Obesity Management and Treatment: Special Consideration in the PD population
April 6 2017
Western Canada PD days

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Assistant Professor and Bariatric Medicine Fellowship Program
Director at University of Ottawa
Outline

- Weight management in general population
  - Lifestyle
  - Surgery
  - Medical

- Focus on PD patients
  - Epidemiology on weight and PD
  - Treatment options
Canadian guidelines for the clinical management of obesity

<table>
<thead>
<tr>
<th>Treatment</th>
<th>BMI category (kg/m²)</th>
<th>≥25</th>
<th>≥27</th>
<th>≥30</th>
<th>≥35</th>
<th>≥40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Behavioural modification</td>
<td></td>
<td></td>
<td></td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Consists of nutrition, physical activity, and cognitive-behavioural therapy</td>
<td>With comorbidities</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Pharmacotherapy</td>
<td></td>
<td></td>
<td></td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Adjunct to behavioural modifications; consider if patient has not lost 0.5 kg per week by 3–6 months after behavioural changes</td>
<td>With comorbidities</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Bariatric surgery</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Consider if other weight loss attempts have failed. Requires lifelong medical monitoring</td>
<td>With comorbidities</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
</tbody>
</table>

✓ Indicates a treatment recommendation for that BMI class. BMI, body mass index
Lau et al. CMAJ 2007;176(8 suppl):Online-1–117
Weight management in general population
- Lifestyle
- Surgery
- Medical

Focus on PD patients
- Epidemiology on weight and PD
- Treatment options
Unintentional weight regain is common after diet-associated weight loss

Follow up range from 4 to 7 years

<table>
<thead>
<tr>
<th>Study</th>
<th>Years of follow-up</th>
<th>% of N in follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anderson et al.</td>
<td>5–7</td>
<td>12%</td>
</tr>
<tr>
<td>Foster et al.</td>
<td>5</td>
<td>47%</td>
</tr>
<tr>
<td>Graham et al.</td>
<td>4.5</td>
<td>43%</td>
</tr>
<tr>
<td>Hensrud et al.</td>
<td>4</td>
<td>88%</td>
</tr>
<tr>
<td>Jordan et al.</td>
<td>5</td>
<td>25%</td>
</tr>
<tr>
<td>Kramer et al.</td>
<td>4</td>
<td>77%</td>
</tr>
<tr>
<td>Lantz et al.</td>
<td>4</td>
<td>48%</td>
</tr>
<tr>
<td>Murphy et al.</td>
<td>4</td>
<td>33%</td>
</tr>
<tr>
<td>Pekkarinen &amp; Mustajoki</td>
<td>5.5</td>
<td>88%</td>
</tr>
<tr>
<td>Stalonas et al.</td>
<td>5</td>
<td>81%</td>
</tr>
<tr>
<td>Stunkard &amp; Penik</td>
<td>5</td>
<td>81%</td>
</tr>
<tr>
<td>Wadden et al.</td>
<td>5</td>
<td>25%</td>
</tr>
<tr>
<td>Wadden &amp; Frey</td>
<td>5</td>
<td>72%</td>
</tr>
<tr>
<td>Walsh &amp; Flynn</td>
<td>4.5</td>
<td>47%</td>
</tr>
</tbody>
</table>

Mean change from baseline to end of diet (kg)
Mean change from baseline to follow-up (kg)

P-values not available

What is Success in Weight Management?

- **Starting weight**
- **Natural course of weight gain**
- **Weight loss phase**
- **Weight maintenance phase**
- **Increasing success**

*Graph showing the stages of weight management.*

- **Months**
- **Years**
Outline

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  - Treatment options
Types of Bariatric Procedures

Scientific Figure on ResearchGate. Available from: https://www.researchgate.net/236089135_Fig1_Figure-1-Common-types-of-bariatric-surgery-procedures-A-Adjustable-gastric-band-B [accessed 16 Sep, 2016]
<table>
<thead>
<tr>
<th>Procedure</th>
<th>Pros</th>
<th>Cons</th>
<th>%EBW* at two years</th>
<th>Mean % weight loss from initial weight</th>
<th>Optimally suited for patients with:</th>
<th>Other comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laparoscopic Adjustable Gastric Banding (restrictive)</td>
<td>Least invasive; removable</td>
<td>25-40%; 5 year removal rate internationally</td>
<td>30-50%</td>
<td>20-30%</td>
<td>Lower BMI; no metabolic disease</td>
<td>Any metabolic benefits achieved are dependent on weight loss</td>
</tr>
<tr>
<td>Vertical Sleeve Gastrectomy (restrictive)</td>
<td>Improves metabolic disease; maintains small intestinal anatomy; micronutrient deficiencies infrequent</td>
<td>No long term data</td>
<td>50-70% (*3- year data)</td>
<td>20-30%</td>
<td>Metabolic disease</td>
<td>Can be used as the first step of staged approach; most common based on 2014 data</td>
</tr>
<tr>
<td>Roux-en-Y Gastric Bypass (mostly restrictive)</td>
<td>Greater improvement in metabolic disease</td>
<td>Increased risk of malabsorptive complications over sleeve</td>
<td>60-75%</td>
<td>25-35%</td>
<td>Higher BMI, GERD, Type 2 DM</td>
<td>Largest data set, more technically challenging than LAGB, VSG</td>
</tr>
<tr>
<td>Biliopancreatic Diversion with Duodenal Switch (Mostly malabsorptive)</td>
<td>Greatest amount of weight loss and resolution of metabolic disease</td>
<td>Increased risk macro- and micronutrient deficiencies over bypass</td>
<td>70-80%</td>
<td>30-40%</td>
<td>Higher BMI, Type 2 DM</td>
<td>Most technically challenging</td>
</tr>
</tbody>
</table>

