Guideline

Pharmacotherapy for obesity management in adults: 2025 clinical practice guideline update

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Abstract

Background: Pharmacotherapy is a key component of comprehensive obesity management, alongside behavioural therapy and metabolic and bariatric surgery. In this guideline, we update the pharmacotherapy recommendations in the 2020 Canadian clinical practice guideline on obesity in adults and in the 2022 pharmacotherapy for obesity management revision to provide current recommendations for clinicians on the efficacy, safety, and appropriate use of pharmacotherapy in the management of obesity in adults.

Methods: This guideline update follows the same methodology as the 2020 Canadian guideline on obesity in adults, adhering to the Appraisal of Guidelines for Research and Evaluation instrument and using the Shekelle framework to assess and grade evidence and to formulate recommendations. Building on the search conducted for the 2022 pharmacotherapy revision, we conducted a systematic literature review (search dates January 2022 to July 2024), supplemented by relevant trials published through May 2025, to identify studies assessing the efficacy of pharmacotherapy for weight management. We also conducted 13 targeted searches on the management of weight-related complications in 13 subpopulations with important adiposity-related health issues. We engaged primary care physicians, obesity medicine specialists, and people with lived experience of obesity to provide feedback on the recommendations.

Recommendations: This update includes 6 new and 7 revised recommendations since the 2022 pharmacotherapy guideline revision (all 2020 pharmacotherapy recommendations are updated). Measures of central adiposity, in addition to ethnicity-specific body mass index and adiposity-related complications, should be used to guide the decision to initiate pharmacotherapy. Obesity pharmacotherapy should be used in conjunction with health behaviour changes and individualized based on a person's specific health needs and in keeping with their values and preferences. Recommendations support long-term use of obesity pharmacotherapy for sustained weight loss and maintenance of weight loss. We provide recommendations for use of specific obesity pharmacotherapies with proven benefit in specific subpopulations — atherosclerotic cardiovascular disease, heart failure with preserved ejection fraction, metabolic dysfunction–associated steatohepatitis, prediabetes, type 2 diabetes, obstructive sleep apnea, osteoarthritis — and for those with certain specific monogenic causes of obesity. We recommend against the use of compounded medications or medications other than those approved for weight loss in people with excess adiposity.

Interpretation: Pharmacotherapy in obesity facilitates clinically meaningful weight loss and important improvements in obesity-related health complications. Clinicians who treat people with obesity with or without obesity-related health complications should appropriately use pharmacotherapy as an integral part of their treatment paradigm.

Sustained weight loss in people with obesity is associated with improvements in health.[1–3] Health behaviour changes alone generally achieve only a modest (3%–5%) weight loss, which is usually not sustained over the long term and may not be sufficient to improve most adiposity-related complications.[4–6] Along with psychological support and metabolic and bariatric surgery, and supported by medical nutritional therapy and physical activity, pharmacotherapy is one of the mainstays of obesity treatment. These treatment options should be used as appropriate for each person to decrease weight and optimize health.[7]

In this guideline, we update the pharmacotherapy recommendations in the 2020 Canadian clinical practice guideline on obesity in adults[7,8] and the 2022 pharmacotherapy for obesity management revision,[9] reviewing the literature pertaining to the efficacy and safety of obesity medications currently approved by Health Canada. Since the last update, 2 new obesity medications, tirzepatide[10] and setmelanotide,[11] have been approved in Canada. Important advancements have also occurred in the field of incretin-based therapies such as glucagon-like peptide 1 (GLP-1) receptor agonists and dual glucose-dependent insulinotropic

polypeptide (GIP)–GLP-1 receptor agonist therapy.[12] Emerging evidence suggests that obesity pharmacotherapies offer additional benefits for certain obesity-related conditions.

In this 2025 update, we build upon the principles established in the 2020 Canadian adult obesity guideline,[8] including a strong emphasis on patient-centred care, shared decision-making, and the recognition and reduction of weight stigma and bias in clinical practice. Recommendations for pharmacotherapy in the management of obesity should always emphasize that patients undergo a comprehensive assessment and that factors contributing to the obesity be addressed where possible. Obesity medications are recommended in conjunction with health behaviour changes, including medical nutrition therapy and physical activity.

All pharmacotherapy recommendations in this update are either updated or new. The recommendations incorporate and reflect advances in the evidence base to support an individualized, evidence-based approach that aligns with patient goals, coexisting obesity-related health conditions, and shared decision-making.

Scope

In this guideline, we inform on the use of pharmacotherapy for management of obesity and weight-related health complications in adults aged 18 years and older. The guideline is primarily intended for primary care clinicians but is relevant for all clinicians who care for adults with obesity with or without weight-related health complications. It may also be used by educators, policymakers, insurers, people living with obesity, and their families.

For patients younger than 18 years, see Obesity Canada's 2025 clinical practice guideline for managing obesity in children.[13]

Recommendations

We developed 13 recommendations (Table 1)[14–47] to guide clinicians on the selection, initiation, and long-term use of obesity pharmacotherapy. Table 2 defines the levels of evidence[48] and grades of recommendations. We provide a summary of the evidence supporting the recommendations below.

Obesity pharmacotherapy, combined with health behaviour changes, should be individualized, with treatment goals informed by the patient's values, preferences, and adiposity-related health complications, in addition to weight loss. Patients may have more than 1 obesity-related health condition for which evidence would support use of different medications for each health condition. In the absence of definitive evidence, we support shared decision-making informed by clinical priorities and patient preference.

In this guideline, we make evidence-based recommendations for medications that are approved for weight management in Canada, even if the medication is not approved for the specific recommendation.

