## Ask, Offer, Act

#### A Pharmacist's Guide to Effective Obesity Management in Canada

Presented by: Michael Boivin, Rph, CDE, CBE 2025-1-21



Canadian Association des Pharmacists pharmaciens Association du Canada



- Presenter's Name: Michael Boivin
- I have the following relationships with commercial interests:
  - Advisory Board/Speakers Bureau: Novo-Nordisk, Emergent BioSolutions, Pfizer, Novavax, GSK, Bavarian Nordic, AbbvieFunding
  - Speaker/Consulting Fees: Teva, Pfizer, Novo Nordisk, mdBriefcase, Kenvue, Abbvie, Astra Zeneca, Boehringer Ingelheim, Moderna, Canopy, Valneva, Abbott Diabetes, GSK
  - I have received an honorarium from CPhA for this presentation



## **Learning Objectives**

Upon completion of this learning activity, participants will be better able to:

- Explain the current evidence-based approach to obesity management using the "Ask, Offer, Act" framework
- 2. Apply strategies to optimize insurance coverage for obesity management medications
- 3. Identify appropriate candidates for obesity pharmacotherapy based on clinical factors and comorbidities
- 4. Select evidence-based treatment options based on patient-specific factors and therapeutic goals



### Is obesity a disease? – New Guidance 2025

#### Diseases

- A distinct pathophysiology that can cause alterations of either a single organ or multiple organs (systemic diseases)
- The ability to cause a specific illness, intended as an objective and subjective experience of ill health

#### lliness

 Illness implies a deviation from the normal functioning of organs and tissues or the whole individual, and is typically associated with specific clinical manifestations—physical and biochemical—that can be used as criteria for disease diagnosis



Rubino, Francesco, David E Cummings, Robert H Eckel, Ricardo V Cohen, John P H Wilding, Wendy A Brown, Fatima Cody Stanford, et al. "Definition and Diagnostic Criteria of Clinical Obesity." *The Lancet Diabetes & Endocrinology*, January 2025, S2213858724003164. <u>https://doi.org/10.1016/S2213-8587(24)00316-4</u>.

## From Preclinical to Clinical Obesity

_		<ul> <li>Increased turnover and release of free fatty acids</li> <li>Mitochondrial damage</li> <li>Dysregulation of adipokines (increased proinflammatory or decreased anti-inflammatory)</li> </ul>						
	Caus							
	• Me	Systemic pathophysiolgy						
	• Env	• Low-grade inflammation						
	• Psy	y • Lipotoxicity						
	• Otł	• Increased renin-angiotensin-aldosterone system activity						
		• Ectopic fat						
Г		• Mechanical: physical stress						
	Mecl	Metabolic or endocrine impaired insulin signalling or hyperinsulinaemia						
	• Alte	<ul> <li>Altered androgen production</li> <li>Haemodynamic: increased blood or plasma volume and cardiac workload</li> </ul>						
	• Apr • Endothelial dysfunction							
	• Sat • Hypercoagulabilty							
Γ		Organ pathonysiology						
	Obes	• Signs and symptoms, alterations of daily activities, or both						
	• Exc							
-		Organ dysfunction (clinical obesity)						
		<ul> <li>Signs and symptoms, alterations of daily activities, or both</li> </ul>						
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		· signs and symptoms, attendions of daily activities, of both						

Adipose tissue pathophysiolay

Rubino, Francesco, David E Cummings, Robert H Eckel, Ricardo V Cohen, John P H Wilding, Wendy J Brown, Fatima Cody Stanford, et al. "Definition and Diagnostic Criteria of Clinical Obesity." *The Lancet Diabetes & Endocrinology*, January 2025, S2213858724003164. <u>https://doi.org/10.1016/S2213-8587(24)00316-4</u>.

## **New Proposed Classification**

	Preclinical obesity	Clinical obesity		
Excess adiposity	(BMI) + (Waist circumference, etc)	(BMI) + (Waist circumference, etc)		
Mechanisms and pathophysiology	Alterations of Alterations of organ structure	Alterations of organ function damage		
Clinical manifestations	Minor or absent (substantially preserved organ function)	Signs and Limitations of Complications symptoms daily activities		
Detection and diagnosis	Anthropometrics, medical history, review of organ systems, and further diagnostic assessment as needed			



Clinical Assessment of Obesity



Rubino, Francesco, David E Cummings, Robert H Eckel, Ricardo V Cohen, John P H Wilding, Wendy A Brown, Fatima Cody Stanford, et al. "Definition and Diagnostic Criteria of Clinical Obesity." The Lancet Diabetes & Endocrinology, January 2025, S2213858724003164. https://doi.org/10.1016/S2213-8587(24)00316-4.