Effect of Weight Loss after Roux-en-Y on Gastrointestinal Hormones and Leptin Concentrations

<table>
<thead>
<tr>
<th>Weight loss after RYGB</th>
<th>Glucagon-Like Peptide-1 (GLP-1)</th>
<th>Peptide YY (PYY)</th>
<th>Leptin</th>
<th>Ghrelin</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>↑</td>
<td>↑</td>
<td>↓</td>
<td>↓</td>
</tr>
</tbody>
</table>
Nutrition in the Patient with Obesity

- Macronutrient Excess
- High potential for micronutrient deficiencies preoperatively in the patient with obesity\(^1,2\)
- Up to 50% of patients with obesity have nutritional deficiencies
- Prevention and management of nutritional deficiencies begins preoperatively

Macronutrients: Proteins

- An elevated protein intake influences body composition changes, sparing fat free mass\(^1\).

- DPI was significantly associated with a greater reduction in BMI and %BF when controlling for (pre-op BMI, exercise and carbohydrate violations).

- It is a predictor of weight loss success after RYGB; associated with other parameters of surgical weight loss such as exercise and fewer carbohydrate violations.

- Promotes satiety and helps to maintain lower overall energy intake\(^2\).

Prevalence of Protein Malnutrition post bariatric surgery

- 0-2%⁹⁻¹¹ after purely restrictive procedures
- 0-13%¹⁻² after RYGB
- 3-18%³⁻⁸ after BPD.

Macronutrients: Proteins

Recommendations:
- A minimum protein intake of 60 g/day
- up to 1.5 g/kg of ideal body weight.
- Higher amounts - up to 2.1 g/kg ideal body weight need to be assessed on an individualized basis (GRADE D)

Protein supplements are helpful in meeting the recommended protein² (both animal and vegetable sources of protein are needed to meet all the essential amino-acid requirements).

Sites of nutrient absorption

- **Esophagus**
  - Water
  - Ethanol
  - Copper
  - Iodide
  - Fluoride
  - Molybdenum

- **Stomach**

- **Duodenum**
  - Thiamin
  - Riboflavin
  - Niacin
  - Pantothenate
  - Biotin
  - Folate
  - Vitamin B₆
  - Vitamin C
  - Vitamins A, D, E, and K
  - Calcium
  - Phosphorus
  - Magnesium
  - Iron
  - Zinc
  - Chromium
  - Manganese
  - Molybdenum

- **Jejunum**

- **Ileum**
  - Water
  - Calcium
  - Phosphorus
  - Magnesium
  - Iron
  - Biotin

- **Large Intestine**
  - Lipids
  - Monosaccharides
  - Amino acids
  - Small peptides
  - Bile salts and acids
  - Sodium
  - Chloride
  - Potassium
  - Short-chain fatty acids

*Many additional nutrients may be absorbed from the ileum depending on transit time.*
Bariatric Surgery: Common Micronutrient Deficiencies

<table>
<thead>
<tr>
<th></th>
<th>Vitamins</th>
<th>Minerals</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A</td>
<td>B1</td>
</tr>
<tr>
<td>RNY</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Sleeve</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>LAGB</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>BPD</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

*Vitamin D deficiency is seen in a significant number of patients with obesity at baseline. However, due to malabsorption, the risk is further increased post-op.

Nutritional Principles Following Bariatric Surgery

- Nutritional advice will depend upon type of bariatric procedure
- Three to five small meals a day
- Chew small bites of food thoroughly
- Avoid consuming liquids during meals, delay for at least 30 minutes after meals
- Protein: At least 60 grams/day, optimally 1.2 to 1.5 grams/kg/day
- Avoid concentrated sweets to minimize dumping and to reduce caloric intake
- High-quality multivitamins are routinely recommended after bariatric procedures, irrespective of deficiencies, which are often recommended to be chewable or liquid
- Other routine supplements often include:
  - Vitamin B12 500 μg/d tablet or sublingual, or 1000 μg/mo IM
  - **Vitamin B1 at least 12 mg/day (At risk pts, 50-100mg/day) (NEW!!!)**
  - Iron at least 27 mg of elemental iron daily, with at least 500 mg vitamin C
  - Calcium citrate 1200-1500 mg/d, preferably with vitamin D
Nephrolithiasis after bariatric surgery

- Mostly calcium oxalate stones
- The risk of kidney stones varies by bariatric procedure
  - Long limb RYGB or DS: 22-28.7%
  - RYGB: 7.65-13%
- Purely restrictive surgery is less associated with kidney stones
- Mean interval between surgery and kidney stones: 1.5-3.6 years

- Hazard ratio for the risk of kidney stone
  - 2.15 for RYGB vs 4.14 for more malabsorptive surgery (DS or long limb RYGB)

