■ CADTH Reports

Real-Time Continuous Glucose Monitoring for People Living With Diabetes

Background

For people living with diabetes, blood glucose monitoring is used in combination with insulin therapy to adjust insulin doses and maintain glucose control. The traditional method is self-monitoring of blood glucose (SMBG) using a glucometer. However, SMBG requires a fingerstick to take a blood sample, which can be painful and time-consuming. Some people find it difficult to practice SMBG at the recommended rates. Additionally, nocturnal or asymptomatic hypoglycemia (low blood glucose) may not be recognized through SMBG, and severe hypoglycemia can lead to coma or death.

Another option is continuous glucose monitoring (CGM), which is a method of glucose testing in which a sensor is inserted into the skin and continuously monitors interstitial glucose concentrations. Real-time continuous glucose monitoring (rtCGM) systems have the capability for alerts and alarms for current and/or impending glycemic events such as hyperglycemia (high blood glucose) or hypoglycemia. In comparison, intermittently scanned continuous glucose monitoring (isCGM) systems, as known as flash glucose monitoring (FGM) systems, measure glucose levels every minute and store 1 value every 15 minutes. However, they require the person using the information to scan the sensor to display information (i.e., it is not done automatically), and only the most recent 8 hours of data are retained.

CADTH undertook 4 rtCGM-related reports in 2022:

- the first compared rtCGM to isCGM (FGM) for people living with type 1 diabetes, type 2 diabetes, or gestational diabetes
- the second compared rtCGM to SMGB for people living with type 1 diabetes
- the third compared rtCGM to SMBG for people living with type 2 diabetes
- the fourth searched for evidence-based guidelines regarding the use of rtCGM for people living with type 1 diabetes or type 2 diabetes.

The details and findings of these 4 reports are summarized here, followed by summaries of additional CADTH work on CGM more broadly (including both rtCGM and isCGM [FGM] systems).

Intermittently Scanned and Real-time Continuous Glucose Monitoring for People With Diabetes

Health Technology Review, July 2022

Purpose

To summarize the evidence on the comparative clinical effectiveness of isCGM versus rtCGM for people living with type 1 diabetes, type 2 diabetes, and gestational diabetes.

Literature Identified

Eight publications met the inclusion criteria: 1 systematic review, 2 randomized controlled trials, and 5 non-randomized studies.

Findings and Key Messages

- Type 1 diabetes – clinical effectiveness: The evidence on the comparative clinical effectiveness of isCGM versus rtCGM for improving time in range, time above range, hemoglobin A1c, and quality of life in people with type 1 diabetes is uncertain. Evidence from some studies suggested there was a significant benefit favouring rtCGM versus isCGM for these outcomes, whereas other studies found no difference between treatment groups.
- Type 1 diabetes – safety: The evidence on the comparative safety of isCGM versus rtCGM in people with type 1 diabetes is also limited and uncertain. Evidence from 1 study suggested that severe hypoglycemic events were more frequent in those using isCGM; however, in other studies, there were no severe hypoglycemic events in either treatment group.
- Type 2 diabetes and gestational diabetes: No studies were identified that evaluated the comparative effectiveness of isCGM versus rtCGM in people with type 2 diabetes or gestational diabetes.

Limitations

Limitations included the fact that none of the primary studies were conducted in Canada; only 2 of the non-randomized studies included children and adolescents; the clinical significance of the time in range outcome measure is uncertain; and none of the studies were blinded (blinding was not possible given that participants need to interact with rtCGM and isCGM [FGM] devices).

Real-Time Continuous Glucose Monitoring for People Living With Type 1 Diabetes

Health Technology Review, August 2022

Purpose

To summarize the evidence on the clinical effectiveness and cost-effectiveness of monitoring glycemia with rtCGM versus SMBG in people living with type 1 diabetes.

Literature Identified

Eight publications met the inclusion criteria: 5 systematic reviews, 1 randomized controlled trial, and 2 economic evaluations.

