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)
OBESITY: FACTS AND FICTIONS

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)

CLASSIFICATION OF WEIGHT AND OBESITY BY BODY MASS INDEX (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>
OBESITY: FACTS AND FICTIONS

BMI AND MORTALITY:
Overall
Combined NHANES I, II, and III data set

<table>
<thead>
<tr>
<th>BMI</th>
<th>25-59 y</th>
<th>60-69 y</th>
<th>≥70 y</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;18.5</td>
<td>1.38</td>
<td>2.30</td>
<td>1.69</td>
</tr>
<tr>
<td>18.5–25</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>25 to &lt;30</td>
<td>0.83</td>
<td>0.95</td>
<td>0.91</td>
</tr>
<tr>
<td>30 to &lt;35</td>
<td>1.20</td>
<td>1.13</td>
<td>1.03</td>
</tr>
<tr>
<td>≥35</td>
<td>1.83</td>
<td>1.63</td>
<td>1.17</td>
</tr>
</tbody>
</table>

Flegal, JAMA, 2005

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><strong>30-35 (Grade 1 Obesity)</strong></td>
<td>0.95</td>
</tr>
<tr>
<td>Above 35 (Grade 2/3 Obesity)</td>
<td>1.29</td>
</tr>
</tbody>
</table>

Flegal, JAMA, 2013

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

Shaw, Cochrane, 2006

More, Cochrane, 2006
FITNESS AND MORTALITY
Aerobics Center Longitudinal Study

25,714 men, 44 years old, 14 year observational study

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Overweight</th>
<th>Obese</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CV death (RR)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fit</td>
<td>1.0</td>
<td>1.5</td>
<td>1.6</td>
</tr>
<tr>
<td>Not fit</td>
<td>3.1</td>
<td>4.5</td>
<td>5.0</td>
</tr>
<tr>
<td><strong>Total death (RR)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>1.0</td>
<td>1.1</td>
<td>1.1</td>
</tr>
<tr>
<td>Not fit</td>
<td>2.2</td>
<td>2.5</td>
<td>3.1</td>
</tr>
</tbody>
</table>


Relative Risk* of Death According to Body Mass and Physical Activity

- *RR* is adjusted for age, smoking status, family history, menopausal status, hormone use, and other factors
- **Reference group** = women with >3.5 hours/week of physical activity and BMI of 25 or less

Estimating Calorie Needs

- **To estimate calories for weight maintenance:**
  - If you are moderately active, multiply current weight (pounds) x 15.

- **To estimate calories for weight loss:**
  - Subtract 500 calories to lose approximately 1.0 pound per week.
  - A pound of fat is about 3500 kcals.
COMPARISON OF ATKINS, ORNISH, WEIGHT WATCHERS, AND ZONE

160 patients, randomly assigned

Intention to treat at 1 year

<table>
<thead>
<tr>
<th></th>
<th>Atkins</th>
<th>Ornish</th>
<th>WW</th>
<th>Zone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wt Loss (kg)</td>
<td>2.1</td>
<td>3.3</td>
<td>3.0</td>
<td>3.2</td>
</tr>
<tr>
<td>Completers (%)</td>
<td>53</td>
<td>50</td>
<td>65</td>
<td>65</td>
</tr>
</tbody>
</table>

Completers at 1 year

<table>
<thead>
<tr>
<th></th>
<th>Atkins</th>
<th>Ornish</th>
<th>WW</th>
<th>Zone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wt Loss (kg)</td>
<td>3.9</td>
<td>6.6</td>
<td>4.6</td>
<td>4.9</td>
</tr>
</tbody>
</table>

Dansinger, JAMA 2005

Weight loss associated with adherence, but not diet type

Each group: 25% lost 5%, 10% lost 10% of initial weight

Each diet reduced LDL/HDL by 10%

No significant effects on BP or glucose

COMPARISON OF WEIGHT LOSS DIETS WITH DIFFERENT MACRONUTRIENTS

RCT of 811 patients, 4 diets: fat/protein/carbs
20/15/65, 20/25/65, 40/15/45, 40/25/35

6 months: 6kg, 7% weight; at 2 years: completers lost 4kg; 15% lost 10% of weight

Results similar for:
- 15% pro v. 25% pro
- 20% fat v. 40% fat
- 35% carbs v. 65% carbs

Attendance highly correlated with weight loss; satiety, hunger, lipids, insulin all equal

Sacks, NRR 2009

Heterogeneity of Response to Weight Loss

Diets: Insulin Resistance

- Insulin sensitive: low carb and high carb both effective for weight loss
- Insulin resistant: low carb more effective
**Very Low Calorie Diets (VLCD) vs Low Calorie Diets (LCD): Meta-analysis of 6 RCTs**

- Trials with direct comparisons
- Short-term: mean 12.7 weeks
- Long-term: mean 1.9 years

<table>
<thead>
<tr>
<th></th>
<th>short-term</th>
<th>long-term</th>
</tr>
</thead>
<tbody>
<tr>
<td>LCDs</td>
<td>9.7</td>
<td>5.0</td>
</tr>
<tr>
<td>VLCDs</td>
<td>16.1</td>
<td>6.3</td>
</tr>
</tbody>
</table>

(p) (0.001) (0.2)

**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

**Weight Loss Diet Tips**

- Ready to lose weight?
- Set realistic expectations.
- Choose diet that is easy to follow and compatible with lifestyle.
- Control portion size (plate method, etc).
- Vegetables, fruit and whole grains
- Maintaining the weight you lose is key.

