Health Quality Ontario

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ONTARIO HEALTH TECHNOLOGY ASSESSMENT SERIES

Continuous Monitoring of Glucose for Type 1 Diabetes: A Health Technology Assessment

KEY MESSAGES

What Is This Health Technology Assessment About?

Type 1 diabetes is a condition in which the pancreas produces little or no insulin. Insulin is a hormone that helps the body's cells use glucose (a type of sugar) for energy. Without insulin, glucose builds up in the blood and can cause serious damage to the body. People with type 1 diabetes must take insulin via injection or an insulin pump, and they should monitor their blood glucose levels several times a day.

Most people with type 1 diabetes use a blood glucose meter to check their blood glucose levels. They prick their finger to obtain a drop of blood, and they apply the blood to a test strip inserted into the meter. This is called self-monitoring of blood glucose. Continuous glucose monitoring is another way to measure blood glucose. It measures a person's blood glucose levels every few minutes via a sensor inserted under the skin.

This health technology assessment evaluates how effective continuous glucose monitoring is for people with type 1 diabetes, if it is good value for money, and the preferences and values of people living with type 1 diabetes and/or their caregivers.

What Did This Health Technology Assessment Find?

People who used continuous glucose monitoring spent more time in the target blood glucose range, less time out of range, and had fewer severe low blood glucose episodes than people who used self-monitoring of blood glucose.

Compared with self-monitoring of blood glucose, the costs of continuous glucose monitoring were higher, with only small increases in health benefits. Publicly funding continuous glucose monitoring for people with type 1 diabetes in Ontario would result in additional costs to the health system over the next 5 years.

Adult patients and parents of children with type 1 diabetes reported very positive experiences with continuous glucose monitoring, but the high cost of using the devices was a barrier to their widespread use.

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ABSTRACT

Background

Type 1 diabetes is a condition in which the pancreas produces little or no insulin. People with type 1 diabetes must manage their blood glucose levels by monitoring the amount of glucose in their blood and administering appropriate amounts of insulin via injection or an insulin pump. Continuous glucose monitoring may be beneficial compared to self-monitoring of blood glucose using a blood glucose meter. It provides insight into a person's blood glucose levels on a continuous basis, and can identify whether blood glucose levels are trending up or down.

Methods

We conducted a health technology assessment, which included an evaluation of clinical benefit, value for money, and patient preferences related to continuous glucose monitoring. We compared continuous glucose monitoring with self-monitoring of blood glucose using a finger-prick and a blood glucose meter. We performed a systematic literature search for studies published since January 1, 2010. We created a Markov model projecting the lifetime horizon of adults with type 1 diabetes, and performed a budget impact analysis from the perspective of the health care payer. We also conducted interviews and focus group discussions with people who self-manage their type 1 diabetes or support the management of a child with type 1 diabetes.

Results

Twenty studies were included in the clinical evidence review. Compared with self-monitoring of blood glucose, continuous glucose monitoring improved the percentage of time patients spent in the target glycemic range by 9.6% (95% confidence interval 8.0–11.2) to 10.0% (95% confidence interval 6.75–13.25) and decreased the number of severe hypoglycemic events.

Continuous glucose monitoring was associated with higher costs and small increases in health benefits (quality-adjusted life-years). Incremental cost-effectiveness ratios (ICERs) ranged from $592,206 to $1,108,812 per quality-adjusted life-year gained in analyses comparing four continuous glucose monitoring interventions to usual care. However, the uncertainty around the ICERs was large. The net budget impact of publicly funding continuous glucose monitoring assuming a 20% annual increase in adoption of continuous glucose monitoring would range from $8.5 million in year 1 to $16.2 million in year 5.

Patient engagement surrounding the topic of continuous glucose monitoring was robust. Patients perceived that these devices provided important social, emotional, and medical and safety benefits in managing type 1 diabetes, especially in children.

Conclusions

Continuous glucose monitoring was more effective than self-monitoring of blood glucose in managing type 1 diabetes for some outcomes, such as time spent in the target glucose range and time spent outside the target glucose range (moderate certainty in this evidence). We were less certain that continuous glucose monitoring would reduce the number of severe hypoglycemic events. Compared with self-monitoring of blood glucose, the costs of continuous glucose monitoring were higher, with only small increases in health benefits. Publicly funding continuous glucose monitoring for the type 1 diabetes population in Ontario would result in additional costs to the health system over the next 5 years. Adult patients and parents of children with type 1 diabetes reported very positive experiences with continuous glucose monitoring. The high ongoing cost of continuous glucose monitoring devices was seen as the greatest barrier to their widespread use.

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OBJECTIVE

This health technology assessment evaluated the clinical benefit, cost-effectiveness, and patient experiences of continuous glucose monitoring compared with usual care (i.e., self-monitoring of blood glucose using a finger-prick and a blood glucose meter) for the management of type 1 diabetes.

BACKGROUND

Health Condition

In Canada, approximately 3.4 million people live with diabetes. It is uncertain how many of those have type 1 diabetes. Some estimates from manufacturers of continuous glucose monitors in Canada, report that approximately 180,000 Canadians have type 1 diabetes, of whom 70,000 live in Ontario. Other estimates suggest that more than 300,000 people in Canada have type 1 diabetes, 150,000 of whom are in Ontario.[1,2]

In type 1 diabetes, the beta cells (insulin-producing cells) in the pancreas are damaged.[3] The role of insulin in the body is to promote entry of glucose into the tissue cells. Inside the cell, glucose is metabolized to release energy, crucial for cell functioning. In most cases, type 1 diabetes is caused by an autoimmune process (the immune system attacks its own cells), resulting in a loss of beta cells. This eventually leads to high levels of glucose in the blood, affecting protein synthesis (protein-building) and other metabolic disorders such as diabetic ketoacidosis (too much acid in the blood).[3] Over the long term, people with diabetes can experience serious complications, including kidney disease, heart disease, stroke, nerve damage, and damage to the eyes, leading to blindness.[1]

Diabetes is considered one of the most burdensome diseases for health care systems because of the time and resource costs related to managing diabetes and its complications.[4]

Clinical Need and Target Population

Patients with type 1 diabetes manage their blood glucose levels by frequently monitoring the amount of glucose in their blood and administering appropriate amounts of insulin to keep their blood glucose levels in the target range. Hyperglycemia (high blood glucose) can result in the long-term diabetes complications listed above. Hypoglycemia (low blood glucose) may lead to loss of consciousness, seizure, or coma.[1]

Type 1 diabetes affects people of all ages and genders. It is the most common type of diabetes in children and teens, accounting for at least 85% of diabetes cases in patients aged less than 20 years.[5]

Current Treatment Options

Typically, people with type 1 diabetes self-monitor their blood glucose levels using a blood glucose meter. Blood glucose levels are usually expressed in millimoles per litre (mmol/L) or milligrams per decilitre (mg/dL). To measure blood glucose levels with a blood glucose meter, a person must prick their finger and squeeze a drop of blood onto a test strip inserted into the meter. The meter then provides a readout of the blood glucose level. People with type 1 diabetes who use a meter usually take readings at regular intervals, including before meals, after meals, before and after physical activity, before driving, and during the night.

A useful laboratory measure for assessing long-term blood glucose management is glycated hemoglobin (A1C), which estimates average blood glucose concentrations over a period of 3 months. This is commonly expressed in terms of National Glycohemoglobin Standardization Program units (%), International Federation of Clinical Chemistry units (mmol/mol), or estimated average glucose (mg/dL). Diabetes Canada (formerly the Canadian Diabetes Association) recommends an optimal A1C of ≤7% to prevent the long-term complications of diabetes.[6]

Health Technology Under Review

Continuous glucose monitoring provides an opportunity for patients to monitor their blood glucose levels more frequently. It is aimed at helping people with diabetes gain a better understanding of their blood glucose control in real time.

Continuous monitoring of blood glucose levels can be used with multiple daily injections of insulin or an insulin pump. Continuous glucose monitors can be separate from an insulin pump (called standalone continuous glucose monitors) or they can be part of a system that is integrated with an insulin pump (called a sensor-augmented insulin pump).[7]

Continuous glucose monitors consist of a sensor inserted underneath the skin, a transmitter, and a small monitor. Every few minutes, the sensor measures blood glucose levels in the interstitial fluid[8] (fluid that surrounds tissue cells) and sends readings via the transmitter to the monitor, which displays the information.[8] For some models, the information can also be transmitted to other devices using Bluetooth technology, so that family members or other caregivers can access blood glucose information.

Continuous glucose monitors that are currently licenced in Canada require regular finger-prick testing to calibrate, usually every 12 hours.[7] Continuous glucose monitors that do not require calibration with a finger-prick are expected to reach the market in 2018. The sensors for continuous glucose monitors are intended to be used for no more than 7 days and must be replaced regularly.[7] Sensors that last 4 months are in development.[9]

Regulatory Information

As of November 2016, Health Canada had granted licenses for continuous glucose monitors from two manufacturers. Medtronic (Brampton, Ontario) and Dexcom (San Diego, California) have licences for several generations of devices. For this assessment, we reviewed any Medtronic or Dexcom device that has been included in peer-reviewed publications since 2010. Table 1 summarizes the devices that have Health Canada licences and met the inclusion criteria for this assessment.

Table 1: Summary of Included Devices

Manufacturer	Device	Year	License Number
Dexcom	G4	2013, 2014	91189
	G5	2016	97937
Medtronic	Glucose sensor	2000, 2009	20654
	REAL-TIME transmitter	2007, 2009, 2013, 2016	73839
	Enlite glucose sensor	2013	90691
	630G	2016	97802

Source: Health Canada.[10]

Medtronic offers a sensor-augmented insulin pump. The continuous glucose monitor is integrated with the pump and includes a "low glucose suspend" feature, which shuts off the administration of insulin for up to 2 hours when blood glucose levels are below a predetermined threshold and the patient is not responding to alerts. This feature may be beneficial for patients with nocturnal (nighttime) hypoglycemia or hypoglycemia unawareness.

The Dexcom continuous glucose monitor is a standalone device, but it can be integrated with the Animas Vibe insulin pump (Animas Corporation, West Chester, Pennsylvania).

Because the scope of this assessment was limited to continuous glucose monitoring devices by manufacturers with Health Canada licences at the time of writing, devices such as the Dexcom SEVEN and the Abbott FreeStyle Navigator were not included in this health technology assessment. Because this assessment was focused on devices used to support patients' continuous monitoring of their blood glucose levels, devices such as the iPRO2 CGM system (license number 85706) and the Abbot Freestyle Libre Pro (license number 97934), which are used only by health care professionals, were also excluded from this assessment.

Ontario Context

Most patients in Ontario are not reimbursed for the cost of purchasing a continuous glucose monitor. Individuals must pay out of pocket or have private insurance that covers these devices.

In Ontario, the cost of a continuous glucose monitor is publicly funded for people who qualify for the Ontario Disability Support Program and the Mandatory Special Necessities benefit, Ministry of Community and Social Services.[11] The Ontario Public Drugs Program offers reimbursement for 3,000 blood glucose test strips per year for certain populations who use insulin to manage their diabetes (i.e., people aged 65 years or older; people who qualify for the Ontario Disability Support Program; Ontario Works recipients; clients of the Trillium Drug Program; residents of long-term care homes or homes for special care; and individuals enrolled in home care).

Ontario's Assistive Devices Program provides funding assistance for insulin pumps for people with type 1 diabetes who are unable to achieve good blood glucose control with multiple daily injections alone.[12] To be eligible, patients must have demonstrated good adherence to diabetes management prior to starting pump therapy. Adults must have been on multiple daily injections for 1 year prior to starting insulin pump therapy; pediatric patients are not required to be on multiple daily injections. Since the cost of an insulin pump is covered as an insured device in Ontario, patients who use an insulin pump with integrated continuous glucose monitoring capabilities need to pay for only the continuous glucose monitoring transmitters and sensors.

International Context

Continuous glucose monitoring is in widespread use around the world, and many insurance providers offer some funding. Table 2 summarizes Canadian and international funding options for continuous glucose monitoring.

Table 2: International Funding of Continuous Glucose Monitoring

Country	Reimbursement Plan	Details of Funding[a]
Canada	Regional funding and private insurance programs	Limited funding regionally; some funding through private insurance companies
Ontario	Assistive Devices Program, Ministry of Health and Long-Term Care	Funding of pump costs for insulin pumps with integrated continuous glucose monitors
	Some private insurance companies	Details vary by insurance company
Czech Republic	Patient capitation model	Partial funding for continuous glucose monitoring devices
France	National insurance funding	Funding for continuous glucose monitoring devices
Germany	National insurance funding	Funding for continuous glucose monitoring devices
Netherlands	Regional insurance funding	Partial funding for continuous glucose monitoring devices
Norway	Tenders; regional	Funding for continuous glucose monitoring devices
Slovenia	National reimbursement funding	Funding for continuous glucose monitoring devices for the pediatric population only
Sweden	Regional insurance funding	Funding for continuous glucose monitoring devices
Switzerland	National reimbursement funding	Funding for continuous glucose monitoring devices
United Kingdom	National Institute for Health and Care Excellence diagnostic assessment	National Health Service funds under specific circumstances; the National Institute for Health and Care Excellence guideline strongly recommends the use of continuous glucose monitoring in young people with impaired hypoglycemic awareness or frequent severe hypoglycemic events and adults who meet certain criteria.[13,14]
United States	Some private insurance companies[b]	Details differ depending on insurance company
	Medicare	Funding for therapeutic continuous glucose monitoring devices

[a]Information was gathered in part from Dexcom (San Diego, California).
[b]Blue Cross/Blue Shield, Aetna, Cigna, Humana, United Healthcare, Kaiser Permanente, Wellpoint.[15]

CLINICAL EVIDENCE

Research Question

Compared with usual care (i.e., self-monitoring of blood glucose using a blood glucose meter), what is the effectiveness of continuous glucose monitoring (using standalone devices or integrated with insulin pumps) in the management of type 1 diabetes?

Methods

Research questions are developed by Health Quality Ontario in consultation with clinical experts, patients, health care providers, and other health system stakeholders.

Clinical Literature Search

We performed a literature search on January 24, 2017, to retrieve studies published from January 1, 2010, to the search date. We used the Ovid interface to search the following databases: MEDLINE, Embase, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Health Technology Assessment, National Health Service Economic Evaluation Database (NHSEED), and Database of Abstracts of Reviews of Effects (DARE); and we used the EBSCOhost interface to search the Cumulative Index to Nursing & Allied Health Literature (CINAHL). Medical librarians developed the search strategies using controlled vocabulary (i.e., Medical Subject Headings) and relevant keywords. The final search strategy was peer reviewed using the PRESS Checklist.[16] We created database auto-alerts in MEDLINE, Embase, and CINAHL and monitored them for the duration of the health technology assessment review, until February 28, 2017.

We performed targeted grey literature searching of health technology assessment agency sites and clinical trial registries. See Appendix 1 for the literature search strategies, including all search terms.

Clinical experts and manufacturers suggested that since continuous glucose monitoring technology has evolved over time, the cut-off year for our literature search should be 2010.

Literature Screening

A single reviewer reviewed the abstracts and, for those studies meeting the eligibility criteria, we obtained full-text articles.

Types of Studies

We included randomized, controlled studies and observational studies that examined (1) the effectiveness of standalone continuous glucose monitors compared with standalone self-monitoring of blood glucose or (2) the effectiveness of continuous glucose monitors integrated with insulin pumps compared with insulin self-management strategies involving insulin pumps or multiple daily injections.

We did not include before-after studies, editorials, case series, or commentaries.

Types of Participants

We included studies of patients with type 1 diabetes. We also considered subgroup analyses by age category.

Types of Interventions

A continuous glucose monitor is any device that provides continuous monitoring of blood glucose, with the results available at any time for patient review. This device may be used alone in conjunction with an insulin pump or multiple daily injections, or it may be integrated into an insulin pump (sensor-augmented pump). Continuous glucose monitors may include additional features, such as high/low glucose alarms or a low glucose suspend option (for sensor-augmented pumps).

Types of Settings

We considered the outpatient setting, with devices used by patients to support management of their blood glucose levels.

Types of Outcome Measures

- Time-related glucose variability: The time a patient spends inside (or outside) the target glucose range is usually preferred to A1C as a measurement of overall glucose management, because A1C can be misleading. Patients may spend their day swinging between high and low blood glucose levels; using A1C, which measures the 3-month blood glucose average, may mask this variability
- Hypoglycemia: Hypoglycemia is categorized by severity. Hypoglycemia occurs when blood glucose levels fall below 4 mmol/L. Severe hypoglycemia is associated with adverse outcomes for patients. Severe outcomes require the assistance of another person and include seizure, loss of consciousness, and hospitalization
- A1C levels: Despite the limitations of A1C (see above), it is commonly used by researchers to evaluate diabetes management. It can provide a good indication of long-term blood glucose levels, since blood cells survive in the body for 3 to 4 months. Diabetes Canada recommends that A1C levels not exceed 7.0%[6]
- User satisfaction: We considered patient satisfaction, with a preference for validated measures of overall satisfaction and health-related quality of life. We also included parent or guardian satisfaction where available

Data Extraction

We extracted relevant data on study characteristics and risk-of-bias items. We used a data form to collect study information about:

- Sources (i.e., citation information, contact details, study type)
- Characteristics of participants, interventions, and comparators
- Methods (i.e., study design, study duration in years, participant allocation, allocation sequence concealment, blinding, reporting of missing data, reporting of outcomes, and whether the study compared two or more groups)
- Outcomes (i.e., outcomes measured, number of participants for each outcome, number of participants missing for each outcome, outcome definition and source of information,

unit of measurement, upper and lower limits [for scales], and times at which outcomes were assessed)

We contacted study authors for clarification as needed.

Health Equity

During scoping, we did not identify any reported health inequities in relation to continuous glucose monitoring for patients with type 1 diabetes. Nonetheless, whenever available, we have reported distributional characteristics for people likely to be affected by equity, as outlined in PROGRESS-Plus.[17]

Statistical Analysis

Analysis was done using Review Manager.[18] We did not conduct meta-analyses because of heterogeneity in the populations, interventions, and outcomes reported in the included studies. Instead, we have presented narrative syntheses. Where specific outcomes reported were consistent across included studies, we used forest plots for visual purposes, but did not pool estimates. Wherever possible, we reported effect sizes, along with 95% confidence intervals.

Quality of Evidence

We evaluated the quality level of the evidence for each outcome according to the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) guidelines.[19,20]. We then rated the studies based on the following considerations: risk of bias, inconsistency, indirectness, imprecision, publication bias, magnitude of effect, and dose-response gradient. We determined the overall quality to be high, moderate, low, or very low using a step-wise, structural methodology. The quality level reflects our certainty about the evidence.

We assessed the risk of bias for each study individually using the Cochrane Risk of Bias Tool to assess randomized controlled trials, and the Risk of Bias Assessment Tool for Non-randomized Studies (RoBANS) for observational studies (Appendix 2).[21,22]

Expert Consultation

Throughout this project, we sought expert consultation on the use of continuous glucose monitoring. Experts consulted included physicians who specialize in endocrinology and diabetes, in both adult and pediatric populations. We also consulted people from industry, specifically Medtronic and Dexcom representatives. The roles of the expert advisors were to inform us of the appropriate use of the technology, contextualize the evidence, and provide insight for our health technology assessment.

Results

Literature Search

The literature search yielded 2,234 citations published between January 1, 2010, and January 24, 2017, after removing duplicates. We reviewed titles and abstracts to identify potentially relevant articles. We obtained the full texts of these articles for further assessment. We searched the reference lists of the included studies, along with health technology assessment websites and other sources, to identify additional relevant studies. Eight citations were added, and 20 full text studies were included in the narrative synthesis.

Figure 1 presents the flow diagram for the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA).

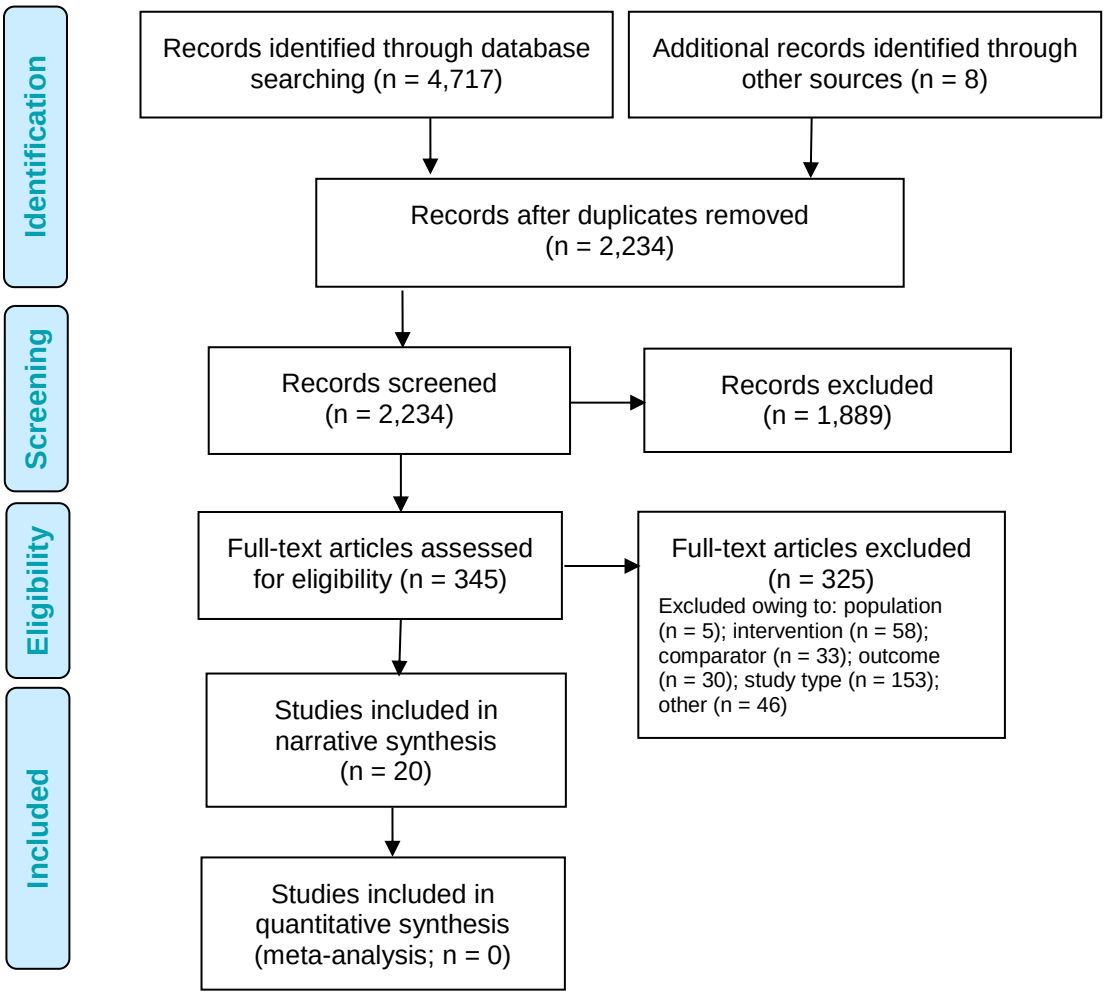

Figure 1: PRISMA Flow Diagram—Clinical Search Strategy

Abbreviation: PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.
Source: Adapted from Moher et al.[23]

Details of the included studies are summarized in Table 3. The studies varied by continuous glucose monitoring device, inclusion criteria, patient age, and follow-up period. We identified 16 randomized controlled trials[24-39] and four observational studies.[40-43] Four studies exclusively focused on pediatric populations.[26,29,34,37]

Table 3: Summary of Included Studies

Author, Year Setting	Study Design (Trial Name)[a] CGM Device	Recruitment Period	Inclusion Criteria					Sample Size, I/C	Intervention	Control	Study Period
			Age, y	Diagnosis	Glucose Control	Insulin Therapy	Other				
Beck et al, 2017[24] United States 24 sites	RCT (DIAMOND) Dexcom G4	October 2014–May 2016	≥ 25	Type 1 diabetes > 1 year	A1C between 7.5% and 10.0%	MDI	Not pregnant	105/53	CGM	SMBG	24 weeks
Bergenstal et al, 2010[25] United States and Canada 30 sites	RCT (STAR 3) Medtronic MiniMed Paradigm REAL-Time	January 2007–December 2008	1–70	Type 1 diabetes ≥ 3 months	A1C between 7.4% and 9.5%	MDI	NA	244/241	SAP	MDI with SMBG	1 year
Bukara-Radujkovic et al, 2011[26] Bosnia and Herzegovina 1 site	RCT Medtronic MiniMed	2006–2007	5–18	Type 1 diabetes ≥ 1 year	A1C ≥ 8%	MDI	NA	40/40	CGM	SMBG	6 months
Hermanides et al, 2011[27] Europe 8 sites	RCT Medtronic MiniMed Paradigm REAL-Time	April 2007–January 2009	18–65	Type 1 diabetes ≥ 1 year	A1C ≥ 8.2%	MDI	NA	43/35	SAP	MDI with SMBG	26 weeks
Hommel et al, 2014[28] Europe 8 sites	RCT, crossover (SWITCH) Medtronic MiniMed Paradigm REAL-Time	January 2008–July 2010	6–70	Type 1 diabetes ≥ 1 year	A1C between 7.5% and 9.5%	CSII > 6 months	CGM-naïve	153 (total sample size)	Sensor on	Sensor off	17 months
Kordonouri et al, 2012[29] Europe 5 sites	RCT (ONSET) Medtronic MiniMed Paradigm REAL-Time	February 2007–October 2008	1–16	Type 1 diabetes ≥ 1 year	NR	CSII	NA	80/80	SAP	CSII with SMBG	1 year