Appendix 1 and Appendix 2 (available at www.cmaj.ca/lookup/doi/10.1503/cmaj.250502/tab-related-content) summarize the effect of each obesity pharmacotherapeutic agent on weight, obesity-related health parameters, standard titration schedules, and common and rare adverse effects. Appendix 3 (available at www.cmaj.ca/lookup/doi/10.1503/cmaj.250502/tab-related-content) provides additional context for several recommendations (subpopulations with heart failure with preserved ejection fraction [HFpEF], metabolic dysfunction–associated steatohepatitis (MASH), obstructive sleep apnea [OSA], and osteoarthritis, and for those with rare genetic monogenic causes of obesity).

We have developed key messages for health care professionals (Appendix 4, available at www.cmaj.ca/lookup/doi/10.1503/cmaj.250502/tab-related-content), key messages for people living with obesity (Box 1), and a clinical decision tool (Appendix 5, available at www.cmaj.ca/lookup/doi/10.1503/cmaj.250502/tab-related-content) and decision table (Appendix 6, available at www.cmaj.ca/lookup/doi/10.1503/cmaj.250502/tab-related-content) to be used together. The full pharmacotherapy guideline update is available on the Obesity Canada website.[7] A visual summary of the guideline is shown in Figure 1.

Assessment

Body mass index (BMI) does not provide information on body composition or fat distribution. The anthropometric measures noted in recommendation 1 (Table 1) correlate strongly with adiposity-related complications and vary by sex and ethnicity.[14–16,49–51] Applying this recommendation to the other recommendations that use BMI in this guideline ensures that people who do not meet ethnicity-specific BMI criteria for obesity, but do meet other sex- and ethnicity-specific anthropometric criteria, are appropriately considered for treatment. Additionally, a patient-centred approach to weight management, which takes obesity-related complications into account, embraces the diverse ways in which excess adiposity can affect health and shifts the focus from weight alone to the management of obesity-related health conditions and overall health.

Initiating pharmacotherapy

The patient and health care professional should work together to identify clear goals of therapy before initiating obesity pharmacotherapy, including a discussion about reasonable expectations of treatment, and potential benefits versus risks of pharmacotherapy (Table 1, recommendation 2). Treatment targets should be determined by the patient's values and preferences as they relate to the patient's health and well-being. The treatment plan should acknowledge the cultural heterogeneity in what is considered acceptable or desirable in terms of body size and shape.[52] In addition to weight loss, treatment targets may include reduction in cardiometabolic risk; improvement, remission, or resolution of adiposity-related complications; maintenance of weight loss; management of appetite or cravings; and improvement in quality of life. The mechanism of action, efficacy, potential adverse effects, tolerability, and contraindications of each agent must be considered in the context of each patient's obesity-related complications and pre-existing medications (Appendix 1 and Appendix 2).

Pharmacotherapy options

Pharmacotherapy for obesity provides clinically meaningful weight loss (Table 1, recommendation 3). In a randomized controlled trial (RCT) of 1961 people with BMI ≥ 30, or BMI ≥ 27 and at

Table 1 (part 1 of 2): Recommendations on pharmacotherapy for the management of obesity in adults

No.	Recommendation	Category of evidence; strength of recommendation
1.	We recommend the use of measures of central adiposity (using sex- and ethnicity-specific cut-offs if applicable), such as waist circumference, waist-to-hip ratio, or waist-to-height ratio, in addition to ethnicity-specific BMI thresholds or adiposity-related complications, to guide the decision to initiate pharmacotherapy.[14–17]	Level 3; grade C
2.	We suggest that the initiation of obesity pharmacotherapy, in conjunction with health behaviour changes, for adults with excess adiposity be personalized to meet individual values, preferences, and treatment goals to support an approach that is safe, effective, culturally acceptable, and affordable for long-term adherence.	Level 4; grade D consensus
3.	Pharmacotherapy for obesity management, in conjunction with health behaviour changes, should be offered to people with BMI ≥ 30,* or BMI ≥ 27* with adiposity-related complications: • Semaglutide 2.4 mg weekly (BMI ≥ 27*) (level 1a; grade A)[18] • Tirzepatide 5 mg, 10 mg, or 15 mg weekly (BMI ≥ 27*) (level 1a; grade A)[19] • Liraglutide 3 mg daily (BMI ≥ 27*) (level 2a; grade B)[20] • Naltrexone–bupropion 16 mg/180 mg twice daily (BMI 27–45*) (level 2a; grade B)[21] • Orlistat 120 mg 3 times daily (BMI 28–47*) (level 2a; grade B)[22] *See recommendation 1.	See recommendation

4.	Pharmacotherapy for obesity management, in conjunction with health behaviour changes, should be used long term, when effective, to:
	• Avoid weight regain and regression of health benefits achieved with pharmacotherapy:
	  • Semaglutide 2.4 mg weekly (level 1a; grade A)[23]
	  • Tirzepatide 10 mg or 15 mg weekly (level 1a; grade A)[24]
	  • Orlistat 120 mg 3 times daily (level 2a; grade B)[22]
	• Maintain weight loss and prevent weight regain following health behaviour changes alone:
	  • Liraglutide 3 mg daily (level 2a; grade B)[25]
	  • Orlistat 120 mg 3 times daily (level 2a; grade B)[26]
	  • Tirzepatide 10 mg or 15 mg (level 2a; grade B)[27]
		See recommendation

5.	Pharmacotherapy should be offered, in conjunction with health behaviour changes, to reduce the occurrence of major adverse cardiovascular events in people with established ASCVD and BMI ≥ 27,* in addition to standard of care for ASCVD: • Semaglutide 2.4 mg weekly[28] *See recommendation 1.	Level 2a; grade B

6.	Pharmacotherapy should be offered, in conjunction with health behaviour changes, to people living with heart failure with preserved ejection fraction and BMI ≥ 30,* in addition to standard of care, for weight loss and:
	• A composite of reduction in cardiovascular death or a worsening heart failure event:
	  • Tirzepatide 15 mg weekly[29]
	• Improvement in heart failure symptoms:
	  • Semaglutide 2.4 mg weekly[30]
	  • Tirzepatide 15 mg weekly[29]
	*See recommendation 1.
		Level 1a; grade A