**BEHAVIORAL ASPECTS OF WEIGHT LOSS**

- Goal setting
- Self-monitoring
- Stimulus control
- Cognitive skills
SUCCESSFUL WEIGHT LOSS MAINTENANCE

- 3000 subjects in National Weight Control Registry: 50-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

SUCCESSFUL WEIGHT LOSS MAINTENANCE

- 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
  - 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
The Neuroendocrinology of Energy Balance

"LONG TERM" PHARMACOTHERAPY OF OBESITY
Review of all RCT’s more than 36 weeks published since 1960
Weight loss in excess of placebo:

<table>
<thead>
<tr>
<th>Medication</th>
<th>% of Initial</th>
<th>kg's</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phen-fen</td>
<td>11.0%</td>
<td>9.6 kg</td>
</tr>
<tr>
<td>Phentermine</td>
<td>8.1%</td>
<td>7.9 kg</td>
</tr>
<tr>
<td>Sibutramine</td>
<td>5.0%</td>
<td>4.3 kg</td>
</tr>
<tr>
<td>Orlistat</td>
<td>3.4%</td>
<td>3.4 kg</td>
</tr>
<tr>
<td>Dexfenfluramine</td>
<td>3.0%</td>
<td>2.5 Kg</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>-0.4%</td>
<td>-0.4 kg</td>
</tr>
<tr>
<td>Diethypropion</td>
<td>-1.5%</td>
<td>-1.5 kg</td>
</tr>
</tbody>
</table>

RIMONABANT

- Meta-analysis of 4 studies
- Rimonabant plus diet vs diet alone, for 1 year or more
  - Rimonabant 20 - 4.9 kg loss (5%)
- Improved waist circumference, BP, HDL, TG
- Attrition 40%: GI, psychiatric, neurological
- Rimonabant 5 mg -1.3 kg loss

RIMONABANT

June 2007

- FDA advisory committee recommends that rimonabant not be sold in the US pending further study of depression and suicidality.
- Sanofi withdraws bid to sell rimonabant in US
OBESITY: FACTS AND FICTIONS

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. 10.0% (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

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

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 15% 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: May 2013

- Still not available.
- Classified as Schedule IV controlled substance
- Available June 7, 2013 as Belviq™

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

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
OBESITY: FACTS AND FICTIONS

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?

Types of Surgery

Restrictive
- Horizontal Gastroplasties
- Vertical Banded Gastroplasty (VGB)
- Silastic Ring Vertical Gastroplasty (SRVG)
- Adjustable Lap-Band

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

Restrictive with Malabsorptive Component
- Roux-en-Y Gastric Bypass (RYGBP)

Restrictive and Mixed Procedures

VBG | Adjustable Gastric Banding | Roux-en-Y GB
OBESITY: FACTS AND FICTIONS

Bariatric Surgery: Weight Change

Resolution of Comorbidities

Gastric Bypass

Sleeve Gastrectomy

Bariatric Surgery – A Systematic Review and Meta-analysis
Buchwald H. et al.
JAMA. 2004; 292(14):1724-37
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%

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

- 30 days 90 days 1 Year
- 2.0% 2.7% 5.2%

Bariatric Surgery and Mortality
Swedish Obese Subjects Study

<table>
<thead>
<tr>
<th></th>
<th>Deaths</th>
<th>HR Rate</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 (approx 850 per year)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Sources: NEJM, 2009

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 5%</td>
<td>26.4</td>
</tr>
<tr>
<td>Gain 0-5%</td>
<td>27.9</td>
</tr>
<tr>
<td>Loss 0-5%</td>
<td>23.5</td>
</tr>
<tr>
<td>Loss 5-10%</td>
<td>14.2</td>
</tr>
<tr>
<td>Loss 10%</td>
<td>18.0</td>
</tr>
</tbody>
</table>

(p for trend = 0.004)

Sources: Arch Surg, 2009
OBESITY: FACTS AND FICTIONS

Nutrition after Bariatric Surgery

<table>
<thead>
<tr>
<th>Gastric Bypass</th>
<th>Lap Band</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multivitamin 2 daily</td>
<td>Multivitamin 1 daily</td>
</tr>
<tr>
<td>(400 mcg folate)</td>
<td>Omeprazole 20 mg daily</td>
</tr>
<tr>
<td>Omeprazole 20 mg daily</td>
<td>Calcium (500mg TID)</td>
</tr>
<tr>
<td>Calcium (500mg TID)</td>
<td>Vitamin D (200 IU TID)</td>
</tr>
<tr>
<td>Vitamin D (200 IU TID)</td>
<td>Vitamin B12 500mcg SL daily</td>
</tr>
<tr>
<td>Iron sulfate 325mg daily (women)</td>
<td></td>
</tr>
</tbody>
</table>

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
OBESITY: FACTS AND FICTIONS

The Magic Formula

"Eat less and exercise more? That's the most ridiculous fad diet I've heard of yet!"