Non-surgical Treatment for Adult Obesity

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Objectives

- Definition, prevalence and cost of adult obesity
- Etiology of obesity
- Health risks associated with obesity
- Options for the treatment of adult obesity
- Non-surgical treatment including:
  - Diet and exercise
  - Behavior modification
  - Pharmacological treatment

Definition of Obesity

- WHO Classification:
  - Underweight < 18.5
  - Normal 18.5 – 24.9
  - Overweight 25 - 29.9
  - Obese Class 1 30 – 34.9
  - Obese Class 2 35 – 39.9
  - Obese Class 3 > 40 (Morbid obesity)

BMI = Weight (kg)/Height (m²)

- Increased health risk
- Substantially increased health risk

<table>
<thead>
<tr>
<th></th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
</table>
| ≥ 80 cm| ≥ 88 cm|≥ 102 cm

Definition of obesity

- Waist circumference
  - may be used independently or in addition to BMI
Prevalence of Obesity

• More than one-third (34.9% or 78.6 million) of U.S. adults are obese. [Journal of American Medicine (JAMA)]
• Among men, obesity prevalence is similar at all income levels
• Higher income women are less likely to be obese than low income women
• No trend between obesity and education among men
• Women with college degrees are less likely to be obese

NCHS data brief no 50. Huntsville, MD: National Center for Health Statistics. 2010

Prevalence of overweight, obesity and extreme obesity among U.S adults aged 20-74

NHANES is National Health Examination Survey. Pregnant females were excluded.
Cost of Obesity

- Cost of overweight and obesity estimated as high as $78.5 billion in 1998
- Half of this total financed by Medicare and Medicaid
- Estimates show that annual burden of obesity has risen to almost 10% of all medical spending
- $147 billion per year in 2008
- Across all payers, obese had medical spending that was $1,429 > spending for normal weight in 2006

Etiology of Obesity

- Genetic components
- Behavioral
- Environmental
- Physiological
- Social
- Cultural

World Health Organization Consultation on Obesity concluded that behavioral and environmental factors are primarily responsible for dramatic increase in obesity during the past 2 decades.

Health risks associated with obesity

Medical Complications
- Pulmonary Disease
- Abnormal Function
- Obstructive Sleep Apnea
- Hypometabolism Syndrome
- Nephrotic Fatty Liver Disease
- Stomal
- Stomachitis Gastroesophageal
- Diverticulitis Disease
- Diabetes
- Hypertension
- Gout
- Severe Pancreatitis
- Cancer
- Breast, Uterus, Colon, Liver, Esophagus, Pancreas, Kidney, Prostate

Idiopathic Intracranial Hypertension
- Headaches
- Stroke
- Cataracts
- Coronary Heart Disease
- Diabetes
- Hypertension

Skin
- Phlebitis

Wound heals

Author: Jordan Fischer

http://mylivewell.org/ckfinder/userfiles/images/Screen
The AMA declared obesity a disease in 2013 at their annual meeting. This decision was supported by the American College of Cardiology and the American Association of Clinical Endocrinologists.

Non-surgical Treatment

- Goals of treatment are to achieve and then maintain clinically meaningful weight loss
- Reduce the risk for obesity-related diseases
- Weight losses of 5% to 10% in initial body weight produce health benefits
- Long term success
  - Maintenance of a 10% weight loss for at least 1 year

Non-surgical Treatment

- Should incorporate multiple approaches
  - Diet, exercise and behavioral strategies
- Options depend on
  - The degree of obesity
  - Presence of co-morbidities
  - Previous weight loss therapies utilized and success of each
  - Characteristics of the individual

Non-surgical treatments

- Dietary approaches
  - Success is dependent on a relative energy deficit not composition
  - May be very-low-calorie diets (VLCDs, <800 kcal/d) or low-calorie diets (LCDs, 800-1500 kcal/d)
  - Produce clinically meaningful weight loss but maintenance is poor
  - 1200 kcal diets produce slower weight loss but can be followed for longer periods of time
  - Better adherence when food and beverage choices are limited and strictly controlled
  - No single approach shown to be effective for all people who are obese
Exercise