Findings and Key Messages

- Clinical effectiveness and safety: Evidence suggests that rtCGM may improve hemoglobin A1c and time in range, and decrease severe hypoglycemia in adults and pediatric patients with type 1 diabetes compared to SMBG. Limited evidence suggests that there was little to no difference between rtCGM and SMBG on quality of life, diabetic ketoacidosis, and severe adverse events.
- Cost-effectiveness: rtCGM may be more cost-effective in the long term than SMBG in adults with type 1 diabetes.

Limitations

Limitations included the fact that none of the clinical effectiveness studies were conducted in Canada; none of the studies were blinded (not possible given that participants need to interact with the devices); many of the studies were funded by device manufacturers; no cost-effectiveness data were available for pediatric patients specifically; the clinical significance of the outcome measures is uncertain; sample sizes were small; there were differences in the types of rtCGM devices used; there was heterogeneity in outcome measures and reporting; trial durations were short; and various other factors that contributed to risk of bias as described in the full report.

Real-Time Continuous Glucose Monitoring for People Living With Type 2 Diabetes

Health Technology Review, September 2022

Purpose

To summarize the evidence on the clinical effectiveness and cost-effectiveness of monitoring glycemia with rtCGM versus SMBG in people living with type 2 diabetes.

Literature Identified

Seven publications met the inclusion criteria: 5 systematic reviews, 1 randomized controlled trial, and 1 economic evaluation.

Findings and Key Messages

- Clinical effectiveness: In adult patients, rtCGM may be favoured over SMBG in improving glycated hemoglobin levels, and in lowering time with extreme low or high blood glucose levels. However, the evidence is uncertain due to limited quality evidence.
- Safety: In adults, limited safety evidence suggests that rtCGM is safe with low rates of adverse events.
- Cost-effectiveness: One cost-effectiveness analysis conducted in Spain found that rtCGM was not a cost-effective option compared to SMBG in adults with type 2 diabetes.
- Pediatric patients: No evidence was identified.

Limitations

Limitations included the fact that it is unclear whether any of the primary studies in the systematic reviews were conducted in Canada (and the randomized controlled trial was not); the cost-effectiveness study was conducted in Spain and therefore its applicability to the Canadian setting is unclear; there were differences in the types of rtCGM devices used (as well as in the medications and insulin used to manage glycemic levels); trial durations were short (follow-up ranged from 48 hours to 9 months); and various other factors that contributed to risk of bias as described in the full report.

Real-Time Continuous Glucose Monitoring: A Review of Guidelines

Health Technology Review, August 2022

Purpose

To summarize evidence-based guidance regarding the use of rtCGM in people living with type 1 or type 2 diabetes (both adult and pediatric populations).

Literature Identified

Six evidence-based guidelines met the inclusion criteria, including 3 of high quality and 3 of moderate quality.

Findings and Key Messages

- Adults with type 1 diabetes:
  - All 4 guidelines that addressed rtCGM for adults with type 1 diabetes strongly recommended it, based on intermediate- to high-quality evidence.
- Adults with type 2 diabetes:
  - All 4 evidence-based guidelines that addressed rtCGM for adults with type 2 diabetes recommended it, based on low- to high-quality evidence.
- Pediatric patients with type 1 diabetes:
  - All 3 evidence-based guidelines that addressed rtCGM for pediatric patients with type 1 diabetes strongly recommended it, based on intermediate- to high-quality evidence.

- Pediatric patients with type 2 diabetes:
  - One expert guideline recommended rtCGM for children and young people with type 2 diabetes based on expert consensus rather than evidence of clinical effectiveness.
  - A second guideline did not make a recommendation, but suggested that research be undertaken on CGM in children and young people living with type 2 diabetes.
  - No other guidelines addressed this patient population.

Limitations

The device capabilities of isCGM (FGM) systems are evolving (e.g., with potential alerts and/or alarms) to become more similar to rtCGM, and the differences between the technology types (and specific devices) will continue to change and evolve over time. Additionally, while the Diabetes Canada guideline was developed for the Canadian context, it was assessed as having a number of limitations due to incomplete reporting of the methods, and the other 5 guidelines were developed for use in the US or England.

