



Joyce Wong, Director, Clinical, Drug Database and Plan Management and one of ESC's clinical pharmacists, Romina Isip, define the term **Cardiodiabetes** and address the growing challenges in the management of these complex diseases in Canada.



THOUGHT LEADERSHIP SERIES

What is Cardiodiabetes?

'Cardio-dia-besity' is a term that captures the complex interrelationship between cardiovascular disease, diabetes, obesity, and metabolic syndrome.

Metabolic syndrome is a cluster of health conditions including high blood pressure, impaired blood sugar levels, and large waist circumference that underlie cardiodiabetes.¹ It is essential to understand the relationship among these chronic conditions within cardiodiabetes due to their prevalence in Canada. In 2022, about one in three individuals in the Express Scripts Canada database submitted a claim for at least one drug used to treat cardiovascular disease, diabetes and/or obesity.

Cardiodiabetes: A Review of ESC Data

As a Pharmacy Benefit Management company, Express Scripts Canada supports the adjudication of drug claims in Canada. Our review delves into the drug data for these three conditions from the private payer perspective and does not address the non-drug options for cardiovascular disease, diabetes, and obesity. These three chronic conditions affected a large proportion of claimants in 2022, where more than 9% of claimants submitted expenses for diabetes medications, close to 30% had claims for cardiovascular medications, and less than 1% had claims for obesity medications. However, findings for cardiodiabetes (i.e., patients having all three conditions) were limited, since not all claimants had coverage for obesity drugs. The majority of drug plans provide coverage for cardiovascular and diabetes medications, while only about a third of members have coverage for obesity drugs.

Analysis of the comorbidity data for cardiovascular disease, diabetes, and obesity drugs provided some interesting insights about the diabetes claimants. In our annual Drug Trend Reports, diabetes has been the second highest therapeutic class by spend for the last 5 years. The increase in the number of claimants each year represented an uptrend for those taking medications for diabetes. Adding to the complexity of the disease, patients with diabetes are at a greater risk of cardiovascular morbidity due to the progressive damage to the heart, nerves, eyes, and kidneys. Consequently, diabetes claimants would likely have claims for drugs used to treat these progressive complications and expand drug claims to beyond the diabetes, cardiovascular, and obesity categories.

Percentage of diabetes claimants with claims associated complications:

Diabetes claimants	2022
Cardiovascular*	82%
Neuropathy	11%
Eye	< 1%
Obesity	< 1%

* Cardiovascular includes drugs for heart disease, high blood pressure and high cholesterol.

As expected, there was a high proportion of diabetes claimants who submitted expenses for cardiovascular drugs in 2022, aligning with clinical practice guideline recommendations for diabetes. Most patients with type 2 diabetes are placed on high blood pressure and/or high cholesterol medications to reduce their cardiovascular risk. The data also revealed that diabetic neuropathy (i.e., nerve damage) has likely developed in 11% of these claimants. With a much smaller correlation, claims for drugs to treat diabetic macular edema and macular degeneration make up less than 1% of diabetes claimants and represented patients with worsening disease. Lastly, only a small portion of diabetes claimants had an obesity drug claimed in 2022, which may be due to either the lack of drug coverage, or that patients may already be on a diabetes drug with inherent weight loss benefit.

In another analysis, the progression of diabetes was observed by examining retrospective data over 5 years. Following the same diabetes claimants from 2018 to 2022, our data showed year-over-year increases in claims for medications used in cardiovascular disease, eye disease, and nerve pain. This pattern, which is associated with the increasing number of medications used over time, was also observed in cardiovascular drug and obesity drug claimants.

In summary, the data revealed significant numbers of people taking medications for cardiovascular disease, diabetes, and obesity. Some claimants had one or more of these disease conditions present and some showed progressive worsening of their disease. In Canada, recent estimates reveal that the costs of cardiovascular disease and diabetes to the healthcare system were about \$21 billion² and \$27 billion³, respectively. Early intervention is the key to halting disease progression of obesity and/or diabetes towards developing serious cardiovascular outcomes. Large population studies would further advance our understanding of the triple threat of cardiometabolic disease, and guide future clinical practice to address the associated health and economic impact of these comorbid diseases.

Challenges to Tackling Cardiometabolic Disease

One of the main challenges in tackling cardiometabolic disease is addressing the stigma related to obesity. Long-standing stigma towards obesity has led to patients facing unequal access to proper chronic disease management strategies that will enable them to achieve the highest level of health (i.e., health equity), including coverage of obesity medications.