Author, Year Setting	Study Design (Trial Name)[a] CGM Device	Recruitment Period	Inclusion Criteria					Sample Size, I/C	Intervention	Control	Study Period
			Age, y	Diagnosis	Glucose Control	Insulin Therapy	Other				
Langeland et al, 2012[30] Norway 1 site	RCT, crossover Medtronic MiniMed Guardian REAL-Time	January 2009–March 2009	18–50	Type 1 diabetes > 3 years	A1C between 7% and 10%	MDI or CSII	> 1 serious hypoglycemic event in previous 6 months Untreated concomitant disease	30 (total sample size)	CGM	SMBG	20 weeks; 4 weeks of intervention, 8 weeks of washout before crossover
Lind et al, 2017[31] Sweden 15 sites	RCT, crossover (GOLD) Dexcom G4	February 2014–June 2016	≥ 18	Type 1 diabetes > 1 year	A1C ≥ 7.5%	MDI	NA	142 (total sample size)	CGM	Usual care	26 weeks of intervention, 17 weeks of washout before crossover
Little et al, 2014[32] United Kingdom 5 sites	RCT, 2 × 2 crossover (Hypo-COMPaSS) Medtronic REAL-Time	NR	18–74	Type 1 diabetes, C-peptide negative	Impaired hypoglycemia awareness	NR	NA	96 (total sample size)	CGM with MDI CGM with CSII	SMBG with MDI SMBG with CSII	24 weeks
Ly et al, 2013[33] Australia[b]	RCT Medtronic Paradigm Veo	December 2009–January 2012	4–50	Type 1 diabetes	Hypoglycemia unawareness/ impaired awareness	CSII > 6 months	Not pregnant	46/49	SAP with low glucose suspend	CSII with SMBG	6 months
McQueen et al, 2014[40] United States 1 site	Retrospective cohort Medtronic MiniMed Paradigm REAL-Time or Dexcom device	2006–2011	≥ 18	Type 1 diabetes	NR	NR	Not pregnant	66/67	CGM with SMBG	SMBG	Up to 10 months
Olivier et al, 2014[34] Canada 2 sites	Pilot RCT Medtronic MiniMed Paradigm REAL-Time	February 2009–January 2011	5–18	Type1 diabetes ≥ 1 year	NR	Injection therapy	NA	10/10	CGM with CSII	CSII with delayed CGM	4 months

Author, Year Setting	Study Design (Trial Name)[a] CGM Device	Recruitment Period	Inclusion Criteria					Sample Size, I/C	Intervention	Control	Study Period
			Age, y	Diagnosis	Glucose Control	Insulin Therapy	Other				
Quiros et al, 2015[41] Europe 8 sites	Retrospective observational study of RCT (SWITCH) Medtronic MiniMed Paradigm REAL-Time	January 2008–July 2010	6–70	Type 1 diabetes ≥ 1 year	A1C between 7.5% and 9.5%	CSII > 6 months	NA	20 (total sample size)	SAP	CSII	3 years
Radermecker et al, 2010[42] Belgium 1 site	Prospective observational controlled trial Medtronic Guardian REAL-Time	NR	Adults	Type 1 diabetes ≥ 1 year	≥ 6 capillary glucose recordings of < 60 mg/dL in 14 days	CSII > 1 year	NA	13 (total sample size)	CGM	SMBG	12 weeks
Rosenlund et al, 2015[35] Denmark 2 sites	RCT Medtronic MiniMed Paradigm Veo	February 2012–December 2014	18–75	Type 1 diabetes	A1C ≥ 7.5%	MDI	GFR at least 45 mL/min/1.73 m^2 No other concomitant disease; no pregnancy	26/29	SAP	MDI with SMBG	1 year
Rubin and Peyrot, 2012[36] United States and Canada 30 sites	RCT (STAR 3) Medtronic MiniMed Paradigm REAL-Time	January 2007–December 2008	7–70	Type 1 diabetes ≥ 3 months	A1C between 7.4% and 9.5%	MDI	< 2 hypoglycemic events in previous year Not pregnant	243/238	SAP	MDI with SMBG	1 year
Slover et al, 2012[37] United States and Canada 30 sites	RCT (STAR 3) Medtronic MiniMed Paradigm REAL-Time	January 2007–December 2008	7–18	Type 1 diabetes ≥ 3 months	A1C between 7.4% and 9.5%	MDI	< 2 hypoglycemic events in previous year	78/78	SAP	MDI with SMBG	1 year
Soupal et al, 2016[43] Czech Republic 1 site	Prospective controlled trial Medtronic MiniMed Paradigm Veo	NR	> 18	Type 1 diabetes > 2 years	A1C between 7% and 10%	MDI or CSII	No concomitant disease; not pregnant or planning pregnancy	27/38	SAP CGM with MDI	SMBG with CSII SMBG with MDI	52 weeks

Author, Year Setting	Study Design (Trial Name)[a] CGM Device	Recruitment Period	Inclusion Criteria					Sample Size, I/C	Intervention	Control	Study Period
			Age, y	Diagnosis	Glucose Control	Insulin Therapy	Other				
Tumminia et al, 2015[38] Italy 1 site	RCT, crossover Medtronic MiniMed Guardian REAL-Time	January–March 2012	18–60	Type 1 diabetes	A1C > 8%	MDI or CSII	Middle-class socioeconomic status; no concomitant disease; not pregnant or planning pregnancy	20 (total sample size)	CGM	SMBG	14 months; 6 months of intervention, 2 months of washout before crossover
van Beers et al, 2016[39] Netherlands 2 sites	RCT (IN CONTROL) Medtronic MiniMed Paradigm Veo	March 2013–February 2014	18–75	Type 1 diabetes	Impaired hypoglycemia awareness	CSII or MDI	No concomitant disease; not pregnant	26/26	CGM	SMBG	44 weeks; 16 weeks of intervention, 12 weeks of washout before crossover

Abbreviations: A1C, glycated hemoglobin; CGM, continuous glucose monitoring; CSII, continuous subcutaneous insulin infusion (insulin pump); GFR, glomerular filtration rate; I/C, intervention/control; MDI, multiple daily injections; NA, not applicable; NR, not reported; RCT, randomized controlled trial; SAP, sensor-augmented pump; SMBG, self-management of blood glucose.

[a]Some studies have been given a trial nickname; where that exists, it has been listed to help identify multiple publications on the same study.

[b]Number of sites not provided.

Results for Time-Related Glucose Variability

We examined glucose variability as a measure of time spent in or out of the target glycemic (normoglycemic) range. Results for time spent in the target glycemic range are presented in Table 4. Results from two randomized controlled trials favoured continuous glucose monitoring over control.

Table 4: Results for Time Spent in Target Glycemic Range

Author, Year	Measure of Glucose Variability	Results[a]		Difference[a]	*P*-value[a]
		Intervention	Control		
Adult Population, RCTs					
Beck et al, 2017[24]	Mean minutes per day within the target range of 70–180 mg/dL	736 (SE 7.59) Change from baseline: +76 min	650 (SE 7.61) Change from baseline: 0 min	Adjusted mean difference: 77 (99% CI 6–147)	.005
van Beers et al, 2016[39]	Mean % time spent in normoglycemia (4.0–10.0 mmol/L)	65.0 (95% CI 62.8–67.3)	55.4 (95% CI 53.1–57.7)	9.6 (95% CI 8.0–11.2)	< .01
Adult Population, Observational Study					
Soupal et al, 2016[43]	Mean % time spent between 4.0 and 10.0 mmol/L	69 (SE 2.12)	59 (SE 2.46)	10 (95% CI 6.75–13.25)	Study authors reported difference as not significant[b]

Abbreviations: CI, confidence interval; RCT, randomized controlled trial; SE, standard error.
[a]CIs, *P*-values, and SE were calculated by the authors of this health technology assessment.
[b]Repeated calculations conducted by the authors of this health technology assessment yielded a significant *P*-value.

The quality of the evidence for time spent in the target glycemic range was moderate for the randomized controlled trials and very low for the observational study. Details of the GRADE assessment can be found in Appendix 2.

Table 5 summarizes the findings for studies that evaluated time spent outside the target glycemic range. Overall, results favoured continuous glucose monitoring over control.

Table 5: Results for Time Spent Outside of Target Glycemic Range

Author, Year	Measure of Glucose Variability	Results		Difference	*P*-value
		Intervention	Control		
Time Spent in Hypoglycemic Range, Adult Population, RCTs					
Beck et al, 2017[24a]	Median minutes per day in hypoglycemia (< 60 mg/dL)	20 (IQR 9–30)	40 (IQR 16–68)	–20	.002[b]
Hermanides et al, 2011[27]	Mean % of time in hypoglycemia (< 4.0 mmol/L)	2.7 (SE 0.53)	2.5 (SE 0.6)	LSM difference at baseline and end of study: 0.2 (95% CI –1.6 to 1.7)	.96
Ly et al, 2013[33a]	Median % of time in hypoglycemia (< 60 mg/dL)	Day[c]: 1.5 (IQR 0.9–3.7) Night[c]: 2.4 (IQR 0.4–5.3)	Day[c]: 3.3 (IQR 1.6–5.9) Night[c]: 6.2 (IQR 4.2–9.9)	Day[c]: −1.8 Night[c]: −3.8	Day[c]: .01[b] Night[c]: < .001[b]
van Beers et al, 2016[39a]	Mean hours per day in hypoglycemia (≤ 3.9 mmol/L)	1.6 (95% CI 1.3–2.0)	2.7 (95% CI 2.4–3.1)	Mean difference −1.1 (95% CI −1.4 to −0.8)	< .001
Time Spent in Hyperglycemic Range, Adult Population, RCTs					
Beck et al, 2017[24a]	Median minutes per day in hyperglycemia (> 250 mg/dL)	223 (IQR 128–383)	347 (IQR 241−429)	−124	< .001[b]
Hermanides et al, 2011[27]	Mean % of time in hyperglycemia (> 11.1 mmol/L)	21.6 (SE 1.91)	38.2 (SE 3.58)	LSM difference between groups at baseline and end of study: −17.3 (95% CI −25.1 to −9.5)	< .001

Abbreviations: CI, confidence interval; IQR, interquartile range; LSM, least square mean; RCT, randomized controlled trial; SE, standard error.
[a]Select results are presented; additional thresholds and permutations of similar results are available in the original study.
[b]Authors reported the *P*-value for the mean difference; the comparison is for the median difference.
[c]Day, 6 a.m. to 10 p.m.; night, 10 p.m. to 6 a.m.

The quality of the evidence for time spent outside the target glycemic range was moderate for the randomized controlled trials in adults. Details of the GRADE assessment can be found in Appendix 2.

Results for Hypoglycemia

Table 6 summarizes the results for hypoglycemia and severe hypoglycemia. Because of variations in how hypoglycemia was reported between studies, it was difficult to develop a summary conclusion. However, in general there did not seem to be a substantial difference in hypoglycemic outcomes between the continuous glucose monitoring groups and the control groups in both adult and pediatric populations.

Table 6: Results for Hypoglycemia

Author, Year	Measure of Hypoglycemia	Results		Difference	*P*-value
		Intervention	Control		
Adult Population, RCTs					
Bergenstal et al, 2010[25]	AUC of rate of patients having blood glucose < 50 mg/dL per day	0.02 (SE 0.03)[a]	0.03 (SE 0.07)[a]	−0.01 (SE 0.003)[a]	.16[b]
Hermanides et al, 2011[27]	Mean number of hypoglycemic episodes (< 4.0 mmol/L) per day	0.7 (SE 0.11)[a]	0.6 (SE 0.12)[a]	0.1 (95% CI −0.2 to 0.5)[a]	.40
Langeland et al, 2012[30]	Mean number of hypoglycemic episodes (≤ 3.1 mmol/L) per 4 weeks	8.2 (SE 0.41)[a]	7.3 (SE 0.36)[a]	0.9 (95% CI 0.85–0.95)[a]	.67[c]
Tumminia et al, 2015[38]	AUC of rate of patients having blood glucose < 70 mg/dL per day	Owing to concerns with the statistical analyses, results are not reported[d]			NS
Adult Population, Observational Studies					
Radermecker et al, 2010[42]	Mean decrease from baseline in number of hypoglycemic episodes (< 60 mg/dL) per 14 days	6.2 (95% CI 2.2–10.2)	0.67 (95% CI −4.7 to 6.0)	Mean difference 5.3 (95% CI −0.49 to 11.55)[a]	.85[a]
Soupal et al, 2016[43]	Mean reduction of % time spent in hypoglycemia	6 (SE 0.87)[a]	7 (SE 1.18)[a,e]	−1 (SE 2.39)[d]	.68
Pediatric Population, RCTs					
Bergenstal et al, 2010[25]	AUC of rate of patients having blood glucose < 50 mg/dL	Owing to concerns with the statistical analyses, results are not reported[d]			.64
Bukara-Radujkovic et al, 2011[26]	Difference in average number of hypoglycemic episodes (< 3.5 mmol/L) per day	0.223	0.175	0.048	NR
Slover et al, 2011[37]	AUC of rate of patients having blood glucose < 60 mg/dL per day (change from baseline)[e]	Age 7–12: 0.05 (SD 0.08)	Age 7–12: 0.03 (SD 0.06)	Age 7–12: 0.02 (SD 0.16)	Age 7–12: .05
		Age 13–18: −0.05 (SD 0.08)	Age 13–18: −0.05 (SD 0.09)	Age 13–18: 0 (SD 0.15)	Age 13–18: .87

Abbreviations: AUC, area under the curve; CI, confidence interval; NR, not reported; NS, not significant; RCT, randomized controlled trial; SD, standard deviation; SE, standard error.
[a]Calculations for SE and CI were conducted by the authors of this health technology assessment.
[b]The reported *P*-value was adjusted for baseline differences, but the SE is for the unadjusted difference.
[c]We could not replicate results for this *P*-value based on the methods and data reported by the authors.
[d]Data were skewed, but the authors used statistical methods that are valid only under a symmetric assumption. Statistical results were questionable.
[e]The study included both patients on insulin pumps and those on multiple daily injections, but these results were for only patients on multiple daily injections.

The quality of the evidence for hypoglycemia was low for the randomized controlled trials in adults, and very low for the observational studies in adults and randomized controlled trials in children. Details of the GRADE assessment can be found in Appendix 2.

Table 7 summarizes findings for severe hypoglycemic events. Results were generally in favour of continuous glucose monitoring.

Table 7: Results for Severe Hypoglycemic Events

Author, Year	Measure of Severe Hypoglycemic Events	Results		Difference	*P*-value
		Intervention	Control		
Adult Population, RCTs					
Little et al, 2014[32]	Severe hypoglycemia requiring the assistance of another person, annualized rate	0.8 (SD 1.8)	0.9 (SD 2.1)	−0.1 (SD 3.63)	.95
Ly et al, 2013[33a]	Severe hypoglycemia, including seizure or coma, 6-month rate per 100 patient-months (change from baseline)	−1.8	0.1	−1.5 (95% CI −2.7 to −0.3)[a]	.02[b]
van Beers et al, 2016[39]	Number of severe hypoglycemic events	14	34	−20	.033[b]

Abbreviations: CI, confidence interval; RCT, randomized controlled trial; SD, standard deviation.
[a]Results generated from a statistical model.
[b]Computed using a nonparametric statistical test.

The quality of the evidence for severe hypoglycemic events was low for the randomized controlled trials in adults. Details of the GRADE assessment can be found in Appendix 2.

Results for A1C Levels

Studies comparing average A1C levels reported results in two ways: change in average A1C levels from baseline, and average A1C levels at the end of the study. The former approach accounts for baseline differences in A1C levels; as a result, our assessment focused only on results derived using this approach. Results for the difference in change in blood glucose levels from baseline to end of study are summarized in Figure 2.

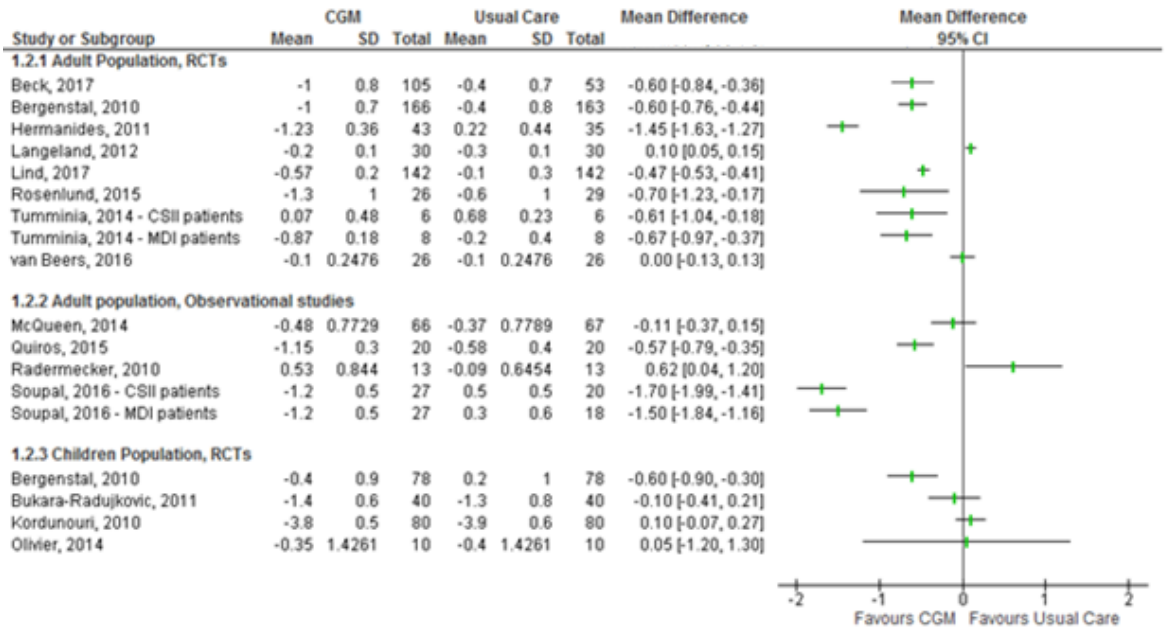

Figure 2: Changes in A1C from Baseline to End of Study

Abbreviations: A1C, glycated hemoglobin; CGM, continuous glucose monitoring; CI, confidence interval; CSII, continuous subcutaneous insulin infusion (insulin pump); MDI, multiple daily injections; RCT, randomized controlled trial; SD, standard deviation.
Note: Olivier et al[34] and Quiros et al[41] reported results for a combined population of adults and children. Tumminia et al[38] reported a crossover design, but their analysis was based on a before-after design.

Sources: Data from Beck et al,[24] Bergenstal et al,[25] Bukara-Radujkovic et al,[26] Hermanides et al,[27] Kordonouri et al,[29] Langeland et al,[30] Lind et al,[31] McQueen et al,[40] Olivier et al,[34] Quiros et al,[41] Radermecker et al,[42] Rosenlund et al,[35] Soupal et al,[43] Tumminia et al,[38] and van Beers et al.[39]

Based on the overall results, continuous glucose monitoring led to a greater reduction in A1C levels than usual care. However, the average A1C values at the end of follow-up were higher than 7% for all studies—above the threshold set by the Diabetes Canada guidelines.[6] As a result, we do not regard the reduction in A1C observed above as clinically important. However, Beck et al[24] reported that 18% of people who used continuous glucose monitoring achieved an A1C ≤ 7.0%; only 2% of the usual care group reached this threshold.

The quality of the evidence for changes in A1C levels was moderate for randomized controlled trials in adults, low for randomized controlled trials in children, and very low for observational studies in adults. Details of the GRADE assessment can be found in Appendix 2.

Results for User Satisfaction

Of the studies that reported user satisfaction, most used well-known measures of quality of life, often measures specific to diabetes. Table 8 presents results reported in the individual studies.

Table 8: Results for User Satisfaction

Author, Year	Measure of User Satisfaction	Results		Difference	*P*-value
		Intervention	Control		
Results for Adult Population, RCTs					
Beck et al, 2017[24]	CGM satisfaction survey, mean score	4.2 (SD 0.4)	NR	NR	NR
Hermanides et al, 2011[27]	Problem areas in diabetes scale	21.0 (SD 19.3)	23.7 (SD 19.4)	LSM change from baseline: −7.9 (95% CI −15.1 to −0.61)	.03
	Hypoglycemia fear survey	24.1 (SD 20.2)	20.3 (SD 16.9)	LSM change from baseline: −3.2 (95% CI −10.0 to 3.7)	.36
	DTSQ	32.4 (SD 3.5)	23.8 (SD 6.2)	LSM change from baseline: 9.3 (95% CI 7.3–11.3)	< .001
Hommel et al, 2014[28]	DTSQ status version, overall treatment satisfaction	NR	NR	1.16	.010
Langeland et al, 2012[30]	DTSQ change version, change in total score	3.93 (SD 8.00)	5.74 (SD 5.83)	−1.81 (SD 16.14)[a]	.47
	SF-36, change in total average	−0.3 (SD 8.5)	−0.3 (SD 9.8)	0 (SD 16.14)[a]	.35
Lind et al, 2017[31]	DTSQ status version, scale total	30.21 (95% CI 29.47–30.96)	26.62 (95% CI 25.61–27.64)	3.43 (95% CI 2.31–4.54)	< .001
Little et al, 2014[32]	DTSQ total satisfaction	30 (SD 5)	30 (SD 5)	—	.79
Rubin and Peyrot, 2012[36]	SF-36, change from baseline	MCS: 0.05 PCS: 1.22	MCS: −1.26 PCS: 0.26	MCS: −1.21[a] PCS: 0.96[a]	NR NR
Results for Adult Population, Observational Studies					
Radermecker et al, 2010[42]	DQOL total score, change from baseline	−2.3 (95% CI −6.4 to 1.7)	0.7 (95% CI −2.5 to 3.8)	−3.0 (95% CI −7.67 to 1.68)[a]	.22[a]
Results for Pediatric Population, RCTs					
Hommel et al, 2014[28]	PedsQL overall health-related quality of life	NR	NR	Child self-rating: −0.31 (SD 0.84) Parent proxy rating: −3.92 (SD 1.18)[b]	Child self-rating: .84 Parent proxy rating: .002

Author, Year	Measure of User Satisfaction	Results		Difference	*P*-value
		Intervention	Control		
Kordonouri et al, 2012[29]	KIDSCREEN-27 psychological well-being	Child self-report: 50.4 (SD 9.2) Proxy/parent: 47.8 (SD 9.3)	Child self-report: 50.3 (SD 10.8) Proxy/parent: 48.6 (SD 10.3)	Child self-report: 0.1 (SD 18.56)[a] Proxy/parent: −0.8 (SD 18.74)[a]	Child self-report: .905 Proxy/parent: .826
Olivier et al, 2014[34]	DTSQ change in total score	NR	NR	−9 (95% CI −16 to −1)	.02
Rubin and Peyrot, 2012[36]	PedsQL overall score, change from baseline	Child self-report: 0.33 Caregiver: 40.19	Child self-report: 1.19 Caregiver: 5.07	Child self-report: 29.14 Caregiver: 35.12	Child self-report: .001 Caregiver: < .001

Abbreviations: CGM, continuous glucose monitoring; CI, confidence interval; DQOL, Diabetes Quality of Life [questionnaire]; DTSQ, Diabetes Treatment Satisfaction Questionnaire; LSM, least square mean; MCS, mental composite score; NR, not reported; PCS, physical composite score; PedsQL, pediatric quality of life inventory; RCT, randomized controlled trials; SD, standard deviation; SF-36, 36-Item Short Form Health Survey.

[a]Results calculated based on information published in original studies.

[b]Publication noted that this was not a clinically meaningful difference.

Results were inconsistent across studies, probably reflecting differences in types of outcomes and survey tools. Therefore, we rated the quality of the evidence for user satisfaction as low for randomized controlled trials in adults and children, and very low in observational studies in adults. Details of the GRADE assessment can be found in Appendix 2.

Summary

We included 20 studies that reported on the use of continuous glucose monitors (as standalone devices or integrated with insulin pumps) compared with usual care. Usual care was typically defined as self-monitoring of blood glucose levels using a finger-prick blood glucose meter.

We did not perform meta-analyses because of the heterogeneity of populations and interventions. All results for outcomes of interest have been summarized narratively (Table 9).

Table 9: Summary of Findings

Outcome	Finding	GRADE
Time-related glucose variability	Continuous glucose monitoring was more effective than usual care in terms of increased time spent in the target glycemic range	Moderate to very low
	Continuous glucose monitoring was more effective than usual care in terms of decreasing time spent outside the target glycemic range	Moderate
Hypoglycemia	There was no substantial difference in hypoglycemic outcomes between patients in the continuous glucose monitoring group and those in the usual care group	Low to very low
	Continuous glucose monitoring was more effective than usual care in reducing severe hypoglycemic events	Low
A1C levels	Results favoured continuous glucose monitoring over usual care in the reduction of A1C levels from baseline	Moderate to very low
User satisfaction	Findings on end-of-study user satisfaction with continuous glucose monitoring compared with usual care were inconsistent	Low to very low
	Findings on children, parent, and caregiver satisfaction with continuous glucose monitoring compared with usual care were inconsistent	Low

Abbreviations: A1C, glycated hemoglobin; GRADE, Grading of Recommendations Assessment, Development, and Evaluation.

We applied the GRADE criteria to assess the quality of evidence (Appendix 2).[19] We applied GRADE to randomized controlled trials in adult populations, observational studies in adult populations, and randomized controlled trials of child populations separately for each outcome, where reported. There were no observational studies in child populations.

Discussion

Main Findings and Clinical Relevance

Continuous glucose monitoring was more effective than self-monitoring of blood glucose for the management of type 1 diabetes, as demonstrated by outcomes such as time spent in target glucose range and severe hypoglycemic events. Interestingly, the majority of the reviewed studies were unable to demonstrate the same effect for hypoglycemia.

Studies evaluating the impact of continuous glucose monitoring on user satisfaction yielded mixed results. These findings may be partly explained by the fact that wearing a sensor or a pump may be perceived as an interruption to children's normal activities. Engaging with parents, caregivers, and children to understand the most practical way to monitor blood glucose is important for effective management of type 1 diabetes. In addition, to avoid diabetes

complications, controlling diabetes at a younger age can reduce the risk of metabolic memory,[44] a condition characterized by persistent diabetes complications despite tight glucose control. Details about parent and child preferences with regard to diabetes management in the Ontario context are provided in the Patient, Caregiver, and Public Engagement section of this health technology assessment.