Bhatti et al., Int. J. of Surg 36(2016)618-623
Nephrolithiasis after bariatric surgery

- Retrospective case control study
- 762 patients
  - 78% RYGB
  - 7.2% very long limb RYGB
  - 6.5% Duodenal switch
  - 2% sleeve gastrectomy
  - 5.6% lap band
- 1:1 matched with control patient with the same BMI
- Assessment of the risk of kidney stones

- Risk of kidney stones similar at baseline between case and control
- New kidney stone event at 10 years: 14% (surgery group) vs 7% (control group) \( p < 0.01 \)
- 94% of stone analyzed: calcium oxalate stones
- Patient with prior history of stone before surgery had a higher risk of kidney stone after bariatric surgery
  - 42% vs 14% at 10 years; HR: 4.1 \( p < 0.001 \)

Lieske et al., kidney Int. 2015 April; 87(4):839-845
Renal Complications after Bariatric Surgery

Lithogenic urinary profile after bariatric surgery

Lithogenic urinary profile after bariatric surgery.

- **Hypocitraturia**
  - Inhibitor of calcium oxalate precipitation via the formation of soluble complex with calcium which reduces calcium oxalate crystallization.
  - Acidosis lead to increasing of renal citrate reabsorption and decreasing excretion in the urine.

- **Low urine volume**
  - Common after bariatric surgery
  - Due to a smaller water intake secondary to smaller stomach
  - 45 patients followed prospectively after RYGB: mean urine volume decreased from 1.8L to 1.4L (p < 0.002)

**Risk of chronic kidney disease**

- Retrospective review of 23 patients diagnosed with calcium oxalate stones or oxalate nephropathy at Mayo Clinic after RYGB or DS.
- 2 patients after RYGB developed oxalate nephropathy diagnosed by renal biopsy.
- No previous history of CKD or kidney stones.
- These 2 patients needed dialysis and 1 patient received kidney transplant.
- At least, 1 similar case at the Quebec Heart and Lung Institute

**At the Quebec Heart and Lung Institute, if history of kidney stone before bariatric surgery → consultation with nephrology and 24h urine collection for citrate, oxalate, sodium, uric acid and calcium.**

**If high 24h urine oxalate, consider choosing a restrictive surgery or RYGB instead of duodenal switch.**

Nelson et al., Surg for Obes and Rel disease, 1(2005)481-485
### Management of oxalate calcium stones

#### Table 3
Strategies, limitations, and solutions to reduce calcium oxalate stone risk after RYGB

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Limitations</th>
<th>Solutions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine output &gt; 2 L/d</td>
<td>Compliance, small stomach pouch</td>
<td>Push fluids high in citrate (i.e., lemonade), downloadable phone application reminders</td>
</tr>
<tr>
<td>Low fat diet (&lt; 25% daily calories)</td>
<td>High prevalence of fatty foods</td>
<td>Early satiety after surgery, patient education</td>
</tr>
<tr>
<td>Low oxalate diet (&lt;80–100 mg/d) for hyperoxaluria</td>
<td>Component in vegetables and “healthy” foods (peanuts, bran, soy), bioavailability variable</td>
<td>Patient education*, downloadable phone applications, “balance” versus avoidance</td>
</tr>
<tr>
<td>Low salt (&lt;2300 mg/d) and animal protein (0.8–1.0 gm/kg/d) intake</td>
<td>Both ubiquitous, particularly in American diet</td>
<td>Patient education, follow Dietary Approaches to Stop Hypertension style diet</td>
</tr>
<tr>
<td>Potassium citrate for hyperoxaluria</td>
<td>Tolerability, absorption efficacy, expense</td>
<td>Dispense as liquid or crystal/powder forms</td>
</tr>
<tr>
<td>Calcium citrate and dietary calcium to bind enteric oxalate</td>
<td>Tolerability, absorption efficacy, compliance, expense</td>
<td>Patient education, low dose chewable Citracal (250 mg) taken 5–6 x daily with small meals</td>
</tr>
<tr>
<td>Probiotics for hyperoxaluria</td>
<td>No commercially available Oxalobacter, unknown efficacy of Lactobacillus sp.</td>
<td>Most yogurts contain protein, calcium, and forms of probiotics</td>
</tr>
<tr>
<td>Vitamin B6 (pyridoxine) for hyperoxaluria</td>
<td>Well studied in primary hyperoxaluria; potential for neurotoxicity at high doses</td>
<td>Consider supplementing 50 mg/d (low dose) x 6 mo then discontinue</td>
</tr>
</tbody>
</table>