7.	Obesity pharmacotherapy, in conjunction with health behaviour changes, for people living with prediabetes should be offered for weight loss and to:
	• Reduce the risk of progression to type 2 diabetes:
	  • Liraglutide 3 mg daily (BMI ≥ 27*) (level 2a; grade B)[31]
	  • Orlistat 120 mg 3 times daily (BMI ≥ 30*) (level 2a; grade B)[32]
	  • Tirzepatide 5 mg, 10 mg, or 15 mg weekly (BMI ≥ 27*) (level 2a; grade B)[33]
	• Achieve normoglycemia:
	  • Semaglutide 2.4 mg weekly (BMI ≥ 30*) (level 1a; grade A)[34]
	*See recommendation 1.
		See recommendation

Table 1 (part 2 of 2): Recommendations on pharmacotherapy for the management of obesity in adults

No.	Recommendation	Category of evidence; strength of recommendation
8.	Obesity pharmacotherapy should be offered, in conjunction with health behaviour changes, to people living with type 2 diabetes for weight loss and improvement in glycemic control: • Semaglutide 2.4 mg weekly (BMI ≥ 27*) (level 1a; grade A)[35] • Tirzepatide 10 mg or 15 mg weekly (BMI ≥ 27*) (level 1a; grade A)[36] • Liraglutide 3 mg daily (BMI ≥ 27*) (level 2a; grade B)[37] • Naltrexone–bupropion 16 mg/180 mg twice daily (BMI 27–45*) (level 2a; grade B)[38] • Orlistat 120 mg 3 times daily (BMI 27–43*) (level 2a; grade B)[39] *See recommendation 1.	See recommendation

9.	Pharmacotherapy may be offered, in conjunction with health behaviour changes, in treating people living with MASH, for weight loss and:
	• Resolution of MASH without worsening of fibrosis:
	  • Semaglutide 2.4 mg weekly (level 2a; grade B)[40]
	  • Liraglutide 1.8 mg daily (BMI ≥ 25*) (level 3; grade C)[41]
	  • Tirzepatide 5 mg, 10 mg, or 15 mg weekly (BMI 27–50*) (level 3; grade C)[42]
	• Improvement in fibrosis without worsening of MASH:
	  • Semaglutide 2.4 mg weekly (level 2a; grade B)[40]
	  • Tirzepatide 5 mg, 10 mg, or 15 mg weekly (BMI 27–50*) (level 3; grade C)[42]
	*See recommendation 1.
		See recommendation

10.	Pharmacotherapy should be offered, in conjunction with health behaviour changes, for weight loss and improvement in apnea-hypopnea index in people who are living with moderate to severe obstructive sleep apnea and BMI ≥ 30,* and who are:
	• Unwilling or unable to use positive airway pressure therapy:
	  • Tirzepatide 10 mg or 15 mg (level 1a; grade A)[43]
	  • Liraglutide 3 mg daily (level 2a; grade B)[44]
	• Using positive airway pressure therapy:
	  • Tirzepatide 10 mg or 15 mg (level 1a; grade A)[43]
	*See recommendation 1.
		See recommendation

11.	Pharmacotherapy for obesity management should be offered, in conjunction with health behaviour changes, for people living with knee osteoarthritis and BMI ≥ 30* for weight loss and reduction in knee pain: • Semaglutide 2.4 mg weekly[45] *See recommendation 1.	Level 1a; grade A
12.	Setmelanotide up to 3 mg daily may be offered for weight management for people with BMI ≥ 30* and: • Bardet–Biedl syndrome (level 2a; grade B)[46] • Genetically confirmed biallelic pro-opiomelanocortin, proprotein convertase subtilisin/kexin type 1, or leptin receptor deficiency due to variants interpreted as pathogenic, likely pathogenic, or of uncertain significance (level 3; grade C)[47] *See recommendation 1.	See recommendation
13.	We recommend against the use of compounded medications, prescription medications, or over-the-counter medications other than those approved in Canada for weight loss in people with excess adiposity.	Level 4; grade D consensus

Note: ASCVD = atherosclerotic cardiovascular disease, BMI = body mass index, MASH = metabolic dysfunction–associated steatohepatitis.

least 1 weight-related coexisting condition, without diabetes, semaglutide 2.4 mg weekly with health behaviour modification resulted in a weight change of −14.9% at 68 weeks, compared with −2.4% with placebo (estimated treatment difference −12.4%, 95% confidence interval [CI] −13.4 to −11.5).[18] The most common adverse effects with semaglutide were transient, mild to moderate nausea, vomiting, and diarrhea, leading to treatment discontinuation in 4.5% of participants versus 0.8% with placebo. Rare adverse effects included gallbladder-related issues (mostly gallstones) in 2.6% of the semaglutide group versus 1.2% with placebo, with pancreatitis reported in 0.2% with semaglutide versus 0% with placebo.[18]

Table 2: Classification of evidence and recommendations*

Levels of evidence	
1A	Evidence from at least 1 meta-analysis of RCTs or individual RCT
2A	Evidence from at least 1 controlled study without randomization
2B	Evidence from at least 1 other type of quasi-experimental study
3	Evidence from nonexperimental descriptive studies, such as comparative studies, correlation studies, and case–control studies
4	Evidence from expert committee reports or opinions or clinical experience of respected authorities, or both
Grades of recommendations	
A	Directly based on level I evidence
B	Directly based on level II evidence or extrapolated from level I evidence
C	Directly based on level III evidence or extrapolated from level I or II evidence
D	Directly based on level IV evidence or extrapolated from level I, II, or III evidence

RCT = randomized controlled trial.
*Note: Levels of evidence and grades of recommendations adapted with permission from BMJ Publishing Group Limited. Shekelle PG, Woolf SH, Eccles M, et al. Developing guidelines. *BMJ* 1999;318:593-6.[48] Large multinational RCTs are now directly classified as level 1a evidence, reflecting their high methodological quality and broad applicability. This change explains the lack of a row for level 1B evidence in this table. For a detailed description of the full methodology and the process of downgrading studies to lower levels of evidence, please refer to the 2020 Canadian adult obesity clinical practice guideline.[8]

