

General Principles of Obesity Pharmacotherapy

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Disclosures

Faculty

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Relationships with commercial interests

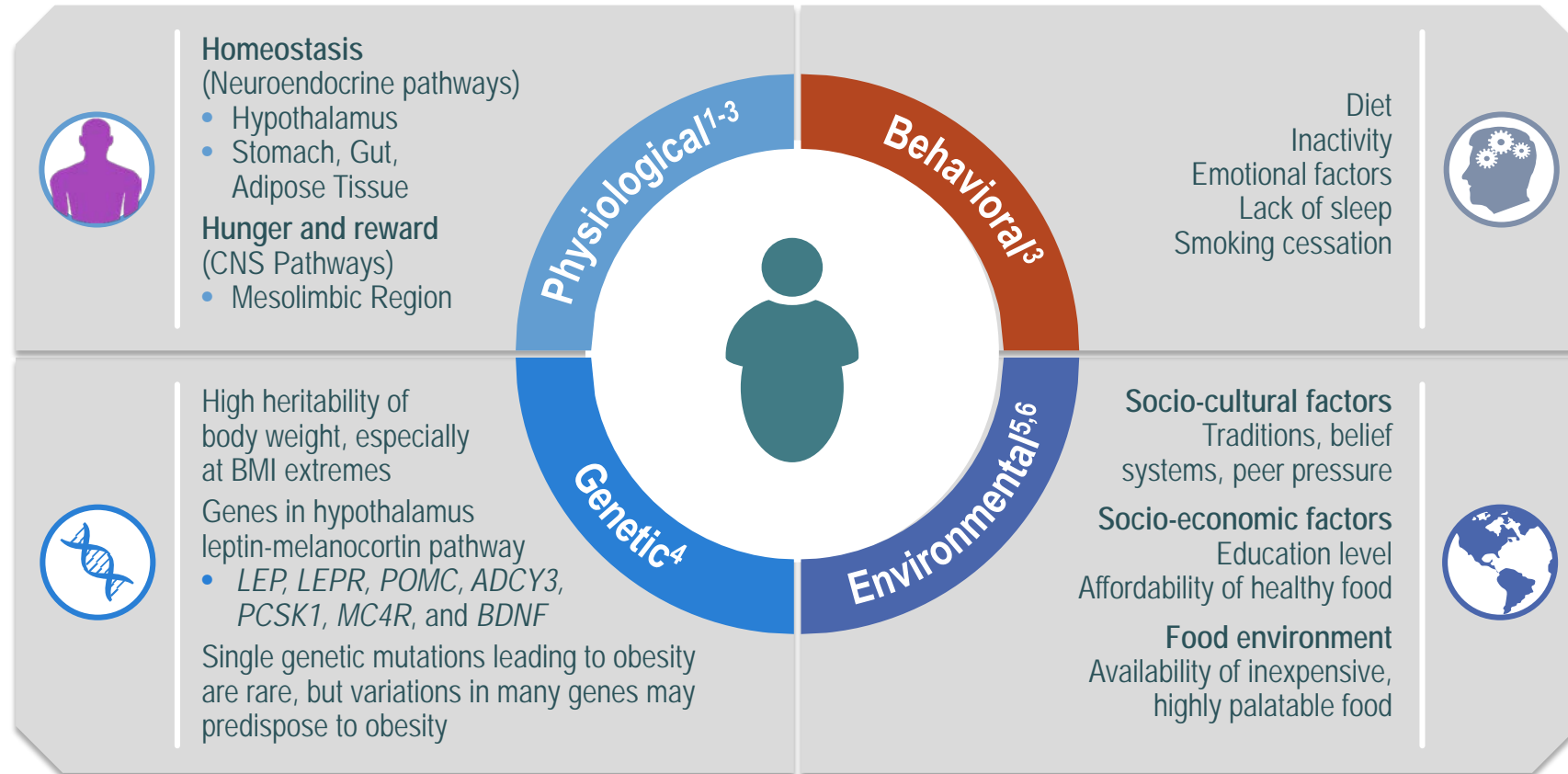
- Speakers Bureau/Honoraria: Novo Nordisk, Valeant
- Consulting Fees: FEMME HOMME Medical

Learning Objectives

1. Understand obesity as a disease of energy homeostasis.
2. Explore the relationship between obesity pharmacotherapy and behavioral interventions in the management of obesity.
3. Review the clinical aspects of initiating obesity pharmacotherapy and patient follow-up.

Why is obesity management difficult?