**Cholestyramine 2-4 g/day with meals (binds bile acid and ↓absorption of oxalate)**

**Vitamin B6 is a cofactor to the transamination reaction of glyoxylate to glycine.**

**When the patient is vitamin B6 deficient, the pathway is shunted for oxalate production instead of glycine.**

*Canales et al, Surg. Obes. Rel. Disease. 10(2014)734-742*

### High Oxalate Foods

<table>
<thead>
<tr>
<th>Category</th>
<th>Foods</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dark Leafy Greens</td>
<td>Swiss Chard, Kale, spinach, collards, dandelion, turnip greens</td>
</tr>
<tr>
<td>Root Vegetables</td>
<td>white/sweet potato, rutabaga, turnips, beets, parsnips</td>
</tr>
<tr>
<td>Other vegetables</td>
<td>carrots, celery, green pepper, brussels sprouts, okra, bamboo shoots</td>
</tr>
<tr>
<td>Fruit</td>
<td>Raspberries, Oranges, Avocado, Tomato puree, Kiwi, Lemon/lime Peels, olives</td>
</tr>
<tr>
<td>Dried fruit</td>
<td>dates, figs, pineapple</td>
</tr>
<tr>
<td>Nuts/Seeds</td>
<td>almonds, walnuts, cashews, peanuts, pistachios, tahini, pumpkin</td>
</tr>
<tr>
<td>Grains</td>
<td>Brown rice, Wheat berries, buckwheat, cornmeal, bulger, millet, wheat flour</td>
</tr>
<tr>
<td>Beverages</td>
<td>tomato juice, carrot juice, rice milk</td>
</tr>
<tr>
<td>Soy</td>
<td>tofu, miso, soy protein isolate, soy flour, soy beans</td>
</tr>
<tr>
<td>Legumes</td>
<td>navy, lentils, fava, refried, red kidney</td>
</tr>
<tr>
<td>Other</td>
<td>cocoa powder, stevia</td>
</tr>
</tbody>
</table>
Kidney stones are highly prevalent after malabsorptive bariatric surgery.

Malabsorptive surgery, previous history of kidney stones and type 2 diabetes are the main risk factors for kidney stones.

High urine oxalate, low urine volume and urine citrate explain the prevalence of the disease among the bariatric population.

Dietary restrictions, calcium citrate and potassium citrate are the main treatment to avoid recurrent kidney stones.
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Three principal treatment modalities for obesity

Bariatric surgery
RYGB, VSG, BPD, LAGB; adjunct to behavioural modifications

Behavioural modifications
Consists of nutrition, physical activity, and cognitive-behavioural therapy

Diet
Physical activities

BPD = biliopancreatic diversion; LAGB = laparoscopic adjustable gastric banding; RYGB = Roux-en-Y gastric bypass; VSG = vertical sleeve gastrectomy.
Three principal treatment modalities for obesity

**Bariatric surgery**
RYGB, VSG, BPD, LAGB; adjunct to behavioural modifications

**Behavioural modifications**
Consists of nutrition, physical activity, and cognitive-behavioural therapy

**Physical activities**

*RYGB = Biliopancreatic diversion; LAGB = laparoscopic adjustable gastric banding; RYGB = Roux-en-Y gastric bypass; VSG = vertical sleeve gastrectomy.*

What is a meal replacement?

- Do not exceed 300 kcal per portion\(^1\).
- Calories from fat < 30%
- Protein $\geq 15g$
- Sugar $\leq 7g$
- Fibres $\geq 5g$
- Be careful about the sodium content (read the nutritional label)
- Vitamin and mineral fortified
- Contain non-nutritive sweeteners
- Wide variety of products (liquid meal replacement, snack bar, soup, hot cereal, frozen entrees, homemade protein shakes, etc.)

\(^1\)Nonas et al. American dietetic association. Managing obesity textbook
Rationale for Meal Replacements (MR)

1. Portion Control
2. Calorie Control
3. Structured eating
4. Improved nutrition
5. High protein
6. Stimulus narrowing: simplify food choices
7. Stimulus control: avoid contact with problem foods/triggers
Two types of meal replacement strategies

1. Full meal replacement (FMR) or low-calorie diet
2. Partial meal replacement (PMR)
The LOOK AHEAD trial  
Wadden TA Obesity 2009;17 (4): 713-722

- Multicentre 10-yr lifestyle/weight management RCT in >5000 patients with DM
- Addition of MR to lifestyle group increased weight loss to 8.6% (0.7% in usual care/control)
- Weight loss directly related to number of MR
  - The higher the reliance on MRs, the higher the odds of achieving weight loss goals
- Replacing 2/3 meals → 8-10% weight loss
Full meal replacement is a strategy for **weight loss**... **BUT**

- Patients on FMR must be medically monitored and **should participate in a multidisciplinary lifestyle program to learn about long-term weight management and maintenance.**

- In Canada, FMR is approved for a LCD of at least 900 kcal/day.

- In the USA, FMR is approved for a VLCD (very low calorie diet) of at least 800 kcal/day.
FMR programs

- Total 6-month program medically supervised
- Weekly lifestyle intervention group session
- Weekly medical appointments
- 6 or 12 weeks of full meal replacements (Optifast® 900)
- Eligibility if BMI>30 with comorbidities
- Can also be used for several weeks before bariatric surgery to shrink the liver.
Objectives of full meal replacement

- A tool to break the vicious cycle of obesity.
- Full meal replacement can result in a 15-20% weight loss

**Optifast ® 900 (4 shakes per day)**

900 kcal/day
90 g of protein
30 g of lipid
67.2 g of carbohydrates
Na 2000mg/day
K 2960 mg/day
Ca 1100mg/day
Phosphorus 1100mg/day
- Total daily allowance of vitamins and minerals
Optifast® 900