We noted several limitations from the primary studies. First, studies that evaluated the effectiveness of continuous glucose monitoring in reducing hyperglycemia recruited patients with high A1C levels. A substantial decrease in A1C would have been required from the patients in these studies to meet the 7% threshold recommended by many experts and clinical practice guidelines. Although the majority of studies did demonstrate a reduction in A1C, the average decrease was not enough to meet the threshold. Second, some studies expressed concerns about missing data.[28,36,37] To address the problem, these studies imputed outcomes by carrying forward the observation from the last visit, but treated the imputed values as if they were real during analysis. In doing so, these studies may have overestimated the precision of point estimates and introduced outcome classification errors. Third, the statistical methods used in some studies[25,32,38] yielded estimates with ranges that covered implausible values. Specifically, the reported standard deviations were larger than the point estimates, suggesting that the area under the curve or the number of hypoglycemic episodes could be negative. As a result, we could not determine the true precision of the point estimates for these studies. Finally, the definition of usual care for some studies included the use of an insulin pump, a mode of insulin administration that is used less in Ontario (there are about 14,000 insulin pump users in Ontario). This means results from these studies may not accurately reflect the effectiveness of continuous glucose monitoring in Ontario, where usual care generally involves multiple daily injections. A comparison of different methods of insulin administration was beyond the scope of this health technology assessment.

Real-World Use of Continuous Glucose Monitoring

Some studies[29,31,35,39] enrolled only patients who exceeded a certain threshold of adherence with glucose monitoring; as a result, the level of adherence in the controlled setting of these studies was likely to be higher than in the general population. Several survey studies have examined adherence and reasons for discontinuation of continuous glucose monitoring in the real world.[45-49] They demonstrated that patients do not use continuous glucose monitoring 100% of the time, and that use tends to taper off over time. The main reasons reported for discontinued use were cost; discomfort with wearing the devices, including sensors falling off; and finding the alarms disruptive.

Ongoing Studies

During scoping, we identified 35 studies on clinicaltrials.gov related to continuous glucose monitoring, glycemic control, and type 1 diabetes. However, we determined that the current literature was sufficient to evaluate the clinical effectiveness of continuous glucose monitoring.

Conclusions

Based on moderate certainty in the evidence, we found that continuous glucose monitoring was more effective than self-monitoring of blood glucose in managing type 1 diabetes for some outcomes, such as time spent in target glucose range and time spent outside target glucose range. Similar findings were obtained for the outcome of severe hypoglycemic events, although there was low certainty in the evidence for this outcome.

ECONOMIC EVIDENCE

Research Question

What is the cost-effectiveness of continuous glucose monitoring compared with self-monitoring of blood glucose in patients with type 1 diabetes?

Methods

Economic Literature Search

We performed an economic literature search on January 25, 2017, for studies published from January 1, 2010, to the search date. We applied methodological filters to the clinical search to limit retrieval to economic evaluations and studies on cost, quality of life, and health utilities.[50]

Database auto-alerts were created in MEDLINE, Embase, and CINAHL and monitored for the duration of the health technology assessment review. We performed targeted grey literature searching of health technology assessment agency sites, clinical trial registries, and Tufts Cost-Effectiveness Analysis Registry. See Clinical Evidence, Literature Search, above, for further details on methods used. See Appendix 1 for literature search strategies, including all search terms.

Finally, we reviewed reference lists of included economic literature for any additional relevant studies not identified through the systematic search.

Literature Screening

A single reviewer reviewed titles and abstracts, and, for those studies meeting the eligibility criteria, we obtained full-text articles. For studies containing several comparators, we extracted only the results for the comparison of interest.

Types of Studies

We included cost-effectiveness or cost-utility analyses that compared continuous glucose monitoring with self-monitoring of blood glucose in adults and children with type 1 diabetes. We examined economic studies that fulfilled the described entry criteria and that had a follow-up time or time horizon of 1 year or greater.

We did not include abstracts, letters, editorials, unpublished studies, or noncomparative studies reporting the costs of continuous glucose monitoring.

Types of Participants

The population of interest was patients with type 1 diabetes, including those with hypoglycemia unawareness.

Types of Interventions

Continuous glucose monitoring can be performed using different devices and technologies (see Background). We looked at studies that compared self-monitoring of blood glucose plus either multiple daily injections or an insulin pump with one or more continuous glucose monitoring interventions:

- Continuous glucose monitoring plus multiple daily injections
- Continuous glucose monitoring plus insulin pump
- Sensor-augmented pump (continuous glucose monitoring integrated with an insulin pump)
- Sensor-augmented pump with a low-glucose suspend feature

Types of Outcomes Measures

We examined the following outcomes: incremental costs, incremental quality-adjusted life-years (QALYs), incremental cost-effectiveness ratios (ICERs), and incremental net benefit.

Data Extraction

We extracted relevant data on the following:

- Source (i.e., name, location, year)
- Populations and comparators
- Interventions
- Outcomes (i.e., health outcomes, costs, and ICERs)

Study Applicability and Limitations

We determined the usefulness of each identified study for decision-making by applying a modified applicability checklist for economic evaluations that was originally developed by the National Institute for Health and Care Excellence (NICE) in the United Kingdom. The original checklist is used to inform development of the institute's clinical guidelines. We modified the wording of the questions to remove references to guidelines and to make them Ontario-specific.

We separated the checklist into two sections. In the first, we assessed the applicability of the study to our research question. A summary of the studies judged to be directly applicable, partially applicable, or not applicable to the research question are shown in Appendix 3. If the study was deemed directly or partially applicable to the research question, we assessed the limitations of the study (minor, potentially serious, or very serious) using the second section of the checklist.

Results

Literature Search

The literature search yielded 256 citations published between January 1, 2010, and January 25, 2017 (with duplicates removed). We excluded a total of 243 articles based on information in the title and abstract. We then obtained the full texts of 13 potentially relevant articles for further assessment. Figure 3 presents the flow diagram for the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA).

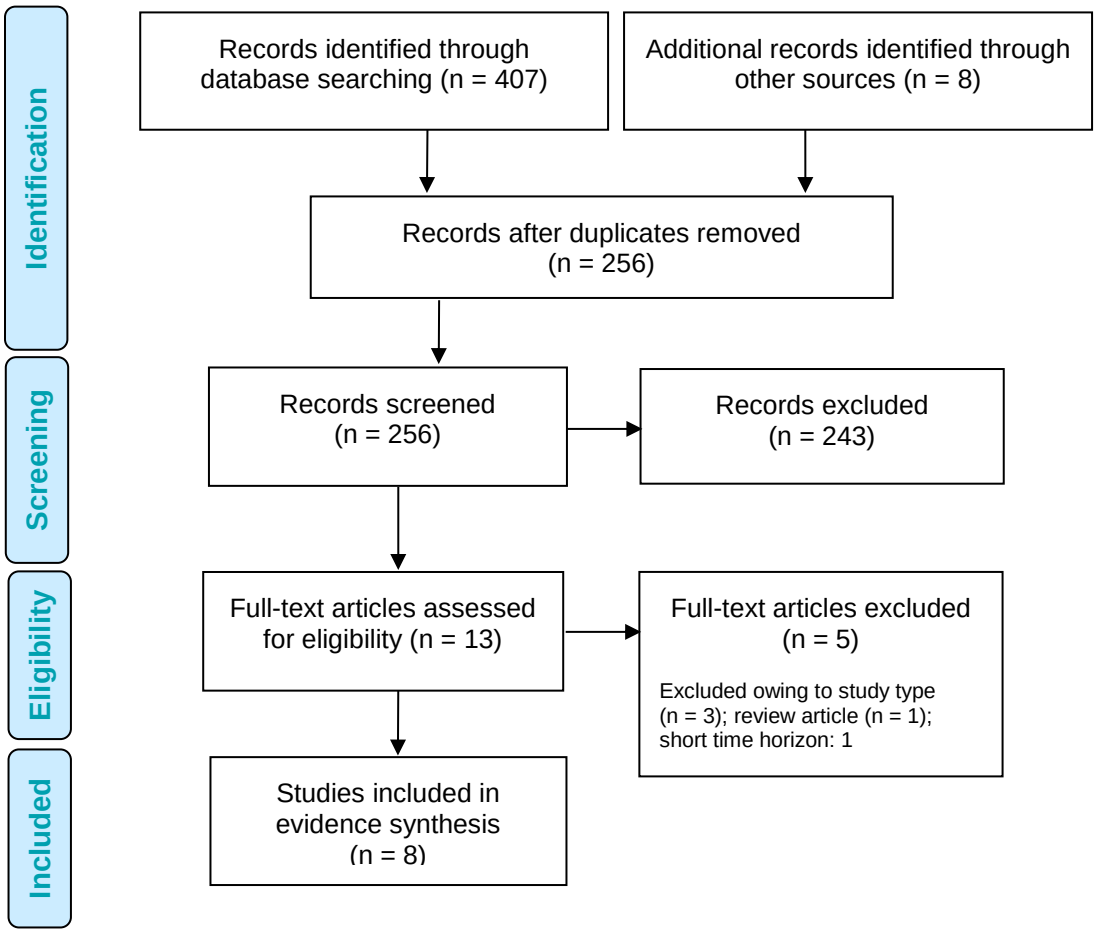

Figure 3: PRISMA Flow Diagram—Economic Search Strategy

Source: Adapted from Moher et al.[23]

Eight studies (seven cost-utility analyses[51-57] and one health technology assessment report by the National Institute for Health and Care Excellence[58]) met the inclusion criteria (Table 10). All studies were based on models. Three cost-utility analyses studies were from United States,[51,52,57] two studies were from the United Kingdom,[53,58] and one each was from Sweden,[54] France,[55] and Denmark.[56] No studies were done in children with type 1 diabetes.

We excluded five studies: one review of the economic literature,[59] one study with a 6-month time horizon,[60] and three costing studies.[61-63] The costing studies were focused on the costs of self-monitoring of blood glucose only, the implications of averting severe hypoglycemic events, and patient time spent on diabetes-related care.

Review of Included Economic Studies

Table 10: Results of the Economic Literature Review—Summary

Name, Year, Location	Study Design and Perspective	Population	Intervention/ Comparator	Results		
				Health Outcomes	Costs	Cost-Effectiveness
Huang et al, 2010,[57] United States	• Cost-utility analysis • Decision analytic model • US societal perspective • Lifetime horizon	Cohort 1: adults with T1D aged ≥ 25 years and A1C ≥ 7.0% Cohort 2: all ages with A1C ≤ 7.0%	CGM SMBG	*Cohort 1* Total QALYs: SMBG 13.75; CGM 14.35 QALYs gained: 0.60 *Cohort 2* Total QALYs: SMBG 16.69; CGM 17.80 QALYs gained: 1.11 Annual discount rate: 3%	2007 US dollars *Cohort 1* Total costs: SMBG $601,070; CGM $659,837 Incremental cost for CGM: $58,767 vs. SMBG *Cohort 2* Total costs: SMBG $2,111,539; CGM $2,198,925 Incremental cost for CGM: $87,386 vs. SMBG Annual discount rate: 3%	*Cohort 1* ICER: $98,679 per QALY gained vs. SMBG *Cohort 2* ICER: $87,386 per QALY gained vs. SMBG
Kamble et al, 2012,[52] United States	• Cost-utility analysis • Decision analytic model • US health care perspective • 60-year horizon	Adults with inadequately controlled T1D; mean age of 41.3 years; mean A1C 8.3%	SAP SMBG MDI	Total QALYs: SAP 10.794; SMBG MDI 10.418 QALYs gained: 0.376 Annual discount rate: 3%	2010 US dollars *3-day sensors* Total costs: SMBG MDI $167,170; SAP $253,493 Incremental cost for SAP: $86,324 vs. SMBG MDI *6-day sensors* Total costs: SMBG MDI $167,170; SAP $230,352 Incremental cost for SAP: $63,182 vs. SMBG MDI Annual discount rate: 3%	*3-day sensors* ICER: $229,675 per QALY gained vs. SMBG MDI *6-day sensors* ICER: $168,104 per QALY gained vs. SMBG MDI
McQueen et al, 2011,[51] United States	• Cost-utility analysis • Decision analytic model • US societal perspective • 33-year horizon	20-year history of T1D, mean age of 40 years	CGM + SMBG with intensive insulin therapy SMBG with intensive insulin therapy	Total QALYs: SMBG 10.289; CGM + SMBG 10.812 QALYs gained: 0.52 Annual discount rate: 3%	2007 US dollars Total costs: SMBG $470,583; CGM + SMBG $494,135 Incremental cost for CGM + SMBG: $23,552 vs. SMBG alone Annual discount rate: 3%	ICER: $45,033 per QALY gained vs. SMBG alone

Name, Year, Location	Study Design and Perspective	Population	Intervention/ Comparator	Results		
				Health Outcomes	Costs	Cost-Effectiveness
Riemsma et al, 2016,[58] United Kingdom	• Cost-utility analysis • Decision analytic model • UK NHS perspective • Lifetime horizon	27-year history of T1D; mean age of 42 years; 38% male	SAP SMBG MDI or SMBG CSII	*SAP vs. SMBG MDI* Total QALYs: SMBG MDI 11.4146; SAP 12.0604 QALYs gained: 0.6458 *SAP vs. SMBG CSII* Total QALYs: SMBG CSII 11.9756; SAP 12.0604 QALYs gained: 0.0849 Annual discount rate: 1.5%	2014 British pounds *SAP vs. SMBG MDI* Total costs: SMBG MDI £61,070; SAP £147,150 Incremental cost for SAP: £86,100 vs. SMBG MDI *SAP vs. SMBG CSII* Total costs: SMBG CSII £90,436; SAP £147,150 Incremental cost for SAP: £56,713 vs. SMBG CSII Annual discount rate: 3.5%	*SAP vs. SMBG MDI* ICER: £133,323 per QALY vs. SMBG MDI *SAP vs. SMBG CSII* ICER: £668,789 per QALY vs. SMBG CSII
Roze et al, 2016,[53] France	• Cost-utility analysis • Decision analytic model • UK NHS perspective • Lifetime horizon	Patients with T1D; mean age 27 years; mean duration of diabetes 13 years; mean A1C 10%	SAP LGS SMBG CSII	Total QALYs: SAP LGS 17.88; SMBG CSII 14.89 QALYs gained: 2.99 Annual discount rate: 1.5%	2013 British pounds Total costs: SAP LGS £125,559; SMBG CSII £88,991 Incremental cost for SAP LGS: £36,568 vs. SMBG CSII Annual discount rate: 3.5%	ICER: £12,233 per QALY gained vs. SMBG CSII
Roze et al, 2015,[54] France	• Cost-utility analysis • Decision analytic model • Sweden societal perspective • Lifetime horizon	Patients with T1D; mean age 27 years; mean duration of diabetes 13 years; mean A1C 8.6%	SAP SMPG CSII	Total QALYs: SAP 13.05; SMPG CSII 12.29 QALYs gained: 0.76 Annual discount rate: 3%	2013 Swedish kronor (SEK) Total costs: SAP SEK 868,897; SMPG CSII SEK 453,791 Incremental cost for SAP: SEK 415,106 vs. SMPG CSII Annual discount rate: 3%	ICER: SEK 60,332 per QALY gained vs. SMPG CSII

Name, Year, Location	Study Design and Perspective	Population	Intervention/ Comparator	Results		
				Health Outcomes	Costs	Cost-Effectiveness
Roze et al, 2016,[55] France	• Cost-utility analysis • Decision analytic model • France health care system perspective • Lifetime horizon	Patients with T1D; mean age 36 years; mean duration of diabetes 17 years; mean A1C 9.0%	SAP LGS SMBG CSII	*Uncontrolled A1C at baseline* Total QALYs: SAP LGS 10.55; SMBG CSII 9.36 QALYs gained: 1.19 *Elevated risk for hypoglycemic events* Total QALYs: SAP LGS 18.46; SMBG CSII 18.30 QALYs gained: 2.99 Annual discount rate: 4%	2014 euros *Uncontrolled A1C at baseline* Total costs: SAP LGS €84,972; SMBG CSII €49,171 Incremental cost for SAP LGS: €35,801 vs. SMBG CSII *Elevated risk for hypoglycemic events* Total costs: SAP LGS €88,680; SMBG CSII €57,097 Incremental cost for SAP LGS: €31,583 vs. SMBG CSII Annual discount rate: 4%	*Uncontrolled A1C at baseline* ICER: €30,163 per QALY gained vs. SMBG CSII *Elevated risk for hypoglycemic events* ICER: €22,005 per QALY gained vs. SMBG CSII
Roze et al, 2017,[56] France	• Cost-utility analysis • Decision analytic model • Denmark societal perspective • Lifetime horizon	Cohort 1: people with T1D and hyperglycemia (baseline A1C 8.1%) Cohort 2: people with T1D at increased risk for hypoglycemic events (owing to impaired awareness of hypoglycemia)	SAP LGS SMBG CSII	*Cohort 1* Total QALYs: SAP LGS 12.44; SMBG CSII 10.99 QALYs gained: 1.45 *Cohort 2* Total QALYs: SAP LGS 13.08; SMBG CSII 11.20 QALYs gained: 1.88 Annual discount rate: 3%	2015 Danish kroner (DKK) *Cohort 1* Total costs: SAP LGS DKK 2,027,316; SMBG CSII DKK 1,801,293 Incremental cost for SAP LGS: DKK 226,023 vs. SMBG CSII *Cohort 2* Total costs: SAP LGS DKK 2,277,868; SMBG CSII DKK 2,109,186 Incremental cost for SAP LGS: DKK 168,682 vs. SMBG CSII Annual discount rate: 3%	*Cohort 1* ICER: DKK 156,082 per QALY gained vs. SMBG CSII *Cohort 2* ICER: DKK 89,868 per QALY gained vs. SMBG CSII

Abbreviations: A1C, glycated hemoglobin; CGM, continuous glucose monitoring; CSII, continuous subcutaneous insulin infusion (insulin pump); ICER, incremental cost-effectiveness ratio; LGS, low-glucose suspend [feature]; MDI, multiple daily injections; NHS, National Health Service; QALY, quality-adjusted life-year; SAP, sensor-augmented pump; SMBG, self-monitoring of blood glucose; SMPG, self-monitoring of plasma glucose; T1D, type 1 diabetes.

Applicability and Limitations of the Included Studies

We assessed the methodological quality of the included studies using an applicability checklist (Appendix 3).

All studies were deemed partially applicable to our research question, because they were partially similar to our base case population and comparators. However, we found no studies that evaluated continuous glucose monitoring from the perspective of Ontario's public health care payer, so the results could not be directly translated to the Ontario context.

All studies included important outcomes related to continuous glucose monitoring and insulin infusion. All studies except those by McQueen et al[51] and Riemsma et al[58] were sponsored by device manufacturers.

All eight studies had important limitations, including the estimation of transition probabilities and treatment effects from various study populations. Also, they did not fully capture hypoglycemic events and two did not specify the use of insulin infusion. The majority of the studies used the Center for Outcomes Research and Evaluation model, which was based on the Diabetes Control and Complications Trial[64] and the United Kingdom Prospective Diabetes Study,[65] and was developed to reflect the natural history of type 1 diabetes.

Discussion

Of the eight eligible studies:

- Two did not specify insulin infusion methods[51,57]
- Three compared continuous glucose monitoring plus a sensor-augmented pump with self-monitoring of blood glucose plus either multiple daily injections[52,58] or insulin pump therapy[54,58]
- Three compared continuous glucose monitoring plus a low-glucose suspend feature with self-monitoring of blood glucose plus insulin pump therapy[53,55,56]

McQueen et al[51] evaluated the cost-effectiveness of continuous glucose monitoring plus self-monitoring of blood glucose versus self-monitoring of blood glucose alone. Both interventions were accompanied by intensive insulin therapy. Inputs to their economic model were obtained mainly from the Diabetes Control and Complications Trial,[64] the UK Prospective Diabetes Study,[65] and the Wisconsin Epidemiologic Study of Diabetic Retinopathy.[66]

Huang et al[57] evaluated the cost-effectiveness of continuous glucose monitoring versus self-monitoring of blood glucose. The authors based their effectiveness data on the Juvenile Diabetes Research Foundation continuous glucose monitoring trials[67-69] and the Diabetes Control and Complications Trial,[64] and they took information on diabetes complications from a modelling study of type 2 diabetes.[70] The authors concluded that continuous glucose monitoring was cost-effective for an adult population aged ≥ 25 years with A1C levels ≥ 7.0%, assuming a willingness-to-pay threshold of $100,000 USD/QALY gained. Continuous glucose monitoring was more cost-effective for all age groups with A1C levels ≤ 7.0%.[57] They found that if the benefits of continuous glucose monitoring were not extended long-term, the ICER would exceed $700,000 USD/QALY gained and would not be cost-effective at commonly used thresholds.

Riemsma et al[58] evaluated the cost-effectiveness of several technologies, including continuous glucose monitoring integrated with a sensor-augmented pump; self-monitoring of blood glucose

plus multiple daily injections; and self-monitoring of blood glucose plus an insulin pump. They obtained short-term effectiveness data on continuous glucose monitoring from a meta-analysis of 19 clinical trials and long-term effectiveness data from the Diabetes Control and Complications Trial,[64] the UK Prospective Diabetes Study,[65] and other literature sources (this meta-analysis was not applicable to the clinical evidence review in this health technology assessment). The authors found that continuous glucose monitoring with a sensor-augmented pump was not cost-effective compared to self-monitoring of blood glucose plus either multiple daily injections or an insulin pump. The study assumed treatment effects to be the mean reduction in A1C from baseline to 12 months. The report concluded that self-monitoring of blood glucose plus multiple daily injections was the most cost-effective option, given the current United Kingdom threshold of £30,000 GBP/QALY gained.[58]

Kamble et al[52] evaluated the cost-effectiveness of continuous glucose monitoring plus a sensor-augmented pump compared with self-monitoring of blood glucose plus multiple daily injections. The authors derived the efficacy of continuous glucose monitoring with a sensor-augmented pump from the STAR 3 adult cohort.[25] They found that continuous glucose monitoring with a sensor-augmented pump did not represent good value for money in adults when considering (1) the significant and ongoing costs associated with continuous glucose monitoring; and (2) the costs of long-term complications in relation to the expected health benefits of 0.376 QALYs.

Roze et al evaluated the cost-effectiveness of continuous glucose monitoring compared with self-monitoring of plasma glucose plus insulin pump therapy. They performed four studies, from the perspectives of the United Kingdom,[53] Sweden,[54] France,[55] and Denmark.[56] All but one[54] used continuous glucose monitoring with a low-glucose suspend feature. The authors used the Center for Outcomes Research and Evaluation diabetes model to determine the cost-effectiveness of continuous glucose monitoring over a lifetime horizon. They derived the clinical effectiveness of continuous glucose monitoring from a patient-level meta-analysis[71] and a Swedish observational study on type 2 diabetes.[72] Overall, the conclusion from all four economic evaluations was that continuous glucose monitoring was likely to be cost-effective compared with self-monitoring of blood glucose and insulin pump therapy.

Overall, the results from the economic evidence review were mixed. McQueen et al[51] demonstrated the cost-effectiveness of continuous glucose monitoring versus self-monitoring of blood glucose (when both interventions were accompanied by intensive insulin therapy, type not specified) at an empirical threshold of $50,000 USD/QALY gained. However, the authors may have modelled a constant decreasing rate of complications from the start of continuous glucose monitoring to approximately 33 years, resulting in relatively favourable ICER values.

Huang et al[57] also demonstrated the cost-effectiveness of continuous glucose monitoring versus self-monitoring of blood glucose, but for a much higher empirical threshold of $100,000 USD/QALY gained, which might not be applicable to Canadian settings. As well, the authors did not specify the method of insulin infusion and found considerable uncertainties around the ICER.

Economic evaluations by Roze et al also demonstrated the cost-effectiveness of continuous glucose monitoring with a low-glucose suspend feature versus self-monitoring of blood glucose and insulin pump from the perspectives of the United Kingdom,[53] Sweden,[54] France,[55] and Denmark.[56]

In contrast, Riemsma et al[58] showed that newer technologies—standalone continuous glucose monitoring and sensor-augmented pumps—were not cost-effective compared with the current standard of self-monitoring of blood glucose plus multiple daily injections.

Lastly, Kamble et al[52] found unfavourable cost-effectiveness results for a sensor-augmented pump versus self-monitoring of blood glucose plus multiple daily injections.

We found no economic evaluations of continuous glucose monitoring in children with type 1 diabetes.

Conclusions

The economic evidence showed mixed results when comparing continuous glucose monitoring with self-monitoring of blood glucose. All studies indicated that continuous glucose monitoring was more effective but also more costly. No studies were conducted in children with type 1 diabetes. No study was conducted from the Ontario or Canadian health care perspective, and many had methodological limitations and uncertainties in the results.

PRIMARY ECONOMIC EVALUATION

The published economic evaluations identified in the economic evidence review addressed our interventions of interest, but none of them took a Canadian perspective. Owing to these limitations, we conducted a primary economic evaluation.

Research Question

What is the cost-effectiveness of continuous glucose monitoring compared with self-monitoring of blood glucose in adult patients with type 1 diabetes from the perspective of the Ontario Ministry of Health and Long-Term Care?

Methods

The information presented in this report follows the reporting standards set out by the Consolidated Health Economic Evaluation Reporting Standards statement.[73]

Type of Analysis

We performed cost-utility and cost-effectiveness analyses. Our cost-effectiveness analysis assessed the cost per life-year saved. Our cost-utility analysis assessed the cost per QALY gained.

Target Population

The target population was adult patients, mean age of 27 years, mean A1C of 8.8%, diagnosed with type 1 diabetes and treated on average for 6 years (range 1 to 15 years).[64,74]

Our target population was based on the Diabetes Control and Complications Trial and the follow-up Epidemiology of Diabetes Interventions and Complications study (n = 1,411), the only randomized controlled trial to follow patients with type 1 diabetes for more than 20 years and report diabetes-related complications.[64,74] The mean age and mean A1C of our target population at baseline and for the disease duration were assumed from the control arm of the Diabetes Control and Complications Trial. The study population had an average baseline A1C that was higher than that reported in some studies of continuous glucose monitoring, but reflected that of the average diabetes population, which tends to keep blood glucose levels higher to avoid severe hypoglycemic events.