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## **Obesity does not get its fair shake**

- Obesity is one of the most prevalent health issues in Canada (based on BMI)
  - 26.8% of Canadians (≥ 18 years) have a BMI in the obesity range
  - 69.4% of males and 56.7% of females in Canada have overweight or obesity
- Obesity significantly impacts the people living with the condition
  - It is estimated that 1 in 10 premature deaths of Canadians aged 20-64 years is attributable to obesity
- Obesity stigmatization has significant effects on the person with obesity
- Increases morbidity and mortality
- Also leads to significant inequities: employment, education and healthcare due to stereotypes (lazy, unmotivated, or lack of selfdiscipline)





## **Obesity impacts almost every organ**



A key learning from today, is we want patients to think beyond the number on the scale. It is the impact of obesity on health and daily function that we want to prevent or address.

#### **Remember: Obesity Care** *≠* **Weight Loss**



limitations of daily living



Musculoskeletal system Chronic, severe knee or hip pain (associated with joint stiffness and reduced range of motion) Lymphatic system

Lower limb lymphoedema (causing chronic pain, reduced range of motion, or both) Ischemic heart disease -8% HF – 3.5% Stroke – 3%



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Rubino, Francesco, David E Cummings, Robert H Eckel, Ricardo V Cohen, John P H Wilding, Wendy A Brown, Fatima Cody Stanford, et al. "Definition and Diagnostic Criteria of Clinical Obesity." The Lancet Diabetes & Endocrinology, January 2025, S2213858724003164. https://doi.org/10.1016/S2213-6587(24)003164. Simon GE et al. Arch Gen Psychiatry 2006;63824–30; Su W et al. J Med Economics 2015;18:886–97; López-Velázquez JA et al. Ann Hepatol 2014;13:166–78; Yildiz BO et al. J Clin Endocrinol Metab. 2008;93:162–68; El-Serag HB et al. Arn J Gastroenterol. 2005;100:1743–50; Prieto-Alhambra D et al. Ann Rev Assoc Med Bras 1992;63:852–8.

# It is Important to Understand the Science of Obesity – Explains the challenge





\*The brain's reward circuitry, especially in the ventral tegmental area and nucleus accumbens. † Especially the dorsolateral pre-frontal cortex. BBB, blood-brain barrier; PYY, peptide YY.

1. Suzuki K et al. Exp Diabetes Res. 2012:824305; 2. Berthoud HR. Curr Opin Neurobiol. 2011;21:888–96; 3. Schwartz A & Doucet É. Obes Rev. 2010;11:531–47.

# The Body Responds to Weight Loss by Increasing Risk of Weight Regain



Weight conservation is an evolutionary protective mechanism to defend against food shortage. It is beyond just "eating less and exercising more" as the brain and CNS respond by adjusting hunger, satiety and energy expenditure.

Morton GJ, et al. *Nature*. 2006;443:289-295; Leibel RL, et al. *N Engl J Med*. 1995;31:621-628; Schwartz A & Doucet É. *Obes Rev*. 2010;11:531–547; Sumithran P et al. *N Engl J Med*. 2011;365:1597–1604; Rosenbaum M et al. *Am J Physiol Regul Integr Comp Physiol*. 2003;285:R183–R192; Rosenbaum M & Leibel R. L. *Int J Obes (Lond)*. 2010 October ; 34(0 1): S47–S55.



