Obesity: Office Evaluation and Management

Oklahoma Chapter Scientific Meeting
October 20, 2017

Andria P. Medina, MD, PhD
Relevant Disclosure and Resolution

Under Accreditation Council for Continuing Medical Education guidelines disclosure must be made regarding relevant financial relationships with commercial interests within the last 12 months.

Andria P. Medina

<table>
<thead>
<tr>
<th>Commercial Interest</th>
<th>Nature of Relevant Financial Relationship What was received?</th>
<th>Nature of Relevant Financial Relationship For what role?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daiichi Sankyo</td>
<td>Travel Support</td>
<td>Consultant</td>
</tr>
</tbody>
</table>

The conflict was resolved by: Not applicable to this presentation.
Practice gap: Internal medicine residents and practicing physicians have indicated less than optimal levels of training and competency in various aspects of obesity assessment and management.
Objectives

• Understand the roles that patient identity and physician attitudes play in treating obesity.

• Know the key elements of evaluating a patient with obesity in the outpatient setting.

• Know when to initiate pharmacologic therapy for obesity.

• Become familiar with data about pharmacologic treatment of obesity.

• Know when to refer a patient with obesity.
Obesity by BMI Definition

<table>
<thead>
<tr>
<th>BMI (kg/m²)</th>
<th>Weight Category</th>
<th>Obesity Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>18.5-24.9</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>25-29.9</td>
<td>Overweight</td>
<td></td>
</tr>
<tr>
<td>30-34.9</td>
<td>Obese</td>
<td>Class I</td>
</tr>
<tr>
<td>35-39.9</td>
<td>Obese</td>
<td>Class II</td>
</tr>
<tr>
<td>40-49.9</td>
<td>Morbidly Obese</td>
<td>Class III</td>
</tr>
<tr>
<td>&gt; 50</td>
<td>Super Obese</td>
<td>Class IV</td>
</tr>
</tbody>
</table>
Prevalence$^1$ of Self-Reported Obesity Among U.S. Adults by State and Territory, BRFSS, 2011

$^1$ Prevalence estimates reflect BRFSS methodological changes started in 2011. These estimates should not be compared to prevalence estimates before 2011.

*Sample size <50 or the relative standard error (dividing the standard error by the prevalence) $\geq$ 30%.
Prevalence\(^1\) of Self-Reported Obesity Among U.S. Adults by State and Territory, BRFSS, 2012

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Prevalence of Self-Reported Obesity Among U.S. Adults by State and Territory, BRFSS, 2013

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Prevalence\(^1\) of Self-Reported Obesity Among U.S. Adults by State and Territory, BRFSS, 2015

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*Sample size <50 or the relative standard error (dividing the standard error by the prevalence) ≥ 30%.
Prevalence\textsuperscript{1} of Self-Reported Obesity Among U.S. Adults by State and Territory, BRFSS, 2016

\textsuperscript{1} Prevalence estimates reflect BRFSS methodological changes started in 2011. These estimates should not be compared to prevalence estimates before 2011.

*Sample size <50 or the relative standard error (dividing the standard error by the prevalence) \( \geq 30\% \).
Cause of Obesity - Energy Balance

- Food
- Drink
- Calories In

- Body functions
- Activity
- Calories Out
Cause of Obesity - Energy Balance
CONTRIBUTORS TO OBESITY

Inside the Person

- Disordered Eating (e.g., binge eating, 'food addiction?')
- Hyper-reactivity to Environmental Food Cues
- Heightened Hunger Response
- Emotional Coping

Outside the Person

- Increased Availability of Energy Dense, Nutrient Poor Foods & Beverages
- Lack of Nutritional Education
- Diet Patterns - Eating away from Home
- Larger Portion Sizes
- Food Insecurity
- Limiting Meals & Meals skiping
- Eating away from home
- Limiting meals
- Lack of Family Meals

- Environmental/Chemical Toxins
- Market Economy
- Food Surplus
- Pervasive Food Advertising