VISITS (weekly)
1 3 6 9 12 15 18 21 24

Transition
1200-1500 Kcal diet

1.5 Hour Workshops
Optifast Lifestyle Education Series weekly for 6 months

Blood work incl Lipid Profile, HbA1c, Insulin, ApoB,
Mean weight loss in first 26 WKS

2804 Patients in the 26 week program – intention to treat analysis
Weekly Average of Normalized Case Trajectories
(1st year)
1. Clinical evidence of a distinct phenotype
   - Obese diet sensitive (ODS)
   - Obese diet resistant (ODR)

2. Mitochondrial Function
   - 50% higher proton leak in ODS vs ODR mitochondria

3. Gene Expression Signatures in Skeletal Muscle & Whole Blood
   - Increased expression of OXPHOS genes in ODS vs ODR subjects

4. Skeletal Muscle Fiber Characteristics
   - Increased proportion of type 1 oxidative fibers in ODS

5. Genetic Discrimination (GWAS)
   - Promising loci
Harper ME. Handbook of Obesity Vol 1, 3rd ed, Chapter 23 p.259-266
LABS reporting variation in weight loss after bariatric surgery

Figure 3. Percent Weight Change Trajectories

A Roux-en-Y gastric bypass

- Group 1 (n=36, 2.1%)
- Group 2 (n=368, 21.5%)
- Group 3 (n=796, 46.5%)
- Group 4 (n=408, 23.8%)
- Group 5 (n=103, 6.0%)

Follow-up Time, y

Percent Weight Change

Changes in DM patients medications on full MR program

- **Accepted for publication Canadian Journal of Diabetes:** Retrospective cohort study (1992 - 2009) on weight, glycemic control, and diabetic medications changes in 317 patients with obesity and Type 2 diabetes on medications in the Optifast full MR program  Shiau J., So D., Dent R.
- 16% weight loss at 6 months
- Decrease or discontinuation of medications were: 92.1% sulfonylureas, 86.5% insulin, 78.8% thiazolidinediones, 77.8% alpha-glucosidase inhibitor, 50% meglitinides, 33.3% DPP4 inhibitors, and 32.8% metformin.
- At 6 months, 30% of patients were no longer on diabetes medications and had significantly better % weight loss compared with those on medications (18.6% vs 16%, p=0.002)
Three principal treatment modalities for obesity

**Bariatric surgery**
RYGB, VSG, BPD, LAGB; adjunct to behavioural modifications

**Pharmacotherapy**
orlistat & liraglutide; adjunct to behavioural modifications

**Behavioural modifications**
Consists of nutrition, physical activity, and cognitive-behavioural therapy

BPD = biliopancreatic diversion; LAGB = laparoscopic adjustable gastric banding; RYGB = Roux-en-Y gastric bypass; VSG = vertical sleeve gastrectomy.

## Features of available pharmacotherapy options

<table>
<thead>
<tr>
<th>Feature</th>
<th><strong>Orlistat (Xenical®)</strong></th>
<th><strong>Liraglutide (Saxenda®)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Drug class</strong></td>
<td>Gastric and pancreatic lipase inhibitor</td>
<td>GLP-1 receptor agonist</td>
</tr>
<tr>
<td><strong>Indication</strong></td>
<td>≥30 kg/m² or ≥27 kg/m² + comorbidity</td>
<td>≥30 kg/m² or ≥27 kg/m² + comorbidity</td>
</tr>
<tr>
<td><strong>Contraindications</strong></td>
<td>• Chronic malabsorption syndrome</td>
<td>• Multiple Endocrine Neoplasia syndrome (MEN2), medullary thyroid cancer (MTC)</td>
</tr>
<tr>
<td></td>
<td>• Cholestasis</td>
<td>• Pregnancy/breastfeeding</td>
</tr>
<tr>
<td><strong>Most common adverse events</strong></td>
<td>• Oily spotting, stool, evacuation</td>
<td>• Nausea, vomiting, dyspepsia</td>
</tr>
<tr>
<td></td>
<td>• Flatus with discharge</td>
<td>• Diarrhea, constipation</td>
</tr>
<tr>
<td></td>
<td>• Fecal urgency, increased defecation</td>
<td>• Abdominal pain</td>
</tr>
</tbody>
</table>

BMI, body mass index; GLP-1, glucagon-like peptide-1.
Why start pharmacotherapy to help maintain diet-induced weight loss? After weight loss with a low-calorie diet (1200–1400 kcal/day): Liraglutide

Pharmacotherapy, in addition to diet and exercise, can help patients achieve clinically relevant weight loss.

Data are mean ± SE
Pharmacotherapy: sibutramine; Pharmacotherapy alone: Patients received a daily dose of 15 mg/day; Lifestyle modification alone: Patients attended 30 lifestyle counselling sessions; Pharmacotherapy + brief therapy: Patients were given sibutramine and received brief lifestyle counselling; Combined therapy: Patients received sibutramine and attended 30 lifestyle counselling sessions.