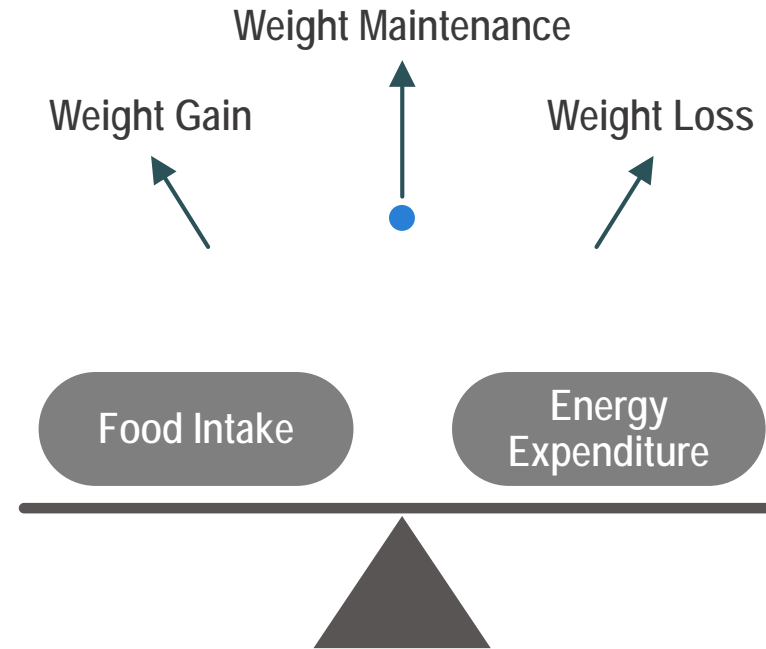
Obesity is a Multifactorial Disease



Obesity is a Disease of Energy Homeostasis

Hormonal Adaptation¹

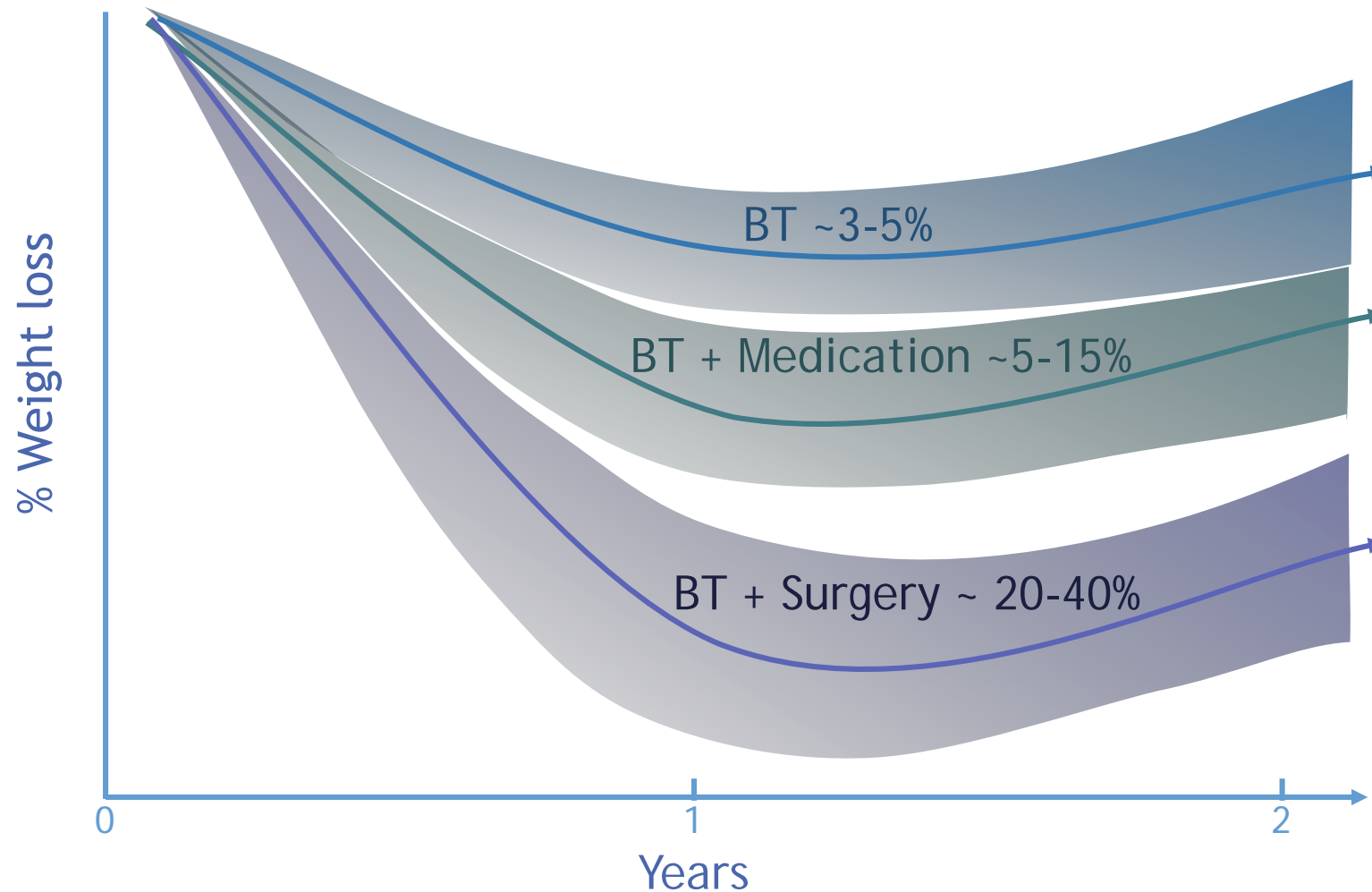
With weight loss, hunger hormone increase and satiety hormones decrease, resulting in an increase in hunger and desire to eat as well as increased risk of weight regain.