Contributors to Energy Storage

- Material Employment
- Birth Order (firstborn vs. lastborn)
- Having Children
- Weight Bias & Stigma
- Low SES & Nutrition Support
- Living in Crime-prone Areas

- Material Stress
- Maternal Obesity
- Maternal Smoking
- Maternal Over-nutrition During Pregnancy
- Maternal Smoking

- Increased Intake
- Material Stress
- Maternal Smoking

- Material Stress
- Maternal Obesity
- Maternal Over-nutrition During Pregnancy
- Maternal Smoking

- Consistent Temperature (e.g., air conditioning/heating, thermoregulation)
- Increased Sedentary Time (e.g., inactive work, inactive job requirements)
- Built Environment (e.g., street design, building design, absence of or poor sidewalks)
- Consistent Temperature (e.g., air conditioning/heating, thermoregulation)
- Increased Sedentary Time (e.g., inactive work, inactive job requirements)
- Built Environment (e.g., street design, building design, absence of or poor sidewalks)

Contributor/Influencer

- Environmental Pressures on Physical Activity
- Biological Medical
- Material Developmental
- Economic
- Food and Beverage Behavior/Environment
- Psychological
- Social

* Potential contributors indicate anything that has been identified in the research literature as a question of investigation and is not intended to be a verbatim of whether or not the causation to which each may or may not contribute.
Treatment Algorithm—Chronic Disease Management Model for Primary Care of Patients With Overweight and Obesity

- Measure weight and height; calculate BMI (see Box 2).
- Assess need to lose weight: BMI ≥ 30 or BMI 25–29.9 with risk factor(s) (see Box 5).
- Assess and treat risk factors for CVD and obesity-related comorbidities (see Box 4).
- Assess weight and lifestyle histories (see Box 5).
- Follow-up and weight loss maintenance (see Box 10).
- Intensive behavioral treatment (see Box 10); reassess and address medical or other contributory factors; consider adding or re-evaluating obesity pharmacotherapy (see Box 12); and refer to an experienced bariatric surgeon (see Box 13).
- Weight loss ≥ 5% and sufficient improvement in health targets (see Box 14).
- High-intensity comprehensive lifestyle intervention (see Box 11a).
- Alternative delivery of lifestyle intervention (see Box 11b).
- Weight loss ≥ 5% and sufficient improvement in health targets (see Box 14).
- BMI ≥ 30 or BMI ≥ 25 with comorbidity—option for adding pharmacotherapy as an adjunct to comprehensive lifestyle intervention (see Box 12b).
- BMI ≥ 30 or BMI ≥ 25 with obesity-related comorbidities—option for adding pharmacotherapy as an adjunct to comprehensive lifestyle intervention (see Box 12c).
- BMI ≥ 30 or BMI ≥ 25 with obesity-related comorbidities (see Box 5).
- No, insufficient risk.
BMI >30 or BMI 25-29.9 w/ risk factors

Risk Factors: Diabetes, pre-diabetes, hypertension, dyslipidemia, increased waist circumference, other obesity related conditions

Box 6: Assess Need to Lose Weight
YES: BMI ≥30 or BMI 25-29.9 with additional risk factor(s):
Weight loss treatment is indicated for 1) obese individuals and 2) overweight individuals with 1 indicators of increased cardiovascular risk (eg, diabetes, prediabetes, hypertension, dyslipidemia, elevated waist circumference) or other obesity-related comorbidities.

NO: BMI <25 or BMI 25-29.9 without additional risk.
Normal weight patients (BMI 18.5-24.9 kg/m²) should be advised to avoid weight gain (Box 7).
Patients who are overweight (BMI 25-29.9 kg/m²) who do not have indicators of increased cardiovascular risk (eg, diabetes, prediabetes, hypertension, dyslipidemia, elevated waist circumference) or other obesity-related comorbidities should be advised to avoid additional weight gain (Box 7).

Circulation, 2014;129:S102-S138
Measure height, weight – calculate BMI

Determine weight category

Assess CVD risk factors and obesity comorbidities

Assess weight and lifestyle
Weight promoting medications

- **Anti-psychotics**
  - Risperidone
  - Lithium
  - Quetipaine
  - Aripiprazole
  - Olazapine
  - Valproic Acid

- **Anti-depressants**
  - Citalopram
  - Duloxetine
  - Venlafaxine

- **Sleep aids**
  - Zolpidem
  - Trazadone

- **Neuropathic Agents**
  - Gabapentin
  - Pregabalin

- **Steroids**
- **B-blockers**
- **Insulin**
- **Hypoglycemic agents**
Physical exam

Clinical / Lab assessments (BP, waist, glucose, lipids)

Management of CVD risk factors and comorbidities

HTN, DLD, DM, Pre-DM, OSA, GERD, NAFLD, Stress incontinence, PCOS, OA, Psychologic disorder
Physical Exam Findings

• Skin:
  • Intertriginous rashes, hirsutism, acanthosis nigricans, skin tags, ulcerations

• Abdomen:
  • Tender RUQ, hepatomegaly, striae distensae (rubra → alba), panniculus morbidus

• Other:
  • OA, joint deformities, gait, fat distribution

• Waist to hip ratio (>1 men, >0.85 women)
• Waist circumference (>40” men, <35” woman)
“Normal-weight central obesity is associated with higher mortality than BMI-defined obesity, particularly in the absence of central fat distribution.”

"How prepared are you to make changes in your diet, to be more physically active, and to use behavior change strategies such as recording your weight and food intake?"

Lose 5-10% body weight in 6 months

*Circulation, 2014;129:S102-S138*
Comprehensive lifestyle intervention first, unless more intensive treatment is warranted.

→ Patients unable to lose weight or sustain weight loss and/or patients with BMI >30 or BMI >27 with comorbidities consider Rx and in patients with BMI >40 or BMI >35 with comorb. consider bariatric surgery referral.
Comprehensive Lifestyle Intervention

• Advise to lose weight
• Self help tools (apps, books, internet)
• Food journal
• Dietician
• Structured programs (Weight Watchers, OA, YMCA)
• High intensity sessions – group or individual
Dietary changes
Associations of fats and carbohydrate intake with cardiovascular disease and mortality in 18 countries from five continents (PURE): a prospective cohort study

Mahshid Dehghan, Andrew Mente, Xiaohua Zhang, Surmathi Swaminathan, Wei Li, Viswanathan Mohan, Romaina Iqbal, Rajesh Kumar, Edelweiss Wentzel-Viljoen, Annika Rosengren, Leela Itty Amma, Alvaro Avezum, Jephath Chifthomba, Rafael Diaz, Rasha Khatib, Scott Lear, Patricia Lopez-Jaramillo, Xiaoyun Liu, Rajeev Gupta, Noushin Mohammadi, Nan Gao, Aytekin Ozgu, Anis Safi, Rameb Serron, Yi Sun, Andrze Szuba, Lungiswa Tsolekile, Andreas Wielgosz, Rita Yusuf, Azfar Hussein Yusufali, Koon K Teo, Surmathy Ranganathan, Gilles Dagenais, Shrikant I Bangdiwala, Shofiqul Islam, Sonia S Anand, Salim Yusuf, and the PURE study investigators

www.thelancet.com  Published online August 29, 2017

 PURE Shakes Up Nutritional Field: Finds High Fat Intake Beneficial

Sue Hughes
August 29, 2017

BARCELONA, SPAIN — A new study of dietary habits around the world is set to shake up the nutritional world. High fat intake—including saturated fat—was associated with lower mortality.
PURE STUDY DESIGN

• Prospective Urban Rural Epidemiology Study
• Recorded dietary intake of 135,335 people, aged 35–70 yrs from 2003-2013
• 18 countries, across all socioeconomic groups
• Median follow-up of 7.4 years
• Primary outcomes - total mortality and major cardiovascular events
  • fatal CVD, non-fatal MI or stroke, and heart failure
• Secondary outcomes - all MI, stroke, CVD mortality, and non-CVD mortality
• Divided by quintiles of nutrient intake (carbohydrate, fats, and protein) based on percentage of energy provided by nutrients
PURE STUDY FINDINGS

• Higher carbohydrate intake
  • Increased risk of total mortality, HR 1.28 [95% CI 1.12–1.46], p=0.0001
  • Not with risk of cardiovascular disease or cardiovascular disease mortality

• Intake of fat (and each type of fat)
  • Lower risk of total mortality
  • Total fat, HR 0.77 [95% CI 0.67–0.87], p<0.0001
  • Total fat and saturated and unsaturated fats were not significantly associated with risk of myocardial infarction or cardiovascular disease mortality
# PURE STUDY FINDINGS

<table>
<thead>
<tr>
<th>Group</th>
<th>HR (95% CI)</th>
<th>P for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbohydrate</td>
<td>1.28 (1.12–1.46)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Total fat</td>
<td>0.77 (0.67–0.87)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Saturated fat</td>
<td>0.86 (0.76–0.99)</td>
<td>0.0088</td>
</tr>
<tr>
<td>Monounsaturated fat</td>
<td>0.81 (0.71–0.92)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Polyunsaturated fat</td>
<td>0.80 (0.71–0.89)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
Dietary changes

• Not a consensus on the “correct diet”
• Important to assess patient’s intake - food tracking
• Develop a strategy that your patient can adhere to
Weight maintenance:
Obesity is a chronic condition. Maximum weight loss by 6 months, then plateau, then regain. Best chance of maintenance is to stayed engaged with long term program.
Adjunct therapies

• Not to replace comprehensive lifestyle intervention
• Pharmacotherapy
• Bariatric Surgery
Pharmacotherapy (FDA-Approved Anti-Obesity Medications)

<table>
<thead>
<tr>
<th>CNS Stimulants/Anorexiant:</th>
<th>Anti-Depressants/Dopamine Reuptake Inhibitors/Opioid Antagonists:</th>
<th>Gastrointestinal Agents/Other:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phentermine</td>
<td>Bupropion/Naltrexone</td>
<td>Orlistat</td>
</tr>
<tr>
<td>Phentermine/topiramate</td>
<td></td>
<td>GLP-1 agonists (liraglutide)</td>
</tr>
<tr>
<td>Lorcanerin</td>
<td></td>
<td></td>
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<tr>
<td>Diethylpropion</td>
<td></td>
<td></td>
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<tr>
<td>Phendimetrazine</td>
<td></td>
<td></td>
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<tr>
<td>Benzphetamine</td>
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<td></td>
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</tbody>
</table>

Other agents: Topiramate, Zonisamide, Bupropion, Metformin, Amylin agonist (pramlintide), SGLT2 inhibitors (canagliflozin, dapagliflozin)
<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism of Action</th>
<th>Study Details</th>
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</thead>
<tbody>
<tr>
<td>Orlistat</td>
<td>Lipase inhibitor</td>
<td>XENDOS</td>
</tr>
<tr>
<td>(Xenical™)</td>
<td></td>
<td>1 yr: 4.0% 4 yr: 2.6%</td>
</tr>
<tr>
<td>(Alli™) - OTC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1999</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lorcaserin</td>
<td>Serotonin (SHT2c) receptor agonist</td>
<td>BLOSSOM BLOOM</td>
</tr>
<tr>
<td>(Belviq™)</td>
<td></td>
<td>1 yr: 3.0%-3.6% 2 yr: 3.1%</td>
</tr>
<tr>
<td>2012</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phentermine/</td>
<td>NE-releasing agent (phentermine)</td>
<td>GABA receptor modulation (topiramate)</td>
</tr>
<tr>
<td>Topiramate ER</td>
<td>(Qsymia®)</td>
<td>EQUIP CONQUER SEQUEL</td>
</tr>
<tr>
<td>(2012)</td>
<td></td>
<td>1 yr: 8.6%-9.3% on high dose; 6.6% on treatment dose</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 yr: 8.7% on high dose; 7.5% on treatment dose</td>
</tr>
<tr>
<td>Naltrexone ER</td>
<td>Opiate antagonist (naltrexone)</td>
<td>Reuptake inhibitor of DA and NE (bupropion)</td>
</tr>
<tr>
<td>Bupropion ER</td>
<td>(Contrave®)</td>
<td>COR I COR-II COR-BMOD</td>
</tr>
<tr>
<td>(2014)</td>
<td></td>
<td>1 yr: 4.2%-5.2%</td>
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<tr>
<td>Liraglutide 3 mg</td>
<td>GLP-1 analog</td>
<td>SCALE Obesity &amp; Prediabetes</td>
</tr>
<tr>
<td>(Saxenda®)</td>
<td></td>
<td>1 yr: 5.6%</td>
</tr>
<tr>
<td>2014</td>
<td></td>
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</table>
EQUIP Trial

- 56-week randomized controlled trial
- 1,267 patients were evaluated (BMI 35-79)
- Primary endpoint: Overall % WL from baseline; pts w/ 5% WL
- Intention to Treat; Last observation carried forward
- Reduced calorie diet and lifestyle modification counseling was offered
EQUIP Trial

![Graph showing mean percent weight loss over weeks and percentage of patients achieving weight loss goals for different treatments.]

**a**

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>3.75/23</th>
<th>15/92</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>498</td>
<td>362</td>
<td>303</td>
</tr>
<tr>
<td></td>
<td>279</td>
<td>416</td>
<td>372</td>
</tr>
<tr>
<td></td>
<td>498</td>
<td>190</td>
<td>149</td>
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<tr>
<td></td>
<td></td>
<td>234</td>
<td>234</td>
</tr>
<tr>
<td></td>
<td></td>
<td>348</td>
<td>498</td>
</tr>
</tbody>
</table>

**b**

Percentage of patients (%)

- Placebo: 17.3, 44.9, 66.7
- PHEN/TPM CR 3.75/23: 18.6, 47.2
- PHEN/TPM CR 15/92: 3.4, 7.3

Comparison:

- ≥5% WL: $P < 0.0001$
- ≥10% WL: $P = 0.0234$
EQUIP TRIAL

- Most common AE: paresthesia, dry mouth, constipation, dysgeusia, insomnia
- Less freq. AE: depression, irritability, alopecia, anxiety, disturbance in attention, and hypoesthesia.
- Serious AE rates were the same across treatment groups
- HR increased 1.2 bmp in high tx group (p=0.08)
- Significant decrease in SBP, DBP, TG, Waist circ, FBG
EQUIP TRIAL

• Primary endpoints:
  • Weight loss from baseline
    • 10.9% weight loss with higher dose
    • 5.1% weight loss with lower dose
    • 1.6% weight loss in placebo group
  • 5% weight loss
    • 67% of patients on higher dose
    • 45% of patients on lower dose
    • 17% of patients on placebo
  • 10% or greater weight loss
    • 47% of patients on higher dose
    • 19% of patients on lower dose
    • 7% of patients on placebo
  • Of note, meaningful weight loss even with taking SSRIs, SNRIs, or bupropion
CONQUER TRIAL

• 56-week phase 3 trial
• Double blind, placebo controlled study
• 2487 patients with BMI 27-45 and two or more comorbidities (hypertension, dyslipidaemia, diabetes or prediabetes, or abdominal obesity)
• Randomized to placebo, phentermine/topiramate 7.5mg/46mg, or phentermine/topiramate 15mg/92mg
• Primary endpoint: Overall % WL from baseline; pts w/ 5% WL
• Intention to Treat; Last observation carried forward

*Lancet* 2011 Apr 16;377(9774):1341-52
CONQUER TRIAL

![Graph showing change from baseline percentage and study completers over weeks.](chart)

**Study completers**
- Placebo: 979, 853, 744, 670, 623, 589, 573, 557, 979, 994
- Phentermine 7.5 mg plus topiramate 46.0 mg: 488, 437, 403, 387, 369, 356, 350, 338, 488, 498
- Phentermine 15.0 mg plus topiramate 92.0 mg: 981, 843, 775, 747, 712, 686, 660, 625, 981, 995

**Graph B**
- Patients % at ≥5% weight loss
  - Placebo (n=979): p<0.0001
  - Phentermine 7.5 mg plus topiramate 46.0 mg (n=488): p<0.0001
  - Phentermine 15.0 mg plus topiramate 92.0 mg (n=981): p<0.0001

**Graph A**
- Change from baseline (%)
  - Placebo
  - Phentermine 7.5 mg plus topiramate 46.0 mg
  - Phentermine 15.0 mg plus topiramate 92.0 mg

*Lancet* 2011 Apr 16;377(9774):1341-52
CONQUER TRIAL

• Primary endpoint:
  • Weight loss
    • 9.8% in patients on high dose
    • 7.8% in patients on 7.5/46 mg
    • 1.2% in the placebo group
  • 5% Weight Loss
    • 70% of patients on high dose
    • 62% of patients on 7.5/46mg
    • 21% of patients on placebo

• 10% or greater weight
  • 48% on high dose, 37% on 7.5/46mg dos, 7% on placebo

Lancet 2011 Apr 16;377(9774):1341-52
SEQUEL TRIAL

• Placebo-controlled, double-blind, 52-wk extension study (total 108 wk)
  • Extension of CONQUER
• 676 patients chose to extend study, stayed in previous groups
• Primary endpoints were the same (WL and pts with 5% WL)
• Secondary endpoints: WL; pts with 10%, 15%, or 20% weight loss; change in waist circ. from baseline
• Efficacy endpoints: changes in BP, lipids, BG, concomitant meds for weight-related comorbidities, and rate of progression to diabetes

Am J Clin Nutr 2012;95:297–308
SEQUEL TRIAL
SEQUEL TRIAL

- Progression to DM2:
  - 54% reduction in pts on 7.5mg/46mg
  - 76% reduction in pts on 15mg/92mg
Phentermine/Topiramate

• Contraindications
  • Pregnancy and breastfeeding
  • Hyperthyroidism
  • Acute angle-closure glaucoma
  • Concomitant MAOI use (within 14 days)

• Caution
  • Tachyarrhythmia
  • Decreased cognition
  • Seizure disorder
  • Anxiety and panic attacks
  • Nephrolithiasis
  • Hyperchloremic metabolic acidosis
  • Dose adjustment with hepatic or renal impairment
  • Concern for abuse potential
  • Combined use with alcohol or depressant
• Who should be considered for pharmacotherapy?
# Treatment

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Calculated BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>25-26.9</td>
</tr>
<tr>
<td>Diet, Activity, Behavioral Tx</td>
<td>With comorbidities</td>
</tr>
<tr>
<td>Pharmacotherapy</td>
<td>With comorbidities</td>
</tr>
<tr>
<td>Weight Loss Surgery</td>
<td>With comorbidities</td>
</tr>
</tbody>
</table>

+ denotes use of indicated treatment regardless of comorbidities
Summary

- Obesity is a chronic, complex disease that affects millions of Americans
- Evaluation and treatment of obesity is evidence-based (algorithm)
- Determine BMI
- Assess for comorbidities
- Treatment includes lifestyle, pharmacotherapy, and bariatric surgery
Bias in Healthcare

[Diagram showing relationships between patient obesity and various factors such as provider attitudes, patient avoidance of care, patient outcomes, provider stereotypes, and provider decision-making.]

Obs. Rev. 2015 April 16(4): 319-326

[Link: https://implicit.harvard.edu]
Thank you