Obesity Pharmacotherapy

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Pharm D, BCPS
Outline

- Case Presentation
- Definition, Prevalence, & Comorbidities of Obesity
- Indications for Drug Therapy
- FDA Approved Medicines for Obesity Treatment
  - sibutramine, phentermine, orlistat
- Other Medicines that Promote Weight Loss
  - DM medicines, antidepressants (SSRIs), anti-epileptics
- Investigational Medicines: Rimonabant
- Summary and Case discussion
Case:  DB

49 y/o obese woman with the following concerns:

- Chronic bilateral knee pain not responding to anti-inflammatory medications
- Inability to exercise due to pain
- Inability to loose weight despite food restriction
<table>
<thead>
<tr>
<th>DB PMH</th>
<th>DB Medications</th>
<th>DB Social History</th>
</tr>
</thead>
<tbody>
<tr>
<td>■ Morbid obesity</td>
<td>■ Diclofenac</td>
<td>■ Disabled/ MA</td>
</tr>
<tr>
<td>■ HTN</td>
<td>■ Lasix</td>
<td>■ +tobacco, no alcohol</td>
</tr>
<tr>
<td>■ Hyperlipidemia</td>
<td>■ Prevacid</td>
<td></td>
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<tr>
<td>■ ↑ TG, ↓ HDL</td>
<td>■ Levothyroxine</td>
<td></td>
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<tr>
<td>■ OSA (Can’t use CPAP)</td>
<td>■ Sertraline</td>
<td></td>
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<tr>
<td>■ OA</td>
<td>■ Benazepril</td>
<td></td>
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<tr>
<td>■ Depression</td>
<td></td>
<td></td>
</tr>
<tr>
<td>■ Insulin resistance</td>
<td></td>
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<tr>
<td>■ Hypothyroidism</td>
<td></td>
<td></td>
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<tr>
<td>■ GERD</td>
<td></td>
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</tr>
<tr>
<td>■ s/p cholecystectomy</td>
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</tbody>
</table>

**DB Social History**

- Disabled/ MA
- +tobacco, no alcohol
DB Exam

- Morbidly obese
  - 285 lb, 5’2”, BMI 52
- Knee exam difficult due to body habitus
- Diffuse tenderness
- ▼ ROM (0-100°)
- No ligamentous laxity
- + Retropatellar crepitus

DB Imaging Data

Standing Plain Films:
Severe OA knees bilaterally
Lateral compartment on R
Medial compartment on L
DB Assessment & Plan

- Morbid obesity and severe bilateral OA of knees
- Referred to Orthopedics
  - TKA is indicated, IF she can reduce weight below 180 lbs.
- Referred to Health ED for dietary counseling
  - Last seen in September, several “no shows.”
- Referred for possible Bariatric surgery
  - WI Medicaid coverage as of 2/05
  - Yes: Gastric bypass for qualified, low risk patients
  - No: Gastric banding
- DB asks whether there are any medications she could take to help her lose weight
Questions

- When diet and exercise are not effective, or adequate exercise is not possible, are there medications to treat obesity that are safe and effective?
- How do I determine which medications are right for which patients?
- What about cost/coverage by local insurance?
Definition of Obesity

- BMI 25-29.9 (Grade 1, overweight)
- BMI 30-39.9 (Grade 2, obese)
- BMI > 40 (Grade 3, Morbidly obese)
- Increased visceral fat
  - Waist > 94 cm in men (waist-to-hip > 0.95)
  - Waist > 80 cm in women (waist-to-hip >0.8)
OBESITY: The percentage of the population older than 15 with a body-mass index greater than 30.

- USA: 31%
- Mexico: 24%
- UK: 23%
- Slovak Republic: 22%
- Greece: 22%
- Australia: 22%
- New Zealand: 21%
- Hungary: 19%
- Czech Republic: 15%

- Canada: 14%
- Spain: 13%
- Ireland: 13%
- Germany: 13%
- Portugal: 13%
- Finland: 13%
- Turkey: 12%
- Belgium: 12%
- Poland: 11%

- Netherlands: 10%
- Sweden: 10%
- Denmark: 10%
- France: 9%
- Austria: 9%
- Italy: 9%
- Norway: 8%
- Japan: 3%
- Korea: 3%
Obesity in the U.S.