## **Obesity Canada Guidelines**

- We have some of the most comprehensive obesity guidelines in the world
  - Background
  - Science
  - Behavioural changes (Medical nutrition therapy/physical activity)
  - Psychological interventions
  - Pharmacotherapy
  - Bariatric surgery
- Let's focus on how to implement into pharmacy practice







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## Meet our Patient – Glen

#### Background

- 42 years old
- Strong family history of obesity and type 2 diabetes
- Dyslipidemia and obstructive sleep apnea

#### Assessment

- BMI = 32 kg/m<sup>2</sup>
- Blood pressure = 145/92 mmHg

#### Medications

Atorvastatin 20 mg daily

#### Discussion

- He mentions that his physician said that he may have some fatty liver disease
- He says his weight is frustrating, he has been eating so much better and not losing weight
- He also says that he finds it embarrassing that he can't keep up with the other fathers when practicing soccer with his son and the team





## Three Simple Actions can Change the Obesity Trajectory





## **Everything Starts with Ask**

- It is about starting patient-focused conversations that encourage engagement
  - "Would you be interested in discussing your weight?"
  - "Would it be alright to discuss your weight?"
  - "Do you have any concerns about your weight?"
- Listen to their response
  - Each person has a different obesity journey
  - You can ask about the impact on their health
  - Some people are **NOT** ready to discuss their weight, that's ok
- Watch the language used
  - Obesity should be viewed as a health condition not a lifestyle issue
  - Avoid terms such as 'obese', 'fat', consider 'person with obesity'
  - Don't minimize the condition or scare them
- Think of obesity like any chronic disease, use the same language







National Institute of Diabetes and Digestive and Kidney Diseases. Talking with Your Patients about Weight. National Institute of Diabetes and Digestive and Kidney Diseases. https://www.niddk.nih.gov/health-information/professionals/clinical-tools-patient-management/weight-management/talking-with-your-patients-about-weight

## **Offer Support and Help**

- If the person is interested:
  - Offer support and evidence-based management
- Remember support, not lecture:
  - Don't provide a lecture on why they need to be treated
  - People with obesity know that their weight can impact their health
- They don't need to feel guilty, they really just need help
  - Remember, most people with obesity have been stigmatized
  - Many don't access standard healthcare due to poor care in the past
  - Not all health conditions are cause by obesity
- Obesity management is hard without significant support
  - We don't make people with hypertension, COPD, asthma, diabetes, or heart failure feel guilty if they need pharmacotherapy to manage their condition
  - Minimizing their obesity, doesn't help the patient and can significantly worsen the relationship with that person





#### Medical Nutrition Therapy Physical Activity

### Act – Managing Obesity by Focusing on the Pillars







## "I just Need to Find the Right Diet"

- Caloric restriction results in short-term reductions in weight (i.e.< 12 months) but not long-term (i.e. > 12 months).
  - Doesn't treat obesity pathology
- Nutrition plans should be:
  - Flexible and person-centric
  - Focusing on health improvements
  - Focusing on food quality, eating patterns and a healthy relationship with food

The key is to eat the best way they can that is sustainable and enjoyable long term.

#### Weight change over 10 years in the Diabetes Prevention Program. (Lifestyle Arm)(n=1079)



Brown, Jennifer, Carol Clarke MHSc, Carlene Johnson Stoklossa, and John Sievenpiper. "Medical Nutrition Therapy in Obesity Management (Updated 2022)," n.d., 28. Bray G.A., Kim K.K., Wilding J.P.H., and null null. "Obesity: A Chronic Relapsing Progressive Disease Process. A Position Statement of the World Obesity Federation." *Obesity Reviews* 18, no. 7 (May 10, 2017): 715–23. https://doi.org/10.1111/obr.12551.



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## **Nutrition Recommendations from the Guidelines**

#### **ADVISE:** Provide/Reinforce Key Nutrition Messages for all Adults

- Meet individual values, preferences and goals that are culturally acceptable, affordable and sustainable
- Use person-first language, patient-centred, weight-inclusive and non-dieting approaches
- Follow Canada' Food Guide for Healthy Eating recommendations (as applicable to the individual)

## Healthy eating is more than the foods you eat.

- Be mindful of your eating habits
- Cook more often
- Enjoy your food
- Eat meals with others
- Use food labels
- Limit foods high in sodium, sugars or saturated fat
- Be aware of food marketing and how it can influence your choices.