Additional CADTH Evidence on Continuous Glucose Monitoring

Continuous Glucose Monitoring for People With Diabetes Receiving Dialysis or With Chronic Kidney Disease

Summary of Abstracts, September 2022

Purpose

To summarize the available evidence on the accuracy and clinical effectiveness of CGM systems versus arterial, venous, or capillary reference samples for people with diabetes who are receiving dialysis or who have chronic kidney disease, and to search for any evidence-based guidelines on the topic.

Findings and Key Messages

- Seven non-randomized studies were identified regarding the accuracy of CGM systems versus arterial, venous, or capillary reference samples for people with diabetes who are receiving dialysis or who have chronic kidney disease.
- While full-text articles were not reviewed or critically appraised, the authors noted that the results generally supported the accuracy of CGM systems.
- No relevant literature was found regarding clinical effectiveness.
- No evidence-based guidelines were identified.

Flash Glucose Monitoring and Continuous Glucose Monitoring for People With Diabetes in Acute Care Settings

Summary of Abstracts, April 2021

Purpose

To summarize the available evidence on the accuracy and clinical effectiveness of CGM systems and FGM systems versus arterial, venous, or capillary reference samples among people with diabetes in acute care settings, and to search for any evidence-based guidelines on the topic.

Findings and Key Messages

- Three randomized controlled trials and 13 non-randomized studies were identified regarding the clinical effectiveness and accuracy of CGM and FGM systems for managing blood glucose levels among people with diabetes in acute care settings.
- While full-text articles were not reviewed nor critically appraised, the authors noted that the findings largely supported improved glycemic management with CGM, with mixed results for accuracy (with concerns about accuracy predominantly in the extremes of glycemic variability).
- One evidence-based guideline was identified from the Diabetes Technology Society.

Hybrid Closed-Loop Insulin Delivery Systems for People With Type 1 Diabetes

Optimal Use, June 2021

Background

Hybrid closed-loop insulin delivery systems (HCLs) combine an insulin pump with a CGM and a computer program. Together, these use information from the CGM to automatically determine insulin needs throughout the day and keep the use within a predetermined blood glucose range. They are called hybrid systems because users must still manually account for insulin needs before and after meals.

Purpose

Across Canada, technologies to manage type 1 diabetes are rapidly evolving. CADTH undertook this Optimal Use project to develop recommendations regarding the use of HCLs for people with type 1 diabetes. It included an assessment of clinical effectiveness and safety, a budget impact analysis, a perspectives and experiences review, and an ethical issues review.

Findings and Key Messages

- HCLs generally increase the amount of time a person is in their target blood glucose range compared with other insulin delivery methods.
- For people with type 1 diabetes and their caregivers, HCLs can decrease the amount of time and energy spent on diabetes management.

- While the short-term data look promising (approximately 6 months), there haven't been any studies that follow research participants for extended periods of time.
- Deciding to fund HCL systems would likely force conversations about reimbursement for CGMs.
- CADTH's expert committee recommended re-evaluating the data in the coming years as more long-term data become available.

Flash Glucose Monitoring Systems in Pediatric Populations With Diabetes

Health Technology Review, April 2021

Purpose

To compare the clinical effectiveness of monitoring glycemia (blood sugar levels) with FGM systems versus SMBG in pediatric patients who require insulin therapy for diabetes. This is because, previously, there was very limited evidence identified for pediatric patients specifically. A second objective was to compare the clinical effectiveness of FGM systems with alerts and/or alarms (e.g., hypoglycemia, hyperglycemia, signal loss) versus systems without alerts and/or alarms.

Literature Identified

Fifteen relevant publications were identified: 3 health technology assessments (HTAs), 5 systematic reviews, 1 randomized controlled trial, and 6 non-randomized studies.

