



Obesity Treatment

“Obesity is a chronic disease requiring enhanced research, treatment, and prevention efforts.”

– *The Canadian Medical Association*

Insights from Dr. Lee Kaplan, MD, PhD

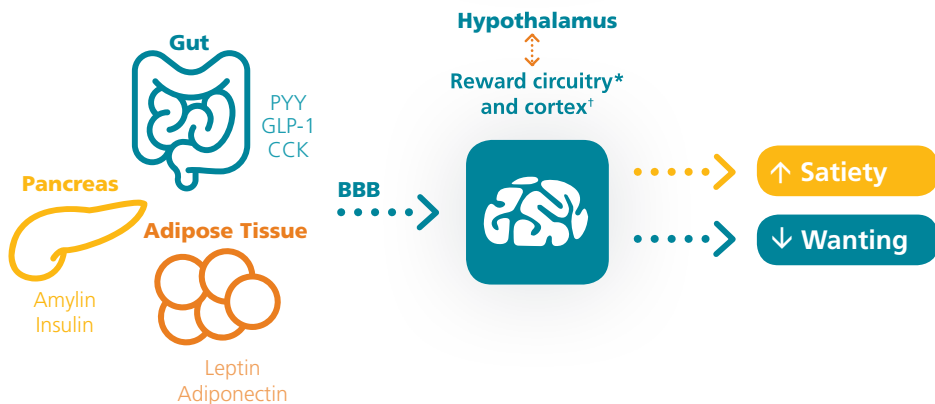
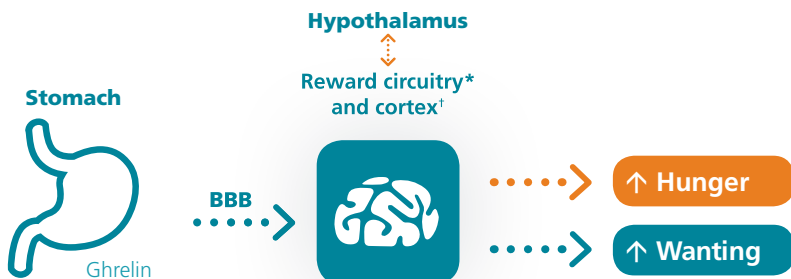


Dr. Lee Kaplan is an obesity medicine specialist whose work focuses on the development of new and more effective strategies for the prevention and treatment of obesity. He notes that:

“Overeating does not cause obesity, obesity causes overeating.”¹



Why are weight loss and weight maintenance difficult?^{2,3}



Insights from Dr. David Macklin, MD, CCFP



Dr. David Macklin is a University of Toronto trained family physician/GP psychotherapist who has been in practice treating obesity for the past 15 years. He states the following:

“Struggling with weight is a **complex, biological, neuro-hormonal**, primarily **genetically-conferred, powerfully environmentally-influenced real medical condition.**”

BBB, blood-brain barrier; CCK, cholecystokinin; GLP-1, glucagon-like peptide-1; PYY, peptide YY.

* The brain's reward circuitry, especially in the ventral tegmental area and nucleus accumbens.

† In particular, the dorsolateral pre-frontal cortex.

The effects of living in an obesogenic environment⁴⁻⁷



Exposure to **cues** in the environment triggers the release of neurotransmitters in the brain. There is a genetic predisposition to be more sensitive to these cues.



This creates **wanting**, the drive and motivation to seek out and consume enjoyable food. This is an innate survival mechanism.

Over time, this associative learning results in **food consumption beyond need**.

The pleasure of consuming enjoyable food reinforces the Pavlovian association between food and these cues. This creates a **reward** system.



It is important to consider that some people are genetically pre-disposed to this conditioning and **wanting**, and have difficulty practising restraint.^{5,6,8} There are pharmacotherapy options available that can address these biological drives and support weight maintenance.⁹⁻¹²

Canadian guidelines for the clinical management of obesity¹²

Obesity management is a combination of:

Behavioural Interventions

Nutrition, physical, and cognitive behavioural therapy.

BMI ≥ 25 kg/m²
+
comorbidities

BMI ≥ 27 kg/m²
+
comorbidities

BMI ≥ 30 kg/m²

BMI ≥ 35 kg/m²

BMI ≥ 40 kg/m²



Pharmacotherapy

Adjunct to behavioural modifications.



Insights from Dr. Michael Vallis,
PhD, R. Psych



Dr. Michael Vallis is a registered psychologist with expertise in adult health psychology, with a clinical focus in the areas of diabetes and obesity. He explains that:

“Obesity is a chronic condition that impacts a person’s overall health. Obesity management strategies should not only focus on weight loss but improving a person’s health and quality of life.”

Bariatric surgery

Consider if other weight-loss attempts have been unsuccessful. Requires lifelong medical monitoring.

Note: For those with BMI ≥ 35 kg/m², bariatric surgery is indicated in those with comorbidities.