Thermogenic Adaptation²

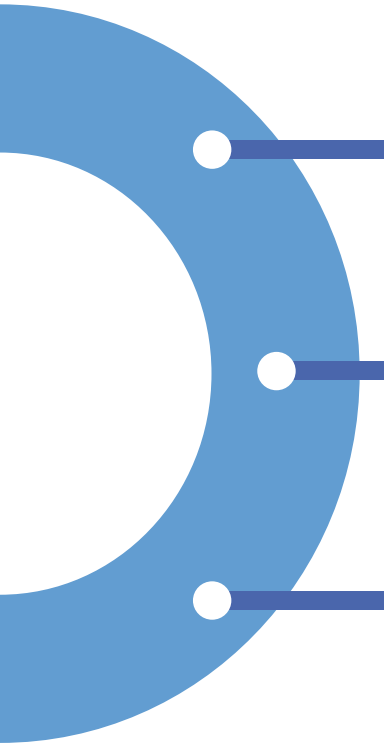
Energy expenditure decreases with weight loss to a greater extent than what would be expected, increasing risk of weight regain.

Behavioral Therapy has Limited Efficacy

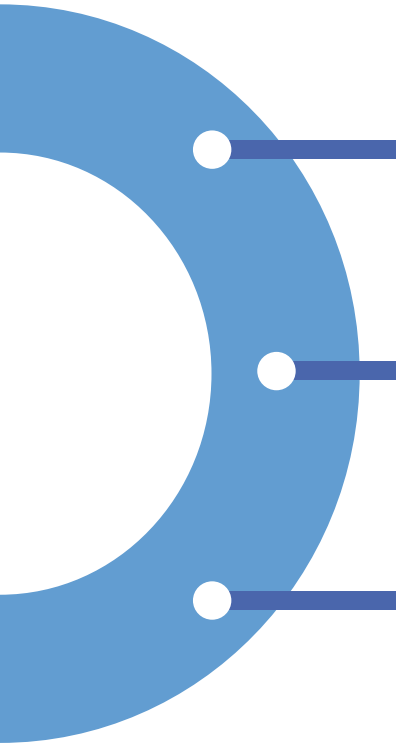


How can we improve obesity outcomes?

Medications Improve Behavior Therapy Outcomes

- 
- Increase the number of patients responding to behavior therapy
 - Increase the magnitude of the response
 - Increase the duration of the response

Behavior Therapy Improves Medication Outcomes

- 
- Increases the number of patients responding to medication
 - Increases the magnitude of the response
 - Increasing the intensity of the behavioral intervention leads to further improvement in outcomes

Clinical Trials for Obesity Medications: Lifestyle Recommendations

Nutrition

- -500 kcal/day (calculated using the WHO algorithm; [Mifflin-St Jeor equation](#) is more common in clinical practice)

Activity

- Minimum 150 min/week of moderate activity

Frequency

- Lifestyle advice given every 12 weeks
- Assessment every 4 weeks
- Self monitoring
Food record – intermittent
Weight

Obesity medications in clinical practice

Obesity Medications in Canada

Drug (trade name)	Health Canada Approval	Mechanism of Action
Orlistat (Xenical®) ¹	1999	Gastrointestinal lipase inhibitor
Liraglutide ² (Saxenda®)	2015	GLP-1 receptor agonist
Naltrexone ER/ Bupropion ER (CONTRAVE®) ³	2018	Opioid receptor antagonist / aminoketone antidepressant

1. Xenical® (product monograph), November 18, 2015, Hoffmann-La Roche Limited, Mississauga, ON; 2. Saxenda® (product monograph), July 12, 2017, Novo Nordisk Canada Inc, Mississauga, ON; 3. CONTRAVE® [product monograph], February 12, 2018, Valeant Canada LP; Laval, QC.