- Does not produce considerable weight loss when used independently
- Important adjunct to weight reducing diet
- $\uparrow$ energy expenditure, $\uparrow$ loss of adipose tissue, and improves dietary adherence
- Physically active obese individuals have a lower risk for morbidity and mortality
- Goal is a minimum of 30 minutes of moderate-intensity activity 5 days/week

Behavior modification

- Target identifying stimuli that signal unhealthy behaviors
- Readiness in initiating positive behaviors
- Recognizing barriers to healthy pursuits
- Important components include:
  - Goal-setting
  - Self-monitoring
  - Frequent contact
  - Feedback
  - Continuous motivation and support

Obesity Treatment Pyramid

- BMI $\geq 40$
- BMI $= 35-39.9$ with 1 obesity related co-morbidity
- BMI $\geq 30$
- BMI $\geq 27$ with 1 obesity related co-morbidity
- BMI $\geq 25$

Pharmacologic agents

- Use in conjunction with diet, exercise and behavioral strategies
- BMI of 30 kg/m² or greater OR BMI of 27 kg/m² with obesity related co-morbidity
- Safe and effective in producing modest but effective weight loss and amelioration of comorbid conditions
- Do not change the physiology of weight regulation in any permanent way
- Include short-term use (3 months) and chronic weight management medications
Pharmacologic agents

**Short-term Medications**
- Phentermine (Adipex)
- Diethylproprion (Tenuate)

**Chronic Weight Loss Medications**
- Orlistat (Xenical)
- Lorcaserin (Belviq)
- Phentermine/topiramate (Qsymia)
- Naltrexone/bupropion (Contrave)
- Liraglutide (Saxenda)

**Comparison of 1 year prospective, randomized, double-blind trials for lorcaserin (BLOOM and BLOSSOM) and phentermine-topiramate (EQUIP and CONQUER)**

<table>
<thead>
<tr>
<th></th>
<th>BLOOM</th>
<th>BLOSSOM</th>
<th>EQUIP</th>
<th>CONQUER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of subjects</td>
<td>3152</td>
<td>4039</td>
<td>1230</td>
<td>2648</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>18-45</td>
<td>18-45</td>
<td>≥ 55</td>
<td>27-45</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27-45</td>
<td>27-45</td>
<td>18-70</td>
<td>18-70</td>
</tr>
<tr>
<td>Comorbid conditions (cardiovascular and metabolic)</td>
<td>At least 1</td>
<td>At least 1</td>
<td>At least 1</td>
<td>≥ 2</td>
</tr>
<tr>
<td>Mean % weight loss compared to placebo</td>
<td>5.8% vs 2.2%</td>
<td>4.8% vs 2.8%</td>
<td>11% vs 1.6%</td>
<td>10.4% vs 1.9%</td>
</tr>
<tr>
<td>Placebo-subtracted weight loss (%)</td>
<td>≥ 4%</td>
<td>2.0%</td>
<td>9.4%</td>
<td>8.8%</td>
</tr>
<tr>
<td>Categorical change vs 5% weight loss compared with placebo</td>
<td>47.5% vs 20.3%</td>
<td>47.2% vs 22%</td>
<td>67% vs 17%</td>
<td>70% vs 21%</td>
</tr>
<tr>
<td>Completion rate</td>
<td>55.4% lorcaserin; 45.1% placebo</td>
<td>55.5%</td>
<td>58.9%</td>
<td></td>
</tr>
</tbody>
</table>

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**Orlistat (Xenical, Alli)**
- Approved by FDA in 1999 as first lipase inhibitor
- Approved as an OTC medication in 2007 at ½ the prescription dose
- 120 mg 3 x day with meals
- Blocks the digestion and absorption of ≈30% of dietary fat
- No systemic SEs
- Other SEs include:
  - Oily spotting, flatus with discharge, fecal urgency, fatty/oily stool, increased defecation

**Phentermine (Adipex, Adipex-p)**
- Appetite suppressant
- Most commonly prescribed centrally acting adrenergic agent
- Schedule IV drug
- Approved for short term use (12 weeks) with 6 months off medication before re-start
- 37.5 mg once a day before breakfast
- Most common SEs include:
  - Restlessness, insomnia, dry mouth, constipation, and increased BP and heart rate
Pharmacologic agents
Phentermine-topiramate ER (Qsymia)