- More than 97 million adults in US are overweight or obese (BMI ≥30)
  - 19.9% of men
  - 24.9% for women

Source: CDC/NCHS, United States, 1960-94 (ages 20-74 years)
Prevalence of Obesity

More than 30% of adults in the US are overweight or obese, and this percentage is rising.

Percentage of people with BMI $\geq 30$ in the US in 2005

*CDC's Behavioral Risk Factor Surveillance System.*
Costs of Obesity

- Costs the US health-care system more than $99 billion each year.
- Consumers also spend over $33 billion annually on weight-reduction products and services.
- Annual health-care costs for patients with BMIs of 20 to 24.9 were 20% lower than costs for patients with BMIs from 30 to 34.9 and almost 33% lower than for patients who had BMIs of 35 or more.
Complications of Obesity

Complications of Childhood Obesity

- **Psychosocial**
  - Poor self esteem
  - Depression
  - Quality of life

- **Neurological**
  - Pseudotumor cerebri
  - Risk for stroke

- **Cardiovascular**
  - Dyslipidemia
  - Hypertension
  - Left ventricular hypertrophy
  - Chronic inflammation
  - Endothelial dysfunction
  - Risk of coronary disease

- **Pulmonary**
  - Asthma
  - Sleep apnea
  - Exercise intolerance

- **Renal**
  - Glomerulosclerosis
  - Proteinuria

- **Gastrointestinal**
  - Pancreatitis
  - Steatohepatitis
  - Liver fibrosis
  - Gallstones
  - Risk for cirrhosis
  - Risk for colon cancer

- **Musculoskeletal**
  - Forearm fracture
  - Blount's disease
  - Slipped capital femoral epiphysis
  - Flat feet
  - Risk for degenerative joint disease

- **Endocrine**
  - Type 2 diabetes
  - Precocious puberty
  - Polycystic ovary syndrome (girls)
  - Hypogonadism (boys)

- **Hernia**

- **DVT/PE**

- **Stress incontinence**
  - Risk of GYN malignancy
<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td><strong>HTN/ hyperlipidemia</strong></td>
<td><strong>CAD/CVA</strong></td>
<td><strong>DM II</strong></td>
</tr>
<tr>
<td><strong>Cancer (Breast, Colon, Prostate)</strong></td>
<td><strong>Meralgia paresthetica</strong></td>
<td><strong>Gallbladder disease</strong></td>
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<tr>
<td><strong>NASH/ NAFLD</strong></td>
<td><strong>GERD</strong></td>
<td><strong>Varicose veins</strong></td>
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<tr>
<td><strong>Endometrial Ca PCOS/ infertility</strong></td>
<td><strong>Surgical Risk/ post-op complications</strong></td>
<td><strong>LE edema/ cellulitis</strong></td>
</tr>
<tr>
<td><strong>Depression</strong></td>
<td><strong>OA</strong></td>
<td><strong>Pulmonary HTN/ OSA</strong></td>
</tr>
</tbody>
</table>
Does weight loss lead to improvement in outcome?

- 10kg loss leads to:
  - Reduction in total cholesterol of 0.25mmol/l
  - Reduction in systolic BP of 6mmHg
  - Reduction in diastolic BP of 3mmHg

- ANY weight loss in people with an obesity related illness leads to:
  - In women - Reduced risk of death, CVD, cancer or diabetes related death
  - In men – Reduced risk of diabetes related death
Metabolic Syndrome: The Role of Obesity

- Obesity
  - FFA
  - Triglycerides
    - HDL
  - Insulin Resistance
    - Blood Glucose
    - Blood Pressure
  - Type 2 Diabetes
  - Cardiovascular Disease
Indications for Drug Therapy in Obesity