Box 1: Key messages for people living with obesity

- Medications are safe and effective for managing weight and weight-related health issues, often in combination with health behaviour changes and psychological interventions.
- The goals in obesity management should include improving health, and should include outcomes that are important to you.
- When choosing a weight-management medication with your health care professional, consider potential benefit to your obesity-related health conditions, effect on weight, potential adverse effects, form (injection v. pill), dosing frequency, interaction with other medications, and cost.
- Health Canada has approved 6 medications for long-term obesity management: liraglutide (Saxenda), naltrexone–bupropion (Contrave), orlistat (Xenical), semaglutide (Wegovy), tirzepatide (Zepbound), and setmelanotide (Imcivree). These medications can help you to achieve and maintain improvements in weight and health complications associated with excess weight. These medications have been proven to be effective for obesity management in clinical trials.
- The dose of weight-management medication should be tailored to you, depending on the goals of treatment, as needed and as tolerated. You may achieve your treatment goals with a dose that is lower than the maximum dose for that medication.
- Weight-management medications are intended as part of a long-term treatment strategy. Stopping medication can lead to weight regain and a loss of the health benefits you've experienced.
- Compounded medications and medications that are not approved for obesity treatment may not be safe or effective for obesity management and should be avoided.

In an RCT of 2539 adults with BMI ≥ 30, or BMI ≥ 27 with at least 1 weight-related complication, but without diabetes, participants were randomly assigned to receive tirzepatide 5 mg, 10 mg, 15 mg, or placebo weekly for 72 weeks, in addition to health behaviour changes. At 72 weeks, the mean weight change with 5 mg, 10 mg, and 15 mg was –15.0%, –19.5%, and –20.9%, respectively, compared with –3.1% with placebo (estimated treatment difference compared with placebo –11.9%, 95% CI –13.4 to –10.45 for 5 mg weekly; –16.4%, 95% CI –17.9 to –14.8 for 10 mg weekly; and –17.8%, 95% CI –19.3 to –16.3 for 15 mg weekly).[19] The most common adverse effects of tirzepatide were mild to moderate gastrointestinal symptoms (nausea, diarrhea, constipation) during dose escalation, with discontinuation rates of 4.3%, 7.1%, and 6.2% for the 5 mg, 10 mg, and 15 mg doses, respectively, and 2.6% in the placebo group. Rare adverse effects with tirzepatide included cholecystitis, which was reported slightly more frequently (0.6%) than with placebo (0%).[19]

In an RCT of 3731 people with BMI ≥ 30, or BMI ≥ 27 with untreated dyslipidemia or hypertension, but without diabetes, liraglutide 3 mg daily with health behaviour modification resulted in weight change of –8.0% versus –2.6% with placebo at 56 weeks (estimated treatment difference –5.4%, 95% CI –5.8 to –5.0).[20] The most common adverse effects with liraglutide were mild to moderate nausea, diarrhea, and constipation, with discontinuation rates from adverse events of 9.9% in the liraglutide group versus 3.8% in the placebo group.[20] Rare adverse effects included gallstones, reported in 0.8% of the liraglutide group versus 0.4% with placebo, with pancreatitis reported in 0.4% of the liraglutide group and less than 0.1% with placebo.[20]

In an RCT of 1742 patients with BMI 30–45, or BMI 27–45 with dyslipidemia or hypertension, but without diabetes, naltrexone–bupropion 16 mg/180 mg twice daily with health behaviour changes was associated with weight change of –6.1% (standard error [SE] 0.3) versus –1.3% (SE 0.3) with placebo at 56 weeks (estimated treatment difference –4.8%).[21] The most common adverse effects with naltrexone–bupropion included nausea, headache, constipation, dizziness, vomiting, and dry mouth. Discontinuation because of adverse events was more common in the naltrexone–bupropion group than in the placebo group (20.1% v. 9.6%).[21]

Adult obesity pharmacotherapy

guideline update

SUMMARY This guideline updates the pharmacotherapy recommendations in the 2020 Canadian clinical practice guideline on obesity in adults[1] and in the 2022 pharmacotherapy for obesity management revision,[2] with 6 new and 7 revised recommendations since the 2022 revision.

ASSESSMENT

- ✓ Anthropometrics:
  - BMI (sex- and ethnicity-specific)
  - Waist circumference
  - Waist-to-hip ratio
  - Waist-to-height ratio
- ✓ Adiposity-related complications

INITIATION OF PHARMACOTHERAPY

- ✓ Identify goals of treatment with patient:
  - Improvement, remission, or resolution of adiposity-related complication(s)
  - Weight loss
  - Weight maintenance
  - Improvement in quality of life
- ✓ Consider individual factors:
  - Values and preferences
  - Contraindications
  - Access and affordability
- ✓ Combine with health behaviour changes:
  - Nutritional therapy
  - Physical activity

PHARMACOTHERAPY OPTIONS

- ✓ Choose medication in accordance with treatment goals and obesity-related health issues*
- ✓ Consider rare monogenic causes of obesity
- ✓ Prescribe medications approved by Health Canada for weight management

*See guideline and appendices for specific pharmacotherapy recommendations and decision-making resources (www.cmaj.ca/lookup/doi/10.1503/cmaj.250502)

1. Wharton S, Lau DCW, Vallis M, et al. Obesity in adults: a clinical practice guideline. *CMAJ* 2020;192:E875-91.
2. Pedersen SD, Manjoo P, Wharton S. Canadian adult obesity clinical practice guidelines: pharmacotherapy for obesity management. Edmonton: Obesity Canada; 2022. Available: https://obesitycanada.ca/wp-content/uploads/2025/03/11-Canadian-Adult-Obesity-CPG-Pharmacotherapy-CPG-2022.pdf

Figure 1: Summary of the guideline recommendations. See Related Content tab for accessible version. Note: BMI = body mass index.