Indication for Obesity Pharmacotherapy

Obesity pharmacotherapy is indicated as an adjunct to behavioral modification (reduced food intake and increased physical activity) in adults with an initial body mass index (BMI) of:

- 30 kg/m² or greater (obesity) or
- 27 kg/m² or greater (overweight) in the presence of at least one weight-related comorbidity

Initiating Obesity Pharmacotherapy: Patients to Prioritize for Medication Initiation

- Patients who have lost weight and are at risk of being unable to sustain current lifestyle
- Patients who have lost weight through behavioral modification and who would benefit from further weight loss
- Patients with a history of weight cycling
- Patients who are actively gaining weight

Initiating Obesity Pharmacotherapy: Key Points in Lifestyle History

At a minimum:

- no active eating disorder
- few skipped meals
- aware of protein target^{1,2}
 - ❖ 1.2 - 1.6 mg/kg ideal body weight, typically 80 - 100 grams/day

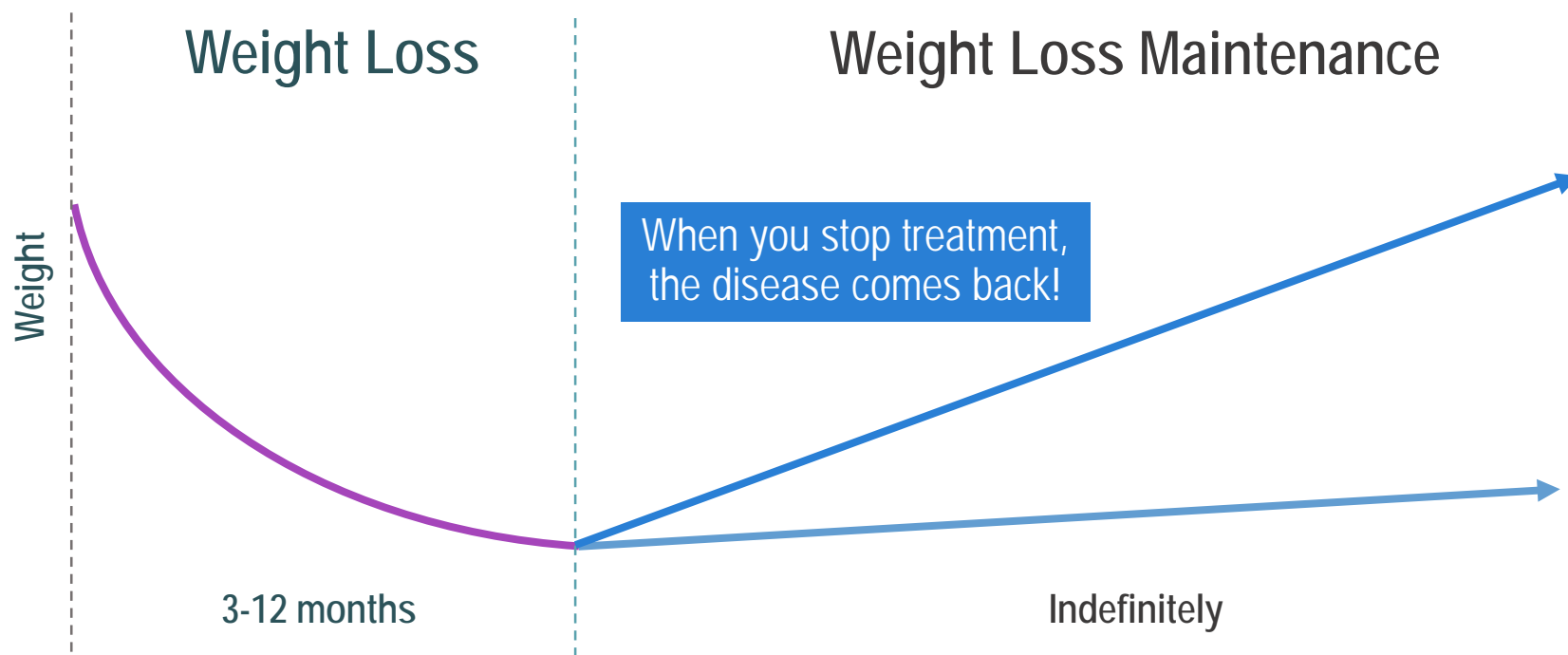
Initiating Obesity Pharmacotherapy: Key Points in Lifestyle Counseling

