Canadian Adult Obesity Clinical Practice
GUIDELINES

2020 Canadian Adult Obesity Clinical Practice Guidelines – Principles for Primary Care

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L'ASSOCIATION CANADIENNE
des MEDECINS et CHIRURGIENS BARIATRIQUE

The CANADIAN ASSOCIATION of
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Contents

- Definition and Context
- Assessment and Screening
- Weight Stigma
- The Science of Obesity
- Approaches to Obesity Management
- Key Messages

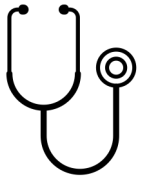
Objectives

- Understand obesity as a chronic, relapsing, multifactorial, neurobehavioural disease, and that guidelines have changed to reflect this understanding.
- Recognize the factors and neurohormonal processes which perpetuate weight gain and frustrate efforts to maintain a lower body weight.
- Describe a multimodal approach to weight management, with a focus on the latest Canadian guidelines, recognizing obesity as a chronic but treatable condition with defined goals but realistic expectations and multiple therapeutic options.

Context

- A comprehensive and current understanding of obesity - pathogenesis and scientific concepts, assessment schemes, psychosocial milieu, new pharmacotherapy, and foundational non-pharmacotherapeutic management, is needed to inform a contemporary and rational approach to obesity prevention and management
- Previous guidelines were published in 2006
- New guidelines published 2020 are extensive (and already ++ read)

New Obesity Definition



Obesity is defined as a prevalent, complex, progressive, and relapsing chronic disease characterized by abnormal or excessive body fat (adiposity) that impairs health

Recommendations and key messages in the guidelines are specific for people living with obesity and may not be applicable or appropriate for people with larger bodies who do not have health impacts from their weight

Definition of Obesity

Obesity has previously been defined by BMI, a measure of size, not health. It is time to move away from a weight centric definition and focus on health.

Obesity as a prevalent, complex, progressive, and relapsing chronic disease characterized by abnormal or excessive body fat (adiposity) that impairs health.

- BMI and waist circumference can be used as screening tools.
- Diagnosis of obesity should be based on the presence of functional, medical, and/or psychosocial impairments related to the presence of abnormal or excess body fat rather than on anthropometric measures alone.

Key Principles of Obesity Management

- Obesity should be managed using evidence-based chronic disease management principles, must validate patients' lived experiences, move beyond the simplistic approaches of "*eat less, move more*", and address the root drivers of obesity.

- People who are living with obesity should have access to evidence-informed interventions, which should include medical nutrition therapy, physical activity, psychological interventions, pharmacotherapy, and surgery.

Initiating the Discussion of Obesity

- We recommend that healthcare providers are aware of their own biases and attitudes toward people living with obesity.
- Approach patients with empathy and sensitivity while acknowledging the complexity of the disease and avoiding stereotypes and oversimplification.
- Create a supportive environment with appropriate equipment (e.g. appropriately sized blood pressure cuffs and gowns, armless chairs in waiting rooms, a private room for weigh-ins).
- Ask for permission to weigh patients to help foster patient comfort and dignity

Screening for Obesity

- Regular assessment of BMI, WC and cardiometabolic risk factors can help identify people at greater risk of developing obesity.
- For most populations, the presence of overweight (BMI ≥ 25 kg/m^2) represents an increased risk and requires further evaluation of other anthropometric, hemodynamic and biochemical parameters.
- In adults with South-, Southeast- or East Asian ethnicity, the recommended BMI cut-off for overweight should be ≥ 23 kg/m^2.
- In special populations such as the elderly, very muscular patients, and those with extreme tall or short stature, the BMI can be misleading and needs to be interpreted with caution.

Assessment of people living with obesity - diagnosis

BMI

Category	BMI (kg/m^2)
Caucasian, Europid, North American	
Underweight	<18.5
Normal	18.5-24.9
Overweight	25-29.9
Obesity class 1	30-34.9
Obesity Class 2	35-39.9
Obesity Class 3	40-49.9
Obesity Class 4	50-59.9
Obesity Class 5	≥60
South-, Southeast- or East Asian	
Underweight	<18.5
Normal range	18.5-22.9
Overweight – At risk	23-24.9
Overweigth – Moderate risk	25-29.9
Overweight – Severe risk	≥ 30

Waist Circumference (cm)

Predominent Ethnicity	Increased abdominal adiposity/Cardio-vascular risk		Significant abdominal adiposity/Greater cardiovascular risk	
	Women	Men	Women	Men
African	71.5	76.5	81.5	80.5
African American	90	80	99	95
Asian	80	85		
Canadian Aboriginal	80	94		
Caucasian Europid/US/Mid-East Mediterranean	80	94	88	102
Chinese	81	83		
Korean	75	80	85	90
Latino central/South American	83	88	90	94
Sub-Saharan African	80	94		

An increased WC may imply

(1) in people with high BMI but < 35: greater risk of cardiometabolic disease

(2) in people with normal BMI: increased abdominal fat and cardiometabolic disease;

(3) in people with BMI > 35: can provide information on efficacy of treatment (adipose distribution can change before BMI)

Metabolically healthy

Absence of increased cardiometabolic risk despite elevated BMI and WC

- Not considered medically healthy because of increased risk of mortality and more likely to suffer obesity-related complications
- No evidence to support long-term benefits of intentional WL - opt for adoption of behaviours that prevent weight gain.

BMI: body mass index **WC:** waist circumference **WL** weight loss

4Ms Framework for Assessment of Obesity

Mental:
- Knowledge/cognition
- Expectations
- Self-image
- Internalized weight-bias
- Mood/anxiety
- Attention
- Addiction
- Eating disorder
- Sleep
- Personality

Mechanical:
- Osteoarthritis
- Sleep apnea
- Plantar fasciitis
- GERD
- Urinary incontinence
- Intertrigo
- Pseudotumor cerebri
- Thrombosis

Metabolic:
- Type 2 diabetes
- Dyslipidemia
- Hypertension
- Gout
- Fatty liver disease
- Gallstones
- PCOS
- Hypogonadism
- Infertility
- CAD, CHF, AF
- Cancer

Mileu:
- Socioeconomic status
- Education
- Occupation
- Access to food
- Disability
- Access to medication

5As Approach to Obesity Assessment and Management

- The use of structured interview formats such as Obesity Canada's 5As of Obesity Management™ can help facilitate discussions about obesity in primary care.
- The main components of the 5As framework include:
  1. ASKING for permission to discuss weight and explore readiness;
  2. ASSESSING obesity-related risks and root causes of obesity;
  3. ADVISING on health risks and treatment options;
  4. AGREEING on health outcomes and behavioural goals; and
  5. ASSISTING in accessing appropriate resources and providers.

Edmonton Obesity Staging System (EOSS)

Stage 0: No apparent obesity-related risk factors, no physical symptoms, no psychopathology, no functional limitations and/or impairment of well-being.

Stage 1: Presence of subclinical risk factors, mild physical symptoms, mild psychopathology, mild functional limitations and/or impairment of well-being.

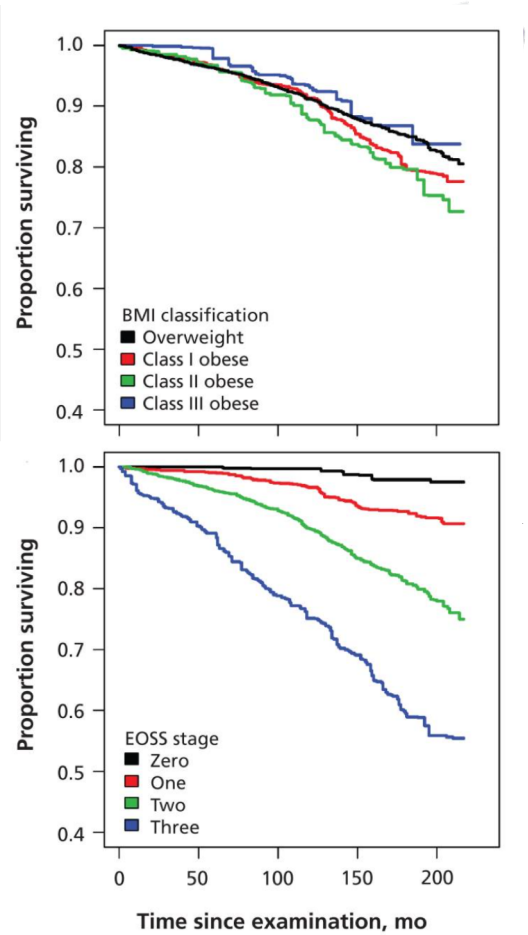
Stage 2: Presence of obesity-related chronic disease, moderate psychopathology, moderate limitations in activities of daily living and/or well-being.

