-moderate intensity primary care interventions have not been shown to be effective (Level A)
• Other approaches (e.g., web- or phone-based) lead to less weight loss and health improvement (Level B)

# Behavioral Therapy for Obesity

| Counseling | • Regular interaction via group or individual contact  
|            |   – Intensive initial counseling frequency |
| Diet       | • Calorie-reduced diet  
|            |   – 1200-1500 kcal for <250 lb; 1500-1800 kcal for ≥250 lb |
| Physical activity | • 150 minutes/week of moderate activity  
|            |   • Strength training desirable |
| Behavioral strategies | • Structured curriculum of behavior change education, including identifying target behaviors and building skills to achieve target behaviors  
|            | • Self-monitoring of food intake, physical activity, and/or weight  
|            | • Goal setting, problem solving, stimulus control  
|            | • Addressing barriers to change  
|            | • Behavioral resources (e.g., portion controlled meals)  
|            | • Regular feedback and guidance from an interventionist  
|            | • Weight maintenance strategies and relapse prevention |
Behavioral Therapy in Patients with Obesity and Diabetes

Comorbidity Improvements With Behavioral Therapy

What About When Standard Behavioral Therapy Isn’t Enough?

• How do we escalate treatment for those who don’t respond to standard behavioral therapy?

• How do we enhance initial weight loss for those who don’t achieve sufficient weight loss to improve health status/risks?

• How do we enhance longer-term weight maintenance and minimize regain?
Clinical Obesity Treatment Modalities

- Self-directed management
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- Pharmacotherapy
- Medical devices
- Surgical therapy
Very Low Calorie Diet with Meal Replacement Products
Clinical Obesity Treatment Modalities

• Self-directed management
• Intensive behavioral therapy
• Structured or medically monitored diets
• Pharmacotherapy
• Medical devices
• Surgical therapy
Which of these best characterizes your beliefs about obesity medications?

A. Weight loss medications are extremely effective; all patients who need to lose a lot of weight should be prescribed medications

B. Weight loss medications are somewhat effective; some, but far from all, patients who need to lose a lot of weight should be prescribed medications

C. Obesity is best treated with judicious diet and exercise behaviors; medications should be avoided as much as possible

D. Weight loss medications don’t work; they should be avoided

E. Weight loss medications are unsafe; they should be avoided
Effect of Weight Loss on Satiety

**Before Meal**
- Baseline Weight
- Weight-10%

**After Meal**
- Baseline Weight

Guidelines For Pharmacotherapy

• Use pharmacotherapy as adjunct to diet, exercise, and behavioral counseling for adults... (Level 1, strong evidence)
  – with BMI 30+; or 27+ with comorbidity;
  – who are unable to lose and successfully maintain weight;
  – who meet label indications

• Assess efficacy and safety monthly for the first 3 months, then every 3 months thereafter (Level 2, weak evidence)

• At 3 months, if loss is 5% or more, continue; if not, discontinue and seek alternative approaches (Level 1, strong evidence)

• Use medications to promote long-term weight loss maintenance (Level 2, weak evidence)

• Use weight-losing and weight-neutral medications as first and second line therapy and discuss weight effects of medications with patients (Level 1, strong evidence)

Obesity Pharmacotherapy

• 4 FDA-approved short-term medications
  – Phentermine accounts for 99% of short-term Rx’s

• 5 FDA-approved long-term medications
  – Orlistat (Xenical/Alli)
  – Phentermine/topiramate ER (Qsymia)
  – Lorcaserin (Belviq)
  – Naltrexone/Bupropion SR (Contrave)
  – Liraglutide 3.0 mg (Saxenda)

• Off-label options
Pharmacotherapy Increases Magnitude and Likelihood of Weight Loss

Pharmacotherapy Increases Magnitude and Likelihood of Weight Loss

Long-term Outcomes - 2 Years

Long-term Outcomes - 3 Years

Long-term Outcomes - 4 Years

Long-term Outcomes - 8 Years

Long-Term Benefits Require Long-Term Use

Outcomes by Responder Status

Pharmacotherapy Improves Weight Maintenance

Combination Therapy

**Pharmacotherapy Improves RFs and Prevents Comorbid Conditions**

<table>
<thead>
<tr>
<th></th>
<th>Orlistat</th>
<th>Lorcaserin</th>
<th>Phentermine/topiramate ER</th>
<th>Naltrexone/bupropion SR</th>
<th>Liraglutide 3.0 mg</th>
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<td>LDL</td>
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### Progression to Diabetes

<table>
<thead>
<tr>
<th>Medication</th>
<th>Medication (%)</th>
<th>Placebo (%)</th>
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<tbody>
<tr>
<td><strong>Lorcaserin</strong>&lt;br&gt;(BLOOM/BLOSSOM)</td>
<td>2</td>
<td>3</td>
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<tr>
<td><strong>Phentermine-tpx</strong>&lt;br&gt;(2 years) (SEQUEL)</td>
<td>&lt;1</td>
<td>4</td>
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<tr>
<td><strong>Liraglutide</strong>&lt;br&gt;(3 years) (SCALE)</td>
<td>3</td>
<td>11</td>
</tr>
<tr>
<td><strong>Orlistat</strong>&lt;br&gt;(4 years) (XENDOS)</td>
<td>2.9</td>
<td>4.2</td>
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</table>
## Completion and Discontinuation