We were unable to develop an economic evaluation of continuous glucose monitoring in children, owing to a lack of data on utilities and probabilities for children with type 1 diabetes.

Perspective

We conducted this analysis from the perspective of the Ontario Ministry of Health and Long-Term Care.

Interventions

We conducted four economic evaluations of continuous glucose monitoring compared with self-monitoring of blood glucose. We took this approach (1) because the clinical review excluded studies that compared continuous glucose monitoring devices with each other and (2) so that

we could consider continuous glucose monitoring devices as a class, without regard to manufacturer or type.

Our review of the economic literature assessed eight possible interventions used in clinical practice (see Economic Evidence Review, Types of Interventions). However, because of a lack of clinical evidence, our evaluation was limited to four interventions. Appendix 4 provides our reasons for including the four interventions and the associated references for the selected studies. Table 11 summarizes the interventions evaluated in the economic model.

Table 11: Disease Interventions and Comparators Evaluated in the Primary Economic Model

Intervention	Comparator
Standalone CGM device plus multiple daily injections	SMBG plus multiple daily injections
Sensor-augmented pump	SMBG plus multiple daily injections
Standalone CGM device plus insulin pump	SMBG plus insulin pump
Sensor-augmented pump	SMBG plus insulin pump

Abbreviations: CGM, continuous glucose monitoring; SMBG, self-monitoring of blood glucose.

We conducted a pairwise comparison (i.e., two at a time) of continuous glucose monitoring and self-monitoring of blood glucose. We considered continuous glucose monitoring devices approved in Canada and produced in 2010 or later. We did not rank the different continuous glucose monitoring devices by cost-effectiveness. For more details about the technologies we assessed, see the Background and Clinical Evidence Review sections.

Discounting and Time Horizon

We applied an annual discount rate of 1.5% to both costs and QALYs.[75] We used a lifelong time horizon for all analyses.

Model Structure

We adapted a transition-state model structure developed by McQueen et al[51] for patients with type 1 diabetes, and we used a Markov cohort model with a 1-year cycle to explore long-term disease progression. Our model included more health states than the McQueen et al model.[51] We also included long-term diabetes complications and short-term acute complications (such as severe hypoglycemia).

Our model consisted of 14 health states (Figure 4). All patients started in the “no complications” state. From the first year onward, they:

- Stayed in the “no complications” state
- Transitioned into one of the initial four diabetes complication health states:
  - Retinopathy
  - Neuropathy
  - Nephropathy
  - Cardiovascular disease
- Died because of diabetes complications or other causes (i.e., entered the absorbing death state)

Patients in any health state could have a severe hypoglycemic event. We counted a number of severe hypoglycemic events for each health state. To account for the episodic nature of hypoglycemia, we estimated the probability of multiple hypoglycemic events for a 1-year cycle, based on the published literature.[76]

From the second year onward, patients could:

- Move to a more severe condition state:
  - Blindness
  - Lower-extremity amputation
  - End-stage renal disease
- Move to a combined complication health state:
  - Nephropathy and cardiovascular disease
  - Neuropathy and cardiovascular disease
  - Retinopathy and cardiovascular disease
  - Neuropathy and nephropathy
- Enter the death state

From the third year onward, patients with nephropathy and cardiovascular disease, neuropathy and cardiovascular disease, or neuropathy and nephropathy could die or transition to the most severe health states:

- Lower-extremity amputation
- End-stage renal disease

After the third year, patients were in the no complications state or had transitioned to any of the complication health states. Figure 4 provides a simplified schematic of the Markov model.

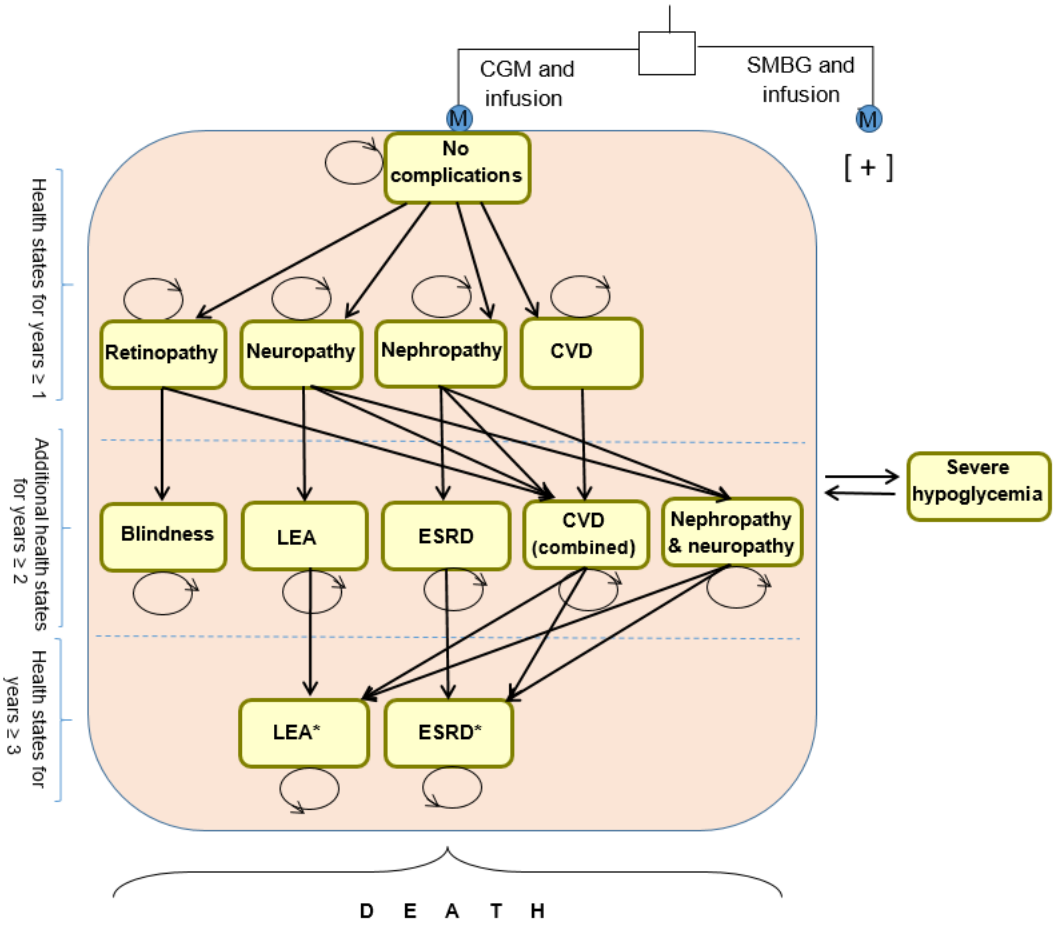

Figure 4: Continuous Glucose Monitoring Versus Self-Monitoring of Blood Glucose—Long-Term Markov Model of Complications in Patients With Type 1 Diabetes[a]

Abbreviations: CGM, continuous glucose monitoring; CVD, cardiovascular disease, ESRD, end-stage renal disease; LEA, lower-extremity amputation; SMBG, self-monitoring of blood glucose.

[a]Straight arrows represent progression to a severe health state; curved arrows represent remaining in the same health state; straight arrows to and from severe hypoglycemia represent the probability of having a hypoglycemic event in any health state. All health states except no complications, retinopathy, neuropathy, and blindness had excess mortality. Infusion includes multiple daily injections or insulin pump. The model structure was adopted from McQueen et al.[51]

*Combined health states.

The Markov health states were based on a description of clinical outcomes from the Diabetes Control and Complications Trial.[76] The macrovascular (cardiovascular disease) and microvascular (retinopathy, nephropathy, and neuropathy) complications of type 1 diabetes occur in later stages of the disease. Therefore, concomitant health states have attributes of both cardiovascular disease and retinopathy, nephropathy, or neuropathy.

- No complications: Patients in this state are free from long-term major adverse events but can have short-term severe hypoglycemic events. They may experience microvascular or macrovascular complications over time, or die from any cause[76]
- Retinopathy: Patients in this state have a growth of easily torn new blood vessels in the retina, as well as macular edema (swelling of part of the retina), which can lead to severe vision loss or blindness. This state includes patients with proliferative

diabetic retinopathy or worse, patients with clinically significant macular edema, and patients undergoing photocoagulation therapy[76]

- Neuropathy: Patients in this state have abnormal and decreased sensation, usually starting in the feet and later in the fingers and hands. When combined with damaged blood vessels, neuropathy can lead to a diabetic foot ulcer, with a high probability of lower-extremity amputation in the later stages[76]
- Nephropathy: Patients in this state have kidney damage. This can lead to chronic renal failure, eventually requiring dialysis. Nephropathy is defined as an albumin excretion rate of 300 mg/24 hours or higher, a serum creatinine level of 2 mg/dL or higher, or the need for dialysis or renal transplantation[76]
- Cardiovascular disease: Patients in this state have conditions that involve narrowed or blocked blood vessels. They might experience any of the following: myocardial infarction (heart attack); stroke; or death secondary to cardiovascular disease, angina, or revascularization (e.g., vascular bypass or angioplasty)[76]
- Severe hypoglycemic event: Severe hypoglycemia is an acute complication of diabetes. A severe hypoglycemic event can result in loss of consciousness or seizure, and risk is known to increase with intensive therapy[76]
- Blindness: Diabetic retinopathy can eventually lead to blindness. Patients in the blindness state have, at most, one-tenth of normal vision in their better eye, even when wearing corrective lenses[77]
- Lower-extremity amputation: Patients in this state undergo amputation of the leg—either above or below the knee—to remove tissue that is ischemic (does not have enough blood supply), infected, or necrotic (dead), or because of an untreatable ulcer. Amputation can be a life-saving procedure[76]
- End-stage renal disease: Patients in this state are in the final stage of chronic kidney disease. Their kidneys no longer function well enough to meet the needs of daily life. Treatments are dialysis or kidney transplantation[76]
- Death: At any point in the model timeline, a patient could die. Death could be the result of diabetes, but all health states are susceptible to death from other causes. This is the absorbing health state

Main Assumptions

The major assumptions for our model were as follows:

- Reduction of A1C with continuous glucose monitoring was associated with a decrease in risk of diabetes-related complications present in the first 12 months, but then the benefit of continuous glucose monitoring slowly declined over a patient's lifetime
- Patients who used continuous glucose monitoring would have better quality of life because they would have less or no worry about hypoglycemia. A hypoglycemic event could occur in any health state and occurred at a constant probability over time, conditional to the treatment strategy
- Our target population was treated for an average of 6 years (range 1 to 15 years)[64,74] before entering the model. To simplify, we assumed that a certain proportion of patients could enter more severe health states, including lower-extremity amputation and end-stage renal disease, as of the second model cycle. We tested this assumption in a scenario analysis by delaying complications for 10 years

Model Parameters

Natural History

We obtained transition probabilities for diabetes complications from the best available literature sources. The Diabetes Control and Complications Trial and the Epidemiology of Diabetes Interventions and Complications study provided more than 20 years of follow-up for a cohort of 1,411 patients with type 1 diabetes who received either intensive or conventional treatment.[76] We derived risk functions for no complications to retinopathy, nephropathy, and cardiovascular disease for the first year and subsequent years using a Weibull function fitted to the data (Table 12).

Table 12: Risk Functions for Type 1 Diabetes Used in the Markov Model

Change of Health State	Study, Year	Function	λ (Scale ÷ Intercept)	γ (Shape ÷ Slope)	R^2 (Goodness of Fit)
No complications to retinopathy	DCCT, 2009[76]	Weibull	0.000025	2.98542	0.988251
No complications to nephropathy			0.000823	1.66710	0.955383
No complications to CVD			0.000086	2.07549	0.91064

Abbreviations: CVD, cardiovascular disease; DCCT, Diabetes Control and Complications Trial.

We also derived transition probabilities from no complications to neuropathy for the first year from the Diabetes Control and Complications Trial and the Epidemiology of Diabetes Interventions and Complications study[74] (Table 13). We obtained probabilities for severe hypoglycemia from the same studies,[76] which reported event rates over 18.5 years of follow-up.

Table 13: Annual Transition Probabilities for the Type 1 Diabetes Markov Model

Parameter	Mean Value	95% CI	Source
First Year Onward			
No complications to neuropathy	0.0235	0.0218–0.0252	DCCT, 2014[74]
Severe hypoglycemic event (acute event from any health state)	0.0982	0.0909–0.1036	DCCT, 2009[76]
Second Year Onward			
Retinopathy to blindness	0.0064	0.0062–0.0066	Early Treatment Diabetic Retinopathy Study Research Group, 1991[78]
Neuropathy to lower-extremity amputation	0.1200	0.1104–0.1296	Jonasson et al, 2008[79]
Nephropathy to end-stage renal disease	0.072	0.006–0.008	McQueen et al, 2011[51] Eastman et al, 1997[70]
Neuropathy to CVD[a]	0.0200	0.0188–0.0212	Klein et al, 2004[66]
Neuropathy to nephropathy	0.097	0.0943–0.0997	Wu et al, 1998[80]
Retinopathy to CVD[a]	0.0155	0.0146–0.0164	Klein et al, 2004[66]
Nephropathy to CVD[a]	0.0224	0.0210–0.0238	Klein et al, 2004[66]

Abbreviations: CI, confidence interval; CVD, cardiovascular disease; DCCT, Diabetes Control and Complications Trial.
[a]Transition probability of having CVD concomitant with retinopathy, nephropathy, or neuropathy.

From the second year, patients could have multiple complications. We obtained transition probabilities for cardiovascular disease concomitant with retinopathy, nephropathy, or neuropathy from Klein et al,[66] who provided 20 years of evidence from the Wisconsin Epidemiologic Study of Diabetic Retinopathy. We obtained the transition probability for neuropathy to nephropathy from Wu et al.[80] We obtained the transition probability from nephropathy to end-stage renal disease from the nephropathy diabetes model,[70] based on the Wisconsin Epidemiologic Study of Diabetic Retinopathy.[51,81] We derived the probability of blindness for patients with proliferative diabetic retinopathy from the Early Treatment Diabetic Retinopathy Study Research Group.[78] We estimated the probability of lower-extremity amputation from patients with peripheral neuropathy in a study by Jonasson et al.[79]

From the third year, patients could move from cardiovascular disease concomitant with retinopathy, nephropathy, or neuropathy to the most severe health states of lower-extremity amputation and end-stage renal disease. Transition probabilities for those states were the same as for the second year.

Intervention Effects

We examined the effectiveness of continuous glucose monitoring in lowering A1C levels from baseline and reducing the number of severe hypoglycemic events.

We estimated the intervention effect of continuous glucose monitoring as the percentage mean reduction from the baseline A1C value. We assumed a mean baseline value of 8.8% for our base case population, consistent with A1C values for the relevant population in clinical studies[64,74] and in studies included in the clinical evidence section of this health technology assessment (Figures 1 and 2). Table 14 shows the mean change in A1C values from baseline to the end of each study for continuous glucose monitoring, calculated for all interventions.

Table 14: Mean A1C Levels, Changes From Baseline With Continuous Glucose Monitoring[a]

Study, Year	Intervention and Comparator	Mean A1C, Baseline (95% CI)	Mean A1C, End of Study (95% CI)	Change (95% CI)
Lind et al, 2017[31]	Standalone CGM plus multiple daily injections vs. SMBG plus multiple daily injections	8.49 (8.41–8.57)	7.92 (7.79–8.05)	−0.57 (−0.78 to −0.41)
Bergenstal et al, 2010[25]	Sensor-augmented pump vs. SMBG plus multiple daily injections	8.30 (8.27–8.33)	7.30 (7.25–7.35)	−1.00 (−1.08 to −0.92)
Quiros et al, 2015[41]	Sensor-augmented pump vs. SMBG plus insulin pump	8.47 (8.33–8.61)	7.38 (7.24–7.52)	−1.09 (−1.37 to −0.81)
Tumminia et al, 2015[38]	Standalone CGM plus insulin pump vs. SMBG plus insulin pump	8.5 (8.38–8.62)	7.82 (7.74–7.90)	−0.68 (−1.04 to −0.18)

Abbreviations: CGM, continuous glucose monitoring; CI, confidence interval; SMBG, self-monitoring of blood glucose.
[a]Note: Values used for deterministic analysis. Point estimates from Tumminia et al[38] were not statistically or clinically meaningful.

We estimated the intervention effect for severe hypoglycemic events as the difference in mean event rates per patient-year between the treatment and control arms. The clinical evidence review revealed no statistically significant difference in rates of severe hypoglycemic events between patients using continuous glucose monitoring and patients receiving usual care. To apply the risk reduction for all continuous glucose monitoring interventions in the model, we selected data from a study by Bergenstal et al[25] because of its higher methodological quality, and because its sample size was the largest. The rate of severe hypoglycemia was 15.31

episodes per 100 person-years in the continuous glucose monitoring group and 17.62 episodes per 100 person-years in the control group.[76] Based on this ratio, we estimated the relative risk (RR) of severe hypoglycemia to be 0.869 (95% CI 0.476–1.586) for continuous glucose monitoring.

However, the average baseline A1C levels in the studies that reported severe hypoglycemia[25,33,39] were well above the target A1C threshold for optimal blood glucose management (> 7%). Hence, the findings from these studies may not reflect the experience of patients at high risk of hypoglycemia. To make sure that patients at highest risk were not overlooked, we conducted sensitivity analyses to cover a wide range of baseline A1C levels, using estimates from two suggested studies (RR 0.174[33] and RR 0.695[39]).

Risk Reduction

Similar to many published economic models[51,65] and one health technology assessment,[58] we represented the efficacy of continuous glucose monitoring using risk reductions for short-term acute events (severe hypoglycemia) and long-term micro- and macrovascular complications resulting from reduced mean A1C levels.

We estimated risk reductions for complication rates based on data from the Diabetes Control and Complications Trial[64,76] which reported the effects of intensive treatment (administration of insulin three or more times per day via pump or injection, self-monitoring of blood glucose at least four times per day, dietary intake, and exercise) on A1C levels and the progression of long-term complications.

We obtained initial relative risks for long-term diabetes complications such as retinopathy, nephropathy, neuropathy, and cardiovascular disease from the Diabetes Control and Complications Trial[64,76] and Martin et al.[82] Assuming a log-linear relationship, we estimated the effect of continuous glucose monitoring on reducing diabetes complications through the change in relative risk for each 1% reduction in mean A1C.[83] Appendix 5 (Table A9) provides detailed examples of these calculations using data from the DIAMOND[24] and GOLD[31] trials.

We obtained a percentage change in A1C for continuous glucose monitoring from studies suggested by the clinical evidence review (Figure 2).

The relative risks for long-term diabetes complications used in the economic model are shown in Table 15.

Table 15: Change in A1C From Baseline and Risk Reduction for Diabetes Complications

Study, Year	Intervention and Comparator	% Decrease in A1C From Baseline (95% CI)[a]	Diabetes Complications, RR (95% CI)			
			Retinopathy	Nephropathy	Neuropathy	CVD
Lind et al, 2017[31]	Standalone CGM plus multiple daily injections vs. SMBG plus multiple daily injections	6.71 (6.02–7.42)	0.794 (0.775–0.813)	0.847 (0.832–0.862)	0.769 (0.748–0.790)	0.859 (0.845–0.872)
Bergenstal et al, 2010[25]	Sensor-augmented pump vs. SMBG plus multiple daily injections	12.05 (11.77–12.33)	0.661 (0.655–0.667)	0.742 (0.737–0.747)	0.624 (0.618–0.631)	0.761 (0.756–0.766)
Quiros et al, 2015[41]	Sensor-augmented pump vs. SMBG plus insulin pump	12.87 (12.66–13.09)	0.643 (0.638–0.647)	0.727 (0.723–0.731)	0.605 (0.599–0.610)	0.747 (0.743–0.750)
Tumminia et al, 2015[38]	Standalone CGM plus insulin pump vs. SMBG plus insulin pump	8.00 (7.63–8.36)	0.760 (0.750–0.769)	0.820 (0.813–0.828)	0.731 (0.721–0.742)	0.834 (0.827–0.841)

Abbreviations: CI, confidence interval; CGM, continuous glucose monitoring; CVD, cardiovascular disease; RR, relative risk; SMBG, self-monitoring of blood glucose.
[a]Data for change in A1C level obtained from Figure 2, calculated based on Table 14 (column 5).

Mortality

We modelled mortality based on diabetes complications and death from other causes. We estimated mortality rates owing to acute complications (including severe hypoglycemia and coma) and long-term diabetes complications using data from the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications study, following patients for 27 years.[84] We used these estimates to model mortality owing to diabetes complications after the first year (Table 16).

Table 16: Annual Mortality for Diabetes Complications States

Parameter	Mean Mortality	95% CI	Source
First Year Onward			
Nephropathy	0.0036	0.0033–0.0039	DCCT, 2015[84]
Severe hypoglycemic event	0.0063	0.0058–0.0068	DCCT, 2015[84]
Death (all-cause mortality, no diabetes), age 27–54 years	0.0020	0.0019–0.0021	DCCT, 2015[84]
Second Year Onward			
Lower-extremity amputation	0.093	0.0845–0.1015	Vamos et al, 2010[85]
End-stage renal disease	0.1640	0.1613–0.1667	Wolowacz et al, 2015[86]
Neuropathy and nephropathy	0.0036	0.0033–0.0039	DCCT, 2015[84]

Abbreviations: CI, confidence interval; DCCT, Diabetes Control and Complications Trial.

For cardiovascular disease alone and cardiovascular disease combined with microvascular complications, we used time-dependent probabilities of death following the onset of congestive heart failure from the Center for Outcomes Research and Evaluation diabetes model[65] (Appendix 6, Table A10).

We used the perioperative mortality of patients who underwent amputation to model excess mortality in the lower-extremity amputation state.[85]

We obtained an excess mortality rate for end-stage renal disease from Wolowacz et al,[86] who examined death rates for diabetes in the United Kingdom Renal Registry.

We calculated age-specific mortality rates for the population without diabetes and estimated nonspecific mortality rates by subtracting diabetes-related deaths from total deaths from all causes.[87]

We used mortality rates from the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications study to calibrate diabetes and nondiabetes mortality rates estimated by the model.[84]

Utilities

Table 17 presents all health state utility values used in the base case analysis.

Table 17: Utilities for Complications Health States

Health State	Mean Utility Value	95% CI	Source
No complications	0.814	0.710–0.918	Clarke et al, 2002,[88] Currie et al, 2006[89]
Severe hypoglycemic event[a]	−0.021	−0.122 to −0.010	Currie et al, 2006[90]
Nephropathy	0.575	0.566–0.584	McQueen et al, 2011[51]
Neuropathy	0.624	0.609–0.639	Palmer et al, 2004[65]
Retinopathy	0.612	0.603–0.621	McQueen et al, 2011[51]
CVD	0.685	0.628–0.742	Palmer et al, 2004[65]
Blindness	0.569	0.493–0.645	Palmer et al, 2004[65]
Lower-extremity amputation	0.534	0.525–0.543	McQueen et al, 2011[51]
End-stage renal disease	0.490	0.450–0.540	Tengs and Wallace, 2000[91]
Combined Health States			
Neuropathy and nephropathy	0.557	0.528–0.577	Sullivan and Ghushchyan, 2006,[92] McQueen et al, 2011[51]
Neuropathy and CVD	0.544	0.532–0.567	McQueen et al, 2011[51]
Nephropathy and CVD	0.516	0.488–0.531	McQueen et al, 2011[51]
Retinopathy and CVD	0.553	0.525–0.572	McQueen et al, 2011[51]
Lower-extremity amputation and CVD	0.511	0.487–0.534	Assumption
End-stage renal disease and CVD	0.447	0.424–0.471	Assumption

Abbreviations: CI, confidence interval; CVD, cardiovascular disease.
[a]Duration of the event and disutility associated with it is explained in the text below.

We obtained the utility for diabetes with no complications from the United Kingdom Prospective Diabetes Study (n = 3,192), which used the EuroQoL EQ-5D instrument to estimate health-related quality of life in patients with diabetes.[88,89] We obtained utilities for diabetes complications such as nephropathy, retinopathy, and lower-extremity amputation from diabetes patients in the US Medical Expenditure Panel Survey (n = 2,778), based on the EuroQoL EQ-5D[92] and from a modelling study by McQueen et al.[51] We obtained utility values for cardiovascular disease, blindness, and neuropathy from the United Kingdom Prospective Diabetes Study[88] and the Center for Outcomes Research and Evaluation diabetes model.[65] We used a utility value for myocardial infarction in the cardiovascular disease health state.[88] We obtained the utility for end-stage renal disease (related to hemodialysis) from Tengs and Wallace.[91] We assumed the highest utility decrement (reduction) for combined health states.

The occurrence and severity of hypoglycemic symptoms were associated with increased patient worry about hypoglycemia and lower health-related quality of life over 1 year of the model cycle. We used a disutility estimate of 0.047 from Currie et al,[90] who examined the fear of hypoglycemia in a survey of 1,305 patients with confirmed type 1 diabetes. The same trial reported a disutility value of 0.122 for the most severe hypoglycemic events. We used both values for our base case analysis.

The evidence was unclear about the duration of severe hypoglycemia. It could last less than an hour, or it could last longer and require an emergency department visit or hospitalization. We assumed that if patients felt unwell owing to a severe hypoglycemic event, they would take time off work. According to a European survey, people who experienced a severe hypoglycemic event took 4 to 7 days off work.[93] We used this period of time to account and adjust for the duration and episodic nature of severe hypoglycemic events over 1 year of the model cycle.

