CoLab Network

Summary Report

Safety Monitoring During Use of Ozempic in People With Diabetes

Report Authors

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Knowledge Translation Support

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This study was conducted by the Canadian Network for Observational Drug Effect Studies (CNODES) through the Post-Market Drug Evaluation CoLab Network.

Executive Summary

Semaglutide is used to help improve blood sugar levels in adults with type 2 diabetes mellitus (T2DM). In Canada, it is available under the brand names Ozempic, Rybelsus, and Wegovy. As the use of Ozempic increases in Canada, there is a need for real-world monitoring of its safety outcomes in people with T2DM. We conducted a cohort study in 4 provinces (British Columbia, Manitoba, Ontario, and Saskatchewan) to demonstrate the feasibility of replicating a US FDA Sentinel TreeScan signal-detection analysis using Ozempic as the case study. We identified 92,428 new users of Ozempic and 46,266 new users of sitagliptin with T2DM. A secondary analysis in the Ontario public drug plan found 44,185 new users of empagliflozin. Although the analysis identified potential safety concerns, this study alone does not establish or confirm safety signals for Ozempic, and further focused studies are necessary. This study is the first of its kind to demonstrate the feasibility of replicating a US FDA Sentinel TreeScan analysis with Canadian data, providing important insights for future studies.

Background

Semaglutide, a glucagon-like peptide 1 (GLP-1) receptor agonist, is available in Canada under the brand names Ozempic, Rybelsus, and Wegovy. These drugs are used to help control blood sugar levels in adults with T2DM. Health Canada is closely monitoring the use of these medications due to their rapid uptake. Guidance is needed on the optimal prescribing of these medications to ensure people with T2DM are benefiting from the treatment with minimal risk. However, data on the real-world safety of these drugs are limited. A recent safety signal identification study by the US FDA compared Ozempic to sitagliptin, a dipeptidyl peptidase-4 (DPP-4) inhibitor with a similar mechanism of action, for treating T2DM. The analysis found that the incidence of gastrointestinal adverse events was relatively higher for semaglutide, with nausea, vomiting, and diarrhea being among the most frequently observed events.

Policy Issue

As Ozempic use increases, there is a need for real-world safety outcome monitoring of the drug in Canada. Guidance is needed on the optimal prescribing of Ozempic to ensure that patients are benefiting from the treatment with minimal risk.

Policy Question

1. Are there potential safety signals associated with the use of Ozempic among adults with diabetes?

Objective

This is 1 of several Common Data Model (CDM) demonstration projects. This project specifically assesses the feasibility of replicating a US FDA Sentinel TreeScan analysis using Canadian data.

Our objective was to use the US FDA Sentinel Ozempic analysis as a case study for 1 of the demonstration projects. Specifically, we aimed to replicate the FDA Sentinel TreeScan analysis using Canadian data, comparing Ozempic to sitagliptin. As an extension to the Sentinel analysis, we added empagliflozin as a secondary comparator because it is the most frequently prescribed sodium-glucose cotransporter-2 (SGLT2) inhibitor in Canada.

Findings

Population

We identified 92,428 new users of Ozempic and 46,266 new users of sitagliptin with T2DM in 4 provinces (British Columbia, Manitoba, Ontario, and Saskatchewan) using provincial administrative health care data transformed into the Sentinel CDM. A secondary analysis in the Ontario public drug plan found 44,185 new users of empagliflozin.

Compared to new users of sitagliptin, new users of Ozempic were relatively younger, less likely to have Alzheimer disease and other dementias, more likely to have high blood cholesterol and depressive disorder, more likely to be living with obesity, and much more likely to be coprescribed insulin.

Compared to new users of empagliflozin, new users of Ozempic were relatively younger, less likely to have a prior heart attack and high blood pressure, more likely to be living with obesity, and more likely to be coprescribed insulin.

Adverse Events

> ***Follow-up*** is defined as monitoring a person's health over time after receiving treatment.

New users of Ozempic were followed for a median of 43 days compared to 103 days for new users of sitagliptin. The primary reasons for the shorter follow-up time were drug discontinuation or switching.

The analysis comparing Ozempic to sitagliptin identified potential safety concerns, including nausea, vomiting, obesity, polyneuropathy (damage to nerves outside of the brain and spinal cord), and other nervous system disorders. However, none of these concerns were identified as signals of increased risk among new users of Ozempic compared with new users of sitagliptin.

Strengths and Limitations

We demonstrated the successful replication of an FDA Sentinel TreeScan signal-detection analysis with Canadian data, with some important considerations.

To eliminate differences in patient characteristics between groups, we used propensity score matching (pairing data from people with similar characteristics). However, this resulted in a significant reduction in the number of patients available for this study. When we switched the comparison drug from sitagliptin to empagliflozin — a more contemporary alternative to Ozempic — there was good balance in patient characteristics, and we could retain more people treated with Ozempic. The small sample size can be considered an additional limitation to identifying any of the potential safety signals.

Implications for Policy-Making

These analyses alone do not establish or confirm safety signals for Ozempic. Further focused studies are necessary to establish the presence of meaningful safety signals.

We have shown that it is possible to use Canadian administrative health data converted into the Sentinel CDM, along with a modified version of the FDA's original analytical program, to replicate the FDA's study methods. Our study provides valuable insights and important lessons for the future use of Canadian data in TreeScan-based analyses.

Considerations

Post-Market Drug Evaluation (PMDE) projects aim to produce health policy issue evidence and are not linked to a recommendation.

This work was intended to inform health policy. Clinical questions regarding treatment recommendations for T2DM should be directed to a health care professional.

For more information on CoLab and its work, visit the **CoLab website**.

For the full scientific report, visit:

Safety of Ozempic for Type II Diabetes

Canada's Drug and Health Technology Agency

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This study was conducted by the Canadian Network for Observational Drug Effect Studies (CNODES) through the Post-Market Drug Evaluation CoLab Network. This work was supported by CADTH and its Post-Market Drug Evaluation Program, through funding provided by Health Canada.

About CADTH: CADTH is a not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs and medical devices in our health care system.

About CoLab: CoLab is a pan-Canadian network of experts in applied research, scientific methods, and data analysis. CoLab members work with CADTH's Post-Market Drug Evaluation Program to produce credible and timely evidence on post-market drug safety and effectiveness.