Weight Management in Primary Care

How we can partner with patients for improved success

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Objectives

1. Definition, classification, and etiology of obesity
2. General Approach to obesity management
3. Specific Dietary Strategies
4. Medications used for weight loss
5. Future Directions
What is Obesity?

Obesity is the state of excess adipose tissue which occurs when energy intake exceeds energy expenditure.

But what is obesity?

Is it a result of lifestyle choices? Is it a disease process? What drives this energy imbalance?
Obesity is a complex disease process

- People with overweightness and obesity don’t live as long

  Yu et al. Annals of Internal Medicine, 2017; 613-621

- It is associated with impaired body function (respiratory, musculoskeletal, etc)

- There are measureable physiologic abnormalities associated with the disease process

- There are specific known gene mutations that lead to the condition
What is known about a genetic component?

• Single Gene Mutations
  o Leptin Deficiency
    - Case Study 9yo girl
  o Leptin Receptor

• Genetic Associations
Recognizing Obesity as a disease process

- Lifestyle choices and disease processes are treated in very different ways.

<table>
<thead>
<tr>
<th>Lifestyle (Homelessness)</th>
<th>Disease (HTN)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Engage with support services</td>
<td>Determine Etiology of Disease process</td>
</tr>
<tr>
<td>Treat consequences of lifestyle choices</td>
<td>Treat with medication and lifestyle changes toward specific goals</td>
</tr>
<tr>
<td>Counseling toward healthier choices</td>
<td>Empowerment of patients and care providers to meet these goals</td>
</tr>
<tr>
<td>&quot;Only so much we can do...&quot;</td>
<td>No fault assessment</td>
</tr>
</tbody>
</table>
Prevalence and disease trajectory

Adult Obesity Rate by State, 2016

Select years with the slider to see historical data. Hover over states for more information. Click a state to lock the selection. Click again to unlock.

Percent of obese adults (Body Mass Index of 30+)

https://stateofobesity.org/adult-obesity
Indicators of Obesity

• Obesity can be measured by body composition analysis (DEXA)

• Obesity can be estimated by:
  o BMI
  o Height/ waist circumference ratio
  o Anthropometry (skin fold thickness)
  o Abdominal CT/ MRI
BMI

• <18.5% - underweight
• 18.6-24.9% - healthy weight
• 25% - 30% - overweight >30% - obese

• For children overweight and obese is determined by percentile:
  o 85th-95th overweight
  o >95th obese
Etiology of Obesity

- Multiple contributing factors:
  - Genetics
  - Behavioral
  - Sleep-wake cycle
  - Hormones
  - Medications
  - Stress management
  - Microbiome
Overweight and obese women (BMI 32.4 ± 1.8 kg/m²) with metabolic syndrome were randomized into two isocaloric (~1400 kcal) weight loss groups, a breakfast (BF) (700 kcal breakfast, 500 kcal lunch, 200 kcal dinner) or a dinner (D) group (200 kcal breakfast, 500 kcal lunch, 700 kcal dinner) for 12 weeks. The two meal plans were either high-calorie breakfast (BF) or high-calorie dinner (D) with a total daily energy of 1400 ± 25 kcal with identical macronutrient content and composition.
Eating during light hours vs. Dark hours affects weight outcomes.
Hormonal Factors

• Elevated cortisol levels in OSA and chronic stress are associated with increased weight.

• Diets that aim to increase growth factor (intermittent fasting) are growing in popularity.

• Falling testosterone/estrogen with age leads to changes in lean muscle mass and fat distribution.
Medications inducing weight gain

- 2015 Metaanalysis in Journal of Clinical Endocrinology

As with other disease processes, important to try and stop contributing factors, as able, prior to adding new therapies

<table>
<thead>
<tr>
<th>Medication</th>
<th>Weight Gain</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>amitriptyline</td>
<td></td>
<td>2.2kg</td>
</tr>
<tr>
<td>mirtazapine</td>
<td></td>
<td>1.5kg</td>
</tr>
<tr>
<td>olanzapine</td>
<td></td>
<td>2.4kg</td>
</tr>
<tr>
<td>quetiapine</td>
<td></td>
<td>1.1kg</td>
</tr>
<tr>
<td>risperidone</td>
<td></td>
<td>0.8kg</td>
</tr>
<tr>
<td>gabapentin</td>
<td></td>
<td>2.2kg</td>
</tr>
<tr>
<td>tolbutamide</td>
<td></td>
<td>2.8kg</td>
</tr>
<tr>
<td>pioglitazone</td>
<td></td>
<td>2.4kg</td>
</tr>
<tr>
<td>glimerpiride</td>
<td></td>
<td>2.1kg</td>
</tr>
<tr>
<td>glyburide</td>
<td></td>
<td>2.6kg</td>
</tr>
<tr>
<td>glipizide</td>
<td></td>
<td>2.2kg</td>
</tr>
<tr>
<td>sitagliptin</td>
<td></td>
<td>0.55kg</td>
</tr>
</tbody>
</table>
Chronic Stress

- Response to acute and chronic stress is mediated differently and has different weight effects
- Regular Exercise!
- Psychology
- Treat underlying anxiety/depression
General Approach to obesity management

• Same as any other disease process...