Stage 3: Established end-organ damage, significant psychopathology, functional limitations and/or impairment of well-being.

Stage 4: Severe disabilities from obesity-related chronic diseases, disabling psychopathology, functional limitations and/or impairment of well-being

Edmonton Obesity Staging System (EOSS)

- EOSS is a measure of the mental, metabolic and physical impact that obesity has had on the patients' health and uses these factors to determine their stage of obesity (from stage 0–4).
- In population studies, EOSS has been shown to be a better predictor of all-cause mortality when compared to BMI or waist circumference measurements alone.



Padwal RS et al. *CMAJ* 2011

Mental Health

- Screen for depression and anxiety
- Screen for attention deficit hyperactivity disorder, post-traumatic stress disorder, chronic grief
- Screen for previous and current forms of physical, psychological and sexual abuse
- Screen for addiction/dependency
- Screen for emotional eating/binge eating disorder
- Assess psychological impact of previous weight journey

Sleep

- Number of hours of sleep per night
- Use of pharmacologic sleeping aids
- Sleep apnea screening

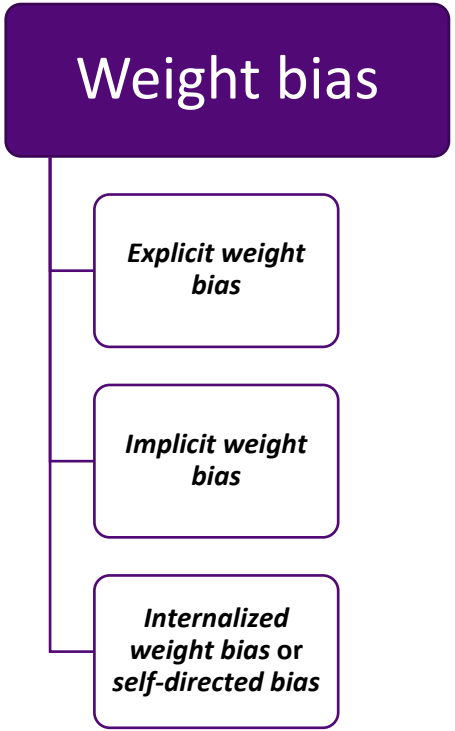
Key Messages Regarding Obesity Assessment In Adults

1. Obesity is a chronic, progressive and relapsing disease, characterized by the presence of abnormal or excess adiposity that impairs health and social well-being.
2. Screening for obesity should be performed regularly by measuring body mass index (BMI) and waist circumference (WC).
3. The clinical assessment of obesity should aim to establish the diagnosis and identify the causes and consequences of abnormal or excess adiposity on a patient's physical, mental and functional health.

Key Messages Regarding Obesity Assessment In Adults (Cont'd)

4. Providers participating in the assessment of obesity should focus on establishing values and goals of treatment, identifying which resources and tools may be needed and fostering self-efficacy with the patient in order to achieve long-term success.
5. A non-judgmental, stigma-free environment is necessary for an effective assessment of a patient living with obesity.

What is weight bias?



Negative weight-related attitudes, beliefs, assumptions, and judgments in society that are held about people living in large bodies

Having overtly negative attitudes toward people with obesity

Having unconscious negative attitudes toward people in large bodies

Extent to which individuals living with obesity endorse negative weight-biased beliefs about themselves

Shaming is ineffective

Individuals with higher IWB report less weight loss, lower physical activity levels, higher caloric intake, greater disordered eating behaviours

Shameful public health messages could inadvertently make the problem worse and harm those most in need of help

Nolan LJ, Eshleman A. Appetite. 2016 01;102:15–24. Pearl RL, Wadden TA, Hopkins CM, Shaw JA, Hayes MR, Bakizada ZM, et al. Obes Silver Spring Md. 2017;25(2):317–22. Kirk, Sara F. L. et al. Qualitative Health Research 2014, Vol. 24(6) 790– 800

"There's such a stigma there that is reinforced. But when I enter the health system, the first place I expect to talk candidly about my issue, I hear the blame. 'Well, you know, if you eat right and exercise, you'll lose weight. It's as simple as that. It's a simple thing.' That's what I get—It's so simple".

Rand, K, Vallis M, Aston M, Price S, Piccini-Vallis H, Rehman L, Kirk SFL, "It is Not the Diet; it is the Mental Part We Need Help with." A Multilevel Study on Obesity and Psychological, Emotional, and Social Well-being, International Journal of Qualitative Studies on Health and Wellbeing, 12(1):1306421

"…weight bias negatively affects patients' engagement in primary health care through their perceived barriers to health care utilization, expectations of differential health care treatment, low trust and poor communication, avoidance or delay of health services, and 'doctor shopping'."

Alberga AS, Edache IY, Forhan M, Russell-Mayhew S. (2019) Weight bias and health care utilization: a scoping review. Primary Health Care Research & Development 20(e116): 1–14

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The Science of Obesity

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Obesity Pathogenesis

- Obesity pathogenesis involves complex biological, psychosocial, and environmental factors
- Body weight is meticulously regulated by the brain
- Obesity is influenced by the social and physical environment in which we live

Energy homeostasis

- Energy surfeit is converted into fat and stored in adipose tissue
- Even small surplus of caloric intake (less than 1%) over energy expenditure can accumulate over years to cause weight gain
- Small cumulative imbalances of energy intake and expenditure can lead to weight gain and obesity
- Biological defence of elevated body weight in individuals with obesity

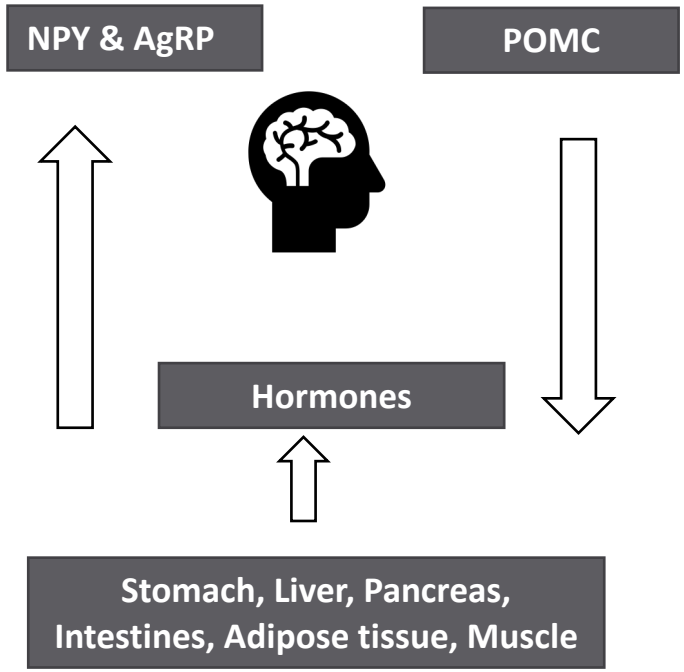
Schwartz et al. (2017).*Endocrine Reviews*, Volume 38, Issue 4, Pages 267–296

The brain and obesity

- The brain plays the most important role in obesity and energy balance
- Biological control of appetite is complex
- Three main areas that regulate appetite
  - The hypothalamus
  - Mesolimbic area
  - Cognitive