## Make it a habit to eat a variety of healthy foods each day.

- Have plenty of vegetables and fruit
- Eat protein foods and choose protein foods that come from plants more often
- Make water your drink of choice
- Choose whole grain foods

## Build a healthy relationship with food and eating

- Take time to eat
- Notice when you are hungry and when you are full
- Plan what you eat
- Involve others in planning and preparing meals.
- Culture and food traditions can be part of healthy eating
- Reconnect to the eating experience by creating awareness of your feelings, thoughts, emotions and behaviours

## Some Nutrition Tips that May Help some Patients

- Smaller plates (e.g. salad plates) if portions are a challenge
- Keep a food diary and consider food tracking app
- Eat slowly to identify satiety cues
- Stop when no longer hungry versus when the plate is finished
- Identify triggers that may be signaling the reward system
- Do not keep calorie-dense snacks and foods in the house
- Prepare meals at home
- Watch calories from beverages

Kushner R, Lawrence V, Kumar S. Chapter 8 - Dietary Intervention. In: Practical Manual of Clinical Obesity. 1 edition. Chichester, West Sussex, UK; Hoboken, NJ, USA: Wiley-Blackwell; 2013.





Lin E, Arussi J. Chapter 4 - Dietary and Lifestyle Strategies for Weight Loss. In: Youdim A, ed. The Clinician's Guide to the Treatment of Obesity. 2015 edition. New York, N.Y.: Springer; 2015:61-75.

### What about exercise, does it work?

- Aerobic physical activity can lead to:
  - Small  $\checkmark$  weight and fat
  - $\psi$  visceral and ectopic fat
  - Favours weight maintenance
  - Improved cardiovascular and mental health
  - Improvement in sleep, energy, self-confidence
- The amount of weight reduction for most patients with physical activity alone is usually relatively small



Consider the context of the patient (e.g. pain, knee OA, sedentary lifestyle) when suggesting a physical activity plan



# Any Weight Reduction with Nutritional and Exercise alone > 5% is an Outlier





### **Psychological Therapy What Does this mean?**

#### **Behavioural therapy:**



- Behavioural 
   →substitution 'instead of going to the pantry, I will....'
- Self-monitoring → journaling
- Stimulus control → E.g. the break room at work
- Goal setting → 'I would like to be able to.....'

#### **Cognitive therapy:**



- Problem solving → E.g. navigating the road home from work past fast food
- Cognitive restructuring 
   recognize
   and change negative thinking; E.g.
   self-bias
- Rather than focusing on having what you want 
   → what you have



## **Obesity Pharmacotherapy**

#### Indication

- Long-term weight management for individuals with a BMI:
  - $\geq$  30 kg/m<sup>2</sup> and no comorbid conditions
  - ≥ 27 kg/m<sup>2</sup> with comorbidities associated with excess adiposity (e.g., type 2 diabetes, hypertension, dyslipidemia, obstructive sleep apnea).

#### **Key Considerations**

- Patient's obesity management goals focusing on health and QoL
- Obesity pharmacotherapy should be considered early as:
  - Health complications increase and progress with time
- Requires long-term treatment as stopping therapy will normally result in weight regain



## **Obesity Medications Approved in Canada**

Agent	Populations Showing Weight Loss Benefits in Clinical Trials*	Average Weight Loss at 1 year	Benefits in adiposity related health parameters	Cost	Provincial Coverage for Obesity Pharmacotherapy
Liraglutide 3mg SC daily	Overweight and Obesity PreDM T2DM MASH OSA	-8.6% vs -2.6% placebo	Remission of preDM A1C MASH parameters Apnea-hypopnea index BP QoL	\$\$\$\$	None
Naltrexone- Bupropion 16/180mg PO bid	Overweight and Obesity T2DM	-6.1% vs -1.3% placebo	A1C Depression scores Cravings QoL	\$\$\$	None
Orlistat 120mg PO tid	Overweight and Obesity PreDM T2DM	-10.2% vs -6.1% placebo	Remission of PreDM A1C	\$\$	None
Semaglutide 2.4mg SC weekly	Overweight and Obesity PreDM T2DM MASH	-14.9% -2.4% placebo	A1C MASH parameters BP Cravings QoL	TBD	None



Crucial to focus on the impact on comorbidities and health parameters than solely the percentage of weight reduction

\*Clinical trials conducted in populations with overweight and obesity, and trials conducted in populations with overweight/obesity and specific comorbidities (preDM, T2DM, MASH, OSA)

Abbreviations: preDM = prediabetes; T2DM = type 2 diabetes mellitus; MASH = metabolic dysfunction associated steatohepatitis; OSA = obstructive sleep apnea; A1C = hemoglobin A1c; BP = blood pressure; QoL = quality of life



### Tailoring Obesity Pharmacotherapy with Some Simple Questions

#### **1.** Does the patient prefer a specific product?

- If yes, take this into consideration when choosing therapy.
- **2.** Is the person  $\geq$  65 years of age?
  - Consider liraglutide 3.0 mg or semaglutide 2.4 mg as these agents have been studied in this age group.