Findings and Key Messages

- The evidence suggests that FGM may improve quality of life, patient satisfaction, diabetes distress, self-efficacy, and frequency of glucose monitoring compared to SMBG in pediatric patients with type 1 diabetes.
- Findings related to other outcomes, such as hemoglobin A1c, glucose time in range metrics, and adverse events were mixed or inconclusive (i.e., in some studies the use of FGM was associated with improved outcomes, while in others it was not).
- No studies were identified that compared the clinical effectiveness of FGM systems with hypoglycemia, hyperglycemia, or signal loss alarms (e.g., the FreeStyle Libre 2) to FGM systems without these features (e.g., the FreeStyle Libre), either in pediatric patients, or in people of any age with diabetes that requires insulin therapy.

Flash Glucose Monitoring System FreeStyle Libre to Monitor Glycemia in Patients With Diabetes

Health Technology Review and Implementation Advice, September 2020

Purpose

To summarize the key findings and recommendations of 2 Canadian provincial HTA reports on FGM systems including clinical, economic, and budget impact analysis results. This information was then considered by members of an ad hoc implementation advice panel to develop advice on the implementation of the recent recommendations for public funding of FGM systems in Canada.

Literature Identified

Ontario and Quebec HTAs were reviewed.

Findings and Key Messages

- Clinical:
  - Both HTAs concluded that FGM systems are superior to SMBG with respect to certain glycemic outcomes (i.e., time in range, frequency and duration of daytime and nocturnal hypoglycemia, and treatment satisfaction). However, there was uncertainty regarding improvement in other outcomes (i.e., A1c and severe hypoglycemic events).
  - Note that there were variations in the clinical benefits according to the type of diabetes (in particular for the time in range outcome).
- Economic:
  - Both HTAs found that the introduction of FGM systems would be expected to increase public health spending. However, the budget impact of introducing FGM systems would be sensitive to the frequency of self-testing associated with SMBG (i.e., the incremental costs of FGM systems would be lower in scenarios in which SMBG users would require a higher frequency of self-testing).
- Patient and clinician perspectives and experiences:
  - There was wide support for the use of FGM systems in terms of physical, emotional, and social benefits.
  - Reduction in, and alternative, to finger pricks, and the ability to see blood glucose trends to better manage their diabetes was widely recognized by patients.
  - Cost was the largest barrier to use.
  - Education for patients and care teams was considered a necessary condition for optimal and beneficial use of FGM systems.

Recommendations

Both HTAs recommended funding FGM systems for patients with type 1 diabetes or type 2 diabetes that require intensive insulin therapy who met specific criteria. The implementation advice panel convened by CADTH offered further commentary and advice on which patients may benefit most from FGM systems.

Notes: Based on the guidance of the Ontario Health Technology Advisory Committee (OHTAC), Health Quality Ontario (HQO), now a part of Ontario Health, recommended publicly funding FGM systems for the following 2 groups of patients: persons with type 1 diabetes who experience recurrent hypoglycemia despite frequent SMBG and efforts to optimize insulin management, and persons with type 2 diabetes that requires intensive insulin therapy – that is, multiple daily injections of insulin or continuous subcutaneous insulin infusion for those who experience recurrent hypoglycemia despite frequent SMBG and efforts to optimize insulin management.

Institut national d'excellence en sante et en service sociaux (INESSS) evaluated the FreeStyle Libre FGMS, and the Comite scientifique permanent de l'évaluation des medicaments aux fins d'inscription (CSMEI) recommended adding the FreeStyle Libre to the list of the prescription drug insurance plan for self-monitoring of glycemia in patients on insulin therapy, provided the economic burden is lessened. If the economic burden of funding the FreeStyle Libre was not reduced for the province, CSEMI recommended that this FGM system be listed as an exceptional drug product for adults aged 18 years and older who meet the following criteria: intensive insulin therapy, frequent or severe hypoglycemic events, and necessity for blood glucose self-monitoring at least 8 times daily.