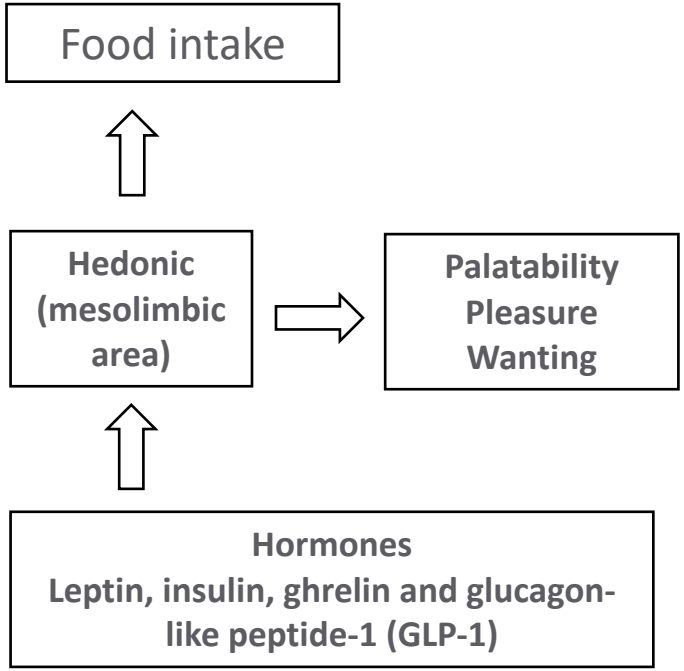
Hypothalamus (homeostatic)

- Arcuate nucleus: hunger centre
- Neurons (co-expressing neuropeptide Y (NPY), agouti-related protein (AgRP)) are activated by hormonal signals from the gut, adipose tissue, and peripheral organs, and stimulate hunger sensation and trigger food-seeking behaviours
- Expression of pro-opiomelanocortin (POMC) and anorexic neuropeptide α-melanocyte–stimulating hormone (MSH) sends satiety signals



Mesolimbic (hedonic)

- Hedonic eating is based on the feelings of reward and pleasure that are associated with seeing, smelling or eating food
- Dopaminergic, opioid and endocannabinoid pathways
- Some people living with obesity may have a heightened anticipation (wanting) of the pleasure of food driven by a dysregulation of dopamine
- Hormonal regulation and cognitive behavioural therapy as targets for obesity treatment



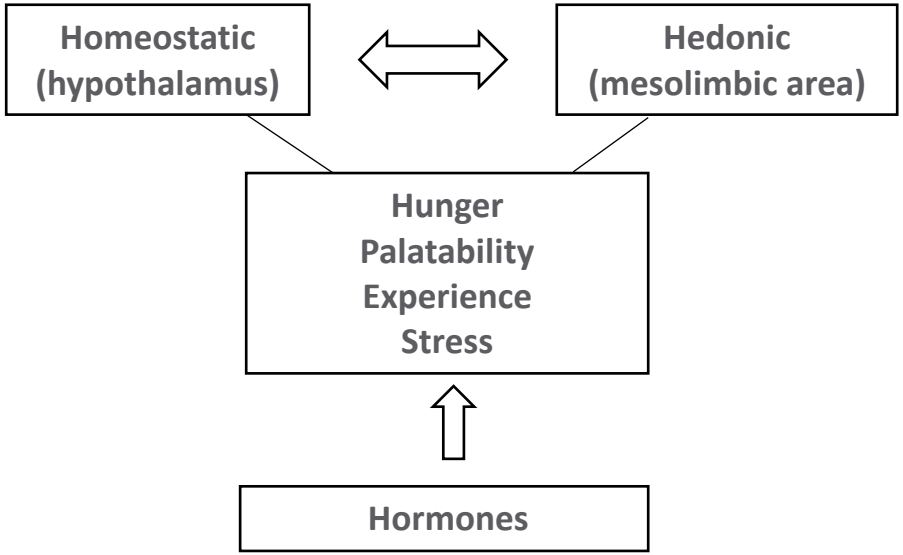
Cognitive (executive functioning)

- Executive functioning and overriding primal behaviours driven by the mesolimbic system
- Optimal conditions: rest, oxygen, decreased stress, and supports
- Dysfunctional connection between the cognitive system and the rest of the brain that leads to the inability to control eating behaviours
- Cognitive areas in the prefrontal cortex exert executive control on the decision to eat and the food choices

Homeostatic and hedonic eating

Significant crosstalk between homeostatic and hedonic eating, which is mediated by many of the endocrine and gut-derived signals

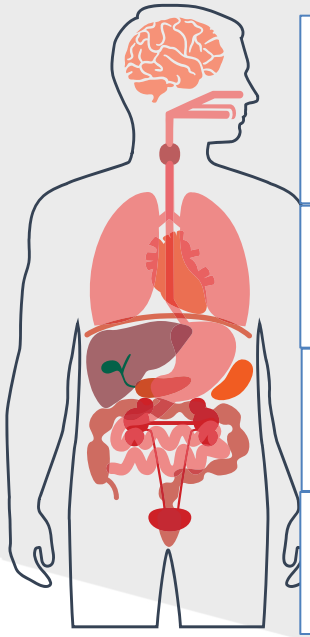
- Leptin, insulin, ghrelin and glucagon-like peptide-1 (GLP-1) also act on the dopaminergic neurons in the midbrain to modulate food reward and hedonic eating
- appetite-suppressing network involves calcitonin gene-related peptide (CGRP) neurons in the parabrachial nucleus (PBN)
- PBN-CGRP neurons are activated by signals associated with food intake, and they provide a signal of satiety



The Role of the Brain in Controlling Eating

Appetite – Reaction to stimuli

Homeostatic eating
Eating for hunger



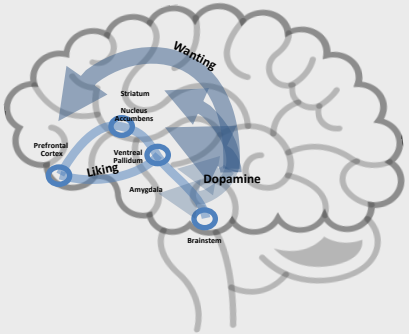
POMC neurons decrease hunger

Ghrelin increases hunger

Leptin decreases hunger

GLP-1 increases satiety

Hedonic eating
Eating for pleasure

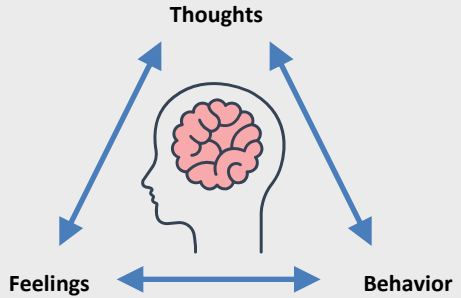


Dopamine controls WANTING, the motivation/drive to eat

Opioid and receptors control LIKING, the pleasure associated with food

Self-regulation

Executive Function
Deciding to eat



Prefrontal cortex regulates eating behaviour and controls the decision to eat certain foods over others

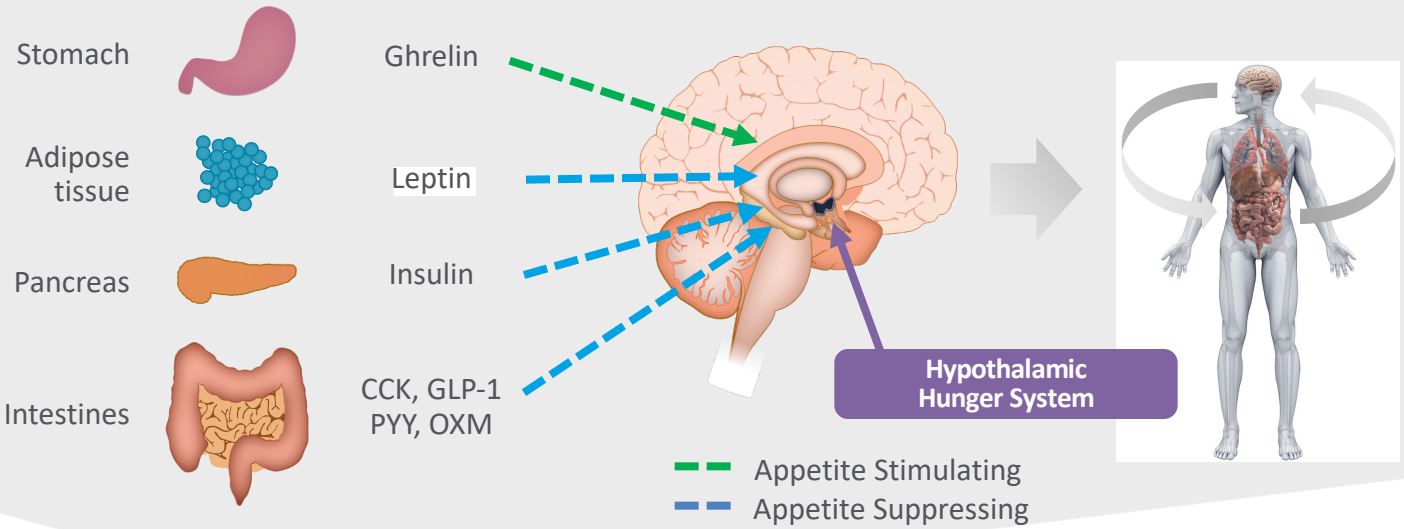
Berridge KC, et al. The American psychologist 2016; 71(8): 670-679

Homeostatic eating – Eating for hunger

Peripheral signals relay information about nutritional status

Signals are integrated in specific regions of the CNS

Control of food intake, Control of energy expenditure, Body weight homeostasis



CCK = cholecystokinin; CNS = central nervous system; GLP-1 = glucagon-like peptide 1; OXM = oxyntomodulin; PYY = peptide YY.

