CURRENT ISSUES IN OBESITY

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Declaration of full disclosure: No conflict of interest

Prevalence of Obesity (Adults)

- Obesity: 33.8%
  - Men: 32.2%  Women: 35.5%
- Overweight + obesity: 68%
  - Men: 72.3%  Women: 64.1%
- Severe Obesity: 6%

Prevalence of Obesity (Children)

- Severe obesity (97 percentile): 11.9%
- Obesity (95 percentile): 16.9%
- Overweight (85 percentile): 31%
- No increase from 1999 to 2008
  (except severe obesity in boys)
CURRENT ISSUES IN OBESITY

Prevalence of Obesity and Trends in Body Mass Index Among US Children and Adolescents, 1999-2010

Obesity Disparities

- Women, 40-59
  - Black: 52%, Hispanic: 47%, Whites: 36%

- Teens
  - Black: 29%, Hispanic: 17.5%, Whites: 14.5%

- Mental illness
  - Overweight + obese: 83%

Obesity Trends* Among U.S. Adults

BRFSS, 2010

(*BMI ≥ 30, or ~30 lbs. overweight for 5’ 4" person)

For a 40 yo woman, with normal BP, lipids, and FBS which BMI is associated with the lowest all-cause mortality?

1. 18
2. 24
3. 28
4. 34
5. 38
CURRENT ISSUES IN OBESITY

CLASSIFICATION OF OVERWEIGHT AND OBESITY BY BMI

<table>
<thead>
<tr>
<th>Obesity Class</th>
<th>BMI (kg/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>&lt;18.5</td>
</tr>
<tr>
<td>Normal</td>
<td>18.5 – 24.9</td>
</tr>
<tr>
<td>Overweight</td>
<td>25.0 – 29.9</td>
</tr>
<tr>
<td>Obesity I</td>
<td>30.0 – 34.9</td>
</tr>
<tr>
<td>Obesity II</td>
<td>35.0 – 39.9</td>
</tr>
<tr>
<td>Extreme Obesity</td>
<td>≥40</td>
</tr>
</tbody>
</table>

BMI AND MORTALITY: Overall

Combined NHANES I, II, and III data set

<table>
<thead>
<tr>
<th>BMI</th>
<th>Combined NHANES I, II, and III data set</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;18.5</td>
<td>1.38 2.30 1.69</td>
</tr>
<tr>
<td>18.5–&lt;25</td>
<td>1.00 1.00 1.00</td>
</tr>
<tr>
<td>25 to &lt;30</td>
<td>0.83 0.95 0.91</td>
</tr>
<tr>
<td>30 to &lt;35</td>
<td>1.20 1.13 1.03</td>
</tr>
<tr>
<td>≥35</td>
<td>1.83 1.63 1.17</td>
</tr>
</tbody>
</table>

MORTALITY AND OBESITY

Meta-analysis of 97 studies of 2.8M people, 270,000 deaths

<table>
<thead>
<tr>
<th>BMI</th>
<th>HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Below 25 (Normal)</td>
<td>1.0</td>
</tr>
<tr>
<td>25–30 (Overweight)</td>
<td>0.94</td>
</tr>
<tr>
<td>Above 30 (Obese)</td>
<td>1.18</td>
</tr>
<tr>
<td>30–35 (Grade 1 Obesity)</td>
<td>0.95</td>
</tr>
<tr>
<td>Above 35 (Grade 2/3 Obesity)</td>
<td>1.29</td>
</tr>
</tbody>
</table>

For a 40 yo woman, with normal BP, lipids, and FBS which BMI is associated with the lowest all-cause mortality?

1. 18
2. 24
3. 28
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5. 38
CURRENT ISSUES IN OBESITY

Epidemic of Inactivity

60% US adults don’t exercise regularly
25% are sedentary

EXERCISE FOR OBESITY
Meta-analysis of 43 RCTs: 3476 participants

- Exercise plus diet vs diet alone
  -1.1 kg

- Increased intensity of exercise
  -1.5 kg

- Exercise without weight loss
  - Reduced: BP, triglycerides, blood sugar

WEIGHT LOSS DIET BOTTOM LINE

- The type of diet does not really matter for weight loss.
- Sticking to the diet does matter
- Calories “trump” macronutrients
- But, select healthy, nutrient rich foods
40 yo woman, BMI 36. Much to your surprise (and satisfaction), she has lost 35 pounds. In order to maintain her new weight, her lifelong daily calorie intake should be:

1. 2000 kcals
2. 1800 kcals
3. 1600 kcals
4. 1400 kcals
5. 1200 kcals

SUCCESSFUL WEIGHT LOSS MAINTENANCE

- 3000 subjects in National Weight Control Registry: 30-lb weight loss for 1-year
- Average weight loss 33 kg (10 BMI units less), average weight maintenance 5.5 years
- 45 years old, 80% women, 97% Caucasian
- 46% overweight as child, 46% one parent obese, 27% both parents

- High levels of physical activity
  - Women 2545 kcal/week, men 3293 kcal/week
  - (1-hour moderate intensity per day
  - Only 9% report no physical activity
- Diet low in calories
  - 1381 kcal day, 24% fat, 19% protein, 56% CHO
  - 4.87 meals or snacks/day
  - Fast food 0.74/week
- Regular self-monitoring of weight
  - 44% weigh once per day; 31% once per week

40 yo woman, BMI 36. Much to your surprise, she has lost 35 pounds. In order to maintain her new weight, her lifelong daily calorie intake should be:

1. 2000 kcals
2. 1800 kcals
3. 1600 kcals
4. 1400 kcals
5. 1200 kcals
In the last year, I have prescribed a medication for weight loss.

1. Yes
2. No

The medication I most commonly prescribe for weight loss is:

1. Phentermine
2. Orlistat (Xenical™, Alli™)
3. Bupropion (Wellbutrin™)
4. Exenatide (Byetta™, Bydureon™)
5. Phentermine/topiramate (Qsymia™)
6. Other

The Neuroendocrinology of Energy Balance

SIBUTRAMINE AND CARDIOVASCULAR OUTCOMES (SCOUT)

- 9804 patients, over 55, with CV disease or diabetes
- Sibutramine vs. placebo, 3.4 year f/u
- Outcomes MI, stroke, cardiac arrest, CV death

Results

- Weight: -1.7 kg
- BP: 1.2 vs. 1.4 mm Hg
- Combined outcome: 11.4% vs. 16.0% (HR 1.16, p = 0.02)
- Nonfatal MI: 4.1% vs. 3.1% (HR 1.28; p = 0.02)
- Nonfatal Stroke: 2.6% vs. 1.9% (HR 1.36; p = 0.03)
- Death: No differences

James, NEJM 2010
CURRENT ISSUES IN OBESITY

LORCASERIN

- Selective serotonin 2C receptor agonist
- RCT of 3,182 adults, 52 week study
- 45% vs. 55% drop-out (lorcaserin vs. placebo)
- 5.8±0.2 kg vs. 2.2±0.1 kg wt. loss
- Frequent adverse events: headache, dizziness, and nausea
- No increase in valvulopathy

Smith, NEJM, 2010

Weight Loss Medications: October, 2010

- Sibutramine (Meridia™): withdrawn by Abbott
  Increased risk of stroke and MI
- Lorcaserin (selective serotonin receptor agonist, more specific than fenfluramine): not approved by FDA
  Animals with increased mammary adenocarcinoma
- Phentermine/topiramate (Qnexa™): not approved by FDA
  Psychiatric adverse events: sleep, anxiety depression: 21% vs. 10% with placebo
  Increased heart rate
  Teratogenicity

Lorcaserin Update: May-June 2012

- FDA panel approved after new round of studies
- Industry sponsored study: 604 patients with type 2 diabetes
  After 1 year, 3.1% more weight loss (criteria >5%)
  38% lost >5% weight vs. 16% on placebo
- Lingering uncertainty re breast tumors, valvular heart disease, psychiatric issues
- Approved June 2012. Trade name Belviq™

Lorcaserin Update: March 2013

- Still not available.
- DEA suggests be classified as Schedule IV controlled substance
CURRENT ISSUES IN OBESITY

Phentermine/Topiramate Update: February-July 2012
- FDA panel approved 20:2
- Industry sponsored study: 4323 subjects
  - 9.3% weight loss
  - Increased heart rate, increased cleft lip
- Recommend post-market monitoring for CV risk and recommendation against use in pregnancy
- Company plans larger trial (11,000 subjects)
- Approved July 2012 (certified pharmacies only). Trade name Qysmia™