We made the following annual adjustments for severe hypoglycemic events. We assumed 5.5 days off work as the duration of a severe hypoglycemic event, and we calculated an annual disutility as follows:

$$-0.122 \times 5.5/365 = -0.0018$$

Using data from another European online survey,[94] we established the proportion of patients with diabetes (40%) who were very worried about hypoglycemia. In this way, we ensured that the total disutility value included the event itself and the fear of hypoglycemia (adjusted for the episodic nature of the event and productivity loss owing to the event):

$$-0.0018 + (-0.047 \times 0.4) = -0.0206$$

These calculations allowed us to develop the overall model disutility for a severe hypoglycemic event (Table 17).

Cost Parameters

Table 18 presents estimates of the health care costs used in our base case analysis. We obtained health care costs for nephropathy, neuropathy, and retinopathy from O'Brien et al.[95] We estimated costs for cardiovascular disease, blindness, lower-extremity amputation, and end-stage renal disease from the Ontario Diabetes Economic Model.[96] This model reflected actual resource-use profiles for a large prospective cohort of people with diabetes (N = 734,113) over 10 years. We calculated costs for cardiovascular disease as an average cost of all costs for ischemic heart disease, myocardial infarction, heart failure, and stroke.[96] We obtained costs for severe hypoglycemic events with an inpatient visit from the Ontario Case Costing Initiative (2014 dollars).[97] When necessary, we inflated costs to 2017 dollars using the Consumer Price Index.[14] There was no direct evidence that continuous glucose monitoring prevented hospitalizations owing to hypoglycemic events,[25,33,39] so we did not consider this possibility in our model.

We assumed that the annual cost of diabetes treatment included the following:

- Insulin
- Diabetes treatment supplies
- Continuous glucose monitoring device and supplies
- Insulin pump system approved by Health Canada

We obtained the annual cost of insulin treatment with multiple daily injections from a systematic review and mixed-treatment comparison meta-analysis report by the Canadian Agency for Drugs and Technologies in Health[98] (Appendix 6, Table A11). We used the cost of insulin lispro (Humalog) cartridges to calculate treatment with an insulin pump (Appendix 6, Table A12). We obtained the annual cost of diabetes treatment supplies, such as needles and syringes, from a

Shoppers Drug Mart pharmacy. All details of treatment supplies calculations are presented in Appendix 6, Table A13.

Dexcom provided costs for a standalone continuous glucose monitoring device and supplies. Animas and Medtronic provided insulin pump costs. We used device warranty times to calculate the annual costs of continuous glucose monitoring devices and insulin pumps. Appendix 6, Table A14, details the costs of the diabetes technologies and supplies. Appendix 6, Table A15, details diabetes treatment costs for the seven interventions presented in Table 18.

Table 18: Average Annual Per-Patient Cost of Diabetes Complications and Interventions in Ontario

	Mean Cost ($)[a]		Source
	First Year	Subsequent Years	
Health State: Diabetes-Related Complications			
Nephropathy	80	13	O'Brien et al 2003[95]
Neuropathy	192	192	O'Brien et al 2003[95]
Retinopathy	492	52	O'Brien et al 2003[95]
Severe hypoglycemic event (in-patient visit)	3,775	3,775	McQueen et al, 2015[97]
Cardiovascular disease	18,682	4,072	O'Reilly et al, 2007[96]
Blindness	3,483	2,482	O'Reilly et al, 2007[96]
Lower-extremity amputation	43,984	6,024	O'Reilly et al, 2007[96]
End-stage renal disease	28,221	12,808	O'Reilly et al, 2007[96]
Intervention (Trade Name)			
Sensor-augmented pump (Dexcom G4 Platinum + Animas Vibe)	11,811	11,811	Dexcom and Animas[b]
Sensor-augmented pump (Dexcom G5 Mobile + Animas Vibe)	11,534	11,534	Dexcom and Animas[b]
Sensor-augmented pump with a low-glucose suspend feature (MiniMed Veo)	9,211	9,211	Medtronic[b]
Standalone CGM plus multiple daily injections (Dexcom G4 Platinum)	10,097	10,097	Dexcom[b]
Standalone CGM plus multiple daily injections (Dexcom G5 Mobile)	8,587	8,587	Dexcom[b]
SMBG plus insulin pump (Animas Vibe or MiniMed Veo)	6,817	6,817	Medtronic and Animas[b]
SMBG plus multiple daily injections	3,677	3,677	Estimate[c]

Abbreviations: CGM, continuous glucose monitoring; SMBG, self-monitoring of blood glucose.
[a]We used 25% of the mean cost for calculations of standard error in our probabilistic sensitivity analysis. All costs are presented in 2017 Canadian dollars.
[b]Manufacturer information.
[c]See Appendix 6, Table A13, for more details.

Analyses

Base Case Analysis

In the base case analysis, we applied a deterministic approach and used actual values or mean values as the model inputs. We presented the results as incremental costs (difference in costs) and incremental QALYs (difference in quality-adjusted life-years) for each continuous glucose monitoring device compared with self-monitoring of blood glucose.

Sensitivity Analyses

A deterministic method may provide the most reliable estimate of cost-effectiveness based on the best available data, but it does not consider the uncertainty of inputs to the model or the possibility of other clinical scenarios. As a result, we performed sensitivity analyses to address the uncertainty of model inputs and clinical scenarios.

We assessed variability and uncertainty in two ways. We conducted one-way sensitivity analyses using plausible ranges of high and low values for the model variables (as suggested by the literature). We also conducted probabilistic sensitivity analyses by assigning distributions to model parameters. In the probabilistic sensitivity analyses, we used gamma distribution to represent the uncertainty of the cost parameters, because cost data are skewed and cannot be negative.[99] We used beta distributions for probabilities and utilities, because those estimates are confined to a range of 0 to 1.[100] We used uniform distribution where a mean estimate of utility value was associated with a high standard error. In Monte Carlo probabilistic simulations, all parameters were randomly sampled from their assigned distributions for a cohort of 1,000 patients. We also estimated the likelihood of each treatment strategy being optimal across a range of willingness-to-pay thresholds.

The estimates used in our one-way sensitivity analyses are presented in Table 19.

Table 19: Sensitivity Analyses for Continuous Glucose Monitoring Model

Parameters	Mean Value	Plausible Range		Source
		Minimum	Maximum	
Discount rates, %	1.5	0	5.0	Paulden et al[75]
Annual Transition Probabilities				
First year onward				
No complications to retinopathy (exponential)	0.0764	0.0461	0.0829	DCCT, 2009,[76] DCCT, 2014[74]
No complications to nephropathy (exponential)	0.0094	0.0008	0.0526	DCCT, 2009[76]
No complications to neuropathy	0.0235	0.0218	0.0252	DCCT, 2009[76]
No complications to CVD (exponential)	0.0045	0.0310	0.0084	Hoerger et al, 2004,[81] DCCT, 2005[101]
No complications to severe hypoglycemic event	0.0982	0.0526	0.1513	DCCT, 2009[76]
Second year onward				
Retinopathy to blindness	0.0064	0.0010	0.1010	Hoerger et al, 2004,[81] McQueen et al, 2011[51]
Neuropathy to lower-extremity amputation	0.1200	0.0620	0.1690	Hoerger et al, 2004,[81] McQueen et al, 2011[51]
Nephropathy to end-stage renal disease	0.072	0.0041	0.096	Hoerger et al, 2004,[81] McQueen et al, 2011[51]
Neuropathy to CVD	0.0200	0.0160	0.0440	Hoerger et al, 2004,[81] McQueen et al, 2011[51]
Neuropathy to nephropathy	0.0970	0.0550	0.1490	Wu et al, 1998[80]
Retinopathy to CVD	0.0155	0.0100	0.0430	Klein et al, 2004,[66] McQueen et al, 2011[51]
Nephropathy to CVD	0.0224	0.0130	0.0340	Klein et al, 2004,[66] McQueen et al, 2011[51]
Utilities				
No complications	0.814	0.710	0.918	Clarke et al, 2002,[88] Currie et al, 2006[90]
Nephropathy	0.575	0.545	0.606	Sullivan et al, 2006[92]
Neuropathy	0.624	0.573	0.632	McQueen et al, 2011,[51] Palmer et al, 2004[65]
Retinopathy	0.612	0.581	0.643	McQueen et al, 2011,[51] Sullivan et al, 2006[92]
CVD	0.685	0.513	0.742	Clarke et al, 2002,[88] and Palmer et al, 2004[65]
Severe hypoglycemia	0.66	0.544	0.764	Vexiau et al, 2008,[102] Marrett et al, 2009,[103] Currie et al, 2006[90]
Blindness	0.569	0.540	0.734	Clarke et al, 2002,[88] and Palmer et al, 2004[65]
Lower-extremity amputation	0.534	0.425	0.644	Clarke et al, 2002,[88] Sullivan et al, 2006[92]
End-stage renal disease	0.49	0.45	0.53	Tengs and Wallace, 2000[91]
Cost, First Year, 2017 Canadian Dollars				
No complications	2,262	1,667	2,262	McQueen et al, 2015,[97] O'Reilly et al, 2007[96]
Nephropathy	80	70	90	McQueen et al, 2015,[97] O'Brien et al 2003,[95] assumption
Neuropathy	192	150	213	O'Brien et al, 2003,[95] assumption

Parameters	Mean Value	Plausible Range		Source
		Minimum	Maximum	
Retinopathy	492	400	642	McQueen et al, 2015,[97] O'Brien et al 2003,[95] assumption
CVD	18,682	7,471	24,170	OCCI, O'Brien et al, 2003[95]
Severe hypoglycemia	3,775	1,500	4,000	Assumption, OCCI
Blindness	3,483	2,738	5,000	McQueen et al, 2015,[97] O'Brien et al, 2003,[95] assumption
Lower-extremity amputation	43,984	31,884	50,000	McQueen et al, 2015,[97] O'Brien et al 2003,[95] assumption
End-stage renal disease	28,221	25,841	81,769	McQueen et al, 2015,[97] O'Brien et al 2003[95]
Relative Risk From Lowering A1C by 1%				
Nephropathy	0.038	0.032	0.043	DCCT, 2009,[76] DCCT, 2014[74]
Neuropathy	0.025	0.020	0.030	DCCT, 2009,[76] DCCT, 2014[74]
Retinopathy	0.029	0.023	0.034	DCCT, 2009,[76] DCCT, 2014[74]
CVD	0.040	0.035	0.045	DCCT, 2009,[76] DCCT, 2014[74]
Severe hypoglycemia	0.061	0.055	0.066	DCCT, 2009,[76] DCCT, 2014[74]

Abbreviations: A1C, glycated hemoglobin; CVD, cardiovascular disease; DCCT, Diabetes Control and Complications Trial; OCCI, Ontario Case Costing Initiative.

Scenario Analyses

In addition to the sensitivity analyses, we conducted several scenario analyses to explore the effects of the most sensitive parameters to the cost-effectiveness results. These scenarios examined the robustness of our results in the face of changes to the relative risk of severe hypoglycemic events and the costs of continuous glucose monitoring devices.

Scenario 1: Variations of Relative Risks for Severe Hypoglycemia Events

In the base case analysis, we used the relative risk of severe hypoglycemia associated with continuous glucose monitoring (RR 0.869) as estimated by Bergenstal et al.[25] Because this estimate was based on a single study, we examined how changes in the probability of a severe hypoglycemic event would influence our base case results. We assumed that the estimated risk reduction would be 20% to 80% of the relative risk:

- RR 0.695, a 20% reduction of the effect
- RR 0.521, a 40% reduction of the effect
- RR 0.348, a 60% reduction of the effect
- RR 0.174, an 80% reduction of the effect

We estimated a range of relative risks for patients with hypoglycemia unawareness.

Scenario 2: Reductions in Costs of Continuous Glucose Monitoring Devices

In scenario 2, we examined the cost of continuous glucose monitoring devices, assuming reductions of 30%, 20%, and 10%.

Scenario 3: Government Funding

In scenario 3, we examined the effect of cost reductions specific to Ontario. In Ontario, provincial funding of insulin, supplies, and blood glucose testing strips varies depending on the age and eligibility of the patient. We considered several scenarios from a patient perspective with various levels of government funding (Table 20):

- Insulin not funded but insulin pump funded
- Funding for insulin and insulin pump
- Funding for insulin, pump, and 75% of the sensor costs
- Funding for insulin pump and 75% of the sensor costs

Table 20: Cost to Patient of Technologies With Various Levels of Government Funding

	Cost to the Patient, $				
Intervention (Trade Name)	Intervention	Insulin Not Covered, Pump Covered	Insulin and Pump Covered	Insulin, Pump, and 75% of Sensors Covered	Pump and 75% of Sensors Covered
Sensor-augmented pump (Dexcom G4 Platinum + Animas Vibe)	11,811	7,520	6,786	5,681	6,415
Sensor-augmented pump (Dexcom G5 Mobile + Animas Vibe)	11,534	7,243	6,509	5,404	6,138
Sensor-augmented pump with a low-glucose suspend feature (MiniMed Veo)	9,211	4,920	4,186	3,406	4,140
Standalone CGM plus multiple daily injections (Dexcom G4 Platinum)	10,097	10,097	8,749	7,644	8,992
Standalone CGM plus multiple daily injections (Dexcom G5 Mobile)	8,587	8,587	7,239	6,134	7,482
SMBG plus insulin pump (Animas Vibe or MiniMed Veo)	6,817	2,333	1,599	1,599	2,333
SMBG plus multiple daily injections	3,677	3,677	2,329	2,329	3,677

Abbreviations: CGM, continuous glucose monitoring; SMBG, self-monitoring of blood glucose.

Scenario 4: Structural Assumption of Treatment Effect to Be Constant for the Rest of a Patient's Life

In our base case scenario, we assumed that a reduction in the risk of diabetes-related complications would occur within the first 12 months. This was similar to the approach taken in the health technology assessment by the National Institute for Health and Care Excellence.[58] In scenario 4, we examined the treatment effect of a reduction in A1C owing to continuous glucose monitoring if it were constant (and maximized) for the rest of a patient's life.

Scenario 5: Delay of Severe Diabetes Complications for 10 Years

According to our model structure, from year 2 onward, a certain proportion of patients could enter more severe diabetes complication health states, including lower-extremity amputation and end-stage renal disease. Although our target population was treated for about 6 years (range 1 to 15 years), in scenario 5, we tested the effect of delaying the development of severe complications for another 10 years.

Generalizability

The findings of this economic analysis are generalizable to adults with type 1 diabetes, but not to children or pregnant women with type 1 diabetes. They may be used to guide decision-making about the specific patient populations addressed in the trials we investigated.

Expert Consultation

Throughout the development of this model, we consulted clinicians who specialize in treating type 1 diabetes and have experience with continuous glucose monitoring. The role of these expert advisors was to review the structure and inputs of the economic model and confirm that the information reasonably reflected the clinical setting. The statements, conclusions, and views expressed in this report do not necessary represent the views of the consulted experts.

Results

Base Case Analysis

The results of the base case analysis are presented in Table 21. Costs, life-years, and QALYs were higher with continuous glucose monitoring than with self-monitoring of blood glucose (usual care). All strategies were associated with ICERs that are generally considered to be very high, suggesting that, compared with self-monitoring of blood glucose, continuous glucose monitoring is not cost-effective at commonly used willingness-to-pay thresholds.

Table 21: Base Case Analysis

Intervention	Average Total Costs, $	Average Total Effects, QALYs	Average Total Effects, LYs	Incremental Cost,[a] $	Incremental Effect,[b] QALYs	Incremental Effect, LYs	ICER $/QALY	ICER $/LY
Standalone CGM Plus Multiple Daily Injections vs. SMBG Plus Multiple Daily Injections								
SMBG + MDI	125,586	18.812	26.411					
CGM + MDI	229,413	18.906	26.520	103,827	0.094	0.109	1,108,812	951,152
Sensor-Augmented Pump vs. SMBG Plus Multiple Daily Injections[c]								
SMBG + MDI	125,586	18.812	26.411					
SAP	258,306	18.944	26.564	132,720	0.132	0.153	1,007,909	868,881
Standalone CGM Plus Insulin Pump vs. SMBG Plus Insulin Pump								
SMBG + insulin pump	177,320	18.812	26.411					
CGM + insulin pump	257,947	18.916	26.531	80,627	0.104	0.121	778,687	669,059
Sensor-Augmented Pump vs. SMBG Plus Insulin Pump								
SMBG + insulin pump	177,320	18.812	26.411					
SAP	258,373	18.949	26.570	81,052	0.137	0.159	592,206	510,755

Abbreviations: CGM, continuous glucose monitoring; ICER, incremental cost effectiveness ratio; LY, life-year; MDI, multiple daily injections; QALY, quality-adjusted life year; SAP, sensor-augmented pump; SMBG, self-monitoring of blood glucose.

[a]Incremental cost = average cost (strategy B) − average cost (strategy A); Costs include all components of direct medical costs without accounting for government funding of insulin treatment, insulin pump, and blood glucose test strips

[b]Incremental effect = average effect (strategy B) − average effect (strategy A).

[c]Difference in outcomes between sensor-augmented pump and self-monitoring of blood glucose plus multiple daily injections was owing to a difference in the relative risk of diabetes complications.

Sensitivity Analyses

One-Way Sensitivity Analysis

We conducted deterministic one-way sensitivity analyses for each parameter using their plausible ranges. Figure 5 shows the results for standalone continuous glucose monitoring with multiple daily injections versus self-monitoring of blood glucose with multiple daily injections. Our model was most sensitive to the relative risk of neuropathy, the relative risk of severe hypoglycemic events, treatment costs, discount rates, and the probability of severe hypoglycemia. Our model was less sensitive to mortality, costs and utilities of complications, and costs of severe hypoglycemic events. One-way sensitivity analyses showed consistent results among all continuous glucose monitoring interventions considered (Appendix 7).

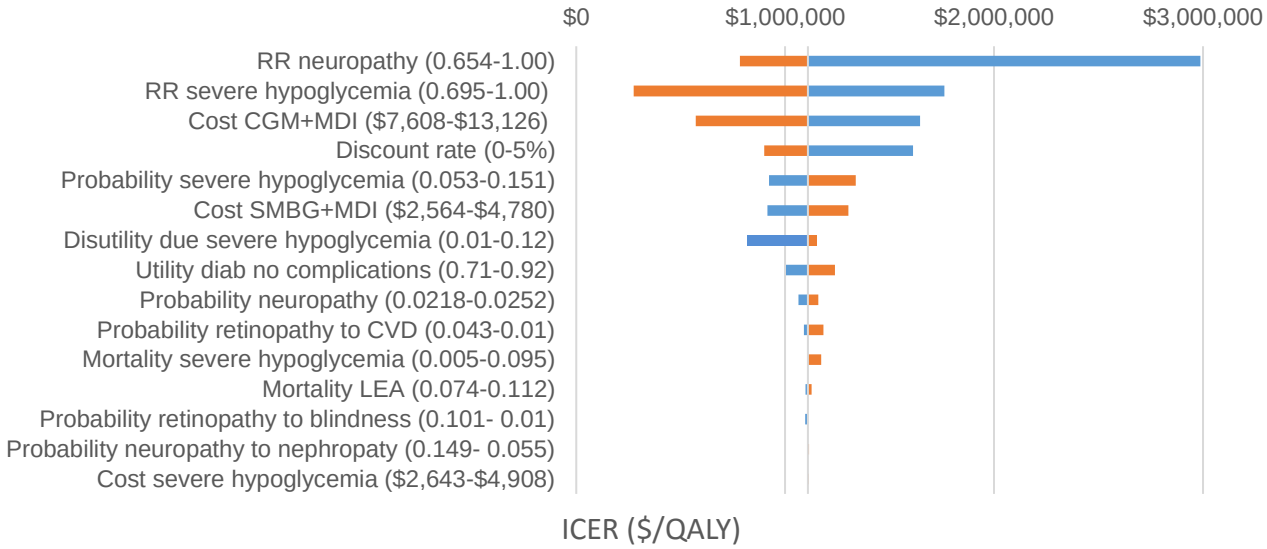

Figure 5: One-Way Sensitivity Analysis: Continuous Glucose Monitoring With Multiple Daily Injections Versus Self-Monitoring of Blood Glucose With Multiple Daily Injections

Abbreviations: CGM, continuous glucose monitoring; CVD, cardiovascular disease; ICER, incremental cost-effectiveness ratio; LEA, lower-extremity amputation; MDI, multiple daily injections; QALY, quality-adjusted life-year; RR, relative risk; SMBG, self-monitoring of blood glucose.
Note: Bars indicate ICER value and directions obtained using the ranges presented in parentheses. Bars indicate ICER values and directions obtained by ranging the model parameters value presented in parentheses. Blue bars indicate ICER values at the upper end of the range, and orange bars indicate ICERs at the lower end. For some parameters, the upper value led to a reduction in ICERs and the lower value led to an increases ICERs.

Probabilistic Sensitivity Analysis

Compared with self-monitoring of blood glucose (usual care), the probability of continuous glucose monitoring being cost-effective was low (Appendix 7, Figure A4). At a willingness-to-pay threshold of $50,000/QALY, the four continuous glucose monitoring interventions had a very small chance of being cost-effective, from 0.1% to 6.6%. There was also large uncertainty around the ICERs associated with these interventions.

Scenario Analyses

Scenario 1: Variations in Relative Risk of a Severe Hypoglycemic Event

The ICERs for the included interventions were higher than $50,000/QALY gained, even considering a favourable relative risk of 0.174 (Table 22). The lowest ICERs were for continuous glucose monitoring with a sensor-augmented pump versus self-monitoring of blood glucose plus an insulin pump. For people with hypoglycemia unawareness, who have a four- to five-fold increased risk of severe hypoglycemia[104,105] (RR 0.521 or RR 0.348), ICERs ranged from $262,255/QALY gained to $571,199/QALY gained.

Table 22: Scenario 1 Results[a]

Intervention	Average Total Costs, $	Average Total Effects, QALYs	Incremental Cost, $	Incremental Effect, QALYs	ICER, $/QALY
RR of Severe Hypoglycemic Event 0.695 (Coefficient 0.8)					
Standalone CGM plus multiple daily injections vs. SMBG plus multiple daily injections					
SMBG + MDI	125,586	18.812			
CGM + MDI	225,987	18.950	100,401	0.138	728,356
Sensor-augmented pump vs. SMBG plus multiple daily injections					
SMBG + MDI	125,586	18.812			
SAP	254,923	18.988	129,336	0.176	734,908
Standalone CGM plus insulin pump vs. SMBG plus insulin pump					
SMBG + insulin pump	177,320	18.812			
CGM + insulin pump	254,558	18.960	77,237	0.148	522,665
Sensor-augmented pump vs. SMBG plus insulin pump					
SMBG + insulin pump	177,320	18.812			
SAP	254,992	18.993	77,672	0.181	**428,747**
RR of Severe Hypoglycemic Event 0.521 (Coefficient 0.6)					
Standalone CGM plus multiple daily injections vs. SMBG plus multiple daily injections					
SMBG + MDI	125,586	18.812			
CGM + MDI	222,540	18.994	96,954	0.182	532,066
Sensor-augmented pump vs. SMBG plus multiple daily injections					
SMBG + MDI	125,586	18.812			
SAP	251,519	19.033	125,932	0.220	571,199
Standalone CGM plus insulin pump vs. SMBG plus insulin pump					
SMBG + insulin pump	177,320	18.812			
CGM + insulin pump	251,149	19.004	73,828	0.192	384,162
Sensor-augmented pump vs. SMBG plus insulin pump					
SMBG + insulin pump	177,320	18.812			
SAP	251,594	19.038	74,273	0.226	**329,228**
RR of Severe Hypoglycemic Event 0.348 (Coefficient 0.4)					
Standalone CGM plus multiple daily injections vs. SMBG plus multiple daily injections					
SMBG + MDI	125,586	18.812			
CGM + MDI	219,096	19.039	93,509	0.226	412,870

Intervention	Average Total Costs, $	Average Total Effects, QALYs	Incremental Cost, $	Incremental Effect, QALYs	ICER, $/QALY
Sensor-augmented pump vs. SMBG plus multiple daily injections					
SMBG + MDI	125,586	18.812			
SAP	248,116	19.077	122,530	0.265	462,659
Standalone CGM plus insulin pump vs. SMBG plus insulin pump					
SMBG + insulin pump	177,320	18.812			
CGM + insulin pump	247,741	19.049	70,420	0.236	297,797
Sensor-augmented pump vs. SMBG plus insulin pump					
SMBG + insulin pump	177,320	18.812			
SAP	248,177	19.082	70,856	0.270	**262,255**
RR of Severe Hypoglycemic Event 0.174 (Coefficient 0.2)					
Standalone CGM plus multiple daily injections vs. SMBG plus multiple daily injections					
SMBG + MDI	125,586	18.812			
CGM + MDI	215,612	19.083	90,026	0.271	332,015
Sensor-augmented pump vs. SMBG plus multiple daily injections					
SMBG + MDI	125,586	18.812			
SAP	244,675	19.122	119,089	0.310	384,647
Standalone CGM plus insulin pump vs. SMBG plus insulin pump					
SMBG + insulin pump	177,320	18.812			
CGM + insulin pump	244,295	19.093	66,974	0.281	238,205
Sensor-augmented pump vs. SMBG plus insulin pump					
SMBG + insulin pump	177,320	18.812			
SAP	244,741	19.127	67,421	0.315	**214,098**

Abbreviations: CGM, continuous glucose monitoring; ICER, incremental cost-effectiveness ratio; MDI, multiple daily injections; QALY, quality-adjusted life-year; RR, relative risk; SAP, sensor-augmented pump, SMBG, self-monitoring of blood glucose.
[a]We used a range of coefficients to estimate the sensitivity of the model results to the parameter "RR of severe hypoglycemic event." We applied different coefficients to the base case RR (0.869) to include all potential scenarios. Relatively low ICERs are shown in bold.

Scenario 2: Reductions in Costs of Continuous Glucose Monitoring Devices

Scenario 2 analyzed the costs of continuous glucose monitoring devices, assuming reductions of 30%, 20%, or 10% (Table 23). Despite significant cost reductions, none of the pairwise comparisons of continuous glucose monitoring versus self-monitoring of blood glucose were cost-effective at common willingness-to-pay thresholds (i.e., $50,000/QALY or $100,000/QALY). At a 30% device cost reduction, ICERs ranged from $383,667/QALY gained to $791,249/QALY gained, suggesting that continuous glucose monitoring was not cost-effective.