Obesity is still not well recognized as a chronic disease and it continues to be stigmatized. Physicians find it hard to initiate conversations surrounding obesity with their patients, unlike cardiovascular disease and diabetes. This may be partly due to some physicians' negative attitudes about obesity⁴, and the historical lack of tolerable and effective treatments. Maintaining long-term weight loss through lifestyle interventions, such as with diet and exercise, are essential but remain challenging. About a third of patients with obesity using this method alone experience a full or partial weight regain.⁵ Although this is partly due to patients slowly reverting to their former habits, there are also pervasive biological mechanisms in the body that promote appetite, reduced satiety and lowered metabolism, resulting in weight regain.⁶

Due to these stigmas, obesity is one of the few chronic conditions for which medications are not readily covered by drug plans. In contrast, most drugs for diabetes and cardiovascular disease are widely covered. From our 2023 Drug Trend Report, although 35% of plan members had coverage for obesity medications, they accounted for less than 1% of overall spend and less than 1% of claimants. In addition, for those who had coverage, plan policies impose maximum limits that do not adequately cover the cost of these medications for chronic use. Treating obesity is equally as important as treating cardiovascular disease and diabetes as it is a driving factor in the progression of these coexisting conditions.

Incorporating diversity, equity, and inclusion philosophies into drug plan design could help establish access to obesity medications. It is important for plan sponsors to ensure their coverage policies are up to date and reflect the current practice guidelines and clinical information on obesity as a chronic disease, rather than a lifestyle choice. Having access to these treatments will not only improve member experience and health, but it may also reduce overall burden of care related to cardiometabolic disease. Plan design can ensure clinically appropriate use of these medications through benefit management techniques such as Prior Authorization.

Another barrier to coverage on public and private drug plans is the need for long-term evidence from the use of obesity medications. Negative reimbursement recommendations cite the lack of long-term data demonstrating meaningful health outcomes associated with sustained weight loss.^{7,8} As a result, the majority of private and public drug plans have taken the same approach and have excluded obesity medications for coverage. The limited coverage for these obesity medications have consequently contributed to the lack of real-world data for patients with obesity. Access to meaningful real-world data to identify and follow patients with cardiometabolic disease could help illustrate not only patient health outcomes, but also its economic impact to payers and the healthcare system.

Weight Management Medications for Cardiometabolic Disease

The prevalence of obesity in the Canadian adult population is steadily increasing,⁹ and without reliable intervention, obesity rates are expected to grow. Obesity is well understood to be a contributing factor in developing type 2 diabetes, high blood pressure, high cholesterol, and other serious chronic conditions.¹⁰ It has also been shown that obesity is an independent risk factor for cardiovascular death and complications, similar to diabetes.¹¹ Early interventions which target weight management may limit the progression to type 2 diabetes and cardiovascular disease.

Substantial and sustained weight loss has been associated with an improvement in blood sugar levels and blood pressure, and a significant reduction in major adverse cardiovascular events seen in patients who have undergone bariatric surgery.¹² Most simply, weight loss is an evidence-based treatment pathway for cardiovascular disease, diabetes, and metabolic syndrome. However, lifestyle modifications and previous drug treatments for weight management have not been able to demonstrate the same substantial cardiovascular benefits as bariatric surgery. This is likely due to the degree of weight loss achieved from surgical intervention (up to 40% of body weight)¹³



compared with lifestyle and/or pharmacological interventions (5–10 % of body weight).¹⁴

A newer drug class called GLP-1 receptor agonists (GLP1-RAs) entered the market in 2010 and since then, these drugs have reshaped the treatment approach to diabetes and obesity. GLP1-RAs show efficacy in lowering blood sugar levels, with added cardiovascular benefit and weight loss. The older GLP1-RAs have been shown to provide modest weight loss and were associated with lower rates of adverse cardiovascular outcomes.^{15,16} Meanwhile, clinical trials for newer GLP1-RAs, such as semaglutide (OZEMPIC®/WEGOVY®) and tirzepatide (MOUNJARO®/ZEPBOUND®), have demonstrated a greater degree of weight loss and better blood sugar management compared to older GLP1-RAs.^{17,18} Furthermore, recent evidence on semaglutide treatment showed a significant 20% reduction in cardiovascular death, non-fatal heart attack, or non-fatal stroke at 5 years – supporting the claim that long-term sustained weight loss leads to clinically meaningful health outcomes.¹⁹ Tirzepatide is the newest drug in the market and is the first dual glucose-dependent insulinotropic polypeptide (GIP) and GLP1 receptor agonist. At this time, trials evaluating the impact of tirzepatide on cardiovascular outcomes are ongoing.²⁰