*P<0.0001 for combined therapy vs. all other groups
†P=0.05 for lifestyle alone and pharmacotherapy + brief lifestyle vs. pharmacotherapy alone

Obesity Treatment

Adapted from Lau DCW et al. Can Med Assoc J 2007;176 (8 suppl):S1-S13

Overweight
BMI ≥ 25 kg/m²

Obese Class 1
BMI ≥ 30 kg/m²

Obese Class 2
BMI ≥ 35 kg/m²

LS + Pharmacotherapy ~ 5-15%

LS + Surgery ~ 20-40%

Lifestyle (LS) ~ 1-5%

0

Years

% Weight loss

1

2

Health behaviour modification

Diet

Physical Activities

Surgery

Pharmacotherapy
Outline

- Weight management in general population
  - Lifestyle
  - Surgery
  - Medical

- Focus on PD patients
  - Epidemiology on weight and PD
  - Treatment options
Is weight gain inevitable for PD pts?

- Average wt gain at end of one year CPD:
  - 9-10% of initial weight or 5-7 kg

- Mechanism:
  - Increased caloric intake from continuous glucose load provided by dialysate
  - Improved appetite experienced by most patients upon initiation of CPD due to improved solute removal
  - With peritonitis, increased glucose absorption

Is weight gain inevitable for PD pts?

- With current available solutions and prescription for PD (including icodextrin glucose sparing regimens), obligatory systemic absorption of 50-150g CHO is inevitable.  
  - Membrane transport status
  - Dwell length
  - Strength of the solution

- No significant difference in the slope of wt change between pts starting HD or PD over two years.  

- US large dialysis provider: wt gain more likely in HD vs PD pts.

References:

Eating behaviour in CAPD vs HD patients

- Three groups of 12 pts (CAPD, HD, healthy matched controls)
  - Mean age 60, no DM
  - CAPD: mean time 10mo, BMI 23,
  - HD mean time 23mo, BMI 22.7
- Fed hash on plate with hidden scale; CAPD did test twice (with or without dialysate)
- VAS concerning appetite and food preferences before and after test meal
- Mean total intake of food: control > HD > PD
- Eating velocity: control > both HD and PD
- CAPD has lowest hunger and desire to eat before meals (with or without dialysate)

Hylander B. Am J. Kidney Disease 1992; 20; 592-597
Genetics may impact weight gain in PD

- Genetics may play an important role

- UCP2 uncouples cellular respiration from ATP synthesis and affects resting energy expenditure

- 126 PD patients and 96 HD patients had body composition compared at baseline and 1 year follow up and were genotyped for UCP2

Wang et al. (Nephrol Dial Transplant 2006)

Courtesy of Dr. B McCormick
PD increases fat mass, particularly truncal fat mass

Stenvinckle et al (J Am Soc Nephrol 2000) looked at body composition after 1 year on PD

Table 1. Body composition, serum leptin, CRP, and plasma insulin levels at the initial state and during peritoneal dialysisa

<table>
<thead>
<tr>
<th>Group</th>
<th>Initial</th>
<th>Follow-Up</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients (n = 36)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>body mass index (kg/m²)</td>
<td>24.1 ± 0.6</td>
<td>24.8 ± 0.7</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>body fat mass (kg)</td>
<td>20.5 ± 1.0</td>
<td>22.9 ± 1.3</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>truncal fat mass (kg)</td>
<td>11.5 ± 0.7</td>
<td>13.2 ± 0.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>lean body mass (kg)</td>
<td>50.8 ± 1.7</td>
<td>49.1 ± 1.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>leptin:body fat ratio (ng/ml per kg)</td>
<td>0.9 ± 0.1</td>
<td>1.3 ± 0.2</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>serum leptin (ng/ml)</td>
<td>20.1 ± 3.8</td>
<td>35.6 ± 6.8</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>C-reactive protein (mg/L)</td>
<td>10 ± 2</td>
<td>12 ± 3</td>
<td>NS</td>
</tr>
<tr>
<td>plasma insulin (mU/L)b</td>
<td>18 ± 2</td>
<td>NA</td>
<td></td>
</tr>
</tbody>
</table>

Courtesy of Dr. B McCormick
Obesity paradox

- In HD patients:
  - Low BMI strong predictor of mortality
  - High BMI not associated with increase in mortality
  - Some studies report high BMI to be protective in HD pts

- In PD patients:
  - PD pts with obesity have equivalent survival to PD pts with normal BMI
  - In general, any survival advantage of obesity in HD is significantly less in PD pts.
  - Possibly pts on PD with obesity and DM have higher mortality compared with similar HD pts.
  - Things to take into account:
    - Survival rates on dialysis change over time
    - PD is often a “temporary” modality, usual at 3-5 years >50% switch to another modality (HD, transplant)
    - PD offered less to patients with obesity

Abbott K. “BMI and PD:”Exceptions to the Exception” in Reverse Epidemiology? Seminars in Dialysis; 20: 561-565
How does Body Composition affect mortality?