Table 23: Scenario 2 Results

Intervention	Average Total Costs, $	Average Total Effects, QALYs	Incremental Cost, $	Incremental Effect, QALYs	ICER $/QALY
30% CGM Device Cost Reduction					
Standalone CGM plus multiple daily injections vs. SMBG plus multiple daily injections					
SMBG + MDI	125,586	18.812			
CGM + MDI	197,492	18.906	71,906	0.094	767,913
Sensor-augmented pump vs. SMBG plus multiple daily injections					
SMBG + MDI	125,586	18.812			
SAP	229,777	18.944	104,191	0.132	791,249
Standalone CGM plus insulin pump vs. SMBG plus insulin pump					
SMBG + insulin pump	177,320	18.812			
CGM + insulin pump	229,483	18.916	52,163	0.104	503,786
Sensor-augmented pump vs. SMBG plus insulin pump					
SMBG + insulin pump	177,320	18.812			
SAP	229,831	18.949	52,511	0.137	383,667
20% CGM Device Cost Reduction					
Standalone CGM plus multiple daily injections vs. SMBG plus multiple daily injections					
SMBG + MDI	125,586	18.812			
CGM + MDI	208,132	18.906	82,546	0.094	881,546
Sensor-augmented pump vs. SMBG plus multiple daily injections					
SMBG + MDI	125,586	18.812			
SAP	239,287	18.944	113,700	0.132	863,469
Standalone CGM plus insulin pump vs. SMBG plus insulin pump					
SMBG + insulin pump	177,320	18.812			
CGM + insulin pump	238,971	18.916	61,651	0.104	595,419
Sensor-augmented pump vs. SMBG plus insulin pump					
SMBG + insulin pump	177,320	18.812			
SAP	239,345	18.949	62,024	0.137	453,180
10% CGM Device Cost Reduction					
Standalone CGM plus multiple daily injections vs. SMBG plus multiple daily injections					
SMBG + MDI	125,586	18.812			
CGM + MDI	218,773	18.906	93,187	0.094	995,179
Sensor-augmented pump vs. SMBG plus multiple daily injections					
SMBG + MDI	125,586	18.812			
SAP	248,796	18.944	123,210	0.132	935,689
Standalone CGM plus insulin pump vs. SMBG plus insulin pump					
SMBG + insulin pump	177,320	18.812			
CGM + insulin pump	248,459	18.916	71,139	0.104	687,053
Sensor-augmented pump vs. SMBG plus insulin pump					
SMBG + insulin pump	177,320	18.812			
SAP	248,859	18.949	71,538	0.137	522,693

Abbreviations: CGM, continuous glucose monitoring; MDI, multiple daily injections; QALY, quality-adjusted life-years; SAP, sensor-augmented pump; SMBG, self-monitoring of blood glucose.

Scenario 3: Government Funding

Scenario 3 considered funding 75% of the cost of sensors, the usual practice by the Ministry of Health and Long-Term Care (Table 24). Continuous glucose monitoring was not cost-effective, even in the most favourable scenario from the purchaser perspective, with ICERs ranging from $402,619/QALY gained to $911,819/QALY gained.

Table 24: Scenario 3 Results

Intervention	Average Total Costs, $	Average Total Effects, QALYs	Incremental Cost, $	Incremental Effect, QALYs	ICER $/QALY
Insulin and Insulin Pump Covered					
Standalone CGM plus multiple daily injections vs. SMBG plus multiple daily injections					
SMBG + MDI	125,586	18.812			
CGM + MDI	229,413	18.906	103,827	0.094	1,108,812
Sensor-augmented pump vs. SMBG plus multiple daily injections					
SMBG + MDI	125,586	18.812			
SAP	186,966	18.944	61,380	0.132	466,133
Standalone CGM plus insulin pump vs. SMBG plus insulin pump					
SMBG + insulin pump	103,443	18.812			
CGM + insulin pump	186,771	18.916	83,328	0.104	804,781
Sensor-augmented pump vs. SMBG plus insulin pump					
SMBG + insulin pump	103,443	18.812			
SAP	187,002	18.949	83,559	0.137	610,523
Insulin Not Covered, Insulin Pump Covered					
Standalone CGM plus multiple daily injections vs. SMBG plus multiple daily injections					
SMBG + MDI	103,372	18.812			
CGM + MDI	207,067	18.906	103,695	0.094	1,107,402
Sensor-augmented pump vs. SMBG plus multiple daily injections					
SMBG + MDI	103,372	18.812			
SAP	174,759	18.944	71,388	0.132	542,135
Standalone CGM plus insulin pump vs. SMBG plus insulin pump					
SMBG + insulin pump	91,344	18.812			
CGM + insulin pump	174,593	18.916	83,248	0.104	804,007
Sensor-augmented pump vs. SMBG plus insulin pump					
SMBG + insulin pump	91,344	18.812			
SAP	174,790	18.949	83,446	0.137	609,694
Insulin Pump and 75% of Sensors Covered					
Standalone CGM plus multiple daily injections vs. SMBG plus multiple daily injections					
SMBG + MDI	125,586	18.812			
CGM + MDI	211,099	18.906	85,513	0.094	913,229
Sensor-augmented pump vs. SMBG plus multiple daily injections					
SMBG + MDI	125,586	18.812			
SAP	168,595	18.944	43,008	0.132	326,617

Intervention	Average Total Costs, $	Average Total Effects, QALYs	Incremental Cost, $	Incremental Effect, QALYs	ICER $/QALY
Standalone CGM plus insulin pump vs. SMBG plus insulin pump					
SMBG + insulin pump	103,443	18.812			
CGM + insulin pump	168,442	18.916	65,000	0.104	627,762
Sensor-augmented pump vs. SMBG plus insulin pump					
SMBG + insulin pump	103,443	18.812			
SAP	168,623	18.949	65,180	0.137	476,237
Insulin, Insulin Pump, and 75% of Sensors Covered					
Standalone CGM plus multiple daily injections vs. SMBG plus multiple daily injections					
SMBG + MDI	103,372	18.812			
CGM + MDI	188,753	18.906	85,381	0.094	911,819
Sensor-augmented pump vs. SMBG plus multiple daily injections					
SMBG + MDI	103,372	18.812			
SAP	156,388	18.944	53,016	0.132	402,619
Standalone CGM plus insulin pump vs. SMBG plus insulin pump					
SMBG + insulin pump	91,344	18.812			
CGM + insulin pump	156,264	18.916	64,919	0.104	626,988
Sensor-augmented pump vs. SMBG plus insulin pump					
SMBG + insulin pump	91,344	18.812			
SAP	156,411	18.949	65,067	0.137	475,407

Abbreviations: CGM, continuous glucose monitoring; MDI, multiple daily injections; QALY, quality-adjusted life year; SAP, sensor augmented pump; SMBG, self-monitoring of blood glucose.

Scenario 4: Structural Treatment Effect Constant for Rest of a Patient's Life

Scenario 4 analyzed the structural assumption of a treatment effect if it were constant for the rest of a patient's life (Table 25). In this scenario, ICERs decreased by 10 to 12 times compared with the base case, ranging from $58,379/QALY gained to $112,979/QALY gained.

Table 25: Scenario 4 Results

Intervention	Average Total Costs, $	Average Total Effects, QALYs	Incremental Cost, $	Incremental Effect, QALYs	ICER $/QALY
Standalone CGM Plus Multiple Daily Injections vs. SMBG Plus Multiple Daily Injections					
SMBG + MDI	125,586	18.812			
CGM + MDI	241,703	19.840	116,117	1.0278	112,979
Sensor-Augmented Pump vs. SMBG Plus Multiple Daily Injections					
SMBG + MDI	125,586	18.812			
SAP	285,827	20.593	160,240	1.7805	89,995
Standalone CGM Plus Insulin Pump vs. SMBG Plus Insulin Pump					
SMBG + insulin pump	177,320	18.812			
CGM + insulin pump	275,981	20.025	98,661	1.2125	81,369
Sensor-Augmented Pump vs. SMBG Plus Insulin Pump					
SMBG + insulin pump	177,320	18.812			
SAP	287,841	20.705	110,520	1.8931	58,379

Abbreviations: CGM, continuous glucose monitoring; MDI, multiple daily injections; QALY, quality-adjusted life-year; SAP, sensor-augmented pump; SMBG, self-monitoring of blood glucose.

Scenario 5: Delay of Severe Diabetes Complications for 10 Years

In scenario 5, severe diabetes-related complications occurred only after the 10th cycle (16 years after diagnosis) to reflect current clinical realities (Table 26). Compared with the base case, a delay in entering a severe diabetes health state until after the 10th cycle increased ICER values by 10% to 30%, depending on the continuous glucose monitoring intervention. This finding was owing to a decrease in incremental effect.

Table 26: Scenario 5 Results

Intervention	Average Total Costs, $	Average Total Effects, QALYs	Incremental Cost, $	Incremental Effect, QALYs	ICER $/QALY
Standalone CGM Plus Multiple Daily Injections vs. SMBG Plus Multiple Daily Injections					
SMBG + MDI	130,228	19.279			
CGM + MDI	235,081	19.354	104,853	0.075	1,397,670
Sensor-Augmented Pump vs. SMBG Plus Multiple Daily Injections					
SMBG + MDI	130,228	19.279			
SAP	264,115	19.380	133,887	0.101	1,328,239
Standalone CGM Plus Insulin Pump vs. SMBG Plus Insulin Pump					
SMBG + insulin pump	182,585	19.279			
CGM + insulin pump	263,892	19.361	81,307	0.082	994,805
Sensor-Augmented Pump vs. SMBG Plus Insulin Pump					
SMBG + insulin pump	182,585	19.279			
SAP	264,156	19.384	81,571	0.104	781,967

Abbreviations: CGM, continuous glucose monitoring; MDI, multiple daily injections; QALY, quality-adjusted life-year; SAP, sensor-augmented pump; SMBG, self-monitoring of blood glucose.

Discussion

Our cost-effectiveness analyses showed that various continuous glucose monitoring interventions were not cost-effective compared with self-monitoring of blood glucose (usual care) at common willingness-to-pay thresholds. All continuous glucose monitoring interventions were more effective but more costly than the corresponding self-monitoring of blood glucose strategies. They were associated with ICERs ranging from $592,206/QALY gained to $1,108,812/QALY gained, much higher than the empirical threshold of $50,000/QALY gained.

The cost-effectiveness results were most sensitive to the relative risk of neuropathy, the risk reduction of severe hypoglycemic events, and the cost of the continuous glucose monitoring device. The results were less sensitive to excess mortality, the costs or utilities of diabetes complications, and the costs of severe hypoglycemic events. Our findings remained robust in all scenario analyses except one, which assumed lifelong effectiveness of continuous glucose monitoring and continuing risk reduction for all complications over a patient's lifetime. Some experts may argue that this is the most realistic scenario, and some economic evaluations have used this approach.

Our results were in agreement with the findings of several cost-effectiveness analyses. A recent health technology assessment by NICE concluded that self-monitoring of blood glucose combined with multiple daily injections was cost-effective compared to continuous glucose monitoring and different insulin infusion options.[31,58] The results for the NICE base case model ranged from £133,323/QALY gained to £730,501/QALY gained ($221,316 CAD/QALY gained to $1,210,495 CAD/QALY gained using an exchange rate of £1 = $1.66 CAD, assessed July 14, 2017). In general, these findings were in line with our results. Differences were related to variations in modelling approach, including the model structure (we used a more simplified approach, while NICE used the CORE global model, including 17 diabetes complication sub-models) and model parameters (we used pairwise comparison for clinical effectiveness, and NICE used indirect comparison). As well, the costs used in the model were different: we used the Ontario health care perspective, and NICE used a United Kingdom perspective.

In our model, the benefits of continuous glucose monitoring were limited to reductions in A1C and fewer severe hypoglycemic events. Lower A1C and better management of A1C lowers the probability of diabetes complications in the long term. Scenario analyses conducted by Huang et al[57] limited to glucose-lowering, with a subsequent reduction in diabetes risk complications, resulted in ICERs from $701,397 USD/QALY gained to $1,185,384 USD/QALY gained. The authors concluded that the benefits from improved glycemic control were relatively small, because complications occurred later in a patient's life, so the benefits of complication reduction were heavily discounted.[57]

Other studies by Roze et al[53-56] and McQueen et al[51] demonstrated the cost-effectiveness of continuous glucose monitoring compared with self-monitoring of blood glucose. These authors may have modelled a continually decreasing rate of complications in the long term with continuous glucose monitoring.

Limitations

Although we used a comprehensive modelling approach, our study had several limitations.

We simplified the clinical pathway of the disease, and although we modelled the most important stages of the disease, we did not model all possible stages.

Evidence for the clinical effectiveness of standalone continuous glucose monitoring in reducing severe hypoglycemia was unclear. A systematic review and meta-analysis of randomized trials indicated that data for the incidence of severe or nocturnal hypoglycemia were sparse and imprecise.[106] The clinical evidence review in this health technology assessment found that there was low certainty about the effectiveness of continuous glucose monitoring to reduce the number of severe hypoglycemic events compared with self-monitoring of blood glucose.

We obtained treatment effects owing to reductions in A1C and severe hypoglycemic events from the clinical evidence review, but we obtained consequent risk reductions for diabetes complications from the Diabetes Control and Complications Trial.[64]

The treatment pattern used in the Diabetes Control and Complications Trial might not match the current standard. The Diabetes Control and Complications Trial (reported in 1993) was a long-term, multicentre randomized clinical trial with a long-term follow-up study (Epidemiology of Diabetes Interventions and Complications study).[64,74] These studies were the only ones to follow patients with type 1 diabetes for more than 25 years. The long-term outcomes from these studies provide a reliable sense of the clinical course expected with modern therapy at the time of the trial, but not with more recent treatment regimens.[76]

The level of treatment adherence achieved during the Diabetes Control and Complications Trial[64] might not be achieved by the general population of patients with type 1 diabetes, so the long-term benefits from the reduction of diabetes complications might be smaller.

We were unable to rank the continuous glucose monitoring devices, because studies that examined and compared devices were excluded from the clinical evidence review.

Owing to the scarcity of utility data and probabilities for children with type 1 diabetes, we did not develop a model for this population. Numerous assumptions would have been required to generate such a model, leading to vast uncertainties.

Finally, our model accounted for the potential impact of severe hypoglycemic events and improved glycemic control in people with type 1 diabetes. We modelled impacts from the reduction of severe hypoglycemic events and from decreased patient worry through improvements in health-related quality of life. The clinical evidence showed a significant decrease in severe hypoglycemic events, but there was a high level of uncertainty with these results (based on the GRADE analysis).

Our results were in agreement with results from other published studies. Future research should evaluate the rates of severe hypoglycemic events more precisely. Severe hypoglycemia should be reported uniformly, with standard cut-offs and definitions.[106] Preferably, results should be reported per patient-year instead of per event.[106]

Conclusion

Compared with self-monitoring of blood glucose (usual care), our base case estimate was that continuous glucose monitoring provides modest incremental benefit at substantial incremental cost. However, there was considerable uncertainty about value for money, given the nature of the available evidence.

BUDGET IMPACT ANALYSIS

We conducted a budget impact analysis from the perspective of the Ontario Ministry of Health and Long-Term Care to estimate the cost burden of publicly funding continuous glucose monitoring devices over the next 5 years. All costs are reported in 2017 Canadian dollars. We forecasted the 5-year budget impact starting from 2018 to address current changes in policy regulation related to government funding of prescription medications for children and youth up to age 24 years.[107] Although we did not conduct a primary economic evaluation in children owing to a lack of data, we did consider a subgroup of the population younger than 24 years in the budget impact analysis. Our reporting and analysis are in accordance with the 2012 International Society for Pharmacoeconomics and Outcomes Research (ISPOR) good practice guidelines for budget impact analyses.[108]

Research Question

What is the 5-year budget impact of publicly funding continuous glucose monitoring devices in patients with type 1 diabetes in the context of the Ontario Ministry of Health and Long-Term Care?

Methods

Target Population

We forecasted the prevalence of diabetes for Ontario's population based on data from the Canadian Diabetes Cost Model, developed by the Canadian Diabetes Association.[109] We applied an annual prevalence rate increase of 0.31% for 2018 to 2022. We obtained a projection of the Ontario population from Statistics Canada.[110] According to the Canadian Diabetes Association, the prevalence of type 1 diabetes ranges from 5% to 10%.

Data from a budget impact analysis by a continuous glucose monitoring manufacturer indicated that about 113,000 people in Ontario had type 1 diabetes in 2017.[111] The manufacturer used the median prevalence (i.e., 7.5%) from the range provided by the Canadian Diabetes Association, above. However, our experts suggested that the prevalence of type 1 diabetes among adults in Ontario in 2017 is 6%; we used that figure to calculate the target population for our model (Table 27). According to Statistics Canada, the number of patients with type 1 diabetes is expected to increase over the next 5 years, from 90,288 in 2017 to 105,932 in 2022.[110]

Based on consultations with experts (endocrinologists, diabetes educators, and manufacturers of continuous glucose monitoring devices), we identified a subgroup of people with hypoglycemia unawareness who would benefit most from continuous glucose monitoring. The prevalence of hypoglycemia unawareness in type 1 diabetes ranges from 20% to 29%.[105,112,113] We used a median prevalence of 25% in our model (Table 27).

Table 27: Ontario Population and Estimated Prevalence of Type 1 Diabetes

Population/Prevalence	2017	2018	2019	2020	2021	2022
Ontario population, n	13,920,500	14,004,100	14,081,900	14,154,600	14,222,100	14,284,300
Projected prevalence of diabetes in Ontario, %	10.81	11.12	11.43	11.74	12.05	12.36
Ontario population with diabetes (type 1 and type 2), n	1,504,806	1,557,256	1,609,561	1,661,750	1,713,763	1,765,539
Prevalence of type 1 diabetes, % (range 5% to 10%)	6	6	6	6	6	6
Ontario population with type 1 diabetes (estimate),[a] n	90,288	93,435	96,574	99,705	102,826	105,932
Ontario population with hypoglycemia unawareness,[a] n (25% of people with type 1 diabetes)	22,572	23,359	24,143	24,926	25,706	26,483

[a]Values used in the budget impact analysis.

In 2018, the Ontario government will start a new pharmacare program that will cover drug costs (including blood glucose test strips and insulin) for children and youth up to 24 years of age.[107] We applied this change to our costing of insulin and test strips for people in this age group. To account for the change in drug funding, we grouped our target populations into three categories (0–24 years, 25–64 years, and 65+ years) and estimated the number of people with type 1 diabetes for each age subgroup (Table 28). See Appendix 8 (Tables A16 and A17) for estimates of government funding by age group.

Table 28: Ontario Populations with Diabetes, Type 1 Diabetes, and Hypoglycemia Unawareness, by Age Group

Age, y	2018	2019	2020	2021	2022
Ontario Population With Diabetes					
0–24	438,362	448,102	457,426	466,974	477,133
25–64	848,956	874,784	899,789	923,958	946,319
65+	269,927	286,676	304,512	322,856	342,112
Total[a]	1,557,245	1,609,561	1,661,727	1,713,787	1,765,564
Ontario Population With Type 1 Diabetes (Prevalence 6%)					
0–24	26,302	26,886	27,446	28,018	28,628
25–64	50,937	52,487	53,987	55,437	56,779
65+	16,196	17,201	18,271	19,371	20,527
Total[a]	93,435	96,574	99,704	102,827	105,934
Ontario Population With Hypoglycemia Unawareness (Prevalence 25% of People with Type 1 Diabetes)					
0–24	6,575	6,722	6,861	7,005	7,157
25–64	12,734	13,122	13,497	13,859	14,195
65+	4,049	4,300	4,568	4,843	5,132
Total[a]	23,359	24,143	24,926	25,707	26,483

[a]Total estimates might not match with those in Table 28 due to rounding.

Resource

We received information from two main manufacturers of continuous glucose monitoring devices: Dexcom (standalone continuous glucose monitoring devices) and Medtronic (sensor-augmented pump with or without a low-glucose suspend feature). Based on this information, we estimated the annual use of continuous glucose monitoring interventions in two scenarios: manufacturer-suggested projections and conservative projections with 20% annual increase in uptake based on the number of current users (Figure 8 and Appendix 8, Table A18).

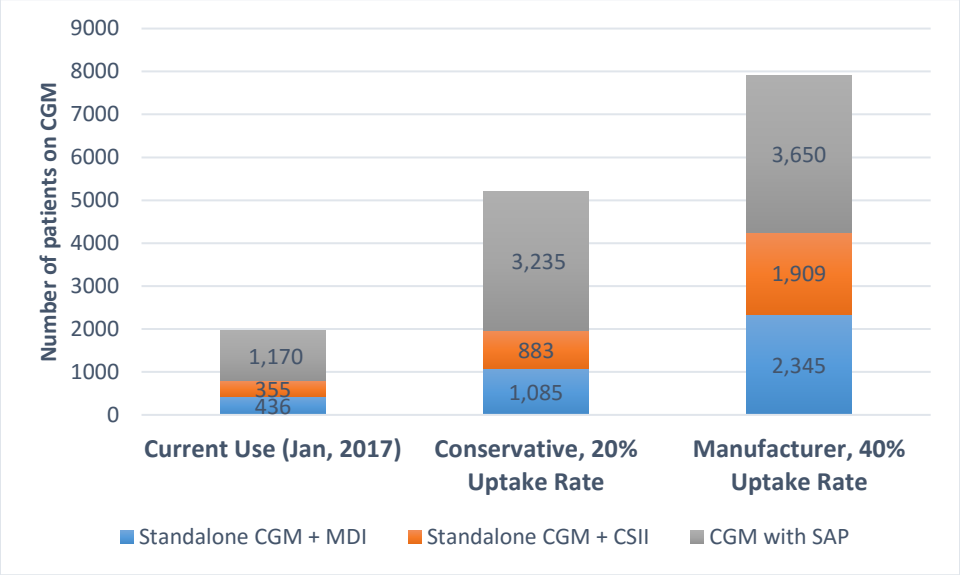

Figure 6: Continuous Glucose Monitoring—Current Use and Projection Scenarios in Ontario, 2018–2022

Abbreviations: CGM, continuous glucose monitoring; CSII, continuous subcutaneous insulin infusion (insulin pump); MDI, multiple daily injections; SAP, sensor-augmented pump.
Source: Information for current use and manufacturer projections provided by Dexcom and Medtronic in January 2017.

Based on Dexcom's projections, the number of patients in Ontario to use standalone continuous glucose monitoring will be about 3,800 to 4,500 in 5 years. This projection was based on a 5% adoption rate at the introduction of continuous glucose monitoring in the United States. Currently, about 800 people use standalone continuous glucose monitoring devices in Ontario. We estimated that a 40% annual increase in uptake would be needed to reach the projected goal.

Based on data from Medtronic, about 1,300 people use continuous glucose monitoring devices integrated with a sensor-augmented pump. Of these, 1,170 have a sensor-augmented pump with a low-glucose suspend feature. Those using a sensor-augmented pump and continuous glucose monitoring are the most motivated, because they fear hypoglycemia (Appendix 8, Table A19). These patients pay out of pocket or through private insurance for continuous glucose monitoring sensors. Based on the experiences of other countries that fund continuous glucose monitoring sensors, sensor use tends to reach a plateau after 5 years, at approximately 30% of sensor-augmented pump users. Medtronic projected a 25% annual increase in the use of sensor-augmented pumps with continuous glucose monitoring.

Table 29 presents the number of patients projected to use standalone continuing glucose monitoring or sensor-augmented pumps with continuous glucose monitoring based on manufacturer information.

Table 29: Estimated Annual Number of Patients Using Continuous Glucose Monitoring in Ontario, Manufacturer Projections

	Year 1	Year 2	Year 3	Year 4	Year 5
Standalone CGM + multiple daily injections	610	855	1,196	1,675	2,345
Standalone CGM + insulin pump	497	696	974	1,364	1,909
Total standalone CGM devices	1,107	1,550	2,171	3,039	4,254
Sensor-augmented pumps	1,768	2,163	2,700	3,276	3,650
Total CGM users	2,875	3,714	4,870	6,314	7,904

Abbreviation: CGM, continuous glucose monitoring.
Totals may appear inexact due to rounding.

However, we used a conservative 20% annual increase of adoption of continuous glucose monitoring based on the number of current users (Table 30) for the following reasons:

- Dexcom obtained its adoption rate for standalone continuous glucose monitoring devices from progressive hospitals with higher-than-average adoption rates
- The infrastructure for continuous glucose monitoring in Canada is still under development; more educators, manuals, and technical support are required for wide implementation

Table 30: Estimated Annual Number of Patients Using Continuous Glucose Monitoring in Ontario, Conservative Projections

	Year 1	Year 2	Year 3	Year 4	Year 5
Standalone CGM + multiple daily injections	523	628	753	904	1,085
Standalone CGM + insulin pump	426	511	613	736	883
Total standalone CGM devices	949	1,139	1,367	1,640	1,968
Sensor-augmented pumps	1,560	1,872	2,246	2,696	3,235
Total CGM users	2,509	3,011	3,613	4,336	5,203

Abbreviation: CGM, continuous glucose monitoring.

Canadian Costs

Reference Case

We assessed the budget impact of funding continuous glucose monitoring for three patient populations:

- The total number of people projected to use continuous glucose monitoring (Table 30)
- The Ontario population with type 1 diabetes and hypoglycemia unawareness (Table 28)
- The entire Ontario type 1 diabetes population (Table 28)

The Ontario government provides funding to people with diabetes, covering some of the medical costs associated with diabetes management. Support varies by age group, type of diabetes, and type of insulin used (Appendix 8, Table A20).

Beginning in January 1, 2018, the provincial government will fund prescription medications for children and youth 24 years of age or younger.[107] This government also funds most types of insulin and blood glucose testing strips for those 65 years or older. For people over age 65, the government also provides an annual grant of $170, paid once per year, for the purchase of needles and syringes to inject insulin.