Phentermine/Topiramate (Qysmia™) Side Effects
- Paraesthesia, dizziness, dysgeusia, insomnia, constipation, dry mouth
- Fetal harm: cleft lip, cleft palate
- Suicidal thoughts or behavior
- Acute angle glaucoma
- Mood disorders: anxiety and depression
- Cognitive dysfunction: concentration memory, language
- Metabolic acidosis and renal failure
- Hypoglycemia (in association with diabetes meds)
- Interactions with alcohol and sedatives

Prescribing Phentermine/Topiramate (Qysmia™)
- Two prescriptions:
  - 14 days on 3.75/23 and
  - 30 days on 7.5/46
- Need DEA #
- Fax to certified pharmacy
- Pharmacy will call patient
- Drug delivered to patient’s home

OTHER INVESTIGATIONAL DRUGS
- Bupropion/naltrexone (Contrave™): Approved by FDA panel 12/10; rejected by FDA 2/11 (concern re heart attacks and CV risk.)
- Bupropion/zonisamide (Empatic™): Phase 3
- Exenatide (Byetta™), Liraglutide (Victoza™): Phase 2/3
- Pramlintide/metreleptin: Phase 2/3
- Cetilistat: Phase 3 in Japan
PRINCIPLES OF DRUG THERAPY

- NIH: BMI > 30 kg/m² or 27 kg/m² with co-morbidity (but in practice almost never)
- Motivated to begin structured exercise and low calorie diet
- Begin medications at completion of one month successful diet and exercise
- Continue medications only if additional weight loss achieved in first month with meds

Wouldn’t It Be Easier Just To Have Surgery?

INDICATIONS FOR BARIATRIC SURGERY

<table>
<thead>
<tr>
<th>Definition</th>
<th>BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt; 25</td>
</tr>
<tr>
<td>Overweight</td>
<td>25-29.9</td>
</tr>
<tr>
<td>Obese, class 1</td>
<td>30-34.9</td>
</tr>
<tr>
<td>Obese, class 2</td>
<td>35-39.9 (with co-morbidity)</td>
</tr>
<tr>
<td>Obese, class 3</td>
<td>40+</td>
</tr>
<tr>
<td>“Superobese”</td>
<td>60+</td>
</tr>
</tbody>
</table>

Types of Surgery

Restrictive
- Horizontal Gastroplasties
- Vertical Banded Gastroplasty (VBG)
- Silastic Ring Vertical Gastroplasty (SRVG)
- Adjustable Gastric Banding
- Sleeve Gastrectomy

Malabsorptive
- Jejunocolic Bypass (JIB)
- Biliopancreatic Diversion (BPD)
- Duodenal Switch
- Long Limb Gastric Bypass

Restrictive with Malabsorptive Component
- Roux-en-Y Gastric Bypass (RYGBP)
CURRENT ISSUES IN OBESITY

Bariatric Surgery: Weight Change

![Graph showing weight change over time for different surgical procedures.]

Bariatric Surgery and Mortality
Swedish Obese Subjects Study

- 4847 subjects, surgery vs. matched control. 10.9 years f/u

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Max weight loss %</th>
<th>Final weight loss %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Gastric bypass</td>
<td>32</td>
<td>25</td>
</tr>
<tr>
<td>Vertical banded Gastroplasty</td>
<td>25</td>
<td>16</td>
</tr>
<tr>
<td>Banding</td>
<td>20</td>
<td>14</td>
</tr>
</tbody>
</table>

Resolution of Comorbidities

![Bar chart showing resolution of comorbidities by surgical procedure.]

35 yo woman, BMI 42 in good health, asks about bariatric surgery. Her surgeon suggests a laparoscopic roux-n-y. Her risk of mortality, DVT, reintervention, or prolonged hospital stay is:

1. 1 in 200
2. 1 in 100
3. 1 in 50
4. 1 in 25
5. 1 in 10
BARIATRIC SURGERY OUTCOMES: 2005-07

- Ten sites, 4776 patients. 3/4 roux-en-y (87% lap); 1/4 lap band
- 30 Day overall mortality: 0.3%
  - lap band 0.0%
  - roux-en-y (lap) 0.2%
  - roux-en-y (open) 2.1%
- Composite (death, DVT, reintervention, 30 + days in hosp): 4.1%
  - lap band 1.0%
  - roux-en-y (lap) 4.8%
  - roux-en-y (open) 7.8%

35 yo woman, BMI 42 in good health, asks about bariatric surgery. Her surgeon suggests a laparoscopic roux-n-y. Her risk of mortality, DVT, reintervention, or prolonged hospital stay is:

1. 1 in 200
2. 1 in 100
3. 1 in 50
4. 1 in 25
5. 1 in 10

57 yo woman, BMI 42 with diabetes, hypertension, and creatinine 1.4 asks about bariatric surgery. Her risk of mortality 30 days post-op is:

1. 1 in 200
2. 1 in 100
3. 1 in 50
4. 1 in 25
5. 1 in 10

57 yo woman, BMI 42 with diabetes, hypertension, and creatinine 1.4 asks about bariatric surgery. Her risk of mortality 30 days post-op is:

1. 1 in 200
2. 1 in 100
3. 1 in 50
4. 1 in 25
5. 1 in 10

Mortality After Surgery
Community Medicare Data: 55-64 year old

<table>
<thead>
<tr>
<th></th>
<th>30 days</th>
<th>90 days</th>
<th>1 Year</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30 days</td>
<td>2.0%</td>
<td>2.7%</td>
<td>5.2%</td>
</tr>
</tbody>
</table>
### CURRENT ISSUES IN OBESITY

**Bariatric Surgery and Mortality**  
Swedish Obese Subjects Study

<table>
<thead>
<tr>
<th></th>
<th>Deaths</th>
<th>HR</th>
<th>MI deaths</th>
<th>Cancer deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>129</td>
<td>0.063</td>
<td>25</td>
<td>47</td>
</tr>
<tr>
<td>Surgery</td>
<td>101</td>
<td>0.050</td>
<td>13</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(p = 0.04)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NNT</td>
<td>77 over 11 years</td>
<td>(approx 850 per year)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SOURCES: NEJM, 2007

**Weight Loss Before Bariatric Surgery**
881 patients with gastric bypass; 6 month program to achieve 10% weight loss; 2/3 lost 5%; 1/2 lost 10%

<table>
<thead>
<tr>
<th>Weight Change</th>
<th>Complications %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gain 0%</td>
<td>28.4</td>
</tr>
<tr>
<td>Gain 0-5%</td>
<td>27.9</td>
</tr>
<tr>
<td>Loss 0-5%</td>
<td>22.5</td>
</tr>
<tr>
<td>Loss 6-10%</td>
<td>14.2</td>
</tr>
<tr>
<td>Loss 10%</td>
<td>18.6</td>
</tr>
</tbody>
</table>

(p for trend = 0.004)

**LONG-TERM OUTCOMES OF LAP BAND**
- 151 patients, single center, 12 year f/u; 54.3% included (82/151)
- Operative mortality: 0
- Mean weight loss: 20.75 kg (BMI decreased from 41.6 to 33.8)
- 60% of patients satisfied; overall quality of life unchanged
- 39% major complications; 60% required re-operation

**Conclusion:** Lap band results in poor long-term outcomes

**Nutrition after Bariatric Surgery**

**Gastric Bypass**
- Multivitamin 2 daily
  - (400 mcg folate)
- Omeprazole 20 mg daily
- Calcium (500mg TID)
- Vitamin D (200 IU TID)
- Iron sulfate 325mg daily
  - (women)
- Vitamin B12 500mcg SL daily

**Lap Band**
- Multivitamin 1 daily
- Omeprazole 20 mg daily
- Calcium (500mg TID)
- Vitamin D (500 IU TID)

**SOURCES:** NEJM, 2009
BARON’S FACTS ABOUT OBESITY

- Environmental changes work: **YES**
- Diets work, but not for long in most people: **YES, BUT THEY DO FOR SOME**
- Exercise improves health independent of weight change and aid in weight maintenance: **YES**
- Continuation of conditions that promote weight loss promotes weight maintenance: **YES**

BARON’S FACTS ABOUT OBESITY

- For children, programs that involve parents and home promote greater weight loss: **MAYBE**
- Provision of meals and meal replacement products promote greater weight loss: **IN THE SHORT TERM**
- Medications can help achieve meaningful weight loss for as long as agents can be used: **BUT WHAT ABOUT LONGER TERM CLINICAL OUTCOMES?**
- Surgery results in long term weight loss and reductions of diabetes and mortality: **WITH COMPLICATIONS IN SOME/MANY AND A HIGH NNT**

GOALS OF MANAGEMENT

- Be as fit as possible at current weight
- Prevent further weight gain
- If successful at 1 and 2, begin weight loss

The Magic Formula

“Eat less and exercise more? That’s the most ridiculous fed diet I’ve heard of yet!”

Casazza, NEJM 2013