- Failure of diet and exercise alone
- Significant obesity related comorbidities even if BMI < 30 (ie 25-30).
- No contraindications to drug therapy
  - Medication interactions
  - Medical conditions that may be adversely affected by the obesity drug

## Model of Obesity Care

| Level 1: Public health initiatives. GP to signpost patients to community based lifestyle intervention |
| Level 2: 1+ practice based intervention, anti-obesity drugs, community dietitian, behaviour modification |
| Level 3: (secondary care) Specialist dietitian, endocrinologist, psychologist, genetic screening, anti-obesity drugs |
| Level 4: (secondary care) Bariatric surgery with support from level 3 service |
Centrally-Acting Anorexigens Approved Post-1938

- 1947 – Desoxyephedrine/methamphetamine (available pre-’38)
- 1956 – Phenmetrazine (Preludin)
- 1959 - Phendimetrazine (Bontril)
- 1959 - Phentermine (Fastin, Ionamin) – W/D CPMP 2000
- 1959 - Diethylpropion (Tenuate)
- 1960 - Benzphetamine (Didrex)
- 1972 - Fenfluramine (Pondimin) – W/D 1997
- 1973 - Mazindol (Sanorex)
- 1997 – Sibutramine (Meridia)
Drugs Approved for Long-Term Treatment of Obesity

- 1996 - Dexfenfluramine (Redux): w/d ‘97
- 1997 - Sibutramine (Meridia)
- 1999 - Orlistat (Xenical)

- Efficacy: Long-term indication drugs
  - Mean loss of 5.0 kg vs. placebo
    - range of placebo-subtracted means across studies 1.5 to 6.0 kg
Drug use data: 1991-2002

Annual volume of antiobesity medications reported in the United States, 1991–2002, IMS HEALTH National Disease and Therapeutic Index. Data for 2002 are an estimate (E) based on January to March 2002 figures. HCl indicates hydrochloride.

Sibutramine

- Mechanism of action:
  - Inhibits norepinephrine and serotonin reuptake
  - Decreases food intake; ?Thermogenic effect?
- Dosing: 5 -15 mg po daily
  - Schedule IV, but approved for long-term use
- Cost: about $105 for a 30 day supply of 10 mg tablets
- Insurance coverage: NC by Unity, PPlus, or Medicaid
**Sibutramine: Efficacy**

- Meta-analysis of healthy obese adults
- Exclusion: patients with CAD
- Concomitant lifestyle, dietary, and behavioral modification
- Primary outcome: weight loss
- Secondary outcomes: cardiovascular, metabolic

<table>
<thead>
<tr>
<th>Dose</th>
<th># trials</th>
<th>Duration</th>
<th>Patients</th>
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</thead>
<tbody>
<tr>
<td>10-15 mg</td>
<td>7</td>
<td>8-12 wks</td>
<td>546</td>
</tr>
<tr>
<td>12 (4-5-3)</td>
<td>12</td>
<td>16-24 wks</td>
<td>1079</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>44-54 wks</td>
<td>2188</td>
</tr>
</tbody>
</table>

Subgroup A used late-observation-carried-forward analysis and had >70% follow up
Subgroup B analyzed only participants who completed the trial
Subgroup C had follow up rates less than 70%
Secondary Outcomes

- Modest increase in BP and HR
- Small improvements in TG, HDL, & glycemic control
- No evidence of improvement of morbidity & mortality
- No dose effect for weight loss.
- 1 trial showed weight loss maintained at 2 yrs
- 2 trials showed regain of 50% of weight at 6-12 months after stopping medicine.