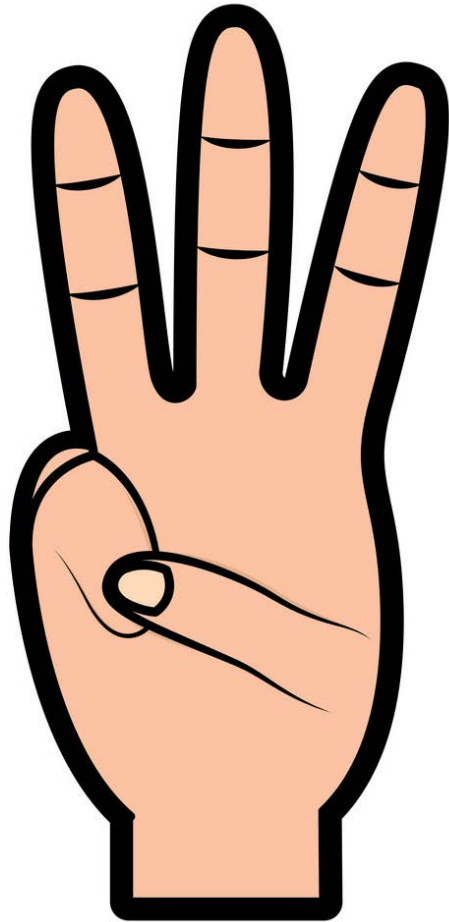
- Maintain a food record; track calories
- Discrete meals and snack; avoid grazing
- Limit liquid calories, eating out, and junk food
- Don't skip meals and reach protein target - otherwise eat only to fullness

Key Issues in Patient Follow-up: Stopping Rule

- After 12 weeks at target dose, obesity medications should be discontinued if 5% weight loss has not been achieved.

Key Issues in Patient Follow-up: Weight Loss Plateau





1. Obesity is a chronic disease.
2. The newest obesity medications alter the neurohormonal regulation of appetite.
3. Obesity medications enhance the effectiveness of behavioral interventions.

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Selecting an obesity medication

Selecting an Obesity Medication: Efficacy and Tolerability

Drug (trade name)	1-year weight loss, placebo- subtracted ¹	≥5% weight loss ¹	≥10% weight loss ¹	Gastrointestinal Side Effects ²
Placebo		23% (median)	9% (median)	
Orlistat (Xenical [®])	2.6 kg	44%	20%	Mitigated by a low-fat diet; >90% of patients discontinue in first year of use
Liraglutide (Saxenda [®])	5.3 kg	63%	34%	Typically transient
Naltrexone ER/ Bupropion ER (CONTRAVE [®])	5.0 kg	55%	30%	Typically transient

Selecting an Obesity Medication: Contraindications and Cautions

Drug (trade name)	Contraindications	Cautions
Orlistat (Xenical®) ¹	Chronic malabsorption Cholestasis	Hepatotoxicity Nephrolithiasis
Liraglutide (Saxenda®) ²	Personal or family history of MTC/MEN2	Gallstones Pancreatitis
Naltrexone ER/ Bupropion ER (CONTRAVE®) ³	Concurrent opiate use Uncontrolled hypertension MAO-I, Tamoxifen	Drug-drug interactions

Selecting an Obesity Medication: Contraindications and Cautions

Drug (trade name)	Hepatic impairment	Renal impairment
Orlistat (Xenical®) ¹	Limited systemic absorption	Limited systemic absorption
Liraglutide (Saxenda®) ²	No significant hepatic clearance Caution in severe hepatic insufficiency	No significant renal clearance Caution in severe renal insufficiency
Naltrexone ER/ Bupropion ER (CONTRAVE®) ³	Decrease dose in mild and moderate hepatic insufficiency Contraindicated in severe hepatic insufficiency	Decrease dose in moderate and severe renal insufficiency Contraindicated in ESRD

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Selecting an Obesity Medication: Patient Characteristics & Preference

Drug (trade name)	Comorbidities	Route of administration	Dosing schedule
Orlistat (Xenical®) ¹	Constipation	Oral	TID
Liraglutide (Saxenda®) ²	Diabetes mellitus High cardiovascular risk Hypertension	Subcutaneous	Daily
Naltrexone ER/ Bupropion ER (CONTRAVE®) ³	Smoking Binge drinking Depression Fertile woman	Oral	BID