1. Mendieta-Zerón H et al. Gen Comp Endocrinol. 2008;155:481-495.

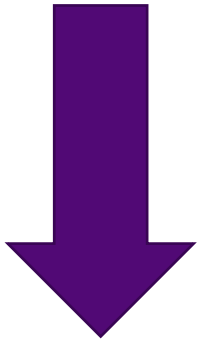
Summary of biological appetite control

- Central neural circuits integrate with signals from the gut
- Adipose tissue and other organs to influence homeostatic and hedonic eating
- Executive control by higher brain centres on the decision of when and what to eat
- These neural networks have also been shown to be altered in obesity

Adipose tissue and food intake

- Leptin is a fat-derived hormone that is secreted by white adipose tissue in proportion to the body's fat mass
- Leptin and insulin bind to their respective receptors in the arcuate nucleus to decrease food intake and increase energy expenditure
- Leptin activates POMC/CART expressing neurons to promote feeding
- Leptin inhibits AgRP/NPY-expressing neurons to increase appetite and decrease energy expenditure
- Leptin resistance also occurs in some people who have excessive adiposity, which can perpetuate the vicious cycle of fat mass accretion

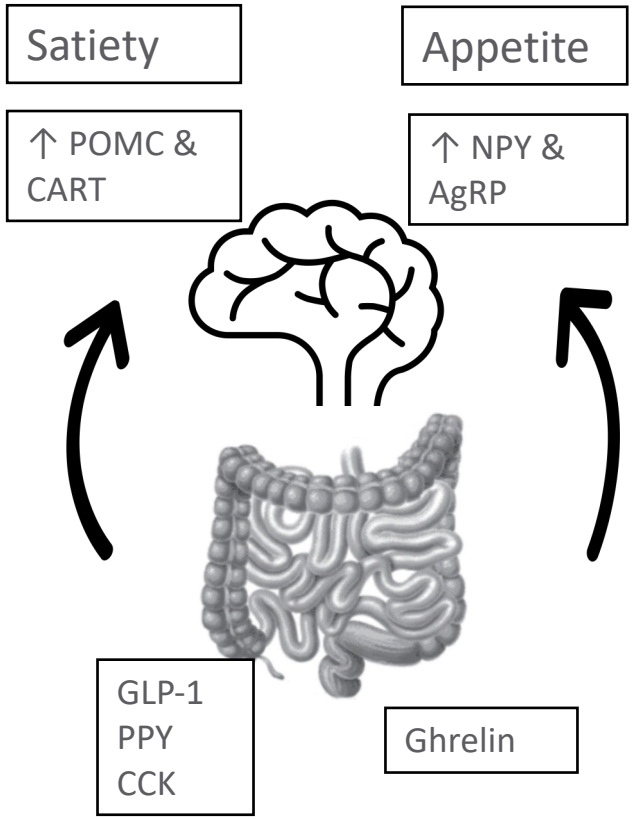
Increased body fat stores, increased leptin levels



Decreased body fat stores, decreased leptin levels

Gut-derived signals

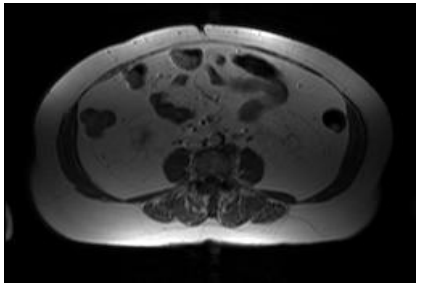
- GLP-1 and peptide YY3-36 (PYY) delay gastric emptying and are potent anorexigenic gut hormones secreted by enteroendocrine L-cells in the small bowel in response to food ingestion
- Promote satiation and satiety by activating the POMC/PYY neurons while reducing hunger via the AgRP/NPY neurons
- Cholecystokinin CCK stimulates gall bladder contractility and pancreatic enzyme secretion, and slows gastric emptying
- Ghrelin is an orexigenic hormone produced in the gastric fundus which increases hunger and stimulates food intake



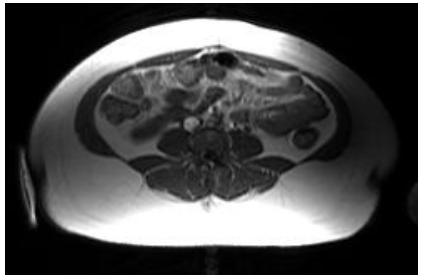
Adipose tissue depots

- Subcutaneous fat accounts for about 85% of total body fat
- Intra-abdominal or visceral fat (15%) – also “ectopic fat”
- Visceral adipose tissue associated with decreased insulin sensitivity, increased expression of proinflammatory adipokines
- An endocrine organ

Visceral



Subcutaneous



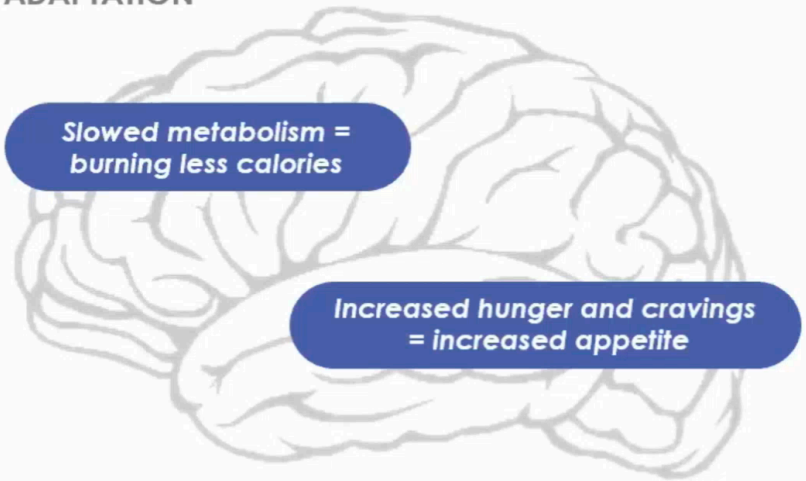
Adipose tissue dysfunction

- Inability to store excess calories in healthy subcutaneous fat depots can lead to increased visceral fat accretion and ectopic fat deposition
- Adipose tissue expansion often leads to dysfunctional changes, which are characterized by inflammation that can lead to augmented production of fat-derived proinflammatory cytokines, or adipokines
- Adipose tissue dysfunction can lead to: comorbidities, such as type 2 diabetes, hypertension, dyslipidemia, non-alcoholic fatty liver disease, cardiometabolic risks and atherosclerotic cardiovascular disease

Brown and beige fat

- Brown adipose tissue involved in whole-body energy homeostasis through non-shivering thermogenesis
- “Beiging” of white fat cells, can be induced by chronic exposure to cold temperatures and, to some extent, exercise
- Further elucidation of the potential roles of brown/beige fat in the regulation of whole-body energy metabolism and glucose/lipid homeostasis is needed