A meta-analysis of 16 RCTs of orlistat 120 mg 3 times daily (n = 10 631 participants) reported a mean placebo-subtracted weight change of –2.9% (95% CI –3.4% to –2.5%) at 1 year.[53] The most common adverse effects with orlistat included oily stool, fecal urgency, and spotting, occurring in 15%–30% of patients and leading to discontinuation in some cases.[53]

Further details on efficacy, potential adverse effects, contraindications, and potential medication interactions are available in Appendix 1, and are reviewed in greater detail in the full guideline on the Obesity Canada website.[7]

Long-term treatment

After weight loss with pharmacotherapy

Obesity medications are intended as part of a long-term treatment strategy (Table 1, recommendation 4). Clinical trials of pharmacotherapy for obesity management consistently show regain of weight and loss or regression of health benefits if treatment is stopped, despite continued health behaviour changes.[22–24,33]

A trial of semaglutide was conducted among 803 people with BMI ≥ 30, or BMI ≥ 27 and with at least 1 weight-related complication.[23] After completing a 20-week run-in period with semaglutide 2.4 mg weekly (achieving a mean weight change of –10.6%), participants were randomly assigned to either continue treatment with semaglutide or switch to placebo for an additional 48 weeks. Participants who continued with semaglutide experienced an additional weight change of –7.9%, whereas those who were switched to placebo regained 6.9% of weight (estimated treatment difference –14.8%, 95% CI –16.0 to –13.5).[23]

For tirzepatide, an RCT was conducted that included 670 participants with BMI ≥ 30, or BMI ≥ 27 and at least 1 weight-related complication, and who completed a 36-week lead-in period with tirzepatide (10 mg or 15 mg weekly), achieving a mean weight change of –20.9%.[24] After a subsequent 52-week double-blind period where participants were randomly assigned to either continue tirzepatide or switch to placebo, participants continuing tirzepatide experienced a further weight change of –5.5%, whereas those who switched to placebo regained 14.0% of their weight (estimated treatment difference –19.4%, 95% CI –21.2 to –17.7).[24]

In a 4-year RCT with 3305 participants, mean weight change was –5.8 kg with orlistat 120 mg 3 times daily versus –3.0 kg with placebo (estimated treatment difference –2.7 kg). Mean weight plateaued after 52 weeks, followed by gradual weight regain.[32]

After weight loss with health behaviour changes

Pharmacotherapy for obesity has also been shown to maintain weight loss and prevent weight regain after health behaviour changes alone (Table 1, recommendation 4). In a trial of 422 participants with BMI ≥ 30, or BMI ≥ 27 with obesity-related complications, who achieved –6.0% weight change with a low-calorie diet, liraglutide 3 mg daily and health behaviour counselling resulted in an additional mean weight change of –6.2% at 56 weeks compared with –0.2% in the placebo group (estimated treatment difference –6.1%, 95% CI –7.5 to –4.6).[25]

Orlistat has been shown to be effective in maintaining weight loss after a very low-energy diet for 8 weeks, with less mean weight regain in the orlistat arm than in the placebo group over 3 years (4.6, standard deviation [SD] 8.6, v. 7.0, SD 7.1 kg with placebo; estimated treatment difference 2.4 kg).[26]

Tirzepatide use was evaluated in 579 participants with BMI ≥ 30, or BMI ≥ 27 with at least 1 weight-related complication, who were able to achieve at least 5% weight loss with a 12-week intensive lifestyle intervention.[27] After an average –6.9% change in body weight with the lifestyle intervention, there was a further mean weight change of –18.4% at 72 weeks with tirzepatide at maximum tolerated dose (10 mg or 15 mg weekly), compared with a weight gain of 2.5% with placebo (estimated treatment difference –20.8%, 95% CI –23.2 to –18.5).[27]

We identified no dedicated RCT evaluating naltrexone–bupropion for prevention of weight regain or long-term maintenance in people with obesity.

Atherosclerotic cardiovascular disease

Obesity is strongly associated with cardiovascular risk factors and is a major driver of atherosclerotic cardiovascular disease, which remains a leading cause of morbidity and mortality worldwide.[54–56] Cardiovascular outcomes with semaglutide 2.4 mg weekly were evaluated among 17 604 people aged 45 years or older with pre-existing cardiovascular disease and BMI ≥ 27, and without type 2 diabetes. Over a mean duration of 40 months of follow-up, the risk of a major adverse cardiovascular event (death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke) was reduced by 20% with semaglutide versus placebo (hazard ratio [HR] 0.80, 95% CI 0.72 to 0.90),[28] as reflected in recommendation 5 (Table 1). Based on these results, Health Canada has approved semaglutide 2.4 mg for reduction in risk of nonfatal myocardial infarction in adults with established cardiovascular disease and BMI ≥ 27.[57]

A cardiovascular outcome trial for tirzepatide is currently under way.[58] In a systematic review of 5 trials, use of liraglutide was not associated with excess cardiovascular risk.[59] Interim results of a cardiovascular outcome trial with naltrexone–bupropion versus placebo, terminated early because of compromised integrity, showed no increase in cardiovascular risk, but could not confirm noninferiority.[60] We did not identify a dedicated RCT for cardiovascular outcomes for orlistat.

Heart failure with preserved ejection fraction

Obesity is common in people with HFpEF, with reported prevalence of up to 84%.[61] The relationship between obesity and HFpEF is complex, and is mediated not only by excess adipose tissue, but also by health complications associated with obesity.[62] Weight loss has been shown to improve exercise capacity in people with HFpEF.[63] Certain obesity pharmacotherapies, when combined with health behaviour changes, have been shown to reduce the risk of cardiovascular death or worsening heart failure and improve heart failure symptoms in people with HFpEF (Table 1, recommendation 6). For further details, please refer to Appendix 3.