Cochrane Review: Sibutramine Long-term Efficacy

- Meta-analysis of RCTs, Sibutramine vs. placebo
  - 3 trials -- weight loss at more than 1 year follow up
  - 2 trials -- weight maintenance at 2 years
- Inclusion: adults BMI>30 or BMI>27 + comorbidities
- Exclusion: patients with DM or uncontrolled HTN
- Results: **4.3 kg (3.6-4.9) more wt loss with sibutramine**
  - 27% more patients maintained 80% of original weight loss at 2 years with sibutramine
- Adverse effects: Small increase in HR and BP

Sibutramine with & without Lifestyle Changes

- 224 obese adults randomized to the following for 1 year:
  - 15 mg sibutramine daily (PCP 8 visits, no counseling)
  - Lifestyle modification alone (30 group sessions, 90 minutes, psychologist)
  - Sibutramine + lifestyle modification (30 group sessions)
  - Sibutramine + brief lifestyle modification (PCP 8 visits, brief counseling)
- All prescribed diet 1200-1500 kcal per day and exercise regimen

*Wadden TA et al. NEJM, 2005.*
# Sibutramine

<table>
<thead>
<tr>
<th>Adverse Effects</th>
<th>Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increase BP, HR</td>
<td>History of CAD, CHF, CVA, glaucoma</td>
</tr>
<tr>
<td>Palpitations, prolong QT</td>
<td>History of arrhythmia</td>
</tr>
<tr>
<td>Tachyarrhythmia (rare)</td>
<td></td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>Predisposition to bleeding</td>
</tr>
<tr>
<td>P450 metabolism</td>
<td>Severe liver or renal disease</td>
</tr>
<tr>
<td>Serotonin syndrome</td>
<td>MAOIs, SSRIs</td>
</tr>
<tr>
<td>HA, insomnia, Sz (rare)</td>
<td>History of seizure</td>
</tr>
<tr>
<td>GI disturbance</td>
<td></td>
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</tbody>
</table>
Phentermine and Diethylpropion

- **Mechanism of action:** Stimulate NE release and inhibit re-uptake
- **Dosing** *(short-term use only -- < 12 weeks)*
  - 18.75 to 37.5 mg once daily or in divided doses
  - Schedule IV
- **Cost:** about $34 for a month supply of 37.5 mg tablets
- **Insurance coverage:** NC by Unity, PPlus, or Medicaid
Phentermine: Efficacy and Safety

- **Meta-analysis:** Included 6 RCTs
- **Duration:** 2-24 wks
- **Dose:** 15-30 mg per day
- **Results:** 3.6kg (0.6-6.0) more wt loss with phentermine
- **No data on side effects or adverse events reported**

*Haddock et al, J Obes Relat Metabolic Disord, 2002.*
# Phentermine

## Adverse Effects

<table>
<thead>
<tr>
<th>HTN, tachyarrhythmia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart valve disorder (rare)</td>
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<tr>
<td>PPH (rare)</td>
</tr>
<tr>
<td>GI disturbance</td>
</tr>
<tr>
<td>Psychosis, agitation</td>
</tr>
<tr>
<td>HA, insomnia, tremor,</td>
</tr>
<tr>
<td>AMS, dizziness</td>
</tr>
<tr>
<td>Decreased libido</td>
</tr>
<tr>
<td>Affect insulin needs in DM</td>
</tr>
</tbody>
</table>

## Contraindications

<table>
<thead>
<tr>
<th>CAD, HTN, glaucoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperthyroidism</td>
</tr>
<tr>
<td>MAOI, SSRI</td>
</tr>
<tr>
<td>History of drug/ethanol abuse</td>
</tr>
<tr>
<td>Psychiatric disease</td>
</tr>
</tbody>
</table>
Orlistat

- **Mechanism of Action**
  - Inhibits pancreatic lipases preventing hydrolysis of ingested fat
  - Less than 1% absorbed
- **Dosing:** 60 – 120 mg prior to each meal.
  - Lower dose OTC (My Alli)
- **Cost:** about $224 for a 1 month supply of 120 mg dose
- **Insurance coverage:** NC by Unity, PPlus, or Medicaid
- **GI side effects:** diarrhea, cramping, flatus, oily discharge, malabsorption of fat soluble vitamins.
- **Only drug interaction:** CSA
Orlistat: Efficacy

