

# How to apply the Canadian Obesity Clinical Practice Guidelines to people with type 2 diabetes

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## About the Author



Dr. Sue Pedersen is a Specialist in Endocrinology & Metabolism and a certified American Board of Obesity Medicine (ABOM) diplomate. She completed her training as an endocrinologist at the University of Calgary in 2005 and has a busy endocrinology practice at the C-ENDO Diabetes & Endocrinology Clinic in Calgary. She is the lead author on the pharmacotherapy chapter of the 2020 and 2022 Canadian Obesity Clinical Practice Guidelines, and a member of the Expert Committee for the 2018 Diabetes Canada guidelines as a co-author of the Weight Management chapter. She is a principal investigator for several studies of diabetes and obesity pharmacotherapy, and a co-author of many of the resultant publications. She has a public information website for healthcare providers and patients about obesity and diabetes ([www.drsue.ca](http://www.drsue.ca)).

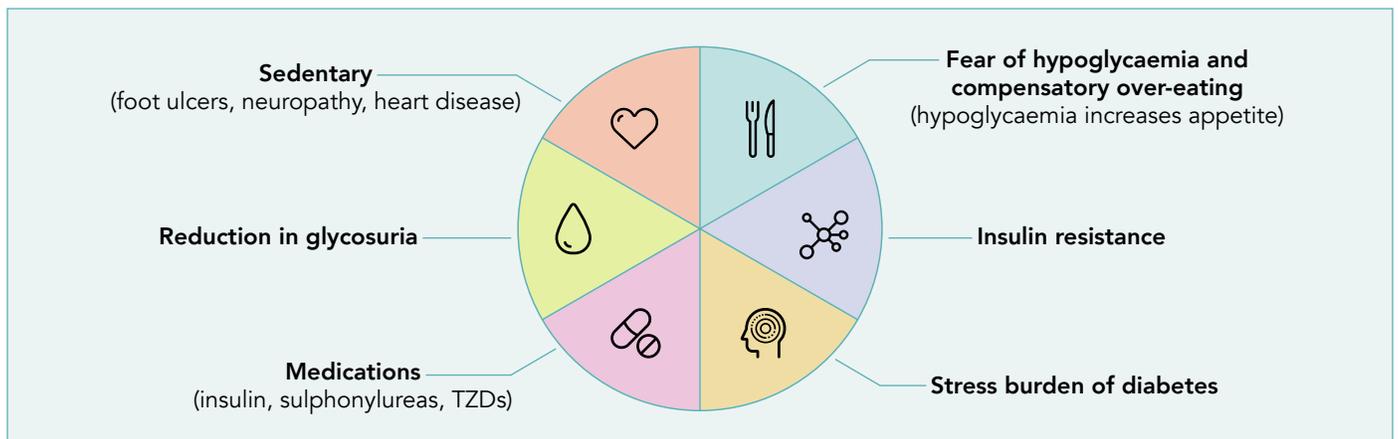
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Approximately 90% of people with type 2 diabetes (T2D) have overweight or obesity. Thus, weight management is a highly relevant clinical issue in this patient population. However, studies of obesity treatment in people with T2D consistently show that people with T2D lose less weight than people who do not have diabetes. There are many reasons why weight loss can be more difficult to achieve for people with diabetes.

Some medications can cause weight gain, as can cessation of hyperglycemia-associated glucosuria with acquisition of glucose control. Complications of DM can

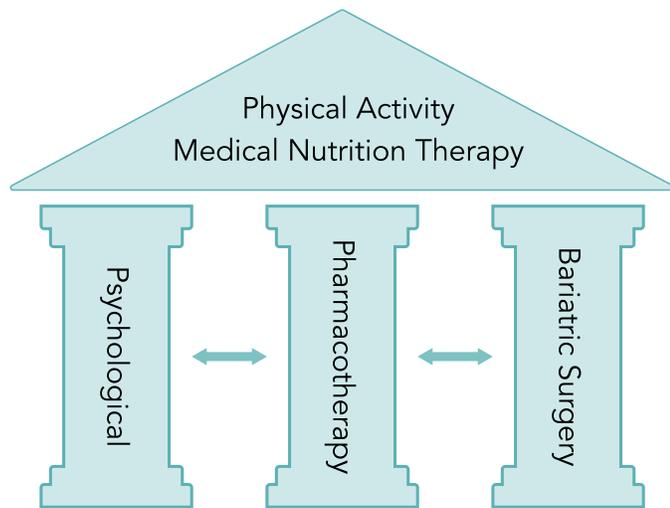
limit physical activity. Hypoglycemia can lead to weight gain, not only because treatment of hypoglycemia requires the ingestion of carbohydrates, but also because some patients may consume more calories than necessary to prevent hypoglycemia ('defensive snacking') or engage in a compensatory increase in food consumption due to fear of hypoglycemia. The stress and burden of diabetes can also lead to emotional eating. Furthermore, insulin resistance is often cited as making weight loss more challenging, though the mechanisms at play here are poorly understood.