Thorough history and physical with focus on weight history and what occurred during times of significant weight changes.

• **Triggers** and **susceptibilities** tend to be different for different people so identifying personal risk factors is important to put together an appropriate treatment plan.
Putting together a personalized weight loss strategy:

• General Guidelines for people who have had success:
  
  National weight control registry:
  • High levels of physical activity (>1 hour/day)
  • Self monitoring weight
  • Eating a low calorie, low fat diet
  • Eating breakfast regularly
  • Maintaining a consistent eating pattern throughout the week
  • Wearable activity trackers (maybe)
Specific Diets

- A to Z diets
- POUNDS lost
- (2009)
But....

- In each of these diet cohorts, the variability within each group was greater than that of the weight loss difference in between the groups.

- **DIETFITS**
  - Reanalysis of the 2007 Data for people with insulin resistance
So more on personalized diets to come….

For now, focusing on what these diets have in common and having your patient choose something that is in line with their tastes and lifestyle needs is most important.

Being able to stick to dietary goals is more important the macronutrient content.
Physical Activity Interventions

Exercise for weight loss

- Works modestly for men. Prevents weight gain in women but with no weight loss benefits.

- LOTS of benefits. Just not weight loss…

Exercise for Weight Maintenance

ACSM recommendations:

- Weight loss 150-250 min/wk of moderate intensity aerobic exercise.
- Prevention of weight regain >250 min/wk
- Resistance training 2-3 days a week
Pharmacologic Intervention

Eligibility: BMI >30 or >28 with co-morbidity
1. Adrenergic Agents
2. Serotonergic Agents
3. Lipase inhibitors
4. GABA receptor antagonist
5. GLP-1 receptor agonists
6. Metformin
7. Combination Pills
Pharmacologic Monitoring and Goals

- Monitor monthly x3 months at least every 3 months after that time
- Effective treatment **>5% weight loss at 12 weeks** for any medication
- If deemed ineffective, trial a different agent or consider a combination pill

- All medication are designed to be used in addition to diet and exercise. None of these medications are designed to “work on their own”

- Weight loss effects are only sustained as long as a person is taken the weight loss medication
Phentermine and diethylpropion
- Approved in 1960 for short term use

- MOA: sympathomimetic amine with pharmacologic properties similar to the amphetamines

- Side effects: elevated on MBP, increase in pulse rate, cardiac ischemia, restlessness, insomnia

- Special considerations: while this medication is only approved for short term use, it has been studied more long term in combination pills. Clinically it is generally used for longer term courses.
Serotonergic Agents

Lorcaserin (Belviq)
• Approved in 2012 for chronic weight management
• MOA: 5HT2c receptor agonist (serotonin agonist)
• Side effects: HA, nausea, dry mouth, fatigue, dizziness
• Special Considerations: use with caution for people on other serotonergic agents
Orlistat (OTC and prescription strength)
  • Approved in 1999 for chronic weight management
  • MOA: A reversible inhibitor of gastric and pancreatic lipases, thus inhibiting absorption of dietary fats by 30%
  • Side effects: Decreased absorption of fat-soluble vitamins, steatorrhea, oily spotting, flatulence with discharge, fecal urgency, increased defecation
  • Special Considerations: this is available OTC at 60mg dose
GABA receptor antagonists

Topiramate (Topamax)

- Off label – used for binge eating and medication associated weight gain. FDA approved in combination drug qsymia in 2012

- MOA: Blocks neuronal voltage-dependent sodium channels, enhances GABA(A) activity, antagonizes AMPA/kainate glutamate receptors, and weakly inhibits carbonic anhydrase.

- Side effects: Parathesias, fatigue, dizziness, memory impairment

- Special Considerations: Teratogenic
Dopamine/ NE reuptake inhibitor

Bupropion (Wellbutrin)

• Off label for binge eating/ impulse control. FDA approved in 2014 as combo pill, contrave

• MOA: The primary mechanism of action is thought to be dopaminergic and/or noradrenergic

• Side effects: tachycardia, insomnia, dry mouth, constipation, n/v

• Special Considerations: contraindicated in people with seizure disorder
GLP-1 receptor agonists

Liraglutide (Victoza or Saxenda)

Adverse effects
- nausea and vomiting
- heart rate
- pancreatitis risk

Efficacy effects
- Insulin biosynthesis
- Beta cell proliferation
- Beta cell apoptosis
- Neuroprotection
- Appetite suppression
- Gastric emptying
- Insulin sensitivity
- Glucose production
Metformin

- Not a medication designed for weight loss but with metabolic outcomes favoring weight loss.
Combination Pills

• Contrave – Bupropion/ Naltrexone. Increase to 180mg/16mg respectively BID. General expectation ~6% greater weight loss that diet and exercise alone.