- FDA approved July 2012
- Catecholamine releaser (phentermine) and an anticonvulsant (topiramate)
- Pregnancy Category X.
- Increased risk of congenital fetal oral cleft formation
- Need for active birth control among child-bearing women
- Measure creatinine before/during treatment
- Common SEs include:
  - Paresthesias, dry mouth, constipation, insomnia, taste alterations (particularly with carbonated beverages)

Pharmacologic agents
Lorcaserin (Belviq)

- Approved by the FDA in 2012
- Selective 5-HT2C receptor agonist
- Thought to decrease food intake through the pro-opiomelanocortin system of neurons
- 10 mg twice a day
- Should NOT be taken with MAOIs
- Caution with SSRIs
- Effect on cardiovascular morbidity and mortality has not been established
- Most frequent SEs include:
  - Headache, dizziness, dry mouth, and nausea

Pharmacologic agents
Naltrexone/buproprion (Contrave)

- FDA approved in 2014
- Tapered dose:

<table>
<thead>
<tr>
<th>TIME</th>
<th>DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 1</td>
<td>1 tablet QD x 7 days</td>
</tr>
<tr>
<td>Week 2</td>
<td>1 tablet BID x 7 days</td>
</tr>
<tr>
<td>Week 3</td>
<td>2 tablets QAM and 1 tablet QPM x 7 days</td>
</tr>
<tr>
<td>Week 4</td>
<td>2 tablets BID</td>
</tr>
</tbody>
</table>
Pharmacologic agents (Contrave)

- Reuptake inhibitor of dopamine and norepinephrine (buproprion) and opioid antagonist (naltrexone)
- Common SEs include: nausea, constipation, headache, vomiting, dizziness
- Contraindications
  - Uncontrolled hypertension
  - Seizure disorder
  - Drug or alcohol withdrawal
  - MAOIs

Pharmacologic agents (Liraglutide (Saxenda))

- Liraglutide (Saxenda)
- Dosage: 3 mg injectable
- GLP-1 agonist
- FDA approved in 2014
- Common SEs include: nausea, vomiting, pancreatitis
- Contraindications
  - Medullary thyroid cancer history
  - Multiple endocrine neoplasia type 2 history

Personalized Risk Assessment

- BMI
- Sex. Race and WC
- Weight gain history, prior treatments
- Blood pressure
- Lipid panel
- FPG, A1C
- Liver function
- Medications
- Diabetes, HTN, CVD, gout, sleep apnea, GERD, NAFLD, PCOS, venous stasis
- Pain, mobility impairment, functional limitation
- Well-being and psychological symptoms

Example of medication use in obese patient

- Patient had visit with surgeon to discuss umbilical hernia repair on 6/2/14.
- Patient's weight was 278 lbs and BP was 163/71
- Surgeon recommended weight loss prior to hernia surgery and referred to weight management clinic
- Patient started on a chronic weight loss medication on 6/10/14 with monthly follow up appointments
- BP was too high for short-term medication
Example of medication use in obese patient

- Weight loss of 40 lbs in a little over 2 months
- Had successful hernia repair
- Continued weight loss of 100 lbs total in 1 year

<table>
<thead>
<tr>
<th>APPOINTMENT</th>
<th>WEIGHT</th>
<th>WEIGHT LOSS</th>
</tr>
</thead>
<tbody>
<tr>
<td>6/02/2014</td>
<td>278</td>
<td></td>
</tr>
<tr>
<td>6/19/2014</td>
<td>266</td>
<td>12 LBS</td>
</tr>
<tr>
<td>7/10/2014</td>
<td>251</td>
<td>15 LBS</td>
</tr>
<tr>
<td>8/07/2014</td>
<td>238</td>
<td>13 LBS</td>
</tr>
<tr>
<td>Total</td>
<td>40 LBS</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion

- Obesity is a chronic disease that predisposes people to numerous serious health disorders
- Efforts to reduce the escalating incidence of obesity are critical
- Treatment options are available and it is essential that these strategies are being recommended to patients
- A multidisciplinary approach is considered the most successful in combating the obesity epidemic

The Surgical Treatment of Obesity and Metabolic Disease

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Medical Director, The Comprehensive Weight Management, Metabolic and Bariatric Surgery Program
The Division of Gastrointestinal and General Surgery
The Ohio State University Wexner Medical Center

National Institute of Health Criteria

- BMI 35-40 in patients with high-risk co-morbidities or severe lifestyle limitations
- BMI > 40 if patient desires surgery and has failed “conventional” treatment modalities
**Obesity is not created equal**

- In the US our population is heterogeneous, yet we apply our BMI criteria to all without taking into account sex, age, or ethnic background.
- There are lower cutoff points for BMI and abdominal obesity metrics among Asians.
- China and Japan define overweight as a BMI of 24 or higher and obesity a BMI of 28 or higher;
- In India, overweight is defined as a BMI of 23 or higher, and obesity, a BMI of 27 or higher.
- The International Diabetes Federation now includes ethnic-specific criteria for the definition of abdominal obesity.

**Current Procedures**

- There are still 4 main operations performed in the US
  - Gastric bypass
  - Sleeve gastrectomy
  - LAGB
  - Biliopancreatic diversion with or without DS

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**Roux-en-Y Gastric Bypass**

- ≤ 30 cc pouch
- 12 -14 mm stoma
- 75-150 cm or longer Roux limb
- BP limb
- Common channel

**Sleeve Gastrectomy**
Adjustable Gastric Banding

- <20 cc gastric “pouch”
- Adjustable “stoma”
- Normal GI anatomy and physiology

Biliopancreatic diversion with Duodenal Switch

- Sleeve (100-200ml)
- BP Limb (350ish cm)
- Alimentary Limb (250ish cm)
- Common channel (50-100 cm)

### Comparison of Procedures

<table>
<thead>
<tr>
<th>Gastric Bypass</th>
<th>Band</th>
<th>Sleeve</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-1.5 hours</td>
<td>&lt;1 hour</td>
<td>1-1.5 hours</td>
</tr>
<tr>
<td>2-3 days in hospital</td>
<td>Same day or 23 hour</td>
<td>2-3 days</td>
</tr>
<tr>
<td>2-6 week recovery</td>
<td>7-10 days</td>
<td>2-4 weeks</td>
</tr>
<tr>
<td>Fastest weight loss</td>
<td>Slower weight loss</td>
<td>Quick weight loss</td>
</tr>
<tr>
<td>Dumping</td>
<td>No dumping</td>
<td>No dumping</td>
</tr>
<tr>
<td>Vitamins mandatory</td>
<td>Recommended</td>
<td>Recommended (B12)</td>
</tr>
<tr>
<td>No NSAIDs</td>
<td>No steroids</td>
<td>No med restrictions</td>
</tr>
<tr>
<td>Regular food in ~2 wks</td>
<td>Regular in 2 weeks</td>
<td>Liquid-y for 1 month</td>
</tr>
</tbody>
</table>

### Comparison of Complications

<table>
<thead>
<tr>
<th>Gastric Bypass</th>
<th>Band</th>
<th>Sleeve</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leak</td>
<td>++</td>
<td>0</td>
</tr>
<tr>
<td>Bleeding</td>
<td>+</td>
<td>0</td>
</tr>
<tr>
<td>Internal hernia</td>
<td>++</td>
<td>0</td>
</tr>
<tr>
<td>Marginal Ulcer</td>
<td>+++</td>
<td>0</td>
</tr>
<tr>
<td>Slip/Erosion</td>
<td>0</td>
<td>+++</td>
</tr>
<tr>
<td>Failure</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>Nutritional Abnormalities</td>
<td>++</td>
<td>0</td>
</tr>
<tr>
<td>GERD</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>
Overall bariatric procedure volume has plateaued

It is felt that there were ~170,000 operations in 2012

It is still a very common operation worldwide...

- It is one of the most commonly performed “elective” general surgery procedures in the US.