- Meta-analysis, 29 RCTs included
- 12 trials with 6 months follow up
  - Mean of 2.59 kg (1.74-3.46) more wt loss with orlistat
- 22 trials with 12 months follow up
  - Mean of 2.89 kg (2.27-3.51) more wt loss with orlistat
- RR diarrhea 3.40, flatus 3.10, and dyspepsia 1.48
  - No difference between 6 and 12 months
- Cochrane review meta-analysis
  - 11 trials with at least 12 months follow up
  - Mean of 2.7 kg (2.3-3.1) more wt loss with orlistat

Orlistat (Xenical) Indications

Among obese patients who meet the criteria for anti-obesity drug therapy, orlistat is most likely to benefit those who:

- Do not feel hungry
- Are not preoccupied with food
- Eat out or order-in often
- Have increased cardiovascular disease risk or multiple cardiovascular risk factors
- Are older
- Take multiple medications

Orlistat is taken 3 times daily with meals
Orlistat- Effect on HgbA1C in T2DM

The improvement in HbA1c achieved with orlistat therapy exceeded that of the placebo group and there was a 0.62% improvement in HbA1c relative to the baseline value for the participants randomized to orlistat.

Figure 4—HbA1c over 1 year of double-blind treatment with placebo (E) or 120 mg orlistat (F). P<0.002, least-squares mean difference from placebo in the change from baseline over 52 weeks.
Orlistat: Long-term Efficacy

- 4-year double blind placebo controlled RCT
- 3,305 patients, BMI>30
- Lifestyle changes + orlistat (120 mg) or placebo
- Primary outcomes: wt loss, time to onset DM II
  - Mean of 2.8 kg more wt loss with orlistat (P<0.001)
  - Incidence of diabetes 6.2% vs 9% (P=0.0032)

Combination Therapy

- 3 small trials
  - 34 women after 1 year on sibutramine with 11.6% mean wt loss randomized to S+O or S + placebo for 16 wks
  - 89 women randomized to diet+O, diet+S, or diet+O+S for 6 months
  - 86 pts randomized to S, O, S+O, or diet for 12 wks
- Sibutramine alone as good as Combination & better than Orlistat alone

Antidepressants: Efficacy

Weight loss with bupropion & fluoxetine vs. placebo at 6 - 12 months

- **Bupropion**
  - Anderson et al., 2002 (89)
  - Croft et al., 2002 (90)
  - Jain et al., 2002 (91)
  - Overall

- **Fluoxetine**
  - Breum et al., 1995 (88)
  - Darga et al., 1991 (82)
  - Goldstein et al., 1994 (80)
  - Marcus et al., 1990 (81)
  - Michelson et al., 1999 (84)
  - O’Kane et al., 1994 (83)

**Mean Difference (95% CI)**
- Anderson et al., 2002 (89): -4.91 (-6.78 to -3.05)
- Croft et al., 2002 (90): -1.17 (-2.25 to -0.09)
- Jain et al., 2002 (91): -2.70 (-3.57 to -1.83)
- Overall: -2.77 (-4.50 to -1.05)

- Breum et al., 1995 (88): -0.70 (-8.53 to 7.13)
- Darga et al., 1991 (82): -3.60 (-4.87 to -2.33)
- Goldstein et al., 1994 (80): 0.40 (-1.70 to 2.50)
- Marcus et al., 1990 (81): -14.50 (-22.62 to -6.38)
- Michelson et al., 1999 (84): -0.20 (-2.59 to 2.19)
- O’Kane et al., 1994 (83): -5.80 (-7.57 to -4.03)

Note: High doses used
Fluoxetine 60 mg daily
Bupropion 400 mg/day

Topiramate

- Topiramate is a novel antiepileptic drug approved by the FDA as an antiseizure medication.
- When reports surfaced that patients enrolled in initial trials of the drug and also in clinical practice were experiencing unexpected weight loss, the effects of the drug on weight began to be studied.
- Mechanism for weight loss is still poorly understood
Topiramate

- 34 patients being treated for epilepsy.
- 12-month open-label trial without dietary intervention, patients took combinations of drugs to treat their epilepsy.