<table>
<thead>
<tr>
<th>Medication</th>
<th>Placebo</th>
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<tbody>
<tr>
<td>Lorcaserin (BLOOM)</td>
<td>55</td>
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<tr>
<td>Naltrexone-Bupropion (COR-1)</td>
<td>50</td>
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<tr>
<td>Phentermine-tpx (CONQUER)</td>
<td>61</td>
</tr>
<tr>
<td>Liraglutide (SCALE)</td>
<td>72</td>
</tr>
<tr>
<td>Orlistat (XENDOS)</td>
<td>52</td>
</tr>
</tbody>
</table>
Long-Term Cardiovascular Safety

Long-Term Cardiovascular Safety

Death from Cardiovascular Causes

Hazard ratio, 0.78 (95% CI, 0.66–0.93)
P=0.007

Phentermine

• Sympathomimetic amine, blunts appetite
• Approved in 1959 for short-term use, schedule IV
• Dosing: 8 to 37.5 mg qAM; use lowest effective dose
• Contraindications: pregnancy, nursing, MAOIs, glaucoma, drug abuse history, hyperthyroidism
• Relative contraindications: uncontrolled hypertension, tachycardia, history of CAD, CHF, stroke, arrhythmia
• Warnings: primary pulmonary hypertension, valvular heart disease, tolerance, risk of abuse, alcohol

Orlistat

- Lipase inhibitor, decreases fat absorption
- Approved 1999; long-term use
- Not scheduled
- 120 mg TID with meals (Rx) or 60 mg TID (OTC)
- Use MVI with fat-soluble vitamins at bedtime
- Contraindications: pregnancy, chronic malabsorption syndrome, cholestasis
- Possible gastrointestinal adverse events
Lorcaserin

- Selective 5-HT2C receptor agonist
- Increases satiety
- Approved in 2012 for long-term use; schedule IV
- Single dose: 10 mg BID
- Contraindications: pregnancy
- Warnings: co-administration with serotonergic or antidopaminergic agents, valvular heart disease, psychiatric disorders (euphoria, suicidal thoughts, depression), priapism
- Discontinue if <5% weight loss after 12 weeks of use

Lorcaserin:
Outcomes by Responder Status

LOR = lorcaserin; PBO = placebo.
Phentermine/Topiramate ER

- Phentermine: sympathomimetic amine; blunts appetite
- Topiramate: increases GABA activity, carbonic anhydrase inhibitor, other; prolongs satiety
- Approved in 2012 for long-term use; schedule IV
- “Recommended” dose: 7.5/46 mg; max: 15/92 mg
- Discontinue if less than 3% weight loss after 12 weeks
- Contraindications: pregnancy (REMS), glaucoma, MAOIs, hyperthyroidism
Naltrexone SR/Bupropion SR

- Bupropion: dopamine/NE reuptake inhibitor
- Naltrexone: opioid receptor antagonist; blocks autoinhibition of POMC neurons and amplifies the effect of bupropion
- Not a controlled substance
- Standard dose: 32/360 mg (2 BID)
- Discontinuation if <5% weight loss after 16 weeks
- Black box warning for suicidal thoughts in adolescents
- Contraindications: pregnancy, MAOIs, uncontrolled hypertension, seizure disorders, chronic opioid use

Contrave (naltrexone SR/bupropion SR) prescribing information. Orexigen Therapeutics, La Jolla, CA.
Liraglutide 3.0 mg

- Glucagon-like peptide 1 (GLP-1) receptor agonist
- Liraglutide 1.8 mg FDA-approved in 2010 for T2DM
- Liraglutide 3.0 mg FDA-approved for primary indication of obesity in December 2014
- Not a controlled substance
- Dosing: weekly escalation by 0.6 mg SC
- Discontinue if <4% weight loss at 16 weeks
- REMs: medullary thyroid carcinoma, acute pancreatitis
Choosing Between Options