- In both HD and PD patients, compared with normal BMI with normal or high muscle mass:
  - Pts with high BMI and low muscle mass (infer high fat mass): ↑ mortality
  - Pts with high BMI and normal or high muscle mass (infer low fat mass): ↓ mortality

- Changes in body fat mass and adipokines in pts starting PD:
  - Prospective study from 2008-2011, 54 patients, BIA, CT, adipokines
  - 54 patients (28 men), BMI 23.6, 61%DM, 35%CHD, 21 pts CAPD, 23 APD
  - By 2 years, 8 deaths, 4 transplants, 23 switched to HD, 27 continued PD
  - Increased at 2 years:
    - Wt incr continuously by 3-4 kg over 2 years
    - Visceral and s/c fat increased at during first 12 months and then did not change
    - Leptin, TC
  - Decreased at 2 years adiponectin
  - Stable: hs-CRP, IL-6
  - Effect of fat mass and adipokines on mortality disappeared after adjusting for age, sex, DM and CVD

Choi S.PDI 2017 in press
Survival No Different Than HD
In the Modern Era

USRDS data comparing adjusted survival among 620,000 HD patients and 64,000 PD patients

HD dark line, PD lighter line

Mehrotra et al. Arch Int Med 2011

Courtesy of Dr. B McCormick
Reversal of Obesity paradox for Renal Transplant Recipients (RTR)?

- 50% RTR have obesity
- Average 10kg wt gain during first year post transplant
  - Resolution of uremic state, better pt condition
  - Obesity preceding transplant
  - Corticosteroid therapy
- Decrease in long-term survival and increase in CVD

Chavalithamrong D. Seminars in Dialysis 2007; 20:544-548
Outline

- Weight management in general population
  - Lifestyle
  - Surgery
  - Medical

- Focus on PD patients
  - Epidemiology on weight and PD
  - Treatment options
Weight loss after dialysis initiation

- Regardless of dialysis modality, weight loss after start of dialysis initiation has been associated with increased risk of mortality.
- No studies have distinguished intentional versus non-intentional weight loss.
- Bottom line: At some point a higher BMI has an impact on an individual and we need to do something for that person.
  - What is the goal? What is the % weight loss?

Abbott K. “BMI and PD:”Exceptions to the Exception” in Reverse Epidemiology? Seminars in Dialysis; 20: 561-565
Do non-glucose solutions attenuate weight gain?

- Observational study of 36 patients treated with long dwell with Extraneal® and 39 treated with long dwell glucose based solution (Kyu-Hyang et al. Nephrol Dial Transplant 2010)

Fig. 3. Serial changes of body composition (body weight, fat mass, lean body mass) in both icodextrin group (A) and non-icodextrin group (B) during initial 3 years measured by BIA (bioelectrical impedance analysis). *P < 0.05, compared with first month in lean body mass gain, †P < 0.01, compared with first month in fat mass gain. A: Changes in the icodextrin group. B: Changes in non-icodextrin group.
### Bariatric surgery to qualify for renal transplant

<table>
<thead>
<tr>
<th>Reference</th>
<th>Relevant Sample Size</th>
<th>Intervention</th>
<th>Length of Intervention</th>
<th>Mean % Weight Loss</th>
<th>Mean % BMI Loss</th>
<th>Follow Up</th>
<th>Proceeded to Transplant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alexander et al. 2007 (9)</td>
<td>25</td>
<td>RYGB</td>
<td>12 months</td>
<td>-</td>
<td>68% excess BMI</td>
<td>12 months</td>
<td>9</td>
</tr>
<tr>
<td>Macloughlin et al. 2012</td>
<td>5</td>
<td>SG</td>
<td>12 months</td>
<td>-</td>
<td>21.5% (median 6 months)</td>
<td>Median 9 months</td>
<td>4 on waitlist</td>
</tr>
</tbody>
</table>

**Thirty-day mortality after bariatric surgery:** 3.5%; One year mortality for patients on waitlist: 7%

<table>
<thead>
<tr>
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<th>Intervention</th>
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<th>Mean % BMI Loss</th>
<th>Follow Up</th>
<th>Proceeded to Transplant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Freeman et al. 2015 (13)</td>
<td>52</td>
<td>SG (vs medical wt loss)</td>
<td>6 months medical weight loss, followed by surgery</td>
<td>15.3%</td>
<td>15.6%</td>
<td>26-73 days post SG</td>
<td>29 achieved target BMI</td>
</tr>
<tr>
<td>Koshy et al. 2008 (14)</td>
<td>3</td>
<td>AGB</td>
<td>12-15 months</td>
<td>15.5%</td>
<td>14.0%</td>
<td>19+ months</td>
<td>3</td>
</tr>
<tr>
<td>Newcombe et al. 2005 (15)</td>
<td>3</td>
<td>AGB</td>
<td>9-28 months</td>
<td>27.8%</td>
<td>24.5%</td>
<td>Variable</td>
<td>3</td>
</tr>
<tr>
<td>Proczyko et al. 2013 (16)</td>
<td>3</td>
<td>RYGB</td>
<td>3 months</td>
<td>-</td>
<td>22.1%</td>
<td>12 months</td>
<td>1</td>
</tr>
</tbody>
</table>
Case reports: bariatric surgery in patients on PD

- Five pts with obesity on CCPD (Nov 2010 and Dec 2011)
- Ave age 41, BMI 43.3, 1LAGB, 4 RYGB
- 3 weeks of hypocaloric liquid diet: ave wt loss 6.8kg
- Night before surgery: regular nocturnal exchanges until the morning of surgery. At the end of the last CCPD session, the peritoneal cavity was drained completely.
  - Preop single iv dose amoxicillin 2g or clindamycin 600mg
- Post-op: 2 resumed CCPD without delay, 3 off dialysis for 24 hours
- Volume titration protocol:
  - POD 1 to 5: 25-50% of original prescription, then increase by 25% q 3-5 days (1.5% dextrose concentration)
- All pts reached their target wt within 8 weeks post op and approved for transplant