Dr. Ulf Smith, Sahlgrenska University Hospital, Göteborg, Sweden
Antiepileptic: Efficacy

Weight loss with topiramate versus placebo at 6 months

Note: High dose, 192 mg/day

Metformin

- 3234 nondiabetic adults with impaired glucose tolerance
  - Mean BMI 34, mean age 51, 68% women
- Randomized to placebo, metformin 850 mg po BID or lifestyle changes for 2.8 years

Knowler et al. NEJM 2002.
Metformin Compared to Others

- 150 women with BMI >30 randomized to the following:
  - Sibutramine 10 mg po BID (Higher than normal dose)
  - Orlistat 120 mg po TID
  - Metformin 850 mg po BID
- All groups also with lifestyle interventions/ nutrition counseling
- No placebo group
- 6 months follow up

<table>
<thead>
<tr>
<th></th>
<th>% decrease BMI</th>
<th>% decrease waist circumference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sibutramine</td>
<td>13.57</td>
<td>10.43</td>
</tr>
<tr>
<td>Orlistat</td>
<td>9.09</td>
<td>6.64</td>
</tr>
<tr>
<td>Metformin</td>
<td>9.90</td>
<td>8.10</td>
</tr>
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</table>

Leptin

• Naturally occurring hormone that plays a role in satiety and weight maintenance.
• Produced in adipocytes
• Its role in weight regulation is related to its effects on the hypothalamus, where it leads to:
  • satiety
  • decreased food intake
  • increased energy expenditure in the periphery
CENTRAL EFFECTS
- Decrease in food intake
- Reversal of hypothalamic thyroid and gonadal dysfunction

PERIPHERAL EFFECTS
- Increase in T cell number and function

INDIRECT EFFECTS
- Improved metabolic profile
- Decrease in insulin
- Decrease in total cholesterol
- Decrease in triglycerides
- Increase in HDL-cholesterol
Leptin

- Initial human trials with recombinant leptin were modestly successful.
- Most subjects in the initial trial developed local reactions at the injection site.
- Weight loss was relatively modest.
- However, the hormone needs to be given subcutaneously and has a short half-life.
- Thus a modified recombinant human leptin (m-leptin) was created that has a longer half-life.
Exenatide

- 336 pts, BMI 34.2+/−5.9
- DM II, mean A1c 8.2+/− 1.1
- 4 wks placebo
- 4 wks 5 μg exenatide BID or placebo
- 26 wks 5 or 10 μg exenatide BID or placebo
- All on metformin
- End of study mean A1c 7.4%
- 50% reached goal of < 7% on 10 μg dose

*DeFronzo RA, et al. Diab Care, 2005.*
Rimonabant

- Cannabinoid-1 receptor blocker
  - Reduces overactivation of the central & peripheral endocannabinoid system
- 3045 pts with BMI>27 and HTN or dyslipidemia
- 4-wk single blind placebo + diet run-in
  - Randomized to 5 mg daily, 20 mg daily, or placebo for 1 year
  - Treated pts re-randomized to placebo or continued rimonabant for 2nd year
- High drop out rate ~ 50% in all groups
- Most common side effect was nausea (11.2% vs 5.8%)

Pi-Sunyer, F. X. et al. JAMA 2006.
Surgery vs. Pharmacotherapy

- RCT, 80 adults BMI 30-35
- Laparoscopic adjustable gastric banding
- Intensive non-surgical program
  - Very low calorie diet (500-550 kcal/day) X 12 wks
  - Orlistat 120 mg added before some meals X 4 wks
  - Orlistat before all meals X 8 wks for total of 6 mo
  - Continued low calorie diet or orlistat + behavioral therapy for long-term maintenance
- Primary endpoint: Change in weight

Mean % of initial weight lost
(initial data carried forward for missing values)