Overview of available pharmacotherapy options in Canada

Product	Orlistat (Xenical®)* ⁹	Liraglutide (Saxenda®)* ¹⁰	Naltrexone/bupropion (Contrave®)* ¹¹
Drug class	Gastrointestinal lipase inhibitor	GLP-1 receptor agonist	Opioid antagonist/NDRI
Initiation dosing	120 mg, three times daily PO	Dose escalation for 5 weeks, once daily SC: Week 1: 0.6 mg Week 2: 1.2 mg Week 3: 1.8 mg Week 4: 2.4 mg Week 5: 3.0 mg (maintenance dose)	Dose escalation for 4 weeks, PO: Week 1: 8 mg/90 mg (1 tablet), once daily, AM Week 2: 8 mg/90 mg (1 tablet), twice daily, AM and PM Week 3: 16 mg/180 mg (2 tablets), AM and 8 mg/90 mg (1 tablet), PM Week 4: 16 mg/180 mg (2 tablets), twice daily PO, AM and PM (maintenance dose)
Maintenance dose	120 mg, three times daily PO	3.0 mg, once daily SC	16 mg/180 mg (2 tablets), twice daily PO, AM and PM
Indication	≥30 kg/m² or ≥27 kg/m² + comorbidity	≥30 kg/m² or ≥27 kg/m² + comorbidity	≥30 kg/m² or ≥27 kg/m² + comorbidity
Contraindications	<ul style="list-style-type: none"> Chronic malabsorption syndrome Cholestasis 	<ul style="list-style-type: none"> Personal or family history of medullary thyroid carcinoma, multiple endocrine neoplasia syndrome (MEN2) Pregnancy or breastfeeding 	<ul style="list-style-type: none"> Uncontrolled hypertension Seizure disorders or history of seizures Use of other bupropion-containing products Bulimia or anorexia nervosa Chronic opioid, opioid agonist/partial agonist use, or acute opiate withdrawal Undergoing abrupt discontinuation of alcohol, benzodiazepines, other sedatives, and antiepileptic drugs Use with MAOIs Use with antipsychotic thioridazine Pregnancy Severe hepatic impairment End-stage renal failure



* Please refer to the Product Monograph for full dosing information.

GLP-1, glucagon-like peptide 1; MAOI, monoamine oxidase inhibitor; NDRI, norepinephrine-dopamine reuptake inhibitor; PO, oral administration; SC, subcutaneous.



Overview of available pharmacotherapy options in Canada (cont.)

Product	Orlistat (Xenical®)* ⁹	Liraglutide (Saxenda®)* ¹⁰	Naltrexone/bupropion (Contrave®)* ¹¹
Most common adverse events	<ul style="list-style-type: none"> • Oily spotting/stool/evacuation • Flatus with discharge • Fecal urgency • Increased defecation • Fecal incontinence 	<ul style="list-style-type: none"> • Nausea, vomiting, dyspepsia • Diarrhea, constipation, abdominal pain, upper abdominal pain, dry mouth • Gastritis, gastroesophageal reflux disease • Flatulence, eructation, abdominal distension • Hypoglycemia, decreased appetite • Injection site conditions (erythema, reactions, pruritus, and rash), fatigue, asthenia • Dizziness, dysgeusia • Increased lipase/amylase • Insomnia • Cholelithiasis 	<ul style="list-style-type: none"> • Nausea, vomiting, dyspepsia • Diarrhea, constipation, upper abdominal pain, abdominal pain, dry mouth • Headache, dizziness, tremor, dysgeusia, migraine, disturbance in attention, lethargy • Insomnia, anxiety, abnormal dreams • Fatigue, irritability, feeling jittery • Influenza, viral gastroenteritis, urinary tract infection • Hyperhidrosis, rash, alopecia, pruritus • Muscle strain • Blood pressure increased, heart rate increased • Tinnitus, vertigo • Hot flush, hypertension • Palpitations • Vision blurred

References:

1. MEDSCAPE. Obesity is a disease, Not a choice, Experts Advise. Available at: https://www.medscape.com/viewarticle/896444#vp_1. Retrieved May 14, 2018.
2. Suzuki K, et al. Obesity and appetite control. *Exp Diabetes Res.* 2012;2012:824305.
3. Berthoud HR. Metabolic and hedonic drives in the neural control of appetite: Who's the boss? *Curr Opin Neurobiol.* 2011;21(6):888-896.
4. Davis C, et al. From motivation to behaviour: a model of reward sensitivity, overeating, and food preferences in the risk profile for obesity. *Appetite.* 2007;48(1):12-19.
5. Berridge KC, et al. Pleasure systems in the brain. *Neuron.* 2015;86(3):646-664.
6. Berthoud HR, et al. Food reward, hyperphagia, and obesity. *Am J Physiol Regul Integr Comp Physiol.* 2011;300(6):R1266-1277.
7. Munzberg H, et al. Hedonics Act in Unison with the Homeostatic System to Unconsciously Control Body Weight. *Front Nutr.* 2016;3:6.
8. Born JM, et al. Differences between liking and wanting signals in the human brain and relations with cognitive dietary restraint and body mass index. *Am J Clin Nutr.* 2011;94(2):392-403.
9. Xenical® (orlistat) Product Monograph. Hoffmann-La Roche Limited. November 18, 2015.
10. Saxenda® (liraglutide) Product Monograph. Novo Nordisk Canada Inc. July 12, 2017.
11. Contrave® (Naltrexone and Bupropion) Product Monograph. Valeant Canada LP. February 12, 2018.
12. Lau DCW, et al. 2006 Canadian clinical practice guidelines on the management and prevention of obesity in adults and children. *CMAJ.* 2007;176(8):1-117.

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