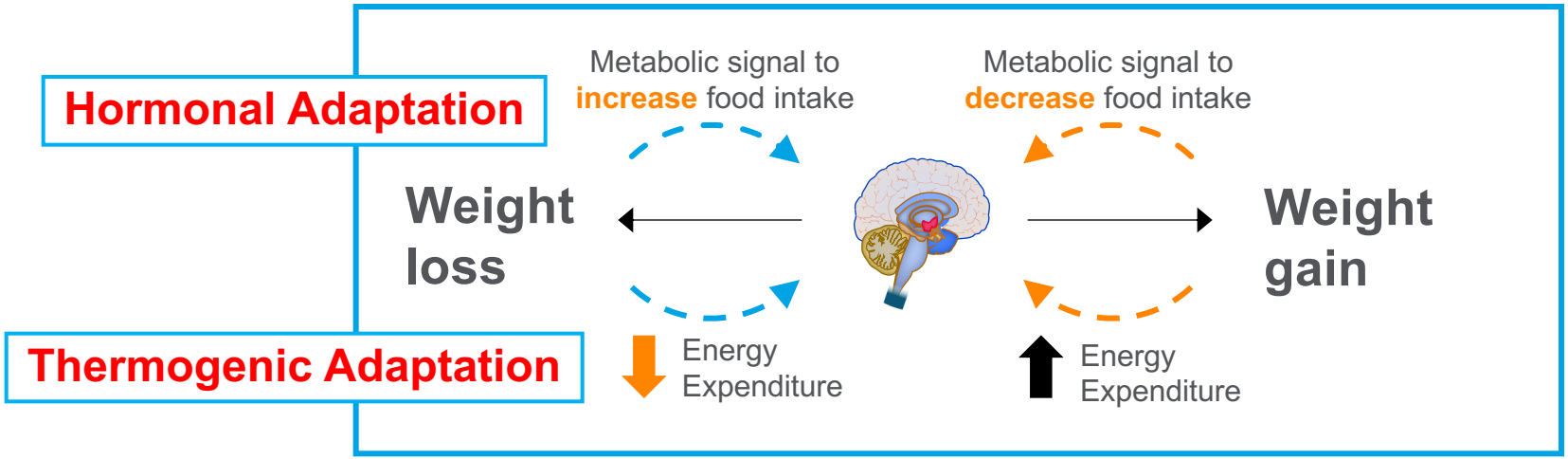
NEUROHORMONAL ADAPTATION



The brain is designed to defend the body against weight loss

What happens when a patient loses weight?
Homeostatic Regulation of Set Point Body Weight

A homeostatic regulatory system prevents deviation from a body weight set point

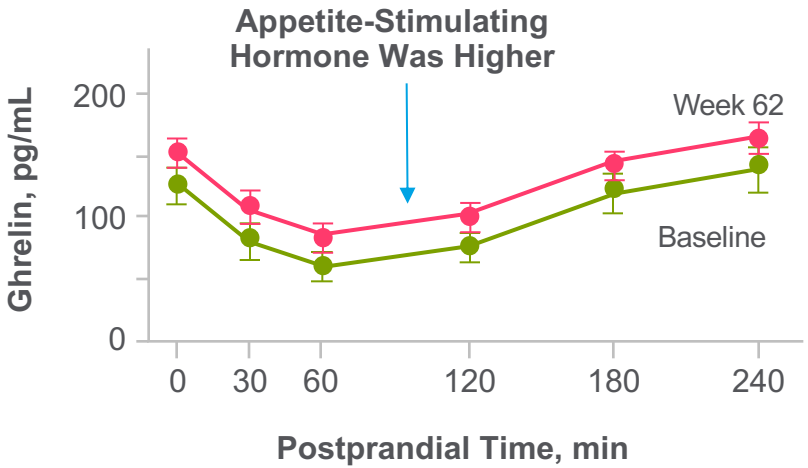


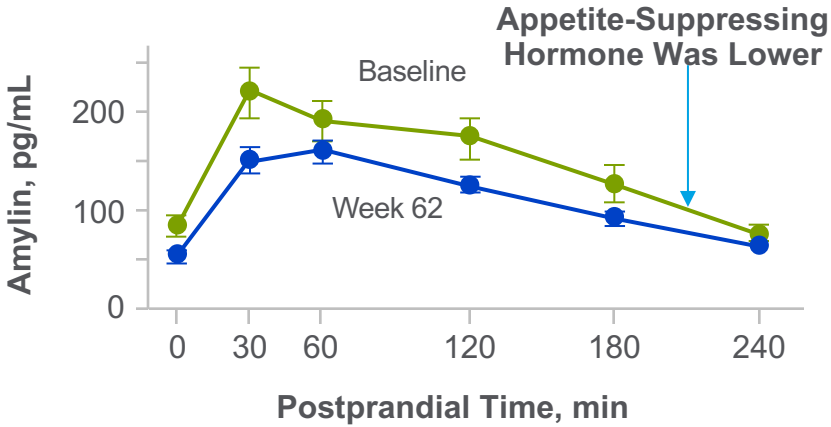
Deviation from this set point elicits a physiological compensatory mechanism
controlling **food intake** and **energy expenditure**

Yu YH et al. Obes Rev. 2015;16:234-247.

Physiological Mechanisms Underlie Weight Regain

Compensatory mechanisms encourage weight regain after weight loss. Circulating mediators of appetite that encourage weight regain after weight loss do not revert to pre-weight loss levels



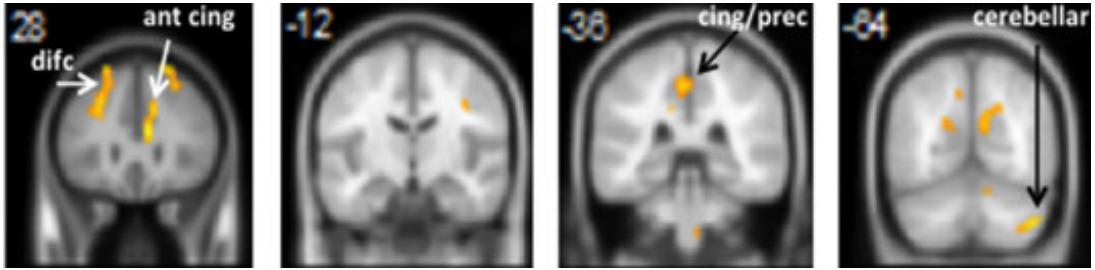


Sumithran P et al. N Engl J Med. 2011;365:1597-1604.

Altered Mesolimbic Reward System Activation in Patients With Obesity

Fed/Satiated State

Individuals with obesity still show reward system activation following a meal compared to lean individuals



Anterior cingulate & dorsolateral frontal cortex

Posterior cingulate cortex

Cingulate & precuneus

Cerebellum

**Images represent subtracted differences in fMRI activation in response to food cues between individuals with and without obesity (with obesity>without).

Repeated dopamine pathway stimulation leads to lower D2 receptor density

Compulsive eating

Loss of control of food intake

Conditioned responses to food

Low activation > High activation

Figure adapted from Puzziferri et al,[2] © 2016 The Obesity Society, with permission from John Wiley and Sons.
Ant cing=anterior cingulate; Cing=cingulate; Dlfc=dorsolateral frontal cortex; fMRI=functional magnetic resonance imaging; NAc=nucleus accumbens; Prec=precuneus.
Puzziferri N et al. Obesity. 2016;24:829-836.


Regained weight
13 of 14 participants regained weight
GAINED 50 lbs.
0
50
100
150
200
LOST 200 lbs.
Weight change (pounds)
"The Biggest Loser" Season 8 (2009)
Six years later
Metabolism slowed
Nearly all contestants had slower metabolism
Body burns 200 more cal. a day
0
200
400
600
Body burns 800 fewer cal. a day
Change in calories burned/day
"The Biggest Loser" Season 8 (2009)
Six years later

Implications for weight maintenance

- Short-term behavioural changes lead to a modest weight loss of 3%–5%, but is often difficult to sustain
- Reduction in energy expenditure and adaptive hormonal responses after weight loss may favour weight regain
- Resting energy expenditure decreased by approximately 15 kcal/kg of weight lost (long term, and likely permanent)
- After long-term diet-induced weight loss, levels of circulating hormones, such as leptin, insulin, GLP-1, CCK, PYY and ghrelin do not revert to levels recorded before weight loss and instead act to encourage weight regain via greater appetite
- Anorexigenic hormones (leptin, insulin, GLP-1) are reduced, whereas levels of the orexigenic hormone ghrelin are increased

Implications for weight maintenance

- for every 1 kg of weight loss, there is an increased drive to eat about 100 calories per day more compared to before the weight loss intervention
- The longer energy intake is restricted, the greater the compensatory food intake
- Feelings of satisfaction ('food reward') increases when calorie intake is restricted, and even sense of smell improves as well – thus more enjoyment of food
- During caloric (dietary) restriction, most of the data also supports that there is a reduction in physical activity as well.
- With exercise induced weight loss, there appears to be an even *greater* drive to eat to regain weight, which gets stronger with longer durations of exercise-induced weight loss. There may also be a decrease in energy burned during regular daily activities (non exercise activity thermogenesis) due to less activity.