Trends

- Vertical Sleeves
- Bands
- Gastric Bypass

Expected Weight Loss

- Lap Band
- UBG
- Gastric Bypass
Weight loss curves


Bariatric Surgery and Change in Mortality


Bariatric Surgery and Diabetes

Bariatric Surgery is effective treatment for diabetes

Table 1. Results of Different Types of Bariatric Surgery*

<table>
<thead>
<tr>
<th>Result</th>
<th>Malabsorptive (BPD)</th>
<th>Restrictive (LACB, VBG)</th>
<th>Combined (RYGB)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excess weight loss, %</td>
<td>72</td>
<td>48–68</td>
<td>62</td>
</tr>
<tr>
<td>Resolution of comorbid condition, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type 2 diabetes</td>
<td>98</td>
<td>48–72</td>
<td>84</td>
</tr>
<tr>
<td>Hypertension</td>
<td>81</td>
<td>28–73</td>
<td>75</td>
</tr>
<tr>
<td>Dyslipidemia improved</td>
<td>100</td>
<td>71–81</td>
<td>94</td>
</tr>
<tr>
<td>Operative mortality rate, %</td>
<td>1.10</td>
<td>0.10</td>
<td>0.5</td>
</tr>
</tbody>
</table>

*BPD = bilipancreatic diversion; LAGB = laparoscopic adjustable gastric banding; RYGB = Roux-en-Y gastric bypass; VBG = vertical banded gastroplasty.

* Mean values from a meta-analysis of 22,094 patients. Data from reference 7.

### Resolution of Co-Morbidities: Hypertension

- All forms of weight loss = in reduction in BP
- Resolution of HTN in 62% with significant improvement 78.8% *
- In DM subset, 69% had resolution at 1yr., 66% at 7yr. **
- Gastric bypass is more effective than vertical banding


### Resolution of Co-Morbidities: Dyslipidemia

- Significant improvement in lipids in 70%
  - Gastric by-pass better than vertical bands
  - HDL improve significantly with vertical bands
- Swedish Obesity Study
  - 2 and 10 yrs, significant improvement in HDL and triglycerides
  - Total cholesterol was not changed

Buchwald, et.al. JAMA 2004, Sjostrom, et.al. NEJM

### Resolution of Co-Morbidities: OSA, NASH, Pseudotumor Cerebri

- NASH – decrease in severity
- OSA - 85.7-93% resolution
- Pseudotumor Cerebri – success rates are higher than results of shunt placement
- No long term studies examining recurrence

### Future


Endoluminal Procedures

- To get a medical device to market takes 4-6 years and $42 million
- Obesity Indication PMA 8-10 years and $90 million

In the Future

Creating the future in obesity...

OSU Study Background: DBS of the behavioral and impulsivity target

- Research shows dysfunction and imbalances of the limbic cognitive circuits which leads to selective preference of impulsive choices vs. behavioral self control and regulation
  - Abnormally active impulsivity center
  - Animal studies of DBS showed improvements
  - Several studies have reported on the safety and efficacy of DBS for alcohol addiction and substance abuse

DBS of Behavioral Target for Obesity at OSU

- Study criteria
  - Age 22-60 years at time of enrollment
  - At least 24 months post Roux-en-Y gastric bypass surgery without evidence of a sustained improvement in BMI after gastric bypass surgery for at least 6 months
  - Anatomically intact bypass confirmed by endoscopy
  - Body mass index (BMI) > 40

We believe that DBS of the Behavioral brain target can improve decision-making, mood, anxiety and behavioral self-control. This study is for those who have not been able to control their body mass index (BMI) through other conventional methods, as well as Roux-en-Y (gastric bypass) surgery.

Left gastric artery embolization

- 5 patients (1 year follow up)
  - BMI >40 but <400#, age > 22 years
  - Primary Outcome Measures: Adverse Events
    - Safety outcomes involving the use of left gastric artery embolization for the purpose of weight loss.
  - Secondary Outcome Measures: Change in BMI
    - Quality of life pre and post procedure to determine the changes of quality in life; everyday activities
    - Appetite hormone levels: Measuring changes in ghrelin, leptin, and CCK before and after left gastric embolization
    - Change in overall weight of subjects