• Qsymia – Toperimate ER/ Phentermine. Increase to 92,g/15mg daily. Titrated to weight loss goals. General Expectation ~9% greater weight loss to diet and exercise alone.

• ***- Lorcaserin/ Phentermine. This is a well researched combination though not available in combination pill yet.
What Medication is the most effective?

• People tend to respond differently to different medications. When deciding on a weight loss medication take into account
  o Individual weight loss triggers (portion control, emotion eating, medication induced weight gain)
  o Co-morbidities

• Be prepared to switch! We find that there is no perfect medication – there is just a perfect medication for that individual. Set the expectation that this will be something that is achieved through follow up and flexibility.
<table>
<thead>
<tr>
<th>Medication</th>
<th>Trade Name</th>
<th>MOA</th>
<th>Side effects</th>
<th>Weight loss Expectations</th>
<th>Who this drug may work for</th>
<th>Doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phentermine</td>
<td></td>
<td>sympathomimetic amine with properties similar to the amphetamines. Stimulation of the hypothalamus to release norepinephrine</td>
<td>Insomnia, anxiety, palpitations and tachycardia, cardiac ischemia</td>
<td>3-4kg (&lt;24 wk trials)</td>
<td>Appetite Suppresant. Low Cost. Higher risk factors</td>
<td>8,15,37.5</td>
</tr>
<tr>
<td>Liraglutide</td>
<td>Saxenda, Victoza</td>
<td>GLP-1 1. Glucose dependent stimulation of insulin secretion 2. reduction in plasma glucagon concentrations 3. Delayed gastric emptying 4. Direct CNS appetite suppression</td>
<td>Nausea and vomiting, pancreatitis, hypoglycemia</td>
<td>5.8kg (1 year)</td>
<td>Looking toward improved DMII control, difficulty with hunger and portion control</td>
<td>3,1.8</td>
</tr>
<tr>
<td>Lorcaserin</td>
<td>Belviq</td>
<td>5HT(2C) receptor agonist</td>
<td>HA, nausea, dry mouth, fatigue, serotonin syndrome</td>
<td>3.6kg (1 year)</td>
<td>emotional eating, appetite suppressent</td>
<td></td>
</tr>
<tr>
<td>Orlistat</td>
<td></td>
<td>Pancreatic and Gastric Lipase Inhibitor</td>
<td>steatorrhea, oily fecal spotting, fecal urgency, increased defecation</td>
<td>2-3.4kg (1 year)</td>
<td>limited systemic side effects (lots of GI side effects)</td>
<td></td>
</tr>
<tr>
<td>Topirimate</td>
<td>Topamax</td>
<td>GABA receptor modulation</td>
<td>Parathesias, fatigue, memory impairment, renal stones, teratogen</td>
<td></td>
<td>Direct appetite suppressent, binge eating tendencies, medication induced weight gain</td>
<td></td>
</tr>
<tr>
<td>Naltrexone</td>
<td></td>
<td>Opioid Receptor Antagonist, Naltrexone acts as an opioid receptor antagonist which is thought to indirectly modulate activation of pleasure and reward centers such as the mesolimbic dopamine system</td>
<td>Hepatocellular injury</td>
<td></td>
<td>Food Cravings</td>
<td></td>
</tr>
<tr>
<td>Metformin</td>
<td></td>
<td>Decreases hepatic glucose production, decreasing intestinal absorption of glucose and improves insulin sensitivity</td>
<td>Diarrhea, Lactic Acidosis</td>
<td></td>
<td>Metabolic syndrome, medication induced weight gain</td>
<td>500mg daily - 1000mg BID</td>
</tr>
<tr>
<td>Bupropion</td>
<td>Wellbutrin</td>
<td>Dopamine and Norepinephrine reuptake inhibitor</td>
<td>Tachycardia, insomnia, HA, agitation, lowers seizure threshold</td>
<td></td>
<td>binge eating tendencies</td>
<td>150mg BID</td>
</tr>
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</table>
Over the counter supplements

- No OTC supplements are FDA regulated.
- In general, none are recommended
Bariatric Surgery

Candidates: BMI >40, BMI >35 with co-morbidity

- Roux-en-Y
- Gastric Sleeve
Future Directions

• **Leptin**
  • Cytokine like amino acid produced by adipocytes
  • Change in leptin levels signal to the CNS (hypothalamus) that fat mass is decreasing. This results in compensatory effects on appetite and energy expenditure aimed to restore the energy balance.

• Microbiome Research
KU Weight Management Services

• KU Weight Management Clinic

• Bariatric Surgery Program