Prediabetes

Between 14.3% and 36.9% of adults with obesity have prediabetes.[64,65] People with prediabetes are at high risk of developing type 2 diabetes, with about 25% progressing to diabetes over 3–5 years.[66] With the caveat that the definition for prediabetes differed across trials, studies showed benefit for obesity pharmacotherapy to reduce the risk of progression to type 2 diabetes, or to facilitate achievement of normoglycemia in people with obesity and prediabetes (Table 1, recommendation 7).

A trial randomly assigned 2254 patients with prediabetes and BMI ≥ 30, or BMI ≥ 27 with dyslipidemia or hypertension, to receive liraglutide 3 mg daily or placebo in addition to health behaviour changes.[31] The time to onset of type 2 diabetes over 160 weeks was 2.7 (95% CI 1.9 to 3.9) times longer with liraglutide 3 mg than with placebo, and the risk of developing diabetes was reduced by 79% with liraglutide (HR 0.21, 95% CI 0.13 to 0.34).[31]

Orlistat was evaluated in a trial that randomly assigned 3305 patients with BMI ≥ 30 and normal (79%) or impaired (21%) glucose tolerance, to receive orlistat 120 mg 3 times daily or placebo, in addition to health behaviour change.[32] At 208 weeks, progression to diabetes was observed in 6.2% in the orlistat group versus 9.0% in the placebo group.[32]

Tirzepatide was evaluated in an RCT that randomly assigned 1032 adults with prediabetes and BMI ≥ 30, or BMI ≥ 27 with at least 1 obesity-related complication, to receive tirzepatide 5 mg, 10 mg, 15 mg weekly (n = 762), or placebo (n = 270), in addition to health behaviour changes.[33] At 176 weeks, the risk of progression to type 2 diabetes was decreased by 93% with tirzepatide compared with placebo (HR 0.07, 95% CI 0.0 to 0.1).[33]

A trial evaluating semaglutide randomly assigned 207 people with BMI ≥ 30 and prediabetes to receive semaglutide 2.4 mg (n = 138) or placebo (n = 69), in addition to health behaviour changes.[34] At 52 weeks, 81% of participants reverted to normoglycemia with semaglutide versus 14% with placebo (odds ratio 19.8, 95% CI 8.7 to 45.2).[34]

We identified no dedicated RCTs evaluating naltrexone–bupropion for the treatment of prediabetes in people with obesity.

Type 2 diabetes

Obesity in people with type 2 diabetes is associated with poorer glycemic control than in those with diabetes who do not have obesity.[67] Clinical trials of the 5 medications we recommend showed improvement in weight as well as glycemic control in people with type 2 diabetes and obesity (Table 1, recommendation 8).

An RCT of 1210 people with BMI ≥ 27 and type 2 diabetes managed with 0–3 oral agents were randomized to semaglutide 2.4 mg weekly, 1 mg weekly, or placebo, in addition to health behaviour changes.[35] At 68 weeks, weight change was superior with semaglutide 2.4 mg at –9.6% at 68 weeks; –7.0% with 1.0 mg; and –3.4% with placebo (estimated treatment difference –6.2%, 95% CI –7.3 to –5.2 for semaglutide 2.4 mg v. placebo). Change in glycated hemoglobin (HbA_{1c}) was similar with semaglutide 2.4 mg (–1.6%, SE 0.1) and 1 mg (–1.5%, SE 0.1), both superior to placebo (–0.4%, SE 0.1) (estimated treatment difference –1.2% for semaglutide 2.4 mg v. placebo; –1.1% for semaglutide 1 mg v. placebo).

In a trial including 938 adults with type 2 diabetes and BMI ≥ 27, tirzepatide (10 mg or 15 mg weekly) plus health behaviour changes led to a mean change of –12.8% and –14.7%, respectively, at 72 weeks, both significantly greater than in placebo (–3.2%) (estimated treatment difference v. placebo –9.6%, 95% CI –11.1 to –8.1 with tirzepatide 10 mg weekly; and –11.6%, 95% CI –13.0 to –10.1 with tirzepatide 15 mg weekly).[36] The HbA_{1c} change was –2.1% with both tirzepatide doses, compared with –0.5% in placebo (estimated difference v. placebo –1.6%, 95% CI –1.74 to –1.37 with tirzepatide 10 mg weekly; and –1.6%, 95% CI –1.76 to –1.37 with tirzepatide 15 mg weekly).

In an RCT including 846 people with BMI ≥ 27 and type 2 diabetes, liraglutide 3 mg daily resulted in –6.0% weight change over 52 weeks, versus –4.7% with the 1.8 mg dose and –2.0% with placebo (estimated difference v. placebo –4.0%, 95% CI –5.1 to –2.1 with liraglutide 3.0 mg daily; and –2.7%, 95% CI –4.0 to –1.4 with liraglutide 1.8 mg daily).[37] Reductions in HbA_{1c} were –1.3%, –1.1%, and –0.3%, respectively (estimated treatment difference v. placebo –0.9%, 95% CI –1.1 to –0.8 with liraglutide 3.0 mg daily; and –0.7%; 95% CI –0.9 to –0.6 with liraglutide 1.8 mg daily).

Naltrexone–bupropion 16 mg/180 mg twice daily was evaluated, in addition to health behaviour changes, among 505 adults with a BMI of 27–45 and type 2 diabetes managed with oral agents or lifestyle. Mean weight change was –5.0% (SE 0.3%) with naltrexone–bupropion versus –1.8% (SE 0.4%) in the placebo group (estimated treatment difference –3.2%).[38] Change in HbA_{1c} was superior with naltrexone–bupropion (–0.6%) versus placebo (–0.1%) (estimated treatment difference 0.5%).

A meta-analysis comprising 2550 patients with type 2 diabetes and BMI 27–43, randomized to orlistat 120 mg 3 times daily or placebo, found that patients treated with orlistat had significantly greater mean change in HbA_{1c} than with placebo (–0.7% v. –0.3%, respectively; estimated treatment difference –0.4%). Weight change in the orlistat group was –3.8 kg compared with –1.4 kg with placebo (estimated treatment difference –2.4 kg).[39]

Metabolic dysfunction–associated steatohepatitis

Metabolic dysfunction–associated steatotic liver disease (MASLD; formerly nonalcoholic fatty liver disease) affects about 25% of adults globally.[68] In people living with obesity, the prevalence of MASLD is about 75%, with MASH (formerly nonalcoholic steatohepatitis) affecting about 34%.[69] Metabolic dysfunction–associated steatotic liver disease is strongly associated with cardiometabolic risk factors.[70] Its management is focused on weight loss in people with obesity;[71] optimization of cardiometabolic risk factors; prevention or delay of progression or regression of MASH or fibrosis; and prevention or management of outcomes such as cirrhosis, hepatocellular carcinoma, and liver transplantation.[72] Certain obesity pharmacotherapies, when combined with health behaviour changes, have been shown to facilitate the resolution of MASH without worsening of fibrosis and lead to improvements in fibrosis without worsening of MASH (Table 1, recommendation 9). For more details on obesity pharmacotherapies that may benefit MASH, refer to Appendix 3.

Obstructive sleep apnea

Obstructive sleep apnea is a common yet underdiagnosed chronic disorder characterized by obstructive apneas and hypopneas from repetitive collapse of the upper airway during sleep, with excess weight being a leading risk factor. Weight reduction can reduce OSA severity and improve related health outcomes.[73] Obesity pharmacotherapy can benefit people with OSA (Table 1, recommendation 10); for more information, refer to Appendix 3.

Knee osteoarthritis

Obesity-related knee osteoarthritis (OA) is caused by both excess joint stress and chronic inflammation. Weight management can reduce pain and improve physical function, and may slow disease progression.[74] Obesity pharmacotherapy can benefit people with OA of the knee (Table 1, recommendation 11); for more information, refer to Appendix 3.

Rare monogenic causes of obesity

Setmelanotide is a daily, subcutaneously administered melanocortin 4 receptor agonist, which has demonstrated benefit in reducing weight and hunger scores in people with rare monogenic causes of obesity (Table 1, recommendation 12). These rare genetic conditions should be considered in people with early childhood-onset obesity (younger than 5 years) and hyperphagia, with a history of parental relatedness, intellectual disability, structural organ defects, or complex endocrinopathy. A referral to a geneticist is suggested to confirm the diagnosis.[75] See Appendix 3 for more information on setmelanotide in certain rare forms of monogenic obesity.

Compounded medications

At the time of publication, we found insufficient evidence to support the use of pharmacotherapies or hormonal treatment strategies for weight loss not discussed in this guideline. Non-Health Canada–approved compounded GLP-1 and GIP–GLP-1 receptor agonists have emerged in the marketplace as a result of supply issues and cost associated with brand-name medications. Because of concerns and uncertainties regarding content, safety, quality, and efficacy, and lack of regulation of products not approved by Health Canada, we recommend against their use (Table 1, recommendation 13).

Methods

Obesity Canada led the development of this guideline update, after a national call for expressions of interest to join the guideline panel. Authors who contributed to the 2020 Canadian adult obesity guideline and the 2022 pharmacotherapy for obesity management revision were invited to reapply, and new contributors were welcomed through this open process. We adhered to the Appraisal of Guidelines for Research and Evaluation (AGREE II) framework[76] and Guidelines International Network (GIN) principles[77] in developing the guideline.

Composition of participating groups

The Canadian Clinical Practice Guideline Executive Committee led by Obesity Canada reviewed applications against the guideline panel criteria, which included clinical expertise in pharmacotherapy in obesity medicine, broad geographical representation, and presence of competing interests.

The guideline was developed by a guideline panel composed of 6 people geographically distributed across Canada. Five authors (S.D.P. [chair], P.M., S.D., A.J., M.P.) are experts in obesity medicine, including 3 in guideline development (S.D.P., P.M., A.J.), and 1 (N.P.) brings extensive experience in guideline development and implementation. Guideline development was further informed by a team of independent methodologists from the McMaster Evidence Review and Synthesis Team (n = 4), who conducted the evidence appraisal following the Shekelle framework[48] to assess levels of evidence and grading of recommendations.

Selection of priority topics

Obesity is associated with more than 200 health conditions,[78] and it was therefore not feasible to evaluate all of them within the scope of this update. Thirteen subpopulations were selected by unanimous consensus of the guideline panel, building upon identified subpopulations in the 2020 guideline.[7] In our selection process, we also incorporated the prevalence and clinical relevance of these conditions in clinical practice, their burden on the health care system, and their importance to patients as identified through lived experience and clinical engagement.

The 13 subpopulations for which search strategies were employed to identify studies of pharmacotherapy comprised atherosclerotic cardiovascular disease, heart failure, prediabetes, type 2 diabetes, MASH and MASLD, dyslipidemia, hypertension, OSA, OA, polycystic ovary syndrome, chronic kidney disease, gastroesophageal reflux disease, and depression. For the subpopulations of polycystic ovary syndrome, chronic kidney disease, gastroesophageal reflux disease, depression, dyslipidemia, and hypertension, we found insufficient data upon which to make recommendations.

Literature review and quality assessment

The McMaster Evidence Review and Synthesis Team conducted a systematic literature review (search dates January 2022 to July 2024), citation screening, methods review, and grading of each included study, based on the search strategy used for the 2020 guideline.[8] Relevant RCTs published between July 2024 and May 2025 were also included in the evidence for this update, as judged by unanimous decision of the guideline panel. The only methodologic revision in this update, compared with the 2020 guideline,[8] is that large multinational RCTs are now directly classified as level 1a evidence, reflecting their high methodological quality and broad applicability (which was previously implemented for the 2022 pharmacotherapy for obesity management revision).[9] Definitions of level of evidence and grading of recommendations are presented in Table 2.

