


cardiovascular disease, diabetes, stroke, osteoarthritis, obstructive sleep apnea, and certain types of cancer.<sup>8</sup> These consequences affect a large proportion of primary care patients; as of 2013, 62% of Canadian adults (aged 18 to 79 years) were estimated to be overweight or obese, based on a calculated BMI of 25 kg/m<sup>2</sup> or greater.<sup>9</sup>

The CTFPHC guidelines deemphasize the role of PCPs in the prevention and treatment of obesity. However, access to bariatric centres is limited in many areas. Given the high proportion of individuals in Canada who are overweight or obese, and the potential health benefits to patients of losing even 5% to 10% of their body weight, PCPs should feel comfortable helping patients achieve weight loss by not only recommending lifestyle modifications, but also suggesting pharmacotherapy when appropriate. Pharmacotherapy for weight management is an important tool, and side effects of currently approved therapy are mainly gastrointestinal in nature.

## Conclusion

Obesity is a chronic disease; building supports, improving available treatments, and implementing best practices will take time. Providing pharmacotherapy for weight management is something family physicians can easily do now to help patients individually, as well as to help fight the obesity epidemic. 

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### Competing interests

None declared

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## CLOSING ARGUMENTS – YES

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- Obesity is a chronic disease and, just like other chronic diseases (eg, diabetes, hypertension), after failed lifestyle changes, patients require pharmacotherapy for treatment.
- Nearly two-thirds of the Canadian population is overweight or obese. As primary care providers (PCPs) are the front line of care, they must be prepared and armed with tools such as medications for weight management.
- Practical algorithms and decision aids exist to assist PCPs in treating patients who are obese or overweight.
- Liraglutide (3.0 mg) and orlistat are currently available in Canada. Both have, at most, potential gastrointestinal side effects. Orlistat has been available since 1999 and liraglutide in 1.2- and 1.8-mg doses has been available in Canada since 2010. Therefore, PCPs already have familiarity with these drugs and should be able to administer them as needed.

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**NO** Obesity is a well recognized risk factor for many chronic health conditions. More than two-thirds of Canadian men (67%) and more than half of Canadian women (54%) are overweight or obese.<sup>1</sup> The primary aim of obesity treatment is to reduce weight-related health risks and improve quality of life. A weight loss of at least 5% has been shown to produce modest improvements in cardiometabolic risk factors and is frequently used in trials as a surrogate.<sup>2</sup>

Neither the US Preventive Services Task Force (USPSTF) nor the Canadian Task Force on Preventive Health Care (CTFPHC) recommends pharmacologic intervention for the management of obesity.<sup>1,3</sup> The CTFPHC guideline states: "For adults who are overweight or obese, we recommend that practitioners not routinely offer pharmacologic interventions (orlistat or metformin) aimed at weight loss. (*Weak recommendation; moderate-quality evidence*)."<sup>1</sup>

This statement hints at offering medication in some "nonroutine" circumstances; however, having tried to look critically at the literature, I am convinced that these drugs are not the answer for most obese Canadians. I will now try to convince you.

## Questions

**Why would we prescribe medication when we have effective, safe nonpharmacologic treatments?** Recent literature reviews by both the USPSTF (2012) and the CTFPHC (update in 2013) recommend offering structured behavioural interventions to obese patients (with body mass index of 30 kg/m<sup>2</sup> or greater). The USPSTF gives this a B recommendation (high certainty that the net effect is moderate).<sup>3</sup> The CTFPHC made this a strong recommendation for obese patients at high risk of diabetes and a weak recommendation for those not at risk. Overall evidence quality was moderate. For patients at high diabetes risk, the absolute reduction in the incidence of new-onset disease was 8.9% (number needed to treat [NNT]=11), with a sustained risk reduction over 10 years.<sup>1</sup> However, practically these programs require additional resources to implement in our primary care environment, they might be difficult to access owing to availability, and they might be expensive and require patient motivation. A potentially easier, safe pharmacologic solution to this epidemic might be welcome. In order to make an informed decision with our patients about the use of obesity medication, we must carefully weigh the benefits *and* the risks of this approach. Unfortunately for by far most Canadians struggling with excess weight and obesity, the balance between benefits and risks is tipped in the wrong direction.

**What are the benefits of available options?** The only medications currently licensed in Canada for the treatment of obesity that have been systematically reviewed are metformin and orlistat, although I will briefly discuss liraglutide as well. Overall study quality in the metformin and orlistat trials was low.

**Metformin:** There are only 2 older randomized controlled trials (RCTs) with weight loss as the only trial outcome. Although intervention participants had a statistically significantly greater weight loss compared with the control group, the mean difference was only about 2 kg.<sup>4</sup>

**Orlistat:** Fifteen RCTs contributed to the most recent systematic review of orlistat; however, generalizability to the typical primary care patient is questionable.<sup>4</sup> All trials had run-in periods excluding patients based on their initial success at reducing calories and increasing exercise, introducing bias likely to overstate efficacy. Included patients were, therefore, likely more motivated, adherent, and responsive than the broader population would be. Maximum study duration was 36 months.


Intervention participants were statistically significantly more likely to lose 5% or more and 10% or more of their baseline body weight as compared with control participants (NNT=4 and NNT=8, respectively) and were statistically significantly less likely to be diagnosed with type 2 diabetes (NNT=28).<sup>4</sup>

**Liraglutide:** This glucagonlike peptide 1 analog is the “new kid on the block” in the pharmacologic war on obesity. A recent large pharmaceutically sponsored RCT showed a significant increase in patients who achieved both 5% and 10% reduction in body weight with 3.0 mg of liraglutide given subcutaneously compared with placebo, with a mean differential weight loss of 5.6 kg over 56 weeks ( $P<.001$ ). The usual recommended dose for type 2 diabetes is 1.8 mg.<sup>5</sup>

**What are the harms of available options?** In the orlistat and metformin trials, participants were statistically significantly more likely to experience gastrointestinal side effects such as oily stool, urgency, abdominal pain, and flatulence (number need to harm of 5).<sup>4</sup> Orlistat was also associated with reduced absorption of fat-soluble vitamins,<sup>3</sup> and an Ontario study showed an association with acute kidney injury.<sup>6</sup> In the liraglutide trial, there was an increase in breast cancers diagnosed in the study group and concerns about the potential for increased risks of pancreatitis and medullary cancer of the thyroid.<sup>6,7</sup> Longer follow-up and close scrutiny for adverse effects is required before we jump on this bandwagon.

It is also critical to note that there are no longer-term studies to confirm medication safety or maintenance of weight loss either while taking or after taking medication. Studies of orlistat during a 12- to 36-month period showed no overall benefit for weight maintenance.<sup>8</sup> In the liraglutide trial, participants gained back an average of 2.9 kg 12 weeks after discontinuing the drug.<sup>6</sup> If long-term treatment is required, orlistat and liraglutide are expensive, at about \$150 to \$300 per month plus daily injections for liraglutide. Metformin is less expensive but also less effective.

## Conclusion

Despite the appeal of pharmacologic interventions to combat this epidemic, a careful review of the benefits and harms finds this approach wanting for by far most Canadians struggling with obesity. Nonpharmacologic approaches are effective, albeit resource intensive, but might have additional benefits in terms of improving overall health and quality of life. Longer-term studies are needed to confirm medication safety and efficacy before we can confidently recommend this strategy to our patients. 

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### Competing interests

None declared

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### CLOSING ARGUMENTS — NO

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- Neither the US Preventive Services Task Force nor the Canadian Task Force on Preventive Health Care recommend the use of medication to treat obesity.
- The balance of benefits and harms of medication appears tipped in the wrong direction, and there are no longer-term studies to confirm the safety of weight-loss medication.
- Effective nonpharmacologic treatment exists, with the potential for health benefits beyond decreasing obesity.

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