3 Advise On obesity risks. Discuss the health benefits of obesity management.

Medical Nutrition Therapy (MNT)

MNT is used in managing chronic diseases and focuses on nutrition assessment, diagnostics, therapy and counselling. MNT should:

a. be personalized and meet individual values, preferences and treatment goals to promote long term adherence

b. be administered by a registered dietitian to improve weight-related and health outcomes

Physical Activity

30-60 mins of aerobic activity on most days of the week, at moderate to vigorous intensity, can result in:

a. small amount of weight and fat loss

b. improvements in cardiometabolic parameters

c. weight maintenance after weight loss

ⓘ **Remember nutrition and physical activity recommendations are important for all Canadians regardless of body size or composition.**

The Three Pillars of Obesity Management that Support Nutrition and Activity

Psychological Intervention

a. Implement multicomponent behaviour modification

b. Manage sleep, time, and stress

c. Cognitive behavioural therapy and/ or acceptance and commitment therapy should be provided for patients if appropriate

Pharmacological Therapy

a. liraglutide

b. naltrexone/bupropion *(in a combination tablet)*

c. orlistat

CRITERIA

BMI ≥30kg/m² or

BMI ≥27 kg/m² with obesity (adiposity) related complications

Bariatric Surgery

ⓘ Procedure should be decided by surgeon in discussion with the patient.

a. Sleeve gastrectomy

b. Roux-en-Y gastric bypass

c. Biliopancreatic diversion with/without duodenal switch

CRITERIA

BMI ≥40 kg/m² or

BMI ≥35 - 40 kg/m² with an obesity (adiposity) related complication or

BMI ≥30 kg/m² with poorly controlled type 2 diabetes

Treating the root causes of obesity is the foundation of obesity management - refer to the 4M framework - *mechanical, metabolic, mental and social milieu*

Key Message #1

Regular physical activity induces a wide range of health benefits in adults across all BMI categories, even in the absence of weight loss

Key Message #2

- Aerobic and resistance exercise can favour the maintenance or improvements in cardiorespiratory fitness, mobility, strength and muscle mass during weight management interventions.
- This can be important, as these outcomes are not targeted and sometimes are negatively affected by other therapies, such as caloric restriction, medications and bariatric surgery.

Physical activity and body composition

- Significant but modest long-term weight loss (about 2 kg) can be expected with exercise alone (e.g., aerobic and resistance) in male and female adults who have overweight or obesity
- In general, nutrition interventions produce a greater weight loss (about 4 kg) compared to exercise alone, and when exercise is combined with diet, there is an additional increase in the amount of weight loss (about 6 kg)
- Obesity management interventions that incorporate exercise generally report either maintenance or gain in fat-free mass

Recommendation #1

Aerobic physical activity (30–60 minutes of moderate to vigorous intensity most days of the week) can be considered for adults who want to:

a) Achieve small amounts of body weight and fat loss (Level 2a, Grade B)

b) Achieve reductions in abdominal visceral fat (Level 1a, Grade A) and ectopic fat such as liver and heart fat (Level 1a, Grade A),even in the absence of weight loss

c) Favour weight maintenance after weight loss (Level 2a, Grade B)

d) Favour the maintenance of fat-free mass during weight loss (Level 2a, Grade B)

e) Increase cardiorespiratory fitness (Level 2a, Grade B)7 and mobility (Level 2a, Grade B)

Recommendation #2

For adults living with overweight or obesity, resistance training may promote weight maintenance or modest increases in muscle mass or fat-free mass and mobility (Level 2a, Grade B)

Recommendation #3

Increasing exercise intensity, including high-intensity interval training, can achieve greater increases in cardiorespiratory fitness and reduce the amount of time required to achieve similar benefits as from moderate-intensity aerobic activity (Level 2a, Grade B)

Recommendation #4

Regular physical activity, with and without weight loss, can improve many cardiometabolic risk factors in adults who have overweight or obesity, including:

a) Hyperglycemia and insulin sensitivity (Level 2b, Grade B)

b) High blood pressure (Level 1a, Grade B)

c) Dyslipidemia (Level 2a, Grade B)

Recommendation #5

Regular physical activity can improve health-related quality of life, mood disorders (i.e., depression, anxiety) and body image in adults with overweight or obesity (Level 2b, Grade B)

Conclusion

- Adults with overweight or obesity should consider increasing physical activity as an integral component of all obesity management strategies
- Physical activity offers a wide range of health benefits that are partly independent of weight loss.
- Sedentary individuals should progress to 30–60 minutes or more of moderate to vigorous intensity aerobic physical activity (e.g., walking, biking) on most days of the week (i.e., aim to accumulate 150 minutes or more per week), engage in strength (resistance) activity at least two days per week, and reduce the amount of daily sedentary time for body weight control and/or health benefits.

Canadian Adult Obesity Clinical Practice
GUIDELINES

Pharmacotherapy in Obesity Management

L'ASSOCIATION CANADIENNE
des MEDECINS et CHIRURGIENS BARIATRIQUE

The CANADIAN ASSOCIATION of
BARIATRIC PHYSICIANS and SURGEONS

obesity canada
obésité canada

Rationale

- Modest (5-10%) and sustained weight loss is associated with improvements in comorbidities associated with obesity
- Behavioural interventions (nutrition and physical activity) generally achieves only a 3-5% weight loss, which is most often not sustained over the long term
- Pharmacotherapy for obesity should be considered to decrease weight and improve metabolic parameters, when behavioural interventions alone have been ineffective, insufficient, or without sustained benefit

Pharmacotherapy for obesity in Canada

- Pharmacotherapy is indicated for chronic weight management in Canada for individuals with a BMI ≥30 kg/m^2, or ≥27 kg/m^2 with comorbidities associated with excess body fat (eg. type 2 diabetes, hypertension, dyslipidemia)

- There are three medications indicated for chronic obesity management in Canada in addition to health behaviour changes: liraglutide (Saxenda®) 3.0 mg, naltrexone/bupropion (Contrave®) in a combination tablet, and orlistat (Xenical®).

Considerations in the use of pharmacotherapy for obesity

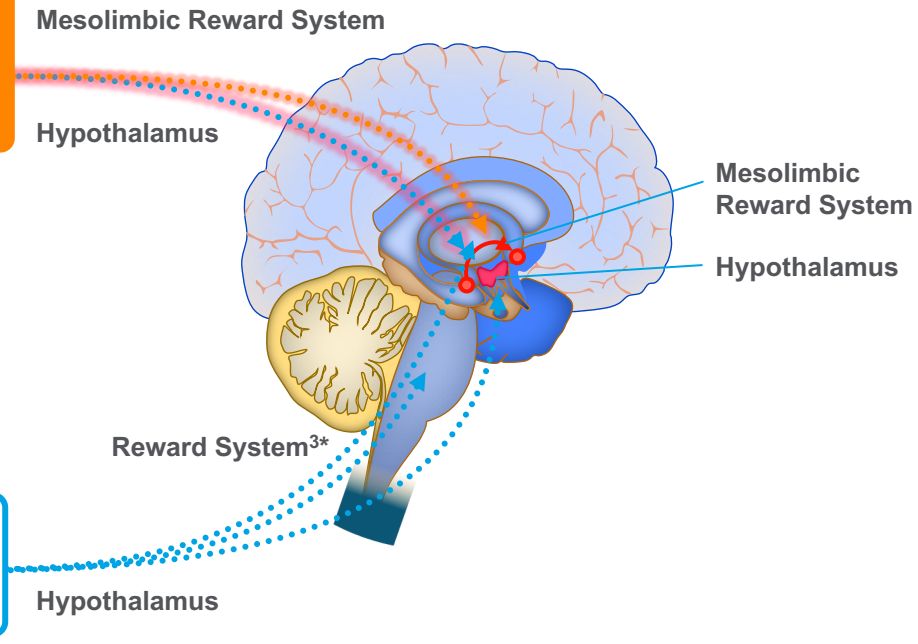
- Mechanism of action
- Side effects/tolerability
- Safety
- Patient comorbidities
- Existing medications
- Mode and frequency of administration
- Cost