Virtual meetings of the guideline panel were held between June 2024 and March 2025. Communication between panel members was conducted via email in between meeting dates. For a detailed description of the full methodology, refer to the 2020 guideline.[8]

Development of recommendations

We followed a pre-established methodology, ensuring that recommendations were grounded in evidence and developed through transparent processes. Briefly, we reviewed the type and strength of the available evidence (level) and used the study reference(s) that provided the highest level of evidence to formulate each specific recommendation. The guideline panel formulated grade D recommendations, labelled as "consensus," based on opinions and clinical experience, both their own and in the published literature. Most recommendations were reached by unanimous agreement; in the rare event where there was not unanimous consensus on wording (not the direction of the recommendation), the guideline panel (excluding N.P.) voted, with a simple majority prevailing. Panel members with a relevant competing interest were precluded from voting. All panel members were in unanimous agreement on the final recommendations. The McMaster Evidence Review and Synthesis Team subsequently reviewed recommendations to ensure that they were aligned with the evidence.

External review

To enhance the guideline's relevance and reduce the risk of bias, we sought feedback from a range of external reviewers (n = 11), including primary care physicians (n = 3), obesity medicine specialists (n = 3), and people with lived experience of obesity (n = 5). Reviewers evaluated the recommendations for clarity, feasibility, and potential bias. Additional input was provided by the Obesity Canada Scientific Advisory Committee (n = 14), which includes clinician–researchers (n = 9), scientists (n = 3), and people with lived experience (n = 2), with expertise spanning obesity prevention, weight bias and stigma, and health systems research. Reviewer feedback led to minor revisions in key messages and text sections, all discussed and agreed upon by the full guideline panel. The recommendations themselves remained unchanged apart from wording and grammatical adjustments, and all changes were agreed upon by all panel members.

Management of competing interests

We used GIN principles to manage competing interests, including quarterly completion of the International Committee of Medical Journal Editors' disclosure of interest forms by all members of the guideline panel and the McMaster Evidence Review and Synthesis Team.[77,79] Obesity Canada adjudicated competing interests through its Clinical Practice Guideline Executive Committee.

Obesity Canada provided nonindustry funding for the use of the services of the McMaster Evidence Review and Synthesis Team and publication fees. Obesity Canada's views have not influenced the content of the guideline. One panel member (N.P.) is a full-time employee of Obesity Canada and did not provide input into the level of evidence, and direction and grading of the recommendations. The other panel members were not remunerated for their services.

Implementation

In Canada, obesity is officially recognized as a chronic disease only by the Alberta provincial government.[80] The federal and other provincial and territorial, and municipal governments, do not recognize obesity as a disease despite declarations by the Canadian Medical Association,[81] multiple provincial medical associations,[82] and the World Health Organization.[83] The lack of recognition of obesity as a chronic disease by public and private payers, health systems, the public, and media has a trickle-down effect, limiting access to treatment (e.g., related to medication costs).

Awareness and implementation of this pharmacotherapy update will require targeted policy action, advocacy efforts, and engagement from people living with obesity, their families, and health care providers, with the goal of improving access and use of pharmacotherapy to improve the health of people living with obesity.

Given the described limitations of BMI-centric assessments of excess adiposity,[14–16,49–51] this guideline will likely help advance future clinical trials of obesity pharmacotherapies to include more comprehensive anthropometric measures as criteria for participation.

Obesity Canada is committed to the implementation of Canadian obesity guidelines,[7,13] in addition to updating and expanding its knowledge mobilization activities for focused updates. Obesity Canada has developed an educational pathway for health care professionals that includes introductory to expert level e-learning courses, microlearnings, and podcasts.[84] Obesity Canada will host the full version of this pharmacotherapy guideline on its website.[7]

Other guidelines

No other Canadian guidelines currently exist specific to obesity pharmacotherapy in adults within Canada; however, obesity guidance is increasingly being integrated into other disease-specific guidelines in Canada. The Canadian recommendations align with international guidelines, best practices, and standards.[85–87]

Gaps in knowledge

Evidence regarding the potential benefit of obesity pharmacotherapy is lacking in several important subpopulations, including polycystic ovary syndrome, chronic kidney disease, gastroesophageal reflux disease, and depression. More evidence is needed to inform on the use of combination therapy (e.g, combining a GLP-1–based therapy with naltrexone–bupropion or orlistat) for weight management, especially given the complex, multifactorial etiology of obesity and the potential benefits of targeting multiple mechanisms of action. Evaluation of quality of weight loss with pharmacotherapy (including quantity of lean muscle lost v. fat, and change in muscle strength and function) needs further exploration. Fertility, conception planning, and ensuring nutritional adequacy while taking obesity pharmacotherapy are also areas requiring more focused evidence. Studies are also needed to inform on management of patients taking GLP-1–based medication in the context of preoperative planning and procedures requiring conscious sedation.

Limitations

Other medications (e.g., phentermine, phentermine–topiramate) are approved for the management of obesity in some countries. In this guideline, we have included only medications that are currently approved in Canada. In addition, as more than 200 health complications are associated with obesity,[78] it was not feasible to search literature for all potential subpopulations. Although we applied principles of equity and inclusion to our recruitment of people with lived experience of obesity to provide input throughout the process, we were unable to engage a breadth of diversity across Canada in a meaningful way, given existing guideline development and update structures. This has been considered a priority for future iterations of guideline development.

Conclusion

Obesity pharmacotherapy is an important treatment option for people living with obesity. Several medications are available that support clinically meaningful and sustained weight loss in addition to important improvements in obesity-related health complications. Pharmacotherapy for obesity management should be considered early in the natural history of obesity, as weight and obesity-related health complications tend to increase and progress with time. Clinicians who treat people with obesity with or without obesity-related health complications should incorporate obesity pharmacotherapy as an integral part of their treatment paradigm.

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