Valle GA. Advances in Peritoneal Dialysis 2012; 28:134-139
Case reports: bariatric surgery in patients on PD

- 27 yo male on PD for 43 months before sleeve gastrectomy
- PMH: ESRD IgA nephropathy, HTN, OSA, hyperuricemia, BMI
- Originally on HD but switched to PD at 2 months:
  - Nightly cycler treatments with 5 exchanges of 3L 2.5% dextrose over 8 hours
  - Last fill consisted of 2.5L 7.5% icodextrin which dwelled for 10 hours
  - Midday exchange 3L 2.5% dextrose
- No peritonitis.
- Difficult time controlling wt and could not be put on transplant list.
  - Heaviest wt=170kg.
  - Day of surgery wt=153.8kg. (9.5% weight loss)

Imam TH. PDI 2013; 33: 710-711
Case reports: bariatric surgery in patients on PD

- Night before surgery:
  - Spent 12 hours on his cycler with no final fill.

- Night of the surgery, PD was held

- Discharge home the next day, restarted nightly PD
  - Initiated on low-volume exchanges with dry days for first 2 weeks
  - At wk 3 and 4, a 1L final fill was added
  - After 4 weeks, resumed presurgical PD regimen
Two years post-op:
- Weight 57.9kg (%EBW loss 91%)
- Albumin 3.7mg/dL to 4.2mg/dL

At 13 months post bariatric surgery, listed on the United Network for Organ Sharing waiting list for renal transplantation.
<table>
<thead>
<tr>
<th>Reference</th>
<th>Relevant Sample</th>
<th>Intervention</th>
<th>Length of Intervention</th>
<th>Mean % Weight Loss</th>
<th>Mean %BMI Lost</th>
<th>Follow Up</th>
<th>Proceeded to Transplant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yanadiga et al. 2014 (24)</td>
<td>28 heart pts; mean BMI 35.6</td>
<td>LVAD+lifestyle counseling</td>
<td>Variable</td>
<td>-</td>
<td>7%</td>
<td>Mean 301 days</td>
<td>Yes: 14 pts</td>
</tr>
<tr>
<td>Sentner et al. 2012 (25)</td>
<td>1 heart pt-glycogen storage dis, LVH, BMI 32.2</td>
<td>900 calorie high protein diet via nasogastric tube feeding</td>
<td>4 months</td>
<td>-</td>
<td>14%</td>
<td>7 yrs</td>
<td>No: symptoms improved</td>
</tr>
<tr>
<td>MacLaughlin et al. 2010 (26)</td>
<td>32 CKD pt; BMI&gt;30 or &gt;28 with comorbidity</td>
<td>Weight management program- diet, exercise, orlistat 3x daily compared with usual care</td>
<td>6 month active intervention with support at 9, 12, 18 and 24 months.</td>
<td>8%</td>
<td>-</td>
<td>24 months</td>
<td>Yes: 3 pts Accepted for transplant listing: 9/26</td>
</tr>
<tr>
<td>Evans et al. 2003 (27)</td>
<td>1 renal pt</td>
<td>Orlistat 3x daily, fat and calorie restricted diet</td>
<td>3 months</td>
<td>Minimal[^2]</td>
<td>-</td>
<td>3+ months</td>
<td>Yes: 1 pt but immunosuppression difficulty</td>
</tr>
</tbody>
</table>
Case 1: Full Meal Replacement

- 52 yo man, T2DM on MDI (300 units/day), HTN, OSA, DVT
- HD Oct 2012, 1 litre fluid restriction + UO
- Ht 5’5”, wt 270.5lbs, BMI 44.5
- Goal for transplant: wt: 231lbs, BMI 38.4, 14.6% wt loss
- Nov 2015: Started Optifast 900 qid
- Feb 2016 wt 227.5lbs, BMI 37.5 (levemir 30 units bid, NR 8 with shakes)
- March 2016: wt 221lbs, 18.2% weight loss: Optifast tid + 3oz protein, 1-2 cups veg
- April 2016: renal transplant
- Feb 2017: wt 244.5lbs. To enroll in official medical program.
Case 2: 43 yo man waiting for 3rd renal transplant
Modified full meal replacement

- PCKD, two deceased donor renal transplant 1982, 1987, on-off smoker, gout, HTN, chronic renal graft disease, cr 251, eGFR 25
- Meds: Lipitor 10mg, cyclosporine 75 bid, vasotec 7.5mg bid, prednisone 10mg qother day, colchicine 0.6mg pm, Imuran 100mg, MV, Rocaltrol, Tums
- Feb 2013: BMI 49.3, wt 223lbs
  - Suggested protein 0.8g/kg to 1g/kg IBW
  - Two Optifast + one Boost Plus Cal=810 kcal/day, 59g ptn (0.9g/kg)
- Aug 2013: BMI 38.7
- Oct 2013: BMI 38.1, wt 172lbs (22% weight loss)
- Feb 2015: BMI 35.8, back on PD
- Feb 2017: renal transplant
Thank you

dr.shiau@leafwmc.com

www.leafwmc.com