According to the Ministry of Health and Long-Term Care, approximately 17% of people in Ontario do not have drug funding through private plans or the Ontario Drug Benefit program. Patients who are not eligible for the Ontario Drug Benefit program can receive a 75% reimbursement for test strips and lancets, up to a maximum of $920 per year, through the Ontario Monitoring for Health Program.[114]

The Assistive Devices Program covers the cost of insulin pumps and related supplies for people of all ages with type 1 diabetes who meet the program's medical eligibility criteria.

Estimated annual per-patient costs for continuous glucose monitoring with various types of government funding for type 1 diabetes presented in Table 31.

We calculated the amount of existing government support for diabetes supplies, blood glucose test strips, and insulin for the different age groups and patient populations (Appendix 8, Tables A16 and A17).

Table 31: Estimated Annual Per-Patient Costs of Continuous Glucose Monitoring When Insulin Pump, Insulin, and Supplies Are Publicly Funded

Intervention	Technology	Year 1, $	Year 2, $	Year 3, $	Year 4, $	Year 5, $
Comparators						
SMBG + multiple daily injections	—	2,329	2,692	2,952	3,134	3,251
SMBG + insulin pump	Animas Vibe	1,599	1,963	2,234	2,432	2,566
Interventions						
CGM + multiple daily injections	Dexcom G4/G5	7,994[a]	8,340[a]	8,479[a]	8,529[a]	8,506[a]
CGM + insulin pump	Integrated	6,647[b]	6,974[b]	7,150[b]	7,232[b]	7,241[b]
SAP with LGS	MiniMed Veo	4,186	4,493	4,731	4,873	4,940
SAP or SAP with LGS	10% SAP; 90% SAP with LGS	4,432	4,741	4,973	5,109	5,170
Average CGM device	40% CGM + multiple daily injections; 60% SAP	5,857	6,181	6,376	6,477	6,505

Abbreviations: CGM, continuous glucose monitoring; LGS, low-glucose suspend [feature]; SAP, sensor-augmented pump; SMBG, self-monitoring of blood glucose.
[a]Average cost of Dexcom G4 Platinum and Dexcom G5 Mobile.
[b]Average cost of Dexcom G4 Platinum + Animas Vibe and Dexcom G5 Mobile + Animas Vibe.

Scenarios

We estimated the annual costs per patient if continuous glucose monitoring were publicly funded by the Ministry of Health and Long-Term Care. We calculated annual per-patient costs for the following scenarios:

- Scenario 1: All direct medical costs (Table 32). We calculated average annual costs per patient from years 1 to 5 based on our model estimates (from deterministic non-discounted cost-utility analyses; see Primary Economic Evaluation).

- Scenario 2: Funding for insulin, pump, and 75% of sensors (Table 33)

For these scenarios, we calculated the funding for blood glucose test strips by age group, because funding varies by patient age.

Table 32: Estimated Annual Per-Patient Costs (All Direct Medical Costs) of Continuous Glucose Monitoring in Ontario

Intervention	Technology	Year 1, $	Year 2, $	Year 3, $	Year 4, $	Year 5, $
Comparators						
SMBG + multiple daily injections	—	3,677	4,039	4,277	4,431	4,515
SMBG + insulin pump	Animas Vibe	6,817	7,175	7,365	7,450	7,458
Interventions						
CGM + multiple daily injections	Dexcom G4/G5	9,342[a]	9,693[a]	9,810[a]	9,830[a]	9,775[a]
CGM + insulin pump	Integrated	11,673[b]	12,075[b]	12,126[b]	12,090[b]	11,980[b]
SAP with LGS	MiniMed Veo	9,211	9,531	9,673	9,701	9,649
SAP or SAP with LGS	10% SAP; 90% SAP with LGS	9,457	9,785	9,918	9,940	9,882
Average for CGM devices	40% CGM + multiple daily injections; 60% CGM + SAP	9,411	9,748	9,875	9,896	9,839

Abbreviations: CGM, continuous glucose monitoring; LGS, low-glucose suspend [feature]; SAP, sensor-augmented pump; SMBG, self-monitoring of blood glucose.
[a]Average cost of Dexcom G4 Platinum and Dexcom G5 Mobile.
[b]Average cost of Dexcom G4 Platinum + Animas Vibe and Dexcom G5 Mobile + Animas Vibe.

Table 33: Estimated Annual Per-Patient Costs of Continuous Glucose Monitoring when Insulin Pump, Insulin, and 75% of Sensor Costs Are Publicly Funded

Intervention	Technology	Year 1, $	Year 2, $	Year 3, $	Year 4, $	Year 5, $
Comparators						
SMBG + multiple daily injections	—	2,329	2,692	2,952	3,134	3,251
SMBG + insulin pump	Animas Vibe	1,599	1,963	2,234	2,432	2,566
Interventions						
CGM + multiple daily injections	Dexcom G4/G5	6,889[a]	7,240[a]	7,389[a]	7,461[a]	7,465[a]
CGM + insulin pump	Integrated	5,542[b]	5,893[b]	6,058[b]	6,157[b]	6,194[b]
SAP with LGS	MiniMed Veo	3,406	3,725	3,959	4,112	4,199
SAP or SAP with LGS	10% SAP; 90% SAP with LGS	3,619	3,942	4,169	4,317	4,399
Average CGM device	40% CGM + multiple daily injections; 60% CGM + SAP	4,927	5,261	5,457	5,574	5,625

Abbreviations: CGM, continuous glucose monitoring; LGS, low-glucose suspend [feature]; SAP, sensor-augmented pump; SMBG, self-monitoring of blood glucose.
[a]Average cost of Dexcom G4 Platinum and Dexcom G5 Mobile.
[b]Average cost of Dexcom G4 Platinum + Animas Vibe and Dexcom G5 Mobile + Animas Vibe.

We also considered a third scenario—a hypothetical situation in which device costs underwent price negotiations, and calculated the budget impact corresponding to device cost reductions of 10%, 20% or 30% (Table 34).

Table 34: Estimated Annual Costs of Continuous Glucose Monitoring Devices With Cost-Reduction Scenarios

	Device Cost, $			
Strategies	**Base Case**	**10% Reduction**	**20% Reduction**	**30% Reduction**
CGM + multiple daily injections (average)	9,342	8,408	7,474	6,539
SAP (average)	11,673	10,505	9,338	8,171
SAP (± LGS)	9,211	8,290	7,369	6,448
Average cost of CGM	9,411	8,470	7,529	6,588

Abbreviations: CGM, continuous glucose monitoring; LGS, low glucose suspend [feature]; SAP, sensor-augmented pump; SMBG, self-monitoring of blood glucose.

Analysis

To address all possible scenarios in Ontario, we conducted the following budget impact analyses:

- Three reference case analyses to estimate the net budget impact of continuous glucose monitoring compared with self-monitoring of blood glucose after accounting for government funding of insulin treatment, insulin pump, and blood glucose test strips:
  - The total number of people projected to use continuous glucose monitoring, based on a 20% annual increase of adoption in Ontario
  - The Ontario population with hypoglycemia unawareness
  - The entire Ontario type 1 diabetes population
- Two sensitivity analyses to estimate the net budget impact of considering all direct medical costs (scenario 1) and different levels of government funding (insulin, insulin pump, and blood glucose test strips, plus 75% of sensor costs; scenario 2) by age group
- Various price negotiation scenarios for the continuous glucose monitoring device (30%, 20% and 10% price reductions; scenario 3)
- Four sensitivity analyses to estimate the net budget impact of price reductions for continuous glucose monitoring devices and 75% of sensor costs (scenario 4)
- Sensitivity analyses of the base case and all above-mentioned scenarios, based on Dexcom's projected 40% annual increase of adoption in Ontario (scenario 5)

We calculated the net budget impact cumulatively: annual costs included the costs of new continuous glucose monitoring devices and expenses for devices introduced in previous years.

Results

Reference Case

Table 35 shows the net budget impact for the reference case, using data on continuous glucose monitoring uptake, the percentage of patients with hypoglycemia unawareness (Tables 28 and 30), the entire type 1 diabetes population, and annual per-patient costs of technologies (Table 31). Appendix 8, Tables A21 to 23, provide the net budget impact by age group.

Table 35: Net Budget Impact of Funding Continuous Glucose Monitoring in Ontario

Intervention	Year 1, $	Year 2, $	Year 3, $	Year 4, $	Year 5, $
Funding CGM Based on a Conservative Projection of a 20% Annual Increase					
CGM	14,192,322	17,835,103	22,441,206	27,412,678	31,857,150
SMBG	5,701,743	7,953,809	10,498,720	13,226,191	15,621,231
Net budget impact	8,490,579	9,881,295	11,942,486	14,186,487	16,235,919
Funding CGM for Entire Population With Hypoglycemia Unawareness					
CGM	120,487,478	131,981,755	140,758,669	147,524,997	152,658,439
SMBG	41,693,554	51,518,633	59,307,520	65,546,416	70,408,816
Net budget impact	78,793,925	80,463,123	81,451,149	81,978,581	82,249,622
Funding CGM for the Entire Type 1 Diabetes Population					
CGM	481,949,914	527,927,021	563,034,675	590,099,986	610,633,755
SMBG	166,774,215	206,074,531	237,230,078	262,185,663	281,753,568
Net budget impact	315,175,698	321,852,490	325,804,597	327,914,323	328,880,187

Abbreviations: CGM, continuous glucose monitoring; SMBG, self-monitoring of blood glucose.

Scenarios

Scenario 1: All Direct Medical Costs

We assessed the budget impact of funding continuous glucose monitoring when considering all direct medical costs (excludes government funding for insulin, insulin pump, and blood glucose test strips) by age group (Table 36).

Table 36: All Direct Medical Costs

Age, [a] y	Year 1, $	Year 2, $	Year 3, $	Year 4, $	Year 5, $
Funding CGM Based on a Conservative Projection of a 20% Annual Increase					
All ages	13,663,640	16,350,489	19,342,798	22,893,882	27,137,269
0–24	3,846,289	4,602,632	5,444,962	6,444,585	7,639,091
25–65	7,448,947	8,913,725	10,545,030	12,480,958	14,794,307
65+	2,368,403	2,834,131	3,352,807	3,968,338	4,703,871
Funding CGM for Entire Population With Hypoglycemia Unawareness					
All ages	121,695,684	125,149,848	126,682,327	127,706,376	128,424,590
0–24	34,257,109	35,229,450	35,660,840	35,949,108	36,151,284
25–65	66,344,309	68,227,400	69,062,855	69,621,132	70,012,677
65+	21,094,266	21,692,998	21,958,632	22,136,137	22,260,629
Funding CGM for Entire Type 1 Diabetes Population					
All ages	486,782,736	500,599,393	506,729,308	510,825,506	513,308,356
0–24	137,028,436	140,917,800	142,643,359	143,796,431	144,495,349
25–65	265,377,235	272,909,602	276,251,421	278,484,528	279,838,092
65+	84,377,065	86,771,991	87,834,527	88,544,547	88,974,915

Abbreviations: CGM, continuous glucose monitoring; NBI, net budget impact.

[a]Ages 0–24 years, full funding of blood glucose test strips (annual cost $1,243); 25–65 years, strips funded to a maximum of $920; 65+ years, full funding of strips and $170 grant for syringes and needles.

Scenario 2: Government Funding for the Insulin, Pump, Strips, and 75% of Sensor Costs, by Age Group

Because government funding is for patients with type 1 diabetes and would involve only the addition of 75% sensor costs, the net budget impact of this scenario (Table 37) was much lower than that of the reference case and scenario 1. Appendix 8, Tables A24 to A26, provide the calculation details. Appendix 8, Table A27, provides details on adopting continuous glucose monitoring for the population with hypoglycemia awareness using a conservative projection.

Table 37: Net Budget Impact of Funding Continuous Glucose Monitoring in Ontario by Age Group—Funding for Insulin, Pump, Strips, and 75% of Sensor Costs

Age,[a] y	Year 1, $	Year 2, $	Year 3, $	Year 4, $	Year 5, $
Funding CGM Based on a Conservative Projection of a 20% Annual Increase					
All ages	6,258,114	7,212,880	8,616,558	10,212,713	11,746,912
0–24	1,738,689	2,003,952	2,393,935	2,837,394	3,263,640
25–65	3,397,447	3,915,777	4,677,815	5,544,347	6,377,243
65+	1,121,977	1,293,151	1,544,808	1,830,972	2,106,029
Funding CGM for Entire Population With Hypoglycemia Unawareness					
All ages	62,186,324	63,630,543	64,296,591	64,842,725	65,295,437
0–24	17,499,740	17,721,986	17,688,562	17,646,273	17,613,612
25–65	33,898,320	34,600,771	34,804,315	34,934,408	34,960,287
65+	10,788,265	11,307,785	11,803,714	12,262,045	12,721,538
Funding CGM for Entire Type 1 Diabetes Population					
All ages	248,745,298	254,522,171	257,186,365	259,370,901	261,063,447
0–24	69,998,960	70,887,946	70,754,249	70,585,090	70,421,580
25–65	135,593,278	138,403,086	139,217,260	139,737,631	139,776,924
65+	43,153,060	45,231,139	47,214,856	49,048,180	50,864,943

Abbreviations: CGM, continuous glucose monitoring; NBI, net budget impact.

[a]Ages 0–24 years, full funding of blood glucose test strips (annual cost $1,243); 25–65 years, strips funded to a maximum $920; 65+ years, full funding of strips and $170 grant for syringes and needles.

Scenario 3: Cost Reductions for Continuous Glucose Monitoring Devices

Table 38 presents the budget impact of including only the costs associated with the continuous glucose monitoring device (i.e., transmitter, sensors, and batteries). Public funding of continuous glucose monitoring would motivate more people to use it, which would stimulate production growth and potentially decrease the costs of production, especially the costs of sensors. Appendix 8, Table A28 provides details of estimated reductions in the cost of continuous glucose monitoring devices.

Table 38: Net Budget Impact of Cost Reductions for Continuous Glucose Monitoring Devices

Intervention	Year 1, $	Year 2, $	Year 3, $	Year 4, $	Year 5, $
Funding CGM Based on a Conservative Projection of a 20% Annual Increase					
Device cost	13,663,640	16,396,368	19,675,642	23,610,770	28,332,924
Device cost + 75% sensor cost	11,396,928	13,676,314	16,411,577	19,693,892	23,632,670
Device cost reduced by 30%	6,394,826	7,673,791	9,208,550	11,050,260	13,260,312
Funding CGM for Entire Population With Hypoglycemia Unawareness					
Device cost	121,695,684	125,704,689	129,684,091	133,627,989	137,530,346
Device cost + 75% sensor cost	99,975,005	103,254,454	106,505,923	109,724,341	112,904,518
Device cost reduced by 30%	55,746,044	57,539,926	59,309,134	61,050,287	62,759,917
Funding CGM for Entire Type 1 Diabetes Population					
Device cost	486,782,736	502,818,757	518,736,363	534,511,956	549,760,390
Device cost + 75% sensor cost	399,900,019	413,017,815	426,023,690	438,897,364	451,257,077
Device cost reduced by 30%	222,984,175	230,159,706	237,236,538	244,201,146	250,678,673

Abbreviations: CGM, continuous glucose monitoring.

We also conducted scenarios involving device cost reductions of 10%, 20%, and 30%. The budget impact of device cost reductions are presented in Appendix 8, Tables A29 to A31. The cost reduction by 30% showed a significant reduction in net budget impact.

Scenario 4: Cost Reductions for Continuous Glucose Monitoring Devices and Government Funding

Appendix 8, Table A32, presents the results of scenario 4, which estimated the budget impact of device cost reductions plus government funding for insulin, insulin pump, blood glucose test strips, and 75% of sensors.

The additional investment to implement this scenario in Ontario, assuming a conservative annual adoption rate of 20%, would be as follows:

- If device costs were reduced as suggested above, the net budget impact would range from $1.9 million to $8.7 million
- If continuous glucose monitoring were funded for those with hypoglycemia unawareness, the net budget impact would range from $23.1 million to $54.3 million
- If continuous glucose monitoring were funded for the entire type 1 diabetes population across all cost reduction scenarios, the net budget impact would range from $92.6 million to $217.1 million

Scenario 5: 40% Annual Increase in Adoption of Continuous Glucose Monitoring in Ontario

The net budget impact would vary from $9.3 million to $27.5 million over the next 5 years (Appendix 8, Table A33). This amount significantly declines when considering various scenarios of government support or reductions in device and sensor costs. Appendix 8, Table A34, also presents the net budget impact of funding continuous glucose monitoring for the entire type 1 diabetes population and for those with hypoglycemia unawareness.

Discussion

The budget impact of funding continuous glucose monitoring would be large compared to the budget impact of many other novel technologies, because of the large number of people with type 1 diabetes and the high cost of supplies (sensors) for continuous glucose monitoring. Based on a projected 20% annual increase in uptake (starting from 2,091 current users), funding continuous glucose monitoring over the next 5 years would cost the province $8.5 million in year 1 to $16.2 million in year 5. Funding continuous glucose monitoring devices for the entire population with hypoglycemia unawareness (26,483 users) could result in extra spending of $78.8 million in year 1 to $82.2 million in year 5.

Of the 5,203 new users of continuous glucose monitoring projected in the next 5 years, an estimated 62% would use integrated monitoring (continuous glucose monitoring with a sensor-augmented pump, with or without a low-glucose suspend feature), and 38% would use standalone continuous glucose monitoring. Budget spending would be expected to increase over time with higher uptake.

A budget impact analysis of introducing Dexcom continuous glucose monitoring in patients with type 1 diabetes with hypoglycemia unawareness in Ontario[111,115] showed a cost savings of $140 million over 5 years. These results were not in line with our findings for several possible reasons.

First, in the Dexcom analysis, the clinical benefits of continuous glucose monitoring were associated with a reduction in emergency department visits and hospital admissions related to severe hypoglycemia patients with in type 1 diabetes. As well, these data were obtained from a European online survey.[93] The survey evaluated the burden of hypoglycemia in insulin-treated patients with diabetes but did not specify methods of blood glucose monitoring. Linking those reductions in emergency department visits and hospital admissions with the use of continuous glucose monitoring may not have been clinically valid.

Second, the potential for continuous glucose monitoring to reduce the number of severe hypoglycemic events and lower A1C versus self-monitoring of blood glucose was unclear. Data on the incidence of severe hypoglycemic events were obtained from short-term (less than 1 year) studies[24,31,39] that showed mixed results. In addition, the rates of severe hypoglycemic events, typically identified as events requiring the assistance of another person (e.g., a seizure, loss of consciousness, or hospitalization), were not properly reported. Longitudinal data from the Diabetes Control and Complications Trial demonstrated that tight control of A1C is associated with a reduction in long-term complications but also with an increased risk of severe hypoglycemic events.[76] The clinical evidence review in this health technology assessment was in agreement with other studies, showing no statistically significant difference in rates of severe hypoglycemic events among patients who used continuous glucose monitoring versus those who used self-monitoring of blood glucose.[106]

Third, we considered patients with hypoglycemia unawareness as a subgroup in our budget impact analysis but did not assess this group in the primary economic evaluation, owing to limited clinical evidence for this population. However, we do agree that patients with hypoglycemia unawareness could benefit most from using continuous glucose monitoring. More research is required to assess the clinical effectiveness of continuous glucose monitoring in patients with hypoglycemia unawareness.

Finally, our primary economic evaluation showed that the cost of continuous glucose monitoring devices was one of the main drivers of the model results. Costs for continuous glucose monitoring are three to four times higher than those for self-monitoring of blood glucose.

Our model-based budget impact analysis provided robust costing parameters and was based on a rigorous systematic review of the best quality evidence to minimize possible biases. Using real-world data from randomized controlled studies was a more robust approach than calculating budget impact based on hypothetical scenarios, as in the Dexcom analysis.

Conclusions

If continuous glucose monitoring were publicly funded in Ontario as an alternative to self-monitoring of blood glucose in patients with type 1 diabetes, the net budget impact for the province would be $8.5 million to $16.2 million over the next 5 years, assuming a 20% increase in adoption each year. Funding continuous glucose monitoring for the entire population with hypoglycemia unawareness would lead to a net budget impact of $78.8 million to $82.2 million over the next 5 years.

PATIENT, CAREGIVER, AND PUBLIC ENGAGEMENT

Objective

The objective of this analysis was to explore the underlying values, needs, impacts, and preferences of those who have lived experience with type 1 diabetes. The treatment focus was continuous glucose monitoring versus usual care (self-monitoring of blood glucose using a finger-stick and a blood glucose meter).

Background

Patient, caregiver, and public engagement provides a unique source of information about people's experiences of a health condition and the health technologies or interventions used to manage or treat that health condition. It includes the impact of the condition and its treatment on the patient, the patient's family and other caregivers, and the patient's personal environment. It also provides insights into how a health condition is managed by the province's health system.

Information shared from lived experience can also identify gaps or limitations in published research (e.g., sometimes typical outcome measures do not reflect what is important to those with lived experience).[116-118] Additionally, lived experience can provide information and perspectives on the ethical and social values implications of health technologies or interventions.

Because the needs, priorities, preferences, and values of those with lived experience in Ontario are not often adequately explored in published literature, we contact and speak directly with people who live with a given health condition, including those who may have experience with the intervention we are exploring.

Type 1 diabetes has a significant impact on people with diabetes and their families, and it substantially affects their quality of life. It is estimated that more than 300,000 people in Canada live with type 1 diabetes, 150,000 of whom are in Ontario.[1,2] This disease strikes both young and old, requires daily management, and lasts for a lifetime.

For this project, we spoke with people who have lived experience: patients with type 1 diabetes and their families. For children with type 1 diabetes, we spoke to their parents about the impact of the disease.

A large number of those we spoke to had experience managing their diabetes using continuous glucose monitoring. Gaining an understanding of the day-to-day experience of managing diabetes, including people's experience with continuous glucose monitoring, helps us assess the potential value of this technology from the perspective of patients and caregivers.

Methods

Engagement Plan

The engagement plan for this health technology assessment focused on consultation to examine the experiences of patients with type 1 diabetes and those of their families and other caregivers, including their experience with continuous glucose monitoring. We engaged people face-to-face, via phone interviews, through written interview responses, and in focus groups.

Primarily, we used qualitative interviews, because this method of engagement allows us to explore the meaning of central themes in the experiences of patients with type 1 diabetes, as well as those of their families and caregivers. Our main task in interviewing is to understand what people tell us and gain an understanding of the story behind their experiences.[119] The sensitive nature of exploring people's experiences of a health condition and their quality of life are other factors that support our primary choice of an interview methodology.

We also held two focus groups, which allowed for more thematic discussion of issues relating to type 1 diabetes in a supportive group environment. Focus groups were split into two main patient populations: adults with type 1 diabetes and parents of children with type 1 diabetes. In comparison to qualitative interviews, focus group discussions focused on commonalities and differences, and on broader experiences of diabetes management and continuous glucose monitoring, rather than on individual stories.

Participant Recruitment

We used an approach called purposive sampling,[120-123] which involves actively reaching out to patients, families, and caregivers with direct experience of the health condition and health technology or intervention being reviewed. We approached a variety of partner organizations, health clinics, diabetes support associations, and foundations to spread the word about this engagement activity and to make contact with patients, families, and caregivers, including those with experience of type 1 diabetes and continuous glucose monitoring.

Inclusion Criteria

We sought to speak with patients with type 1 diabetes and their families who actively manage their diabetes. Patients were not required to have direct experience with continuous glucose monitoring.

We sought broad geographic, cultural, and socioeconomic representations to elicit possible equity issues in accessing and using continuous glucose monitoring devices.

Exclusion Criteria

We did not set specific exclusion criteria.

Participants

We conducted interviews and focus groups with 59 individuals. We interviewed 45 patients and families one on one, either in person or over the phone. We conducted two interviews via written correspondence, and we held two six-person focus groups.

Those interviewed included adults with type 1 diabetes and parents of children with type 1 diabetes. The children ranged in age from less than 2 years old to 16 years old. We recruited participants from across Ontario.

The majority of participants had direct experience with continuous glucose monitoring. Because no participants received continuous glucose monitoring devices immediately upon diagnosis of type 1 diabetes, they were able to compare their experiences of diabetes management with and without these devices.

Approach

At the beginning of the interview and focus groups, we explained the role of Health Quality Ontario, the purpose of the health technology assessment, the risks of participation, and how personal health information would be protected. We gave this information to participants both verbally and in a printed letter of information (Appendix 9). We then obtained participants' verbal consent before starting the interview and focus groups. With participants' consent, we audio-recorded interviews and then had the recordings transcribed.

Interviews lasted 20 to 90 minutes. They were loosely structured and consisted of a series of open-ended questions. Questions were based on a list developed by the Health Technology Assessment International Interest Group on Patient and Citizen Involvement in Health Technology Assessment.[124] Questions focused on the impact of type 1 diabetes on patients' and families' quality of life, their experiences with treatment options, and their perceptions of the benefits or limitations of using continuous glucose monitoring to manage diabetes. See Appendix 9 for our interview guide.

The focus groups lasted approximately 90 minutes each. They were loosely structured and guided by a series of open-ended questions, based on the interview guide. Questions focused on commonalities and differences in diabetes management and continuous glucose monitoring, allowing members to explore themes surrounding the topic.

Data Extraction and Analysis

We used a modified version of a grounded-theory methodology to analyze interview transcripts, focus group transcripts, and survey results. The grounded-theory approach allowed us to organize and compare information across participants. This method consisted of a repetitive process of obtaining, documenting, and analyzing responses while simultaneously collecting, analyzing, and comparing information.[125,126] We used the qualitative data analysis software program NVivo (QSR International, Doncaster, Victoria, Australia) to identify and interpret patterns in interview, focus group, and survey data. The patterns we identified then allowed us to highlight the impact of health conditions and treatments on the patients, family members, and caregivers we interviewed.