#### 3. Does the patient have any comorbidities?

• There are many options that can be impacted by the patient's comorbidities

#### 4. What is the weight reduction goal?

• The weight reduction with the approved agents (greatest to lowest weight reduction vs. placebo): semaglutide 2.4 mg > liraglutide 3.0 mg > naltrexone/bupropion > orlistat

#### 5. Is there a preferred method or frequency of administration?

- Oral: Orlistat, naltrexone/bupropion
- Injectable: Liraglutide 3.0 mg, semaglutide 2.4 mg
- **Frequency**: 3/day orlistat, 2/day naltrexone/bupropion, 1/day liraglutide, 1/week semaglutide

#### 6. Cost and coverage

Can vary for each person with obesity









# Tailoring Obesity Pharmacotherapy based on Comorbidity

Comorbidity	Orlistat	Liraglutide 3.0 mg	Nal/Bu	Semaglutide 2.4 mg
Use in cardiovascular disease or high CV risk				(Preferred)
Depression	<b>S</b>	$\checkmark$	<b>S</b>	$\checkmark$
History of medullary thyroid cancer or pancreatitis				
Metabolic dysfunction-associated steatotic liver disease (MASLD)		$\checkmark$		
Obstructive sleep apnea		<b>S</b>		
Opioid use or history or seizure	<b>S</b>	<b>S</b>		<b>~</b>
Uncontrolled tachycardia or hypertension				
Tobacco use			<b>S</b>	

Pedersen SD, Manjoo P, Wharton S. Canadian Adult Obesity Clinical Practice Guidelines: Pharmacotherapy in Obesity Management (2022 Update). Accessed October 29, 2022.

<u>https://obesitycanada.ca/guidelines/pharmacotherapy</u>. c



### **Effect of Pharmacotherapy on Weight Loss**

	Liraglutide 3.0 mg	Naltrexone/bupropion	Orlistat	Semaglutide 2.4 mg
Effect on % weight loss at 1 year, placebo subtracted	-5.4%	-4.8%	-2.9%	-12.4 %
% of patients achieving ≥ 5% weight loss at 1 year	<b>63.2%</b> (vs. 27.1% in placebo)	<b>48%</b> (vs. 16% in placebo)	<b>54%</b> (vs. 33% in placebo)	<b>86.4%</b> (vs 31.5% with placebo)
% of patients achieving ≥ 10% weight loss at 1 year	<b>26%</b> (vs. 14% in placebo)	<b>25%</b> (vs. 7% in placebo)	<b>33.1%</b> (vs. 10.6% in placebo)	<b>69.1%</b> (vs 12.0% with placebo)
Effect on maintenance of previous weight loss	-6.0% additional placebo-subtracted weight loss at 1 year	Not studied	2.4 kg less weight regain (vs. placebo over 3 years)	<b>50.5%</b> (vs 4.9% with placebo)



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Pedersen SD, Manjoo P, Wharton S. Canadian Adult Obesity Clinical Practice Guidelines: Pharmacotherapy in Obesity Management. Published online August 4, 2020. Accessed August 4, 2020.

https://obesitycanada.ca/quidelines/pharmacotherapy. Wilding JPH, Batterham RL, Calanna S, et al. Once-Weekly Semaglutide in Adults with Overweight or Obesity. N Engl J Med. 2021;384(11):989-1002. doi:10.1056/NEJMoa2032183

## Common Issues: "I have stopped losing weight"

- Assess adherence, administration and other modulators of weight (e.g. stress, sleep, medications)
- Frame the importance of health goals
  - Focus on health and not the numbers on a scale
  - · Has the patient reached their obesity management goals?
- Managing plateauing
  - Focus on the "Best weight"
  - Consider changing pharmacotherapy if patient goals are not met



"The drug stopped working. I'm not losing any more weight. Is there anything stronger?"