- Statistically significant improvement in metabolic syndrome in surgical group: 35% of pts in both groups initially, 24% of pts in non-surgical group and 3% of pts in surgical group at 2 yrs
- Surgical group adverse events: 1 port site infection, 4 prolapse of posterior gastric wall, 1 cholecystitis
- Non-surgical group adverse events: 1 diet intolerance, 8 orlistat intolerance, 4 cholecystitis

## Summary

- Weight loss with obesity medicines is modest
- Obesity medicines are not a substitute for diet and exercise
- Weight loss is often not maintained after drug is discontinued
- Most obesity medicines are not covered by insurance

<table>
<thead>
<tr>
<th>Drug</th>
<th>Wt loss</th>
</tr>
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<tbody>
<tr>
<td>Sibutramine</td>
<td>4-5 kg</td>
</tr>
<tr>
<td>Phentermine</td>
<td>3-4 kg</td>
</tr>
<tr>
<td>Orlistat</td>
<td>2-3 kg</td>
</tr>
<tr>
<td>Metformin</td>
<td>2 kg</td>
</tr>
<tr>
<td>Exenatide</td>
<td>2-3 kg</td>
</tr>
<tr>
<td>Bupropion</td>
<td>2-3 kg</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>Mixed</td>
</tr>
<tr>
<td>Topamax</td>
<td>6-7 kg</td>
</tr>
<tr>
<td>Rimonabant</td>
<td>6-7 kg</td>
</tr>
</tbody>
</table>
Novel treatments

- Neuroendocrine regulation of energy balance
- Inhibit anabolic molecules
  - Neuropeptide Y, Melanin concentrating hormone
- Stimulate catabolic signals
  - Leptin receptor agonists
- Gastric peptides
  - GLP-1, Ghrelin inhibitors
NICE Indications for Bariatric Surgery

- BMI > 40
- BMI > 35 + co-morbidity eg DM, high BP
- Failure to achieve/maintain adequate weight loss after 6/12 non-surgical intervention
- Receiving specialist obesity service treatment
- Commitment to long-term follow-up
- Fit for anaesthetic/procedure
- First line treatment if BMI > 50
Types of Procedure

- **Restrictive**
  - Gastric band (reversible)
  - Sleeve gastrectomy (irreversible)

- **Malabsorptive**
  - Biliopancreatic diversion +/- duodenal switch (gastric pouch attached to ileum)

- **Mixed Restrictive / Malabsorptive**
  - Roux-en-Y bypass
  - Mini gastric bypass (less small bowel bypassed)
Laparoscopic Gastric Band

Complications: Slippage, leakage, infection, migration
Roux-en-Y Bypass

Complications: Anastamotic leak, stoma stenosis, GI ulcers or bleeding, small bowel obstruction
Long-term surgical complications

- Nausea and vomiting
  - Over-eating, band too tight, stenosis

- Dumping syndrome
  - Flushing, light-headed, palpitations, fatigue, diarrhoea (triggered by sugar intake)

- Malnutrition
  - Thiamine, B12, Copper (neurological signs)
  - Iron, folate, calcium, fat soluble vitamins
  - Hyperoxaluria

- Inadequate weight loss or weight regain
  - Behavioural
  - Inadequate pre-operative assessment
Selecting a Medicine for Obesity Treatment

1. Cost an issue?  
   - NO  
   - Sibutramine contraindicated?  
     - YES  
     - Orlistat  
     - NO  
     - Sibutramine  
   - YES  
   - Co-existing DM or insulin resistance?  
     - NO  
     - Co-existing depression?  
       - NO  
       - Consider adding exenatide  
       - YES  
       - Consider bupropion  
   - YES/No  
   - On metformin?  
     - NO  
     - Metformin  
   - YES  
   - Consider adding exenatide
Case Application

- Benefit of medications without lifestyle changes is questionable
- Sibutramine and orlistat likely cost prohibitive for this patient with Medicaid.
- Consider changing anti-depressant to bupropion
- Consider adding metformin due to insulin resistance
- Gastric banding best option, but likely not covered
- Gastric bypass next best option, but not without risk