Current obesity pharmacotherapy approved for long-term use in Canada

Naltrexone/bupropion[1]
μ-opioid antagonist +
DA/NE reuptake inhibitor

Liraglutide[2]
GLP-1 receptor agonist

Orlistat[4]
Lipase inhibitor

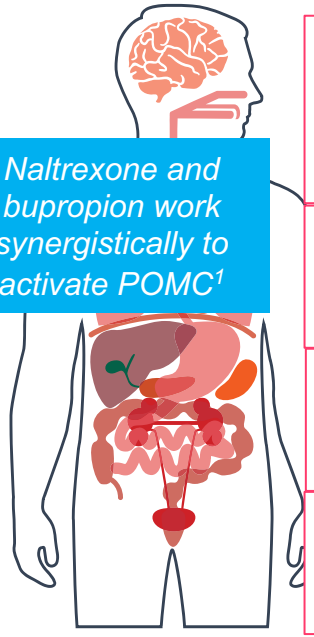


DA=dopamine; GLP-1=glucagon-like peptide-1; NE=norepinephrine. *GLP-1s have been shown to modulate food reward and hedonic eating

1. Ornellas T, Chavez B. P T. 2011;36(5):255–262; 2. Shah M, Vella A. Rev Endocr Metab Disord. 2014;15(3):181–187; 3. Reproduced from the Canadian Adult Obesity Clinical Practice Guidelines [The Science of Obesity. Lau, C.W., Wharton, S. 1-7, copyright notice] with permission from Obesity Canada/ Obésité Canada; 4. Yanovski SZ et al. JAMA. 2014;311:74-86.

The role of the brain in controlling eating

Homeostatic eating



Naltrexone and bupropion work synergistically to activate POMC[1]

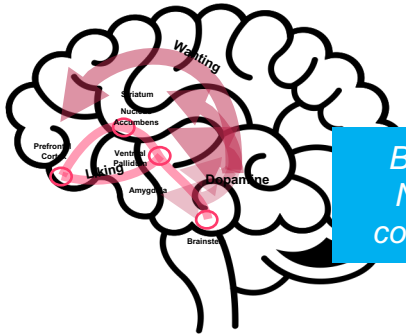
POMC neurons decrease hunger

Ghrelin increases hunger

Leptin decreases hunger

GLP-1 increases satiety

Hedonic eating



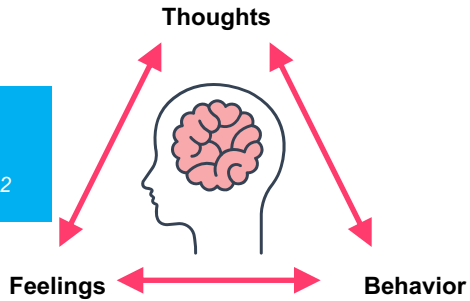
Bupropion is a NDRI used to control cravings[2]

Dopamine controls WANTING, the motivation/drive to eat

Opioid and cannabin receptors control LIKI the pleasure associate food

Naltrexone blocks the mu-opioid receptor to reduce liking[3]

Executive Function



Behavioural interventions

ower sustainable aviours in controlling ng

1. Berridge KC, et al. The American psychologist. 2016; 71(8): 670-679 2. Billes & Greenway. Expert Opin Pharmacother. 2011;12:1813–26. 3. Tek C. Patient Prefer Adherence. 2016;10:751–759.

Recommendation 1

Pharmacotherapy for weight loss can be used for individuals with BMI ≥ 30 kg/m^2 or BMI ≥ 27 kg/m^2 with adiposity-related complications, in conjunction with medical nutrition therapy, physical activity and psychological interventions (liraglutide 3.0 mg [Level 2a, Grade B)], naltrexone/bupropion combination [Level 2a, Grade B],4 orlistat [Level 2a, Grade B]).

Recommendation 2

Pharmacotherapy may be used to maintain weight loss that has been achieved by health behaviour changes, and to prevent weight regain (liraglutide 3.0 mg or orlistat) (Level 2a, Grade B).

Recommendation 3

For people living with type 2 diabetes and a BMI ≥ 27 kg/m^2, pharmacotherapy can be used in conjunction with health behaviour changes for weight loss and improvement in glycemic control: liraglutide 3.0 mg (Level 1a, Grade A); naltrexone/bupropion combination (Level 2a; Grade B), orlistat (Level 2a, Grade B).

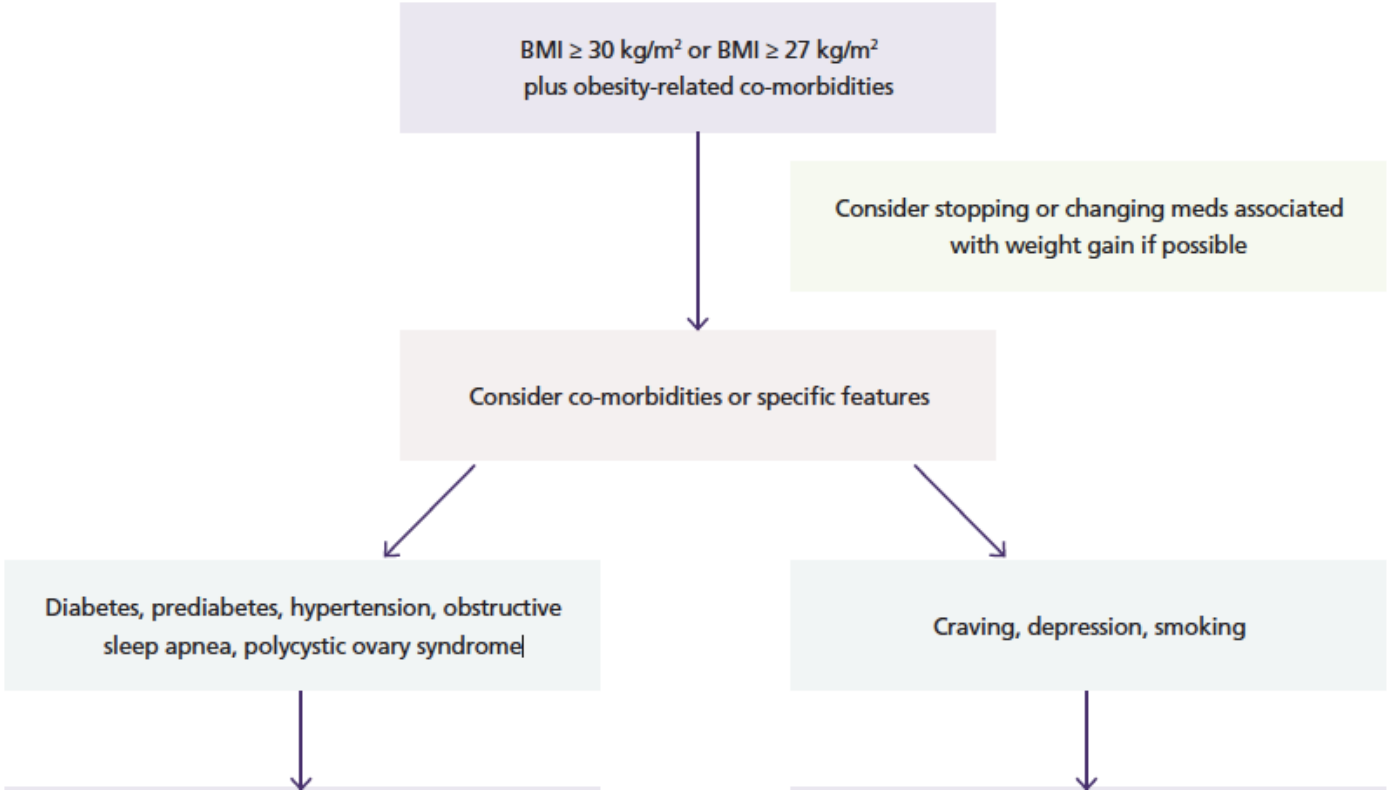
Recommendation 4

We recommend pharmacotherapy in conjunction with health behaviour changes for people living with prediabetes and overweight or obesity (BMI > 27kg/m^2) to delay or prevent type 2 diabetes. (Liraglutide 3.0 mg (Level 2a, Grade B); orlistat (Level 2a, Grade B).