**<u>Remember:</u>** Obesity is a chronic progressive disease Always set realistic expectations before and during treatment



## **Common Issue: Length of Therapy**

- Obesity is a chronic disease. Most patients will need to stay on medication to maintain weight loss
  - 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







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## **GLP-1 RA Adverse Effects**

- Patient Education
  - Most GI-related adverse effects are temporary
  - Small meals, stop when full, avoid overeating, avoid high-fat or spicy foods
- Titration
  - Titrate as per product monograph
- Management
  - Includes slowing titration, discontinuing or switching treatment

#### Iffective management of GI side effects





## **GLP-1 RAs Destroy Muscle Mass!**



FFM, fat-free mass; FM, fat mass; SMM, skeletal muscle mass.

Conte, Caterina, Kevin D. Hall, and Samuel Klein. "Is Weight Loss–Induced Muscle Mass Loss Clinically Relevant?" *JAMA* 332, no. 1 (July 2, 2024): 9. https://doi.org/10.1001/jama.2024.6586.



## Pillar 3 – Bariatric Surgery

- Bariatric surgery is considered in a patient with a:
  - BMI ≥ 40 kg/m<sup>2</sup>
  - BMI ≥ 35 kg/m<sup>2</sup> with an obesity-related comorbidity (e.g. diabetes, cardiovascular disease, sleep apnea)
- Bariatric surgery is the most effective weight reduction intervention and is associated with significant improvement in comorbidities and mortality risk
- Access, referrals and wait time to this treatment is an issue in most parts of Canada



Biertho L, Hong D, Gagner M. Canadian Adult Obesity Clinical Practice Guidelines: Bariatric Surgery: Surgical Options and Outcomes.
 Published online August 4, 2020:13. Shiau J, Biertho L. Canadian Adult Obesity Clinical Practice Guideline: Bariatric Surgery:
 Postoperative Management. Published online August 4, 2020:15.



## **Managing Glen**

#### **Clinical Considerations**

- Has multiple health conditions that are related to obesity
- Obesity impacting daily life
- His liver disease could also impact choice

#### **Pharmacist's Course of Action**

- Glen is interested in obesity management
- Pharmacist reviews behaviour change
- Glen is interested in pharmacotherapy
- They review the different treatment options (risks and benefits)

#### Background

- 42 years old
- Strong family history of obesity and type 2 diabetes
- Dyslipidemia and obstructive sleep apnea

#### Assessment

- BMI = 32 kg/m<sup>2</sup>
- Blood pressure = 145/92 mmHg
- Medications
  - Atorvastatin 20 mg daily

#### Discussion

- He mentions that his physician said that he may have some fatty liver disease
- He says his weight is frustrating, he has been eating so much better and not losing weight
- He also says that he finds it embarrassing that he can't keep up with the other fathers when practicing soccer with his son and the team





# Glen is prescribed a GLP-1 RA, but it was rejected by his insurer

- Can you talk about how insurance companies determine coverage of these products for this type of patient?
- Can you review the duration of therapy discussion and prior authorization for medications like this?
- What do you recommend pharmacists do if the claim is rejected?





## **Obesity and Comorbidities**

## **Meet our Patient – Preet**

- Background
  - 57 years old
  - Myocardial infarction

#### Assessment

- BMI = 28 kg/m<sup>2</sup>
- Blood pressure = 128/72 mmHg
- LDL-C = 1.7 mmol/L

#### Medications

- Rosuvastatin 20 mg daily
- Telmisartan 80 mg daily
- Indapamide 2.5 mg daily
- Bisoprolol 5 mg daily
- ASA 81 mg daily
- Discussion
  - She is in to pick up refills
  - She has lost a tremendous amount of weight since her MI.
    - Eating better and exercising multiple times per week





### **Obesity management can impact comorbidities**



38 CV, cardiovascular; GERD, gastro-esophageal reflux disease; HFpEF, heart failure with preserved ejection fraction; MASLD, metabolic dysfunction-associated steatotic liver disease; MASH, Metabolic dysfunction-associated steatohepatitis; OA, osteoarthritis; OSA, obstructive sleep apnea; PCOS, polycystic ovary syndrome; T2D, type 2 diabetes Garvey WT et al. Endocr Pract, 2016;22(Suppl. 3):1–203; Look AHEAD Research Group. Lancet Diabetes Endocrinol, 2016;4:913–21; Lean ME et al. Lancet, 2018;391:541–51; Benraoune F and Litwin SE. Curr Opin Cardiol, 2011;26:555–61; Sundström J et al. Circulation, 2017;135:1577–85.



### **Obesity Management and Pharmacotherapy is Changing Disease Course**



## LOTS of new data showing a change in disease course for:

- Underlying cardiovascular disease
- Heart failure with preserved ejection fraction (HFpEF)
- Prediabetes
- Chronic Kidney Disease (CKD)
- Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD)



## Main inclusion / exclusion criteria of SELECT



\*>60 days prior to the day of screening.

†Symptomatic PAD evidenced by intermittent claudication with ankle-brachial index less than 0.85 (at rest), or peripheral arterial revascularisation procedure, or amputation due to atherosclerotic disease. ‡Gestational diabetes was allowed.

BMI, body mass index; HbA1c, glycated haemoglobin; MI, myocardial infarction; NYHA, New York Heart Association; PAD, peripheral artery disease; SELECT, semaglutide effects on cardiovascular outcomes in people with overweight or obesity.

1. Ryan DH et al. Am Heart J 2020;229:61–9; 2. Lingvay I et al. Obesity (Silver Spring) 2023;31:111–22.

## Semaglutide Significantly Reduced MACE Risk



Lincoff, A. Michael, Kirstine Brown-Frandsen, Helen M. Colhoun, John Deanfield, Scott S. Emerson, Sille Esbjerg, Søren Hardt-Lindberg, et al. "Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes Cahlenge Association des Journal of Medicine, November 11, 2023, NEJMoa2307563. https://doi.org/10.1056/NEJMoa2307563.

## Semaglutide for HFpEF in Obesity (STEP HFpEF)



6MWD, 6 minute walking distance; BMI, body mass index; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; hsCRP, high sensitivity, c-reactive protein; KCCQ, Kansas City Cardiomyopathy Questionnaire; NN, Novo Nordisk; NT-proBNP, NT-proB-type natriuretic peptide; NYHA, New York Heart Association; SOC, standard of care; T2D, type 2 diabetes.





# Semaglutide Reduced HF Symptom Burden and Weight



#### \* KCCQ-CSS quantifies HF symptoms, physical function, quality of life and social function

Kosiborod, Mikhail N., Steen Z. Abildstrøm, Barry A. Borlaug, Javed Butler, Søren Rasmussen, Melanie Davies, G. Kees Hovingh, et al. "Semaglutide in Patients with Heart Failure with Preserved Ejection Fraction and Obesity." *New England Journal of Medicine*, August 25, 2023, NEJMoa2306963. <u>https://doi.org/10.1056/NEJMoa2306963</u>.

![](_page_42_Picture_4.jpeg)

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# Semaglutide lowers the risk of diabetes development

 Semaglutide 2.4 mg weekly in people with obesity and prediabetes

#### Results:

- Significant reduction in body weight
- Significantly more people reaching normoglycemia
- Reduction of the risk of type 2 diabetes

![](_page_43_Figure_6.jpeg)

 McGowan, Barbara M, Jens M Bruun, Matt Capehorn, Sue D Pedersen, Kirsi H Pietiläinen, Hanna Angelene Kudiyanur Muniraju, Maria Quiroga, Anette Varbo, and David C W Lau.
 "Efficacy and Safety of Once-Weekly Semaglutide 2·4 Mg versus Placebo in People with Obesity and Prediabetes (STEP 10): A Randomised, Double-Blind, Placebo-Controlled, Multicentre Phase 3 Trial." *The Lancet Diabetes & Endocrinology* 12, no. 9 (September 2024): 631–42. <a href="https://doi.org/10.1016/S2213-8587(24)00182-7">https://doi.org/10.1016/S2213-8587(24)00182-7</a>.

![](_page_43_Picture_8.jpeg)

## Semaglutide in People with CKD without Type 2 Diabetes

- Semaglutide 2.4 mg weekly in people with CKD with obesity (no diabetes)
- Results:
  - Significant reduction in the amount of albumin spilling in the urine
  - More research is required to determine the role in improving outcomes in people with CKD

![](_page_44_Figure_5.jpeg)

![](_page_44_Picture_7.jpeg)

# Semaglutide and metabolic dysfunction-associated steatohepatitis (MASH)

- Press release on the potential benefit of semaglutide in MASLD
- Could change the course of this highly prevalent condition
- You will be hearing more about this highly relevant condition

#### Press release

2:45 PM November 19 2024

## ESSENCE Phase 3 trial results demonstrating statistically significant and superior improvements with semaglutide 2.4 mg in people with MASH presented at AASLD 2024 - The Liver Meeting®

- The trial achieved both its primary endpoints, with semaglutide 2.4 mg demonstrating statistically significant and superior improvements in liver fibrosis with no worsening of steatohepatitis, as well as resolution of steatohepatitis with no worsening of liver fibrosis in people with MASH compared to placebo.<sup>1</sup>
- Supportive secondary endpoints showed improvements in liver enzymes, including alanine transaminase (ALT), aspartate transaminase (AST), and gamma-glutamyl transferase (GGT), as well as the Enhanced Liver Fibrosis (ELF)<sup>TM</sup> test.<sup>1</sup>
- One in 20 adults in the US are living with metabolic dysfunction-associated steatohepatitis (MASH)<sup>2</sup>, with MASH progressing to cirrhosis in 20% of all cases.<sup>3</sup>

https://www.novonordisk-us.com/media/newsarchive/news-details.html?id=171986

![](_page_45_Picture_11.jpeg)

### **Tirzepatide for Obesity in Canada- Not yet available**

![](_page_46_Figure_1.jpeg)

#### Tirzepatide in people with obesity and prediabetes

- Jastreboff, Ania M., Carel W. le Roux, Adam Stefanski, Louis J. Aronne, Bruno Halpern, Sean Wharton, John P. H. Wilding, et al. "Tirzepatide for Obesity Treatment and Diabetes Prevention." New England Journal of Medicine 0, no. 0. Accessed November 14, 2024. https://doi.org/10.1056/NEJMoa2410819

![](_page_46_Picture_5.jpeg)

47 Packer, Milton, Michael R. Zile, Christopher M. Kramer, Seth J. Baum, Sheldon E. Litwin, Venu Menon, Junbo Ge, et al. "Tirzepatide for Heart Failure with Preserved Ejection Fraction and Obesity." New England Journal of Medicine, November 16. 2024. NEJMoa2410027. https://doi.org/10.1056/NEJMoa2410027

#### **Clinical Considerations**

**Managing Preet** 

- She had a previous MI and is overweight
- The use of semaglutide 2.4 mg significantly lowers her risk of 3 point MACE

#### **Pharmacist's Course of Action**

- Discuss how a treatment can lower her risk of a stroke, another MI or cardiovascular death
- She is interested in any therapy that can reduce her risk of another heart attack and would like the pharmacist to discuss this with her primary care provider

#### Background

- 57 years old
- Myocardial infarction

#### Assessment

- BMI = 28 kg/m<sup>2</sup>
- Blood pressure = 128/72 mmHg
- LDL-C = 1.7 mmol/L

#### Medications

- Rosuvastatin 20 mg daily
- Telmisartan 80 mg daily
- Indapamide 2.5 mg daily
- Bisoprolol 5 mg daily
- ASA 81 mg daily
- Discussion
  - She is in to pick up refills
  - She has lost a tremendous amount of weight since her MI.
    - Eating better and exercising multiple times per week

![](_page_47_Picture_25.jpeg)

![](_page_47_Picture_27.jpeg)

### Preet's Semaglutide was denied by her Insurer

- This patient was rejected for obesity management as her BMI was too low. Any suggestions on how to address?
- Will the new outcome data shown impact the coverage of these agents for patients?
- Any other suggestions or tips that you can provide pharmacists regarding coverage access of these medications?

![](_page_48_Picture_4.jpeg)

![](_page_48_Picture_5.jpeg)

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https://obesitycanada.ca/guidelines/pharmacotherapy

![](_page_49_Picture_29.jpeg)

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![](_page_50_Picture_23.jpeg)

## Thank you

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![](_page_52_Picture_0.jpeg)

Canadian Association des Pharmacists pharmaciens Association du Canada