Choosing Between Options

**Drug factors**
- Contraindications
- Dual benefits
- Studied populations

**Patient factors**
- Patient preferences
- Adverse events
- Prior experiences
- Access

**Physician factors**
- Provider knowledge/comfort
## Contraindications and Cautions

<table>
<thead>
<tr>
<th>Clinical Scenario</th>
<th>Avoid/Caution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevated seizure risk</td>
<td>Naltrexone/bupropion</td>
</tr>
<tr>
<td>History of recurrent kidney stones</td>
<td>Phentermine/topiramate, orlistat</td>
</tr>
<tr>
<td>History of glaucoma</td>
<td>Phentermine/topiramate</td>
</tr>
<tr>
<td>Uncontrolled hypertension</td>
<td>Naltrexone/bupropion, phentermine</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>Phentermine</td>
</tr>
<tr>
<td>Moderate-to-severe renal impairment</td>
<td>Do not exceed half-dose: phentermine/topiramate, naltrexone/bupropion</td>
</tr>
<tr>
<td></td>
<td>Caution: liraglutide, lorcaserin</td>
</tr>
<tr>
<td>Moderate-to-severe hepatic impairment</td>
<td>Do not exceed half-dose: phentermine/topiramate, naltrexone/bupropion</td>
</tr>
<tr>
<td></td>
<td>Do not exceed one-quarter dose: naltrexone/bupropion</td>
</tr>
<tr>
<td></td>
<td>Caution: liraglutide, lorcaserin</td>
</tr>
<tr>
<td>SSRI use</td>
<td>Caution: lorcaserin</td>
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</tbody>
</table>

SSRI = selective serotonin reuptake inhibitor.
# Dual Benefits

<table>
<thead>
<tr>
<th>If Patient has Obesity and...</th>
<th>Consider (But not Explicitly Approved)...</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking</td>
<td>Naltrexone/bupropion</td>
</tr>
<tr>
<td>Depression</td>
<td>Naltrexone/bupropion</td>
</tr>
<tr>
<td>Migraines</td>
<td>Phentermine/topiramate ER</td>
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<td>Diabetes</td>
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<tr>
<td>Chronic constipation</td>
<td>Orlistat</td>
</tr>
<tr>
<td>Elevated LDL</td>
<td>Orlistat</td>
</tr>
</tbody>
</table>
Studied populations

- Adolescents
- Older adults
- Post-pregnancy
- Menopause
- Post-bariatric surgery
- Extreme obesity
Patients with Extreme Obesity (BMI >45)

Choosing Between Options

**Drug factors**
- Contraindications
- Dual benefits
- Studied populations

**Patient factors**
- Patient preferences
- Adverse events
- Prior experiences
- Access

**Physician factors**
- Provider knowledge/comfort
Few Eligible Patients Are Prescribed Obesity Pharmacotherapy

# Prioritize Weight-Losing or Weight-Neutral Medications

<table>
<thead>
<tr>
<th>Category</th>
<th>Weight Gain Associated With Use</th>
<th>Alternatives (Weight Reducing in Parentheses)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>Insulin, sulfonylureas, TZDs, mitiglinide</td>
<td>(Metformin), (acarbose), (miglitol), (pramlintide), (exenatide), (liraglutide), (SGLT2 inhibitors)</td>
</tr>
<tr>
<td>Hypertension medications</td>
<td>β-blocker</td>
<td>ACE inhibitors, calcium channel blockers, angiotensin-2 RAs</td>
</tr>
<tr>
<td>Antidepressants and mood stabilizers</td>
<td>Amytriptyline, doxepin, imipramine, nortriptyline, trimipramine, mirtazapine, paroxetine</td>
<td>(Bupropion), nefazodone, fluoxetine</td>
</tr>
<tr>
<td>Oral contraceptives</td>
<td>Progestational steroids</td>
<td>Barrier methods, intrauterine devices</td>
</tr>
</tbody>
</table>

Clinical Obesity Treatment Modalities

- Self-directed management
- Behavioral tools
- Intensive behavioral therapy
- Structured or medically monitored diets
- Pharmacotherapy
- Medical devices
- Surgical therapy
Which of these best characterizes your beliefs about bariatric surgery?

A. Bariatric surgery is extremely effective and safe; all patients who need to lose a lot of weight should strongly consider surgery

B. Bariatric surgery is somewhat effective and safe; many, but far from all, patients who need to lose a lot of weight should consider surgery

C. Obesity is best treated with judicious diet and exercise behaviors; surgery should be avoided as much as possible

D. Bariatric surgery doesn’t work – I’ve seen people regain all their weight; surgery should be avoided

E. Bariatric surgery is unsafe; it should be avoided
Guidelines For Bariatric Surgery

• Advise patients with BMI $\geq 40$ (or $\geq 35$ with comorbidity) that bariatric surgery may be an appropriate option to improve health (Grade A)
• Offer referral to an experienced bariatric surgeon for consultation and evaluation (Grade A)
• Insufficient evidence to recommend for or against surgery for BMI $<35$
• No clear guidance for medical devices

Medical Devices for Obesity Treatment

VBLOC

Gastric Balloons

Gastric Band

Bariatric Surgery

Sleeve Gastrectomy

Roux-en-Y Gastric Bypass
Bariatric Surgery Has Long Term Data

Bariatric Surgery Improves Mortality

Trajectories of Weight Change After Surgery

Combining Modalities Works Better

Adapted from Wadden, et al. NEJM, 2005.
Combining Modalities Works Better

Combining Modalities Works Better

- Surgery
- Medication

25% BWL
40% BWL
Today

• Obesity epidemiology and background
• Why is it so hard to lose/maintain weight?
• Key clinical guidelines for obesity management
• Evidence-based treatment options for obesity
Thank you

Scott Kahan, MD, MPH
kahan@jhu.edu