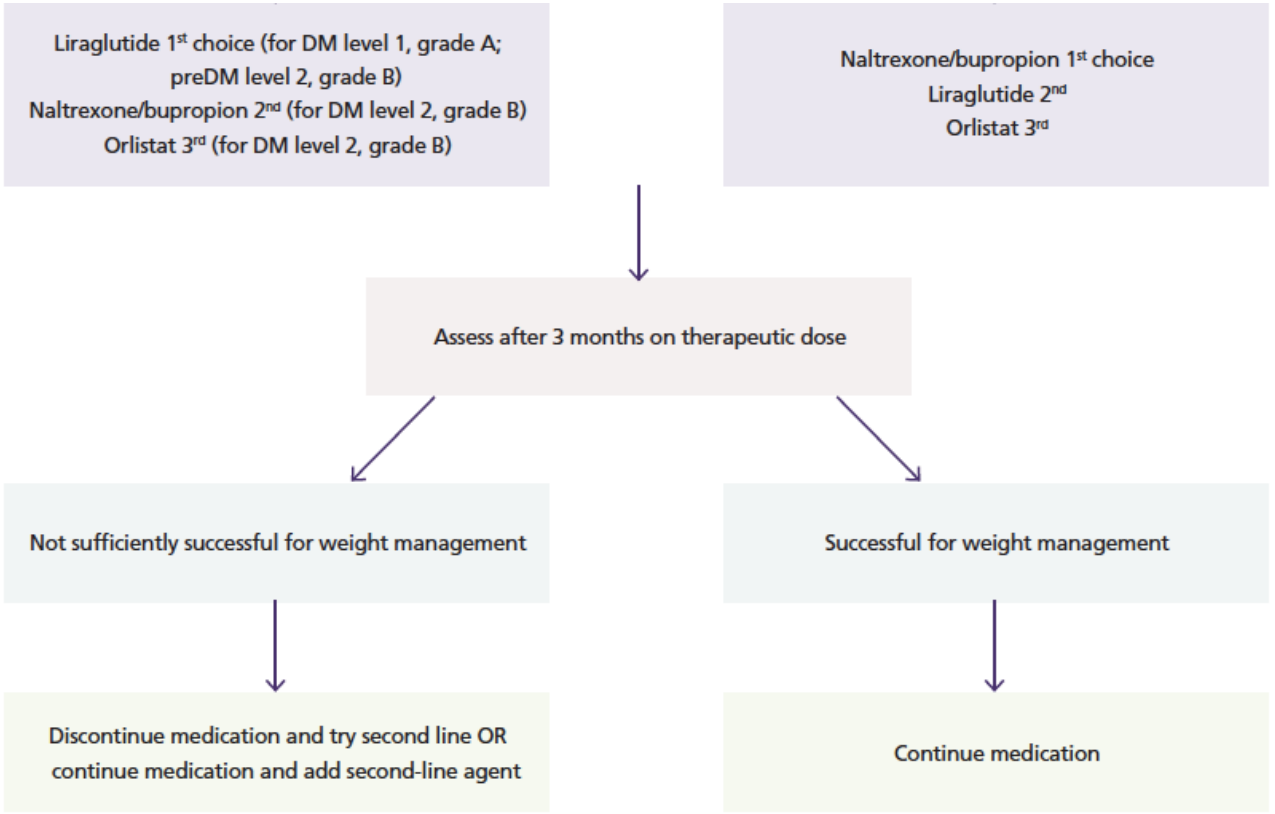
Recommendation 5

We do not suggest the use of prescription or over-the-counter (OTC) medications other than those approved for weight management (Level 4, Grade D, Consensus).

Algorithm: Choice of Obesity Pharmacotherapy



Algorithm: Choice of Obesity Pharmacotherapy



Pharmacotherapy for obesity

	Orlistat	Liraglutide	Naltrexone/bupropion
Mode of administration	Oral	Subcutaneous	Oral
Dose/frequency	120 mg TID	3.0 mg daily	16/180 mg BID
Effect on % weight loss at 1 year, placebo subtracted	-2.9%	-5.4%	-4.8%
Effect on weight over longer term, placebo subtracted	-2.8kg at 4 years	-4.2% at 3 years	Not studied
% of patients achieving ≥ 5% weight loss at 1 year	54% (vs 33% in placebo)	63.2% (vs 27.1% in placebo)	48% (vs 16% in placebo)
% of patients achieving ≥ 10% weight loss at 1 year	26% (vs 14% in placebo)	33.1% (vs 10.6% in placebo)	25% (vs 7% in placebo)
Common side effects	Loose, oily stools, flatus	Nausea, constipation, diarrhea, vomiting	Nausea, constipation, headache, dry mouth, dizziness, diarrhea
Rare side effects	• Liver failure • Nephrolithiasis • Acute kidney injury	Pancreatitis Cholelithiasis	• Seizure • Worsening of depression
Drug interactions	• Fat-soluble vitamins • Levothyroxine • Cyclosporine • Oral anticoagulants anticonvulsants16	May affect absorption of medications due to slowing of gastric emptying	• Medications metabolized through CYP2D6 enzymes • Dose adjustment when used with CYP2B6 inhibitors • Avoid if using CYP2B6 inducers • Possible CNS toxicity if used with other dopaminergic drugs

When should we stop pharmacotherapy?

- Pharmacotherapy is intended to be part of a long-term treatment strategy
- If ≥5% weight loss not achieved after 3 months on full/maximum tolerated dose:
  - What was the patient's previous weight trajectory?
  - What factors could be impeding weight loss efforts?
  - Consider trying a different medication if no other evident etiologies of lack of success are apparent

Why do people with DM2 have more difficulty losing weight?

- Medications **that can cause weight gain** including insulin, sulfonylureas, meglitinides, and thiazolidinediones.
- Cessation of glycosuria as DM2 is brought under control (no more “calories lost” in the urine).
- Compensatory overeating to avoid hypoglycemia
- Stress, unhealthy relationship with food
- Complications of diabetes impairing physical activity
- Insulin resistance mechanisms

Optimization of diabetes medical therapy

- For people with type 2 diabetes, the 2020 Diabetes Canada Guidelines recommend consideration of GLP-1 receptor agonists or SGLT2 inhibitors if weight reduction is a priority.
- This is separate to considerations of these medications for cardiovascular, renal, and heart failure benefits.
- Metformin still first-line.
  - Improves insulin resistance
  - Increases GLP-1 levels, alters gut microbiome, affects mitochondria
  - Some individuals secrete greater amounts of intestinal peptide (GDF15) which reduces appetite.

Potential Mechanisms of Weight Loss with SGLT2-inhibitors

- **(not just)** urinary glucose excretion – approximately 300 calories/day
- There is actually increased food intake
- However, increased energy expenditure as well
- Shift from carbohydrate metabolism to fat metabolism
- Significant heterogeneity in response

Brown et al. Obesity Rev. 2019

Semaglutide for weight loss in type 2 diabetes – STEP 2 Trial

Among GLP-1 receptor agonists currently available for the treatment of diabetes, semaglutide 1.0 mg q weekly has shown the greatest weight loss effect in patients with type 2 diabetes.

- Recent trial assessed 2.4 mg q weekly compared to 1.0 mg compared to placebo in double-blind double-dummy trial in obese/overwt with DM2
- At 68 weeks, more patients (2/3) lost > 5% body weight, mean weight loss was 9.6%, 2/3 reached A1c of <6.5%.
- GI side effects were mostly mild-moderate

Davies et al. Lancet. 2021.

Summary

- Obesity is more than counting calories: complex interplay between individual, environmental, and societal factors
- The body adapts during periods of weight loss to protect itself
- Feeding behavior is influenced by peripheral and central signals in the brain
- There is a neural basis for hunger and patients with obesity have neurological differences from those without obesity
- Different options for obesity pharmacotherapy have distinct neural and physiological targets for their actions
- Multiple treatment modalities fit into the framework of a long-term approach to obesity management as a chronic disease

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Thank you!

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