Results

Lived Experience of Type 1 Diabetes

During the interviews and focus groups, patients with type 1 diabetes and their family members repeatedly emphasized the daily burden and stress of managing this disease. People with type 1 diabetes have to regularly monitor their blood glucose levels and make adjustments by administering insulin. Therefore, multiple times per day, every day, year after year, patients and families must make calculations and decisions about the amount of insulin to take. Participants emphasized that while these calculations and injections may eventually become routine, they are of vital medical importance, and errors can have grave health consequences in both the short and long term.

Diagnosis

Adult patients with type 1 diabetes and parents of children with type 1 diabetes described the overwhelming and emotional experience of diagnosis. Often, they had no previous experience or knowledge of type 1 diabetes. A short hospital stay, which included rapid education about

diabetes and its management, was a common experience. They often encountered a steep learning curve in attempting to understand the disease and its day-to-day medical management:

> *Yeah, it's insane. Absolutely. My husband and I, we were discharged after about an hour of training. After spending a weekend in the hospital, we had the clinic people come in and train us, and they sent us home. And even though I'm a nurse and we're both fairly intelligent people, we sat in bed that night and we're like, "What the heck are we doing?"*
>
> *I had no idea. I knew there was a difference between type 1 and type 2, and I knew the basics about it, but I had no idea the daily management that is involved in type 1 diabetes.*

Adult patients and parents of newly diagnosed children reported quickly learning that daily management of diabetes extends beyond merely injecting insulin. Adjustments to food choices and activity levels were new concerns they needed to learn about:

> *You have to learn how to count carbs and everything, and estimate … For me, I like everything to be an exact science, but I had to learn that nothing is an exact science with this disease. It's kind of trial and error, and it's so unpredictable.*
>
> *The [blood glucose] was so unpredictable with his activity level. Being so little, we just didn't know what to expect or how different foods were going to react.*
>
> *You have to try and eliminate reasons why this is happening and adjust basal insulin rates and bolus insulin rates, and it was just a different language to me. You know, you just start researching, and basically I've spent the last 2 years online reading and reading.*

While newly diagnosed adults tended to focus on the informational burden of the diagnosis, parents of children often spoke of its emotional impact. These parents repeatedly reported fearing and doubting their ability to keep their children alive and healthy. Managing this challenging disease in young children, with little background knowledge, was daunting:

> *So, it was really hard at first with the multiple finger pokes and the daily injections. There were months where we would have to—my husband would have to hold her down and basically restrain her while I gave her injections.*
>
> *But the emotions were overwhelming, and as a parent, you're trying to hold it together, because all the education was done in front of my child. I would have preferred a moment where they took her away and just let me digest it—you know, say everything I was feeling, because you can't say, "I'm scared."*
>
> *…Because you're trying to stay brave for your child whose whole world was turned upside down.*
>
> *We were diagnosed over a weekend. Friday was our education, and then we had to return Monday and Tuesday for more education … That was the scariest weekend of my life, because I did not feel I was equipped to take care of my child, for the first time ever. And I have three kids, and it was the first time ever in my life as a mother I felt very ill-equipped.*

While patients and families expressed appreciation for the support the medical system provided at the time of diagnosis, they often still felt the support was inadequate, owing to the overwhelming nature of the medical management that diabetes requires. Patients and families often reported feelings of abandonment, of being left to self-manage the disease with a perceived lack of proper training or preparation:

> *So, it was very traumatizing and very upsetting, but even then we didn't really understand what this meant. They said, "They have diabetes," and we thought, "Okay, she'll have to have a shot every day." Like, that's kind of all we thought that this disease was. We had no idea just how complex it is and how it can affect every aspect of what she does in her day-to-day life.*

> *The clinic was good in terms of giving the basic information that we needed, and they gave us pretty much all we could chew at that time; because it's overwhelming. There's a lot of content that's coming at you, and you basically are getting trained to be a nurse in a week.*

Day-to-Day Impact of Type 1 Diabetes

While events surrounding the diagnosis of type 1 diabetes were unique to each person, those interviewed consistently reported the overwhelming nature of the diagnosis. Similarly, almost all of those interviewed referred to significant and profound changes in their daily life, including their quality of life. The descriptions of this impact generally fell into three categories: social, emotional, and other.

Social Impact

The social impact of type 1 diabetes was more commonly reported among parents of children with type 1 diabetes than among adults with the disease. People who were diagnosed as adults spoke of adjustments they had to make in their work life or in social settings, but overall expressed less social impact:

> *But I do notice that I do a lot of exercise, a lot of walking. I belong to quite a few groups that go out and walk around and do things like that, and I have to make sure that I stop everybody. "Sorry, guys, you're going to have to wait. I've got to test." And I have to do it about every 20 minutes when I'm out.*

On the other hand, children who were newly diagnosed faced increased social challenges, at a time when social interactions are less established and comfortable. Several parents spoke of wanting to minimize the changes brought on by type 1 diabetes. As much as possible, they did not want the disease to change their child's life:

> *For her, it was important to be back with her friends, and because we didn't disrupt her life so much, she just kind of kept going.*

> *She has a couple of other kids in the school … in high school specifically, who refused to talk about their diabetes or refused to tell anybody that they had it, because they felt that they were an outcast.*

Parents of children with type 1 diabetes reported that a particularly challenging time for their children was during school. Parents would often be required to educate classmates, teachers,

and administrators about type 1 diabetes and how their children would manage it. For younger children, this required that more responsibility be placed on teachers. For older children, it could mean a disruption in class while the child managed their blood glucose:

> *So I become quite a momma bear and threatened—not threatened—but explained to them what could happen … I did [it] quite a few times. I insisted on always training the teachers and training the staff.*
>
> *And [my daughter with type 1 diabetes] was actually saying to me yesterday how it really bothered her that no matter how many times she would say something to a teacher and how many times they were great and they understood about the diabetes, they would still turn to her and say, "Why are you eating in class?"*
>
> *When the boys were younger, they had to go to the office to check their blood sugar or inject—when they were first diagnosed, before they were on a pump—because they didn't want to scare any of the other kids.*

Additionally, children were involved in sports and physical activities at school. This required extra-careful management of sugar and insulin to avoid catastrophic low blood glucose levels:

> *Well, it just affects every aspect of our lives … especially for her. She plays volleyball, a higher-level volleyball, and she has to plan hours in advance for the physical activities. And there's even gym class or, you know, a school trip where they walk somewhere, she has to—an hour in advance—make sure her blood sugar is at a safe level to sustain that physical activity so she doesn't go low in the middle of it. So she has to plan pretty far in advance.*

Emotional Impact

Parents consistently reported the emotional impact of type 1 diabetes. They often spoke of the near-constant fear and anxiety they experienced in caring for their child. The health of their child became something never to be taken for granted, and parents often reported wrestling with the daily struggle of keeping their child healthy and the fear of failure. This emotional burden had a large impact on the parents, their children, and their extended families:

> *And, yeah, just a feeling of, "I can't control this. I can't control this disease for [my son]." And, of course, then there's the [thought], "Is my kid going to die from a low blood sugar that I slept through, that I didn't catch?"*
>
> *And it's incredibly … it's hard to describe, but incredibly frustrating, and there's some shame involved in … not being able to do this properly for your child. Even though you know in your rational mind, it's not really possible. But you're always striving to do a better job for your child, for sure.*
>
> *So there was all that, and as a result, I wasn't sleeping within the first month, I don't think—and that was contributing to my anxiety and my inability to go to work, and it was seriously impacting our quality of life as a family.*
>
> *And, you know, that level of fear and anxiety takes a toll. Takes a toll on [my son], takes a toll on us, takes a toll on your relationship. You know, it can become your focus. Because it's your child.*

Additionally, parents spoke of their contrasting desires to keep their children safe by observing them and testing their blood glucose, but also wanting to allow them independence and to be as "normal" as possible. Parents also reflected on the challenge of ensuring their children were responsible and diligent in their diabetes management. In young children, parents took on this responsibility. However, as their child grew older and gained more independence, parents attempted to cultivate a sense of responsibility in their child to manage their own diabetes, without eliciting resentment or rebellion. Parents reported the emotional burden that this caused and the challenges in allowing their child to manage their condition independently, knowing the potential long-term consequences of poor diabetes management:

> *The hardest thing for a parent to do is giving their child their independence with a type 1.*

> *I think she might have been maybe 10 or 11, and she went out to a movie with her friends, and she was having so many problems with her blood sugar. I dropped her off, and then I cried because I knew she would have no idea what the movie was about. Her friends were all excited that all the parents let them go to a movie for the first time by themselves, and [my daughter] was going to be there testing her blood sugar and not being able to eat the popcorn…*

> *It scares me because … my boys are just, like, "Yeah, whatever, it's diabetes." In my head, all I can picture is my friend Kevin; he's got multiple amputations because he didn't care enough. And that's what I don't want for my boys. And, of course, I panic and think about it, like, "Hey, by the way guys, got to check your sugar more."*

To help alleviate these emotional burdens, parents spoke of linking with other parents, often through social media. They often received comfort from other parents. Parents found a huge benefit in being able to reach out and speak about their concerns, their fears, and the challenges they faced in managing their child's diabetes:

> *For me, a big piece was the emotional healing that I was going through … I needed to know that we weren't alone, because it does feel very isolating if you don't know anybody who's doing this, who's dealing with this. And I wanted to be able to do it better. And so by connecting with other families—there's just a lot of learning to be had.*

Other Impacts

Changes to sleeping patterns was the most common impact mentioned by parents of children with type 1 diabetes. Informed of the risk of hypoglycemia overnight (through their health providers or their own research), parents reported the need to wake up multiple times to test their child's blood glucose and make any necessary corrections. This had huge impact on both the parents and the child. A large number of parents reported being so worried about their child's blood glucose that they intentionally kept levels high, reasoning that the long-term effects of high blood glucose were not as dire as the immediate effects of a hypoglycemic event:

> *Absolutely, and the worst-case scenario is a low in the middle of the night. So, some people who don't have continuous glucose monitoring go with the 12, three, and six program, which means for the duration of the time their child lives*

> *in their house, they're going to wake up at midnight, three, and six and check him.*
>
> *And we weren't getting sleep because we never got to the point [of comfort]. Like, we'd check her at midnight, we'd check her at three, and we kept doing this and doing this, and we were never comfortable not checking her.*
>
> *It was just not as good management, because we ran him higher. That was the way to be safe. He sat at 14 to 16, 14 to 18, overnight because that was the way to keep him safe, because it's so dangerous for him to go low.*

Information About Continuous Glucose Monitoring

Rarely did adult patients or parents of children with type 1 diabetes report that they first heard of continuous glucose monitoring at the time of diagnosis. In fact, patients and families often reported that the information they received about continuous glucose monitoring did not initially come from their health care provider. Often, it was first conveyed through social media support groups for patients and families with type 1 diabetes. Sometimes, continuous glucose monitoring devices were introduced when patients sought out an insulin pump.

While the initial information may not have come from health care providers, both parents and adult patients reported seeking the opinion and approval of their health care team before choosing to invest in continuous glucose monitoring technology:

> *I didn't even know it existed. I basically sat there and thought, "There's got to be something, some kind of technology out there, that will make this easier," and I was really surprised the clinic, like I said, didn't suggest it. It's so expensive.*
>
> *And then obviously we learned about continuous glucose monitoring when we were learning about the pump, because they go hand in hand very often*.
>
> *Well, we spoke fairly extensively to [a doctor] at Sick Kids, and he spoke of the benefits and any kinds of disadvantages, so it was good advice from him. But I think it was more just our own understanding [that made us choose continuous glucose monitoring].*

Barriers to Using Continuous Glucose Monitoring

Financial Barriers

Adult patients and parents of children with type 1 diabetes were asked about their perceptions of the existing barriers to more widespread use of continuous glucose monitoring, and what barriers they had encountered. They consistently reported that the greatest barrier was cost. Even patients who reported that they used their devices in a limited, targeted way to simply learn about their blood glucose patterns often said that they would use the devices more if they were cheaper:

> *Like I said, we learned about continuous glucose monitoring when she went on the pump, but it wasn't ever something we'd considered, because, well, we're not paying for that, right? And we don't have any outside medical insurance either. We're self-employed farmers, so, you know, it's completely out of pocket.*

Patients and parents spoke often of the compromises they made to afford continuous glucose monitoring, such as extending the sensors beyond their recommended usage:

> *The sensors are only supposed to be used for a week, and if you want to you can go online and find out how to extend that sensor to maybe 2 weeks or 3 weeks, depending on how old the kid is and how active they are. That's what people do.*

> *That money could be groceries or set aside for their education, and that we won't be able to afford, because we're paying for diabetes supplies, so it's a catch-22 for a lot of families, I think. We want it! What are we going to do? Like, in the future, the kids don't go to [college] because we were trying to save their life now with continuous glucose monitoring? Yeah.*

Many of those interviewed expressed their gratitude that they had private insurance or could purchase a continuous glucose monitoring device, but acknowledged that there were many families and individuals for whom the cost is simply prohibitive. Often, owing to the social and online connectivity around dealing with type 1 diabetes management, those interviewed knew of other families who could not afford continuous glucose monitoring devices. When interviewed, those who could not afford the devices often expressed their emotional pain and frustration at not being able to provide the care they felt their child required:

> *You know, we're fortunate in the sense that we can afford it, right? Thankfully. And I say that all the time, because there are families that just can't.*

> *I couldn't possibly afford to pay for that, although if I didn't have the coverage, knowing what I know now and having used it for the last 3½ years, we can't live without it. This is a tool that we absolutely have to have to take care of my child.*

> *She's been wanting it for 2 years, and she just can't afford [a continuous glucose monitoring device]. She actually texted me a month or two ago because overnight her son had had a severe hypoglycemic episode with a seizure, and they had to call 911. He was OK; it doesn't seem to be any permanent damage or anything like that, but it was shattering for her. I mean, she's doing nights all alone, she's doing all of it alone. Those are the stories for me where I think, "There's got to be a better way," and that a continuous glucose monitoring device shouldn't be a luxury item. It should be accessible for everybody, in my mind.*

> *And you want, you really want, to do your best, the best for your child. You want to offer your child the best that's available, right? And sometimes you can't, and that's horrible, right? You should be able to give them the best kind of therapy.*

On occasion, when speaking of the prohibitive cost of continuous glucose monitoring, patients lamented that their insulin pump was funded by insurance or through government funding, but not the continuous glucose monitoring device. A large number of patients spoke about choosing a continuous glucose monitoring device over a pump, if given the choice:

> *And we love the benefit of the pump. Like, it's very easy to just roll with whatever she wants to eat, and it's very convenient. But we have always said if we ever have to give up a device, it would be the pump. We would never give up the continuous glucose monitoring device, because that information that we have access to is invaluable to us.*

> *I would give up my pump before my continuous glucose monitoring device if I had to. Yeah. And pumps are great. They offer us a ton of flexibility. But from a safety and peace-of-mind standpoint, the continuous glucose monitoring device is my comfort.*

Other Barriers

While cost was the barrier most often mentioned by adult patients and parents of children with type 1 diabetes, it was not the only barrier. A number of those interviewed spoke about the lack of information about continuous glucose monitoring. People also felt that perhaps adult patients who had managed their diabetes one way for many years were reluctant to use a newer technology:

> *I have a mom with type 1 and a son with type 1, so two generations apart. My mom uses multiple daily injections. She doesn't use a pump. While she is really, really glad that [my son] has a continuous glucose monitoring device, she doesn't have one. Well, for her, cost is a huge barrier for the device. And she's been type 1 since she was 51; she's now 75. So there is a feeling of, "I've done this."*

> *And I think that there would be the unknown, maybe just not enough information or not having tried it yet to see what the benefits were.*

> *I mean not everybody can afford [it], and the knowledge is not there. I mean, obviously, the older generation probably doesn't even know that this is out there, that it's available, that it's easy. People might be intimidated by technology.*

Use of Continuous Glucose Monitoring

Those who were able to afford and use continuous glucose monitoring reported that the benefits were numerous and important. However, occasionally the value of continuous glucose monitoring was different for adult patients and parents. Often, this difference could be attributed to the level of comfort in managing diabetes. Adults may have been managing their diabetes for many years, and continuous glucose monitoring was only the latest in a long line of tools used to assist in their management. For parents of newly diagnosed children, however, continuous glucose monitoring was more than a tool. It served as way to keep their child safe and healthy.

Many of those interviewed—both adults and parents of children with type 1 diabetes—spoke of an unauthorized feature of a particular continuous glucose monitoring device, known as Nightscout. With this feature, it was possible to program the device to wirelessly transmit blood glucose readings to other electronic devices, such as smart phones or smart watches. This feature was originally developed by parents and has since spread widely via the Internet and social media.

Nightscout was not an original feature of this particular continuous glucose monitoring device, but a large number of people with diabetes and parents reported its benefits. The next generation of continuous glucose monitoring devices is expected to include the ability to transmit readings wirelessly, much as Nightscout has done for the older device.

Overall, the benefits of continuous glucose monitoring, including the Nightscout feature, fell into three general categories: social, emotional, and medical and safety benefits.

Social Benefits

Adult patients who used a continuous glucose monitoring device spoke less often about its social benefits than parents of children with diabetes. Being able to check blood glucose levels discreetly instead of using finger pricks and a blood glucose meter was mentioned as a nice option, but adult patients placed less emphasis on it. They seemed less concerned with the social impact of their diabetes management, although they appreciated the ability to manage it discreetly. In addition, they reported that continuous glucose monitoring could have a positive impact on their employment, especially if work required long periods in a car or travelling:

> *I'm 50 years old. I don't really care about people around me, so if they don't like me testing in front of them, that's too bad, whether I'm in a restaurant or in a board meeting. I mean, it's a little bit uncomfortable, and you have to interrupt people in the middle of their lectures or whatever, [and] everybody stops and looks at you. At this point, I don't really worry about it.*

> *What I see with continuous glucose monitoring is the freedom of being able to know what your glucose is at all times, for exercising … sometimes it hinders me in doing things because I have to drag along my test kit. I have to stop in the middle of my walks or my exercise, in the middle of a class, where I have to interrupt everybody.*

In contrast, parents of children with type 1 diabetes often spoke of the social freedom that continuous glucose monitoring provided for their children. They perceived it as being very beneficial for their child's quality of life. Parents often expressed the desire to minimize the impact that diabetes would have on their child's life—to allow their child to be as "normal" as possible. Many parents felt that continuous glucose monitoring allowed their child to get closer to this ideal; they could manage their diabetes in a way that was as socially unobtrusive as possible.

Parents also felt more comfortable allowing their child a larger degree of freedom. The Nightscout feature mentioned above enhanced this by allowing remote monitoring of blood glucose levels:

> *It gives her independence … She didn't have her mother constantly over her shoulder. And what happens when mom's constantly over your shoulder after your diagnosis? You start to resent type 1. You know what I mean?*

> *But now … I can say yes a lot more, she can have freedom to be out. And there's also a—you know, as a 13-year-old girl, with anything, you want to be the same as everybody else. You don't want to stand out at all.*

> *Diabetes interrupts and disrupts; continuous glucose monitoring took away a lot of that disruption and interruption.*

This social benefit extended to others in the circle of the child's care. Parents reported that teachers, sport coaches, friends, and other family members were more comfortable being responsible for a child with type 1 diabetes when that child had a continuous glucose monitoring device. Continuous glucose monitoring allowed for easier management of diabetes, providing greater information about blood glucose levels and reporting trends, thereby reducing the potential need for drastic intervention by carers:

> *[With Nightscout,] we're alerted when she's high or low, so we can help her deal with it from anywhere. So that comforts her coaches and her teachers and everybody as well, knowing that she's going to be alerted and she's not just going to drop and hit the floor.*

> *And I have a friend who I'm eternally grateful to, because continuous glucose monitoring made her comfortable enough to say, "I want to have [your son] for a sleepover," and we'd never had that before, ever. So it meant that he could go and do things that kids do all the time, and it meant that we could back off a little.*

Emotional Benefits

Many parents reported the fear, anxiety, and sense of failure they felt in trying to care for their child with type 1 diabetes. Constantly trying to manage the fluctuations of blood glucose was described as exhausting and frustrating. Parents who were able to provide continuous glucose monitoring for their child reported a noticeable reduction in these emotions. Continuous glucose monitoring allowed a sense of safety and security that had been lacking.

Parents also reported their increased comfort in allowing their child to grow and manage their diabetes more independently because of continuous glucose monitoring:

> *Then, after my maternity leave ended, I thought, "You know, I can't put her in someone else's care. I can't relinquish this and trust that she will still be okay." But with [continuous glucose monitoring] and getting comfortable with that, we started to be able to relinquish some of that need to monitor her ourselves. She actually went to preschool, which we didn't think she would do.*

> *So as much as it gave to me as a parent, in that safety net and not worrying, it gave to my child that sense … the normalizing of what it's like to be a normal 10-year-old kid …*

> *We've kind of said it, but just to reiterate, it has changed our lives, especially for [our son] for nighttime, especially for school. It's just that peace of mind. Just to have other people look after him, it gives us peace of mind, too.*

> *My job is to raise my children to be good people and to be the best they can be. But with my daughter, it felt good to teach her how to manage her chronic lifelong illness. And having the continuous glucose monitor there to explain to an 8-, 9-, 10-year-old what happens when you eat, it's concrete. That was a turning point as well for us, because she started to connect what she eats with her blood sugar.*

While the emotional benefits of continuous glucose monitoring were reported most often by parents of children with diabetes, a number of adult patients also remarked on the comfort it provided:

> *I also suffer from stress and anxiety, which is caused a lot by my health issues, and knowing what your blood sugar is all the time really helps, because, you know, I would test 10 to 20 times a day to keep my blood sugar in very good control. And so, being able to look at my [continuous glucose monitoring device]*

all the time, and being able to know what my blood sugar is, has definitely improved my life, [and] the way I live my life.

If either [my son with type 1 diabetes] or I don't have [continuous glucose monitoring] for even a couple of hours, we feel really weird, because we're so used to having information. And it's almost like, well, I can't survive without it, but, yeah, I find it really beneficial as well.

Medical and Safety Benefits

Beyond the social and emotional benefits of continuous glucose monitoring, both adults and parents of children with type 1 diabetes were far more likely to report the perceived medical and safety benefits of the device. Adult patients who had been managing their diabetes for many years often described continuous glucose monitoring as a useful educational tool to learn about their own body and how different factors affected their blood glucose levels:

This is just another tool that helps keep me away from hospitals.

Given my background, I know these continuous glucose monitoring devices are just a tool. They're never to be trusted 100%; so we still test his blood sugar when we don't get the reading. It's more helpful, I find, to get the trends, to find out when he goes up and when he goes down.

This ability to see trends of blood glucose levels rather than the isolated data points provided by finger-prick monitoring was a common feature perceived to have enormous medical benefit. This perception on the part of patients and parents was consistent with clinical findings on the benefits of continuous glucose monitoring. People reported that knowing trends allowed for more aggressive insulin dosing; parents and adult patients could use the trend data to adjust dosing immediately, rather than waiting for the next finger prick. This was felt to be especially helpful in children—parents felt that changes in hormones, activities, and diets often caused wild fluctuations in blood glucose levels. The increased comfort with aggressive insulin dosing helped patients keep their A1C (glycated hemoglobin) levels lower, to the overall benefit of their health.

I was always going high overnight, and I didn't know it, because I wasn't waking up in the middle of the night to test myself. When I saw that … consistently happening, then I could start taking action to address that. And that in itself allowed me to improve my A1C fairly significantly.

For [my son,] I'm making adjustments sometimes on a daily basis, based on what his blood sugar is doing. For me, having [continuous glucose monitoring], honestly, I couldn't do it without it, because I'm able to get that data reporting just by plugging it in, and I can see what the trends are, and I can make adjustments on the fly so easily.

I think every parent tries for a good A1C. And so it's allowed us to improve significantly, I believe, with continuous glucose monitoring, because I make changes more frequently, and I can see trends more easily, and so we have been able to get better control. So I think, like, when he was diagnosed he was 9.1, and his last one was 6.8, which is good.

> *With [continuous glucose monitoring,] I can be far more aggressive with [dosing] to bring down her high blood sugar. Like, if I talk to people, if they don't have a continuous glucose monitoring device, I would never suggest that to them, because too much insulin can kill them. Without a [continuous glucose monitoring device], I would never risk it, ever.*

A number of parents of children with type 1 diabetes reported that prior to continuous glucose monitoring, they had kept their child's blood glucose deliberately high, in fear of hypoglycemic events. Parents knew that this was putting their child at risk for long-term complications, but felt it was safer than risking low blood glucose levels in the short term. Continuous glucose monitoring helped to alleviate this risk, allowing better management decisions and better blood glucose control:

> *You are shooting in the dark without continuous glucose monitoring. You cannot make educated choices about treatment without continuous glucose monitoring … Without a continuous glucose monitoring device, you kind of have to run them higher.*

> *Like, that 5.5 [mmol/L], is that a steady 5.5 and she's going to be OK, or is that a 5.5 and she's dropping quickly? You just don't know off that one piece of information. Whereas with [continuous glucose monitoring], you have the trends and the directions, and it allows you to adjust your reactions to suit it.*

> *So I said, "Do you want me to wake you up? I can keep on checking and wake you up." She says, "No, I want to sleep, because sleep is precious." So she just says, "Let me run myself high so I don't have to worry, and I can actually sleep through the night and I'll wake up in the morning." And it breaks my heart for me to hear my 17-year-old say that.*

Commonly, both patients and parents commented that more information was helpful in managing the diabetes in the short and long term. Continuous glucose monitoring provided that information. It allowed for data tracking and uploading to computers, which was useful for seeing longer-term trends and make adjustments:

> *When I was seeing my A1C dropping, it was making me really happy, and I was glad to be on [continuous glucose monitoring]. But at the same time, I do always think about the long term and the best systems I can use … to make sure that I have the best control I have now, because I know it's going to affect later on. So seeing that it was impacting my A1C right now, I knew that even that was beneficial for the future.*

> *But we knew, we said, "We've researched it, this is what we want, like, we can cope better with the more information we have." It's the unknown that makes us nervous.*

From a safety perspective, parents of children with diabetes were almost universal in their praise for continuous glucose monitoring. And while adult patