Obesity
What's it all about, anyway?
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Why do we care?

- Obesity is a terribly prevalent problem in our country.
- Obesity is associated with or the direct cause of many life threatening conditions.
- It's not just about keeping people alive, their quality of life is an issue too.
- Obese individuals have increased all-cause mortality, with or with endocrine abnormalities.
Objectives, hour 1

- Understand the causes of obesity
- Learn contributing factors
- Identify physiologic changes in the obesity process
Objectives, hour 2

- Overcoming the hurdles to treatment
- Treating the whole patient—social, family, environment
- Medical interventions
Obesity is defined as a BMI of 30 or greater.

In 2012, more than 1/3 of adults 20 years and older in the US were obese.

An additional 30% is classified as overweight (25-29.9 BMI).

Relatively stable over the past 10 years, but a 21% increase in the rate of obesity in women over 60.
Adverse health outcomes

- Most strongly associated with HTN
  - Lipid disorders
  - Heart disease
  - Stroke
  - Diabetes
  - Osteoarthritis
Liver disease

Gallbladder disease

Sleep apnea

Abnormal menses

Infertility
Adverse health outcomes

- Breast cancer
- Endometrial cancer
- Colon cancer
- Prostate cancer
- Behavioral health issues
Risk factors for obesity

- Race: more common in Native American, black, and Mexican Americans
- Having 1 obese parent increases risk 2-3 times
- Low income status
- Resource-rich country (USA, UK, Greece, Italy, Malta, Portugal, and Spain)
Environmental factors

“Obesogenic environment” evolved in the 1970s

- Diminishing Family presence at meals (especially children)
- Decreased physical activity
- Increased portion size
- Increasing trend of glycemic index in foods
- Sugar-containing beverages
Appetite

Complex hormone regulation

Some stimulate appetite: GHRELIN, neuropeptide Y, melanin-containing hormone, GH-releasing hormone, norepinephrine, orexin-A and B

Norepinephrine and neuropeptide Y appear to stimulate predominantly carbohydrate intake.
Appetite suppressing hormones

- Leptin appears to indicate whether fat stores are adequate for growth and reproduction.
- GLP-1 inhibits food intake and slows gastric emptying.
- Cholecystokinin decreases food intake
- Pancreatic polypeptide, oxyntomodulin, peptide YY 3-36
The brain

- Key modulator of body weight
- Nucleus of the tractus solitarius, the hindbrain
- The arcuate nucleus at the base of the hypothalamus
- Paraventricular nucleus
- Ventromedial hypothalamus
- Lateral hypothalamus
- Amygdala
Genes

- Challenging to identify
- 97 genes have been associated with obesity
- Environmental factors appear to modify the known genetic associations with BMI.
- Single gene defects: FTO on chromosome 16, Prader-Willi on chromosome 15, Bardet-Biedl, Leptin gene
Leptin gene

- Lep gene codes for a protein called leptin.
- Leptin-deficient mice have hyperphagia, insulin resistance, infertility, and hyperinsulinemia.
- Administration of leptin reverses all these conditions.
- Leptin receptor deficiency has also been described.
Other associated genes

- Prohormone convertase (PSCK1)—associated with early onset obesity, especially in caucasians.

- Melanocortin-4 receptor (MCR4)—deficiency associated with early-onset obesity and taller-than-average height.

- Proopiomelanocortin (POMC)

- Brain-derived neutrophic factor (BDNF)

- Tropomycin-related kinase B (TrkB)

- Single-minded 1 (SIM1)
Obesity-susceptible loci discovered in four waves of genome-wide association studies for BMI (blue), three waves of genome-wide association studies for waist circumference (purple) and WHRadj (red), and two waves of genome-wide association studies for extreme and early-onset of obesity (green). Each Venn diagram represents the loci of one paper.

BMI: body mass index; WHRadj: waist-to-hip ratio (adjusted).


Graphic 87759 Version 3.0
So, why do people really gain weight?

- Energy intake is higher than energy expenditure.

  (But of course it's way more complicated than that!)
Obese individuals do not seem to adapt well to weight loss (handling and storage of calories).

Obese individuals require fewer calories after weight loss than their never obese counterparts.

This can persist for years after weight loss.
Weight gain

- Gut microbiome
- Energy expenditure
  - 70% used for basal metabolic processes
  - 10% dissipated through the thermic response to food
  - The rest is activity and exercise—fidgeting can increase energy expenditure by 25%!
Ghrelin

(Gremlin)
Ghrelin

- A 28-amino-acid peptide
- In the motilin family of peptides
- Stimulates secretion of growth hormone, increases food intake, and produces weight gain
- Produced in the stomach
- Increases during periods of fasting or negative energy balance
In obese individuals, postprandial suppression is impaired.

It signals starvation.
Leptin

- Produced primarily in fat cells, especially large ones
- Member of the cytokine family
- BMI and body fat are strongly correlated to leptin.
- Overeating increases serum leptin concentration.
- Conversely, fasting decreases the level.
And now for the fun part!

You can wake up now
What are we going to do about it?

- Learn how to approach this special patient.
- Understand that this is a complex process.
- It's not just about pushing back from the table.
- It's not just about the BMI.
So, let's give everyone leptin and/or ghrelin blockers. Problem solved, right?
“I think you should be more explicit here in step two”
<table>
<thead>
<tr>
<th>Clinical recommendation</th>
<th>Evidence rating</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI should be calculated for all patients 18 years and older, and those with obesity should be referred for intensive, multicomponent behavioral interventions.</td>
<td>B</td>
<td>2</td>
</tr>
<tr>
<td>Increased physical activity should be recommended for weight loss in combination with diet and behavioral modifications.</td>
<td>B</td>
<td>20</td>
</tr>
<tr>
<td>Physicians should consider medications for weight loss in patients with a BMI of 30 kg per m² or greater, or 27 kg per m² or greater who also have comorbidities and have unsuccessfully tried diet and lifestyle modification first.</td>
<td>C</td>
<td>26</td>
</tr>
<tr>
<td>Patients with a BMI of 40 kg per m² or greater and those with a BMI greater than 35 kg per m² who also have obesity-related comorbidities should be referred for consideration of bariatric surgery. Patients with a BMI greater than 30 kg per m² who also have obesity-related comorbidities may be candidates for adjustable gastric banding.</td>
<td>B</td>
<td>36</td>
</tr>
</tbody>
</table>

*BMI = body mass index.*

*A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to [http://www.aafp.org/afpsort](http://www.aafp.org/afpsort).*
### Table 1. Weight Classifications

<table>
<thead>
<tr>
<th>Classification</th>
<th>Body mass index (kg per m²)</th>
<th>Prevalence (%)</th>
<th>Waist circumference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>&lt; 18.5</td>
<td>NA</td>
<td>—</td>
</tr>
<tr>
<td>Normal weight</td>
<td>18.5 to 24.9</td>
<td>NA</td>
<td>Male &lt; 40 in (102 cm)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Female &lt; 35 in (89 cm)</td>
</tr>
<tr>
<td>Overweight</td>
<td>25 to 29.9</td>
<td>33.6</td>
<td>—</td>
</tr>
<tr>
<td>Class 1 obesity</td>
<td>30 to 34.9</td>
<td>20.4</td>
<td>Male ≥ 40 in</td>
</tr>
<tr>
<td>Class 2 obesity</td>
<td>35 to 39.9</td>
<td>8.1</td>
<td>Female ≥ 35 in</td>
</tr>
<tr>
<td>Class 3 obesity</td>
<td>≥ 40</td>
<td>6.4</td>
<td></td>
</tr>
</tbody>
</table>

NA = not available.

Information from references 1 and 3.
BMI

- It is a surrogate, not direct, measurement of body fat.
- Can be misleading
- Particularly true in extremes of age where (in elderly) muscle mass decreases and body fat increases.
- High fitness levels
- Differs between the sexes (more accurate in females)
Racial differences—Asians tend to have higher body fat mass than Caucasians, and in Polynesians or African Americans the reverse is true.

Should not be your only measurement!
Yes, BMI is the tool most often used in the office, but waist circumference is helpful too.

Central adiposity is in itself a risk for morbidly and mortality.

Waist circumference has been shown to have a linear association with all-cause mortality in white individuals.
Other methods for measuring body composition

- Skin fold thickness—inconsistent and only measures fat under the skin
- Bioelectrical impedance analysis (BIA)
- DEXA scan—measures body mineral content and lean soft tissue mass, estimates fat by subtracting from total body mass.
- Hydrostatic weighing
- CT
- MRI (costly and limited access)
Step 1: the approach

- Remember that this person is likely already unhappy with their weight.
- They have probably tried and failed many diets or supplements.
- An answer of “diet and exercise” is NOT what will help.
<table>
<thead>
<tr>
<th>Technique</th>
<th>Example</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ask permission to discuss behavior-change topic</td>
<td>&quot;Would it be okay if we talked about your weight today?&quot;</td>
<td>When patient gives permission, he or she is more open to the conversation</td>
</tr>
<tr>
<td>Show empathy</td>
<td>&quot;Losing weight is very challenging.&quot;</td>
<td>Aids in building rapport, particularly in difficult discussions</td>
</tr>
<tr>
<td>Scale motivation (0 = low to 10 = high)</td>
<td>&quot;On a scale of 0 to 10, with 10 being the highest, how motivated are you to try to lose weight?&quot;</td>
<td>Assesses motivation to change; if very low, the patient may not be ready for change; if high, additional intervention strategies may be successful</td>
</tr>
<tr>
<td>Scale confidence (0 = low to 10 = high)</td>
<td>&quot;On a scale of 0 to 10, with 10 being the highest, how confident are you that you can lose weight?&quot;</td>
<td>Identifies need for interventions to overcome obstacles</td>
</tr>
<tr>
<td>Inquire about the scores on above scales</td>
<td>&quot;Why did you choose 3 instead of 2? What would help you move from 3 to 4?&quot;</td>
<td>Furthers the conversation on thinking about behavior change</td>
</tr>
<tr>
<td>Use decisional balance technique (explore pros and cons of change vs. no change)</td>
<td>&quot;What are the pros of losing weight?&quot; &quot;What are the pros of not losing weight?&quot; &quot;What are the cons of losing weight?&quot; &quot;What are the cons of not losing weight?&quot;</td>
<td>Helps patient and physician understand barriers to and motivators for change</td>
</tr>
<tr>
<td>Listen for change talk and reinforce it; let the patient take ownership by generating ideas for change</td>
<td>Patient: &quot;I think I could try to walk more.&quot; Physician: &quot;That's a fantastic idea that will help you move toward your goal.&quot;</td>
<td>Provides encouragement and helps promote confidence in patients</td>
</tr>
</tbody>
</table>

Information from references 11 and 12.
Helpful hints in the approach

- Cheerleader vs Preacher
- People want their doctor’s help!
- There is no deadline, we’re in this for the long haul.
- Expect excuses!
<table>
<thead>
<tr>
<th>Medication type</th>
<th>Promote weight gain</th>
<th>Weight neutral/variable</th>
<th>Promote weight loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antidepressants</td>
<td>Amitriptyline, doxepin, imipramine, mirtazapine (Remeron), nortriptyline (Pamelor), paroxetine (Paxil), phenelzine (Nardil)</td>
<td>Citalopram (Celexa), desvenlafaxine (Pristiq), duloxetine (Cymbalta), escitalopram (Lexapro), fluoxetine (Prozac), sertraline (Zoloft), venlafaxine</td>
<td>Bupropion (Wellbutrin)</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>Chlorpromazine, clozapine (Clozaril), olanzapine (Zyprexa), paliperidone (Invega), quetiapine (Seroquel), risperidone (Risperdal)</td>
<td>Aripiprazole (Abilify), haloperidol, ziprasidone (Geodon)</td>
<td>—</td>
</tr>
<tr>
<td>Cardiovascular agents</td>
<td>Amlodipine (Norvasc), atenolol, felodipine, metoprolol, nifedipine, propranolol</td>
<td>Angiotensin-converting enzyme inhibitors</td>
<td>—</td>
</tr>
<tr>
<td>Diabetic agents</td>
<td>Insulin, meglitinides, sulfonylureas, thiazolidinediones</td>
<td>Dipeptidyl peptidase-4 inhibitors</td>
<td>Alpha-glucosidase inhibitors, glucagon-like peptide-1 agonists, metformin, pramlintide (Symlin), sodium glucose cotransporter-2 inhibitors</td>
</tr>
<tr>
<td>Hormones</td>
<td>Estrogens, steroids</td>
<td>—</td>
<td>Progestins, testosterone</td>
</tr>
<tr>
<td>Hypnotics</td>
<td>Diphenhydramine (Benadryl)</td>
<td>Benzodiazepines, trazodone</td>
<td>—</td>
</tr>
<tr>
<td>Mood stabilizers</td>
<td>Lithium</td>
<td>Oxcarbazepine (Trileptal)</td>
<td>—</td>
</tr>
<tr>
<td>Seizure medications</td>
<td>Carbamazepine (Tegretol), gabapentin (Neurontin), pregabalin (Lyrica), valproate (Depacon)</td>
<td>Lamotrigine (Lamictal), levetiracetam (Keppra), phenytoin (Dilantin)</td>
<td>Felbamate (Felbatol), topiramate (Topamax), zonisamide (Zonegran)</td>
</tr>
</tbody>
</table>

Medical conditions that contribute to weight gain

- Thyroid disease
- Cushing syndrome
- PCOS
- Sleep apnea

Optimize treatment of these conditions first.
Diet
—*but don't call it that!*
Diet

- Multitude of options
- Structure is key
- Aim for 500 calories per day below total calorie intake needed to maintain weight.
- Eliminate high calorie foods.
- Following a specific diet
Diet

- Eliminate high calorie drinks.
- Weight Watchers
- Jenny Craig
- Nutri System
- Prescribed diets: New Direction, Ideal Protein, etc.
- Can be expensive and must be followed closely
Diet

- Low calorie
- Low fat
- Low carb
- Low glycemic index
- Ketogenic
- Intermittent fasting
Diet

- Overall results of dietary changes are modest.
- Specific diet is not as important as adhering to “A” diet, because there are minimal long-term differences between them when studied.
- Patient preference should be a determining factor in the choice.
My personal belief: low carb

No starvation

Stable sugar=fewer cravings

Drawback: if you cheat, you will gain weight!
Exercise

The part nobody wants to do
Exercise

- When you burn more calories, you lose more weight.
- At least 150 minutes of moderate-intensity aerobic activity per week
- Or at least 75 minutes of vigorous-intensity aerobic activity per week
- Increases in physical activity by any level are associated with decreased cardiovascular risk.
- There is a strong inverse association between increased exercise capacity and all-cause mortality.
<table>
<thead>
<tr>
<th>Activity category</th>
<th>Mild intensity</th>
<th>Moderate intensity</th>
<th>Vigorous intensity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gym activities</td>
<td>Slow swimming</td>
<td>Body pump</td>
<td>Climbing</td>
</tr>
<tr>
<td></td>
<td>Tai chi</td>
<td>Moderate swimming</td>
<td>Jumping rope</td>
</tr>
<tr>
<td></td>
<td>Yoga or Pilates</td>
<td>Water aerobics</td>
<td>Swimming competitively</td>
</tr>
<tr>
<td>Physical activities</td>
<td>Walking &lt; 3 mph</td>
<td>Ballroom dancing</td>
<td>Aerobic dancing</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bicycling (&lt; 10 mph)</td>
<td>Bicycling (≥ 10 mph)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>General gardening</td>
<td>Hiking uphill or with a heavy pack</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Walking briskly (3 mph)</td>
<td>Intense gardening (continuous digging or hoeing)</td>
</tr>
<tr>
<td>Sporting activities</td>
<td>Golf</td>
<td>Horseback riding</td>
<td>Racewalking, jogging, or running</td>
</tr>
<tr>
<td></td>
<td>Hunting</td>
<td>Leisurely canoeing</td>
<td>Canoeing</td>
</tr>
<tr>
<td></td>
<td>Sport fishing</td>
<td>Tennis (doubles)</td>
<td>Mountain biking</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tennis (singles)</td>
<td></td>
</tr>
</tbody>
</table>

* mph = miles per hour.

Information from references 23 and 27.
Excuses

- This is where I hear the most excuses.
- Help your patients outsmart themselves.
- They must get brutally honest with themselves and find the time to do it.
- The best exercise regimen is one the person will actually do.
- Find something they don't hate, hopefully with time and some results they will like it or find something they do like.
Behavioral therapy

- USPSTF recommends physicians offer obese individuals intensive counseling.
- Address barriers to change
- Setting goals
- Self monitoring
- Motivational interviewing
Behavioral therapy

- Workplace interventions/challenges
- Reduction of screen time
- Arm yourself with counselors who are confident in handling obesity and related issues.
- Identify strengths
Medical therapies

What you've been waiting for!
Rule #1 in my practice: medical conditions have to be controlled before we begin.

You actually have to be overweight to get medications.

There is no magic bullet for weight loss. I'll do my part, but you have to do your part.

Don't think in terms of “diet.” Diets are temporary. Weight loss needs to be approached as long-term.
Medical therapies

- A viable and helpful tool
- Use them appropriately and you have nothing to fear.
- Helping someone lose weight is not “cheating.”
- Work with a patient’s endocrine system and you’ll fare much better.
- More thyroid is, in most cases, NOT the answer.
Supplements are of benefit if there is a deficiency.

Research is lacking on many popular supplements.

Natural doesn't necessarily equal beneficial (think poison ivy).

If people are willing to pay for these, I think it indicates a degree of motivation.
Orlistat (Xenical)

- Lipase inhibitor
- 60 or 120 mg TID
- Inhibits absorption of dietary fat
- Weight loss up to 7.5 pounds
- Side effects: fecal incontinence, urgency, flatulence, increased defecation, oily stools
Orlistat

- Contraindicated in cholestasis or chronic malabsorption syndrome
- Has fallen out of favor for the most part
Stimulants

- Phentermine, phendimetrazine, etc.
- Strengths vary
- 1-3 times daily
- Mean weight loss 7.9 pounds
- Approved by FDA for short-term weight loss (12 weeks)
Stimulants

- Major drug interactions with anti-depressants
- Addiction potential
- Adverse effects: palpitations, tachycardia, elevated BP, CNS effects, constipation
- Avoid in patients with heart disease, uncontrolled hypertension, narrow-angle glaucoma.
Phentermine/topiramate (Qsymia)

- Stimulant/antiepileptic
- 7.5/46 or 15/92 per day
- Same side effects as stimulants, plus dysgeusia, paresthesia
- Risk of kidney stones at 1 year of use
- Mean weight loss of 14.8 or 19.6 pounds, dose dependent
Qsymia

- Contraindications: glaucoma, hyperthyroidism, use of MAOI in 14 days
- Many have used phentermine and topiramate instead to defray the cost.
Lorcaserin (Belviq)

- 5-HT2C receptor agonist
- 10 mg BID
- Mean weight loss 7 pounds
- Can cause serotonin syndrome
- Side effects: back pain, constipation, cough, dizziness, dry mouth, fatigue, headache, hypoglycemia, nausea
Lorcaserin

- Taken for 1-2 years
- Weight loss not sudden
Naltrexone/bupropion (Contrave)

- Opioid antagonist/antidepressant
- Dosing up to 2 8/90 mg tablets BID
- Study duration: 56 weeks
- Mean weight lost: 10.4-10.8 pounds
Contrave

- Side effects: constipation, diarrhea, dizziness, dry mouth, headache, insomnia, nausea, vomiting

- Contraindications: abrupt discontinuation of alcohol, benzo, barbiturates, or antiepileptics; anorexia, bulimia, long-term opioid use, seizure disorder, uncontrolled hypertension, use of an MAOI in 14 days

- If it hasn't worked by 4-6 weeks, it isn't going to work.
Liraglutide (Saxenda, Victoza)

- Glucagon-like peptide-1 inhibitor
- Slows transit time through the gut
- 0.6 up to 3 mg SC daily
- 20-56 weeks study
- Up to 13 lb mean weight loss
Saxenda

- Side effects: abdominal pain, constipation, decreased appetite (yay!), diarrhea, dizziness, fatigue, headache, hypoglycemia, increased lipase levels, nausea, vomiting

- Contraindications: personal or family history of medullary thyroid cancer or multiple endocrine neoplasia type 2

- Expensive, Saxenda not covered by most insurance
Disclaimer: these are my opinions formed by clinical experience. I am not employed by any of the companies that make these medications.
Stimulants

- They work for a short time, probably 3 months.
- Good for the patient who just wants a jump start.
- When they stop working, it is hard to get patients to stop taking them.
- They give people energy. This is why they are addictive.
- If still working, I will continue the prescription.
- Close follow up!
Phentermine/topiramate

- When first introduced, there was a complicated online registry.
- Expensive
- Kills appetite/makes things taste funny.
- Results in my practice similar to phentermine alone
Orlistat

- Now available without a prescription
- Not used much any more
- Fecal incontinence is BAD when someone is trying to improve their self image.
Lorcaserin

- I haven't used much due to cost
- Use with caution in diabetics due to increased risk of hypoglycemia.
Naltrexone/bupropion

- Some people just can't stand the side effects.
- Most side effects are workable.
- Dosage flexibility
- Costs $30-90 per month
- Ok to use long-term
Naltrexone/bupropion

Well-suited for “food addicts”
Liraglutide

- Super expensive if not covered
- Well-suited to diabetics, hyperglycemia patients, PCOS and those with metabolic syndrome.
- Victoza instead?
- Daily injection—major hurdle to some individuals
No approach works for every person. You must be flexible.

It takes an integrated approach to decide the best plan of diet, exercise, counseling for each patient.

The best diet or exercise plan is the one the patient will actually do.

Weight management is not for the faint of heart.


5. Diet and Physical Activity for Cardiovascular Disease Prevention: Jeffrey B. Lanier, MD, David C. Bury, DO, and Sean W. Richardson, DO. American Family Physician, June 1, 2016.