**Figure 1:** Reasons weight loss can be more difficult to achieve in people with diabetes<sup>1,2,3,4</sup>

Weight loss is associated with improvement in various comorbidities related to obesity, including glycemia. Among individuals with prediabetes, one kilogram of weight loss is associated with a 16% relative risk reduction in the development of T2D.<sup>5</sup> An approximate 15% weight loss from baseline with

lifestyle intervention can lead to remission of T2D,<sup>6</sup> especially when the duration of diabetes is short. While these data for lifestyle interventions are encouraging, the vast majority of people who lose weight with the help of lifestyle intervention are not able to maintain the weight loss over the long term due to natural biology which drives weight regain through increase in ghrelin, reduction in satiety hormones, and a reduction in resting energy expenditure.<sup>7</sup> Another challenge is that these interventions may be difficult to implement in real-world clinical practice.

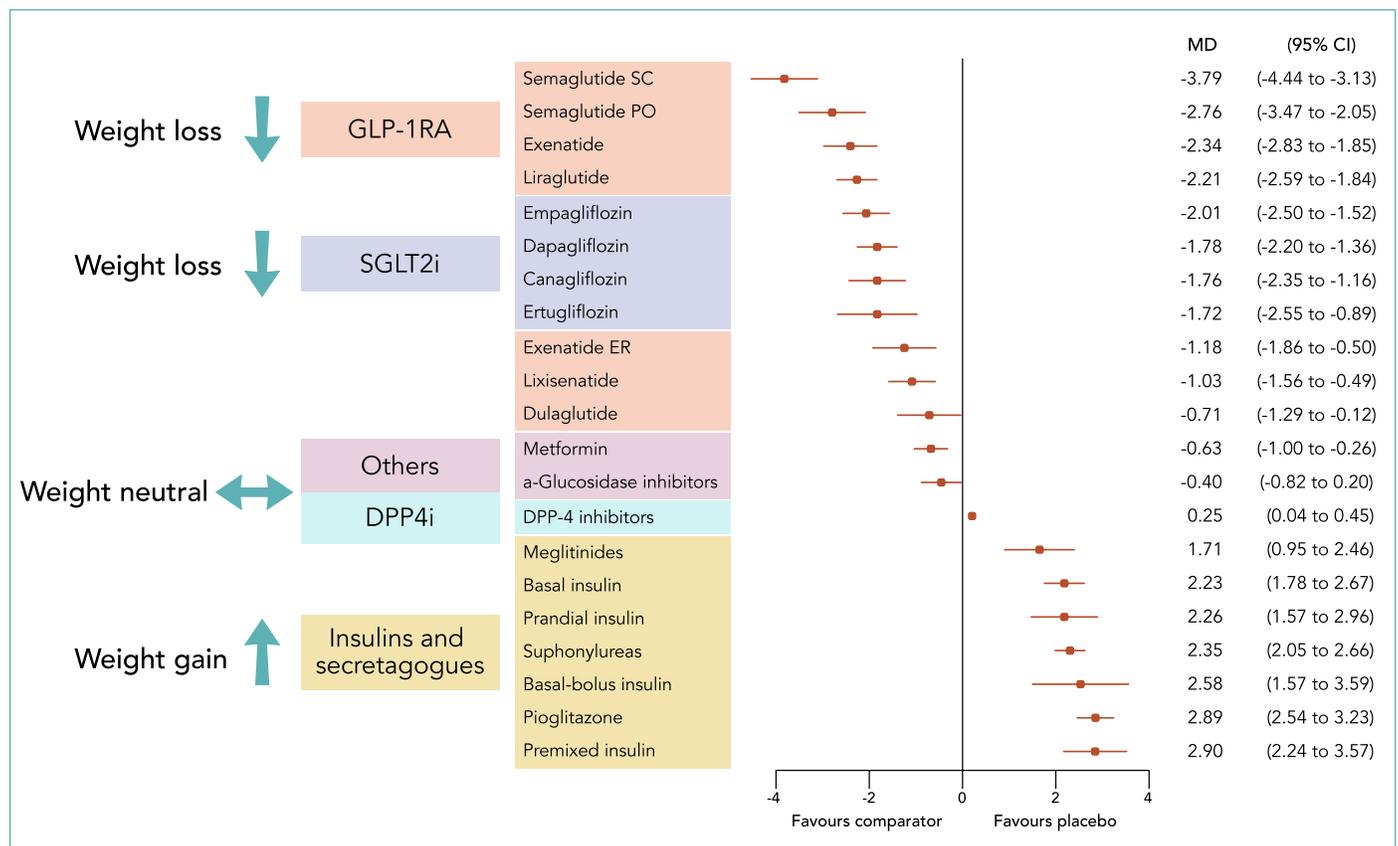


**Figure 2:** Three pillars of obesity management that support medical nutrition therapy & physical activity.

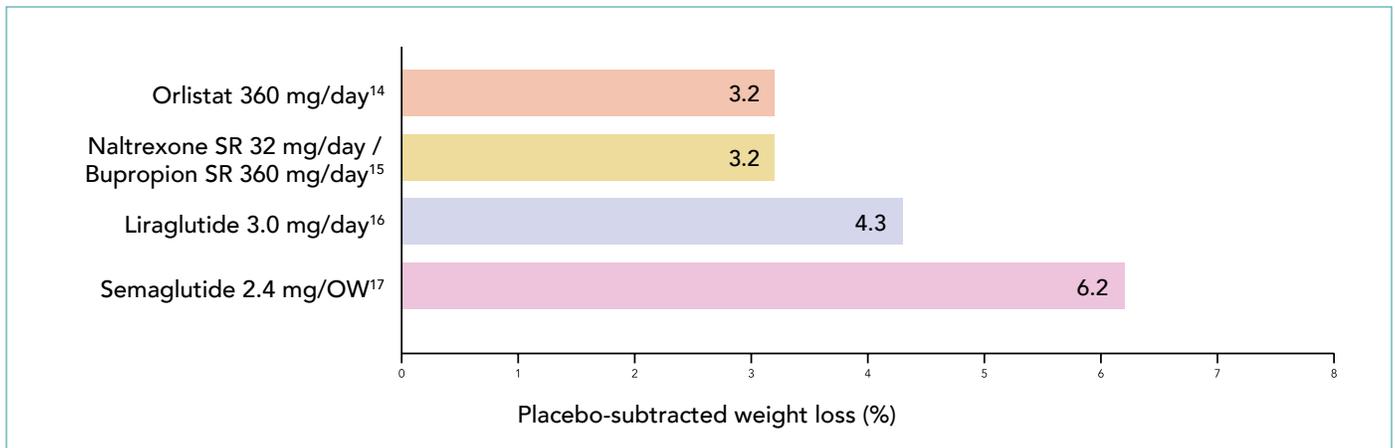
### So what do the Canadian obesity guidelines recommend for people with T2D?

The three pillars of obesity management that support medical nutrition therapy and physical activity are psychological support, pharmacotherapy, and/or bariatric surgery (Figure 2).

The Canadian obesity guidelines recommend choosing therapy from these pillars as appropriate for each patient. Lifestyle approaches, which include medical nutrition therapy and physical activity, are not sufficient interventions in and of themselves; rather, the pillars of treatment facilitate adherence to healthier lifestyles.<sup>8</sup>



**Figure 3:** Effects of glucose-lowering agents on body weight: network meta-analysis of 394 trials. Adapted from Kakotrichi P et al.<sup>13</sup>



**Figure 4:** Efficacy of approved obesity pharmacotherapy in people with type 2 diabetes. All treatment differences for obesity pharmacotherapy were significant,  $p < 0.001$  vs. placebo.<sup>14,15,16,17</sup>  
 SW: Sustained Release; OW: Once Weekly

## Medical Nutrition Therapy

There are numerous nutritional approaches that can improve glycemia with or without a small amount of weight loss.<sup>9</sup> These approaches include following the Mediterranean dietary pattern, a vegetarian diet, low glycemic index, a DASH (Dietary Approaches to Stop Hypertension) diet, and the inclusion of pulses (e.g. beans), vegetables, and nuts as part of one's routine nutritional consumption. It is recommended that nutrition plans should be personalized to ensure that they meet individual values and preferences and are safe, effective, nutritionally adequate, culturally acceptable, and affordable for long-term adherence. It is recommended to consider intensive lifestyle interventions that target a 7–15% weight loss to increase the likelihood of remission of T2D.<sup>9</sup>

## Physical Activity

Meta-analyses have consistently shown improvements in Hemoglobin A1c (A1c) following structured or supervised aerobic and/or resistance exercise training in people with T2D, even in the absence of weight loss.<sup>10</sup> Numerous studies have demonstrated that exercise with or without dietary interventions can reduce the risk of type 2 diabetes by 38–58% among people with prediabetes.<sup>11</sup>

## Pharmacotherapy

According to the Obesity Canada guidelines, when choosing the most appropriate medications for glycemic control, the effect of glucose-lowering pharmacotherapy on weight should be considered.<sup>12</sup> GLP-1 receptor agonists and sodium/glucose cotransporter

2 (SGLT2) inhibitors are associated with weight loss in addition to improving glycemic control. Other agents such as metformin, DPP-4 inhibitors, and acarbose are typically weight-neutral. Insulin, insulin secretagogues, and thiazolidinediones (TZDs) are associated with weight gain. As GLP-1 receptor agonists and SGLT2 inhibitors address the coincident goals of weight loss, glycemic control, and cardiorenal protection, they should be prioritized for the treatment of T2D.

When used in conjunction with health behaviour changes, obesity pharmacotherapy can facilitate weight management, improve glycemic control, and reduce the need for other glucose-lowering medication for people with T2D and a BMI  $\geq 27$  kg/m<sup>2</sup>.<sup>12</sup>

Figure 4 illustrates the placebo-subtracted weight loss efficacy of approved obesity pharmacotherapies in people with T2D. This depiction illustrates an indirect treatment comparison and is not from head-to-head trials. Readers should note that patients differ in terms of background glucose lowering medication, the duration of their T2D, and other important demographic and disease-related factors.

Orlistat is a pancreatic lipase inhibitor, inhibiting the absorption of ingested fat and thereby creating a caloric deficit. A meta-analysis of patients with T2D and obesity found that patients treated for 6 or 12 months with 120 mg orlistat t.i.d. had significantly greater reduction in A1c compared with placebo (0.74% vs. 0.31%, respectively).<sup>18</sup> The average weight loss in the orlistat group was 3.8kg compared to a loss of 1.4kg for patients in the placebo arm. The primary reason for improvement in glycemic control with orlistat is weight loss.

Liraglutide is a GLP-1 receptor agonist that acts centrally to improve satiation and satiety and reduce

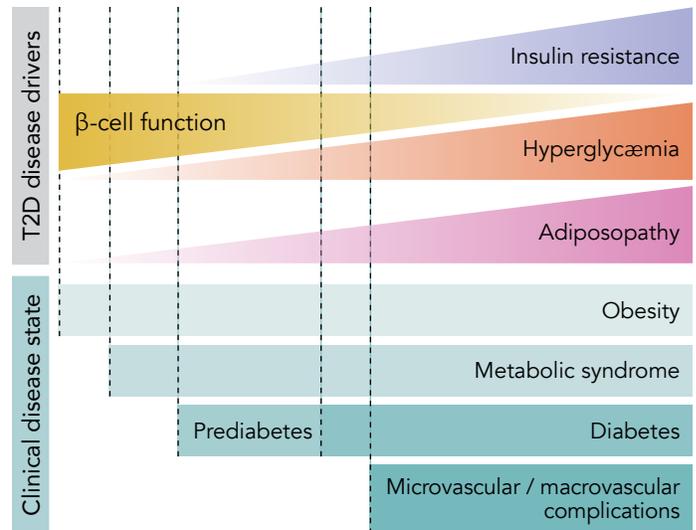
hunger, with a transient effect to decrease gastric emptying.<sup>19,20</sup> Liraglutide is approved for T2D at a dose of 1.2 mg or 1.8 mg daily, with near-maximal efficacy for A1c lowering at the 1.8 mg dose. It is approved for long-term obesity management at a dose of 3.0 mg daily for people with or without T2D. In people with obesity and T2DM managed with 0-3 oral agents, the SCALE randomized clinical trial found that in conjunction with health behaviour change, liraglutide 3.0 mg reduced weight by -6.0%, vs -4.7% with liraglutide 1.8 mg and -2.0% with placebo at 56 weeks.<sup>21</sup> A1c was reduced by 1.3% in the liraglutide 3.0 mg group, 1.1% in the liraglutide 1.8 mg group, and 0.3% in those receiving placebo.

Naltrexone/bupropion is approved for obesity management as a combination tablet, which works by inducing satiety centrally and reducing cravings.<sup>22</sup> Used along with health behaviour changes in adults with a BMI of 27–45 kg/m<sup>2</sup> and T2D managed with oral agents or diet, naltrexone/bupropion-treated patients achieved a 5% weight reduction from baseline, compared with 1.8% with placebo, and achieved a 0.5% greater reduction in HbA1c vs placebo. The change in A1c was correlated with the change in body weight.

Semaglutide is a GLP-1 receptor agonist that acts centrally to improve satiation and satiety, reduce hunger, and reduce cravings.<sup>23</sup> Semaglutide is approved for treatment of T2D at a dose of 0.5 mg, 1.0 mg, or 2.0 mg weekly, with near-maximal therapeutic efficacy for A1c lowering at the 1.0 mg dose. Semaglutide is approved in Canada for long-term obesity management at a dose of 2.4 mg weekly, in people with or without T2D. Among people with overweight or obesity and who have T2D managed with oral agents or health behaviours alone, semaglutide 2.4mg with health behaviour modification resulted in a superior weight loss of 9.6% at 68 weeks, compared to a loss of 7.0% with semaglutide 1.0 mg and 3.4% with placebo. Reduction in A1c was 1.6% with semaglutide 2.4 mg, 1.5% with semaglutide 1.0 mg, and 0.4% with placebo.

## Bariatric Surgery

Bariatric surgery can be considered for people with BMI  $\geq 40$  kg/m<sup>2</sup> or BMI  $\geq 35$  kg/m<sup>2</sup> with T2D, to induce control and remission of T2D in combination with best medical management, over best medical management alone.<sup>24</sup> Bariatric surgery should also be considered in patients with poorly controlled T2D and Class I obesity (BMI between 30 and 35 kg/m<sup>2</sup>)<sup>10</sup> despite optimal medical management. Remission rates of diabetes at three years have been reported at 79% and 95% in Roux-en-Y gastric bypass and duodenal switch groups, respectively, compared to no response with



**Figure 5:** Obesity management disrupts type 2 diabetes progression.<sup>28</sup>

medical intervention alone. Long-term outcome data from a randomized controlled trial found that 29% of patients who underwent Roux-en-Y gastric bypass and 23% who underwent sleeve gastrectomy maintained A1c levels of 6.0% or lower at 5 years, with or without the use of diabetes medications, compared to 5% of patients who underwent intensive medical therapy alone.<sup>25</sup> Predictors of diabetes remission include higher preoperative serum C-peptide, younger age, shorter duration of diabetes, and lack of need of insulin therapy preoperatively.<sup>26</sup> In people who experience diabetes remission, it is important that routine screening for diabetes continues lifelong, as recurrence of diabetes is common.

## Treating obesity earlier disrupts the natural history of T2D

Weight gain, central adiposity, and insulin resistance, which ultimately lead to hyperglycemia, are typically present decades before a diagnosis of T2D. As shown in Figure 5, treatment in the early years of obesity provides the opportunity to prevent comorbidities related to excess adiposity. At the stage where metabolic syndrome has developed, treatment of obesity is targeted towards resolution of metabolic syndrome and prevention of prediabetes. During the prediabetes stage, potential outcomes of obesity management include remission of prediabetes and prevention of T2D, whereas if the same intervention is started after the onset of T2D, goals of treatment center on glycemic control or perhaps T2D remission. Once diabetes-related complications have developed, the focus is on treating or preventing progression of

those complications, in addition to glycemic control.

While there are important benefits to treating obesity across the continuum, by treating obesity earlier, we have the potential to disrupt the natural history of T2D. As such, a focus on weight management must start as early as possible in the continuum of metabolic disease.

As most patients with T2D will benefit from having a primary weight-centric approach to diabetes management, the 2022 ADA/EASD guidelines have been updated to prioritize weight management alongside glycemic control and cardiorenal protection in their diabetes pharmacotherapy algorithm<sup>27</sup>—an important addition to the treatment paradigm!

### Clinical Pearls

- When any weight management treatment modality is initiated in a person with T2D, it is important to consider any needed reduction in insulin or secretagogues for avoidance of hypoglycemia.
- As weight decreases, reduction in other medications (eg. hypertension medications, thyroid hormone treatment for hypothyroidism) may be required, and these parameters should be monitored.
- For any patient who experiences remission of T2D or prediabetes with any treatment modality, it is essential that glycemic control is re-evaluated regularly to screen for recurrence.

### Financial Disclosures

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