There are several investigational treatments in the pipeline that target appetite-regulating hormones like GLP-1, GIP, and glucagon for the treatment of obesity and diabetes. Recently, clinical trials for new diabetes treatments are required to include cardiovascular outcome data. Diabetes drugs that exhibit cardiovascular benefit are generally favoured in clinical practice guidelines, which subsequently influences prescribing practices. Clinical research further emphasizes the interrelationship between cardiovascular disease, diabetes, and obesity, as well as the value of exploring treatment modalities that target all three conditions. More than ever, there is great awareness among patients about the existence of these treatments, which places great pressure on healthcare providers and payers for equitable access to these obesity medications. A growing number of patients are demanding more support in navigating available services and interventions associated with obesity management.²¹

Cardiometabolic: Key Takeaways

Cardiometabolic is on the rise. A review of ESC claims data revealed that a large proportion of claimants suffer from cardiovascular disease and diabetes. Due to limitations in coverage for obesity medications, patients living with obesity were underreported in our data compared to Canadian estimates.²² The number of different medications accessed by these claimants was also shown to increase over time, which have been attributed to disease worsening.

Drug management of cardiometabolic involves a multi-pronged approach, which focuses on obesity interventions alongside cardiovascular and diabetes treatments. Newer drugs in the market have the potential to address each aspect of cardiometabolic and provide long-term health outcomes from cardiovascular complications. These health outcomes could translate to reductions in the overall drug spend, as well as in the number of medications accessed by patients.



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¹ [What is Metabolic Syndrome? | American Heart Association](#)

² [Connected by the numbers | Heart and Stroke Foundation](#)

³ [Diabetes. 360 Recommendations](#)

⁴ Alberga AS, Nutter S, MacInnis C, Ellard JH, Russell-Mayhew S. Examining Weight Bias among Practicing Canadian Family Physicians. *Obes Facts*. 2019;12(6):632-638. doi: 10.1159/000503751. Epub 2019 Nov 8. PMID: 31707395; PMCID: PMC6940460.

⁵ [Weight cycling is associated with adverse cardiometabolic markers in a cross-sectional representative US sample | Journal of Epidemiology & Community Health](#)

⁶ [Understanding weight regain after a nutritional weight loss intervention: Systematic review and meta-analysis – ScienceDirect](#)

⁷ [Semaglutide \(Wegovy\) \(cadth.ca\)](#)

⁸ [Liraglutide \(Saxenda\) \(cadth.ca\)](#)

⁹ Health Canada Health Fact Sheets, Overweight and obese adults, 2018. Release date June 2019. Accessed Sep 2023. [Overweight and obese adults, 2018 \(statcan.gc.ca\)](#)

¹⁰ Valenzuela PL, Carrera-Bastos P, Castillo-García A, Lieberman DE, Santos-Lozano A, Lucia A. Obesity and the risk of cardiometabolic diseases. *Nat Rev Cardiol*. 2023 Jul;20(7):475-494. doi: 10.1038/s41569-023-00847-5. Epub 2023 Mar 16. PMID: 36927772.

¹¹ [Diabetes Canada | Clinical Practice Guidelines - Chapter 23: Cardiovascular Protection in People with Diabetes](#)

¹² Doumouras, Aristithes G et al. Bariatric Surgery and Cardiovascular Outcomes in Patients With Obesity and Cardiovascular Disease: A Population-Based Retrospective Cohort Study. *Circulation* vol. 143,15 (2021): 1468-1480. doi:10.1161/CIRCULATIONAHA.120.052386

¹³ [Effects of Bariatric Surgery on Cardiovascular Function | Circulation \(ahajournals.org\)](#)

¹⁴ [Obesity and Cardiovascular Disease: A Scientific Statement From the American Heart Association \(ahajournals.org\)](#)

¹⁵ [Dulaglutide and cardiovascular outcomes in type 2 diabetes \(REWIND\): a double-blind, randomised placebo-controlled trial – The Lancet](#)

¹⁶ [Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes | NEJM](#)

¹⁷ Powell-Wiley, Tiffany M et al. "Obesity and Cardiovascular Disease: A Scientific Statement From the American Heart Association." *Circulation* vol. 143,21 (2021): e984-e1010. doi:10.1161/CIR.0000000000000973

¹⁸ [Tirzepatide versus Semaglutide Once Weekly in Patients with Type 2 Diabetes | NEJM](#)

¹⁹ [Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes | NEJM](#)

²⁰ [Find Lilly Clinical Trials : A Study of Tirzepatide \(LY3298176\) Compared With Dulaglutide on Major Cardiovascular Events in Participants With Type 2 Diabetes \(SURPASS-CVOT\) | Learn About Our Research](#)

²¹ [Benefits Canada Healthcare Survey Report 2023 | Benefits Canada.com](#)

²² Health Canada Health Fact Sheets, Overweight and obese adults, 2018. Release date June 2019. Accessed Sep 2023. [Overweight and obese adults, 2018 \(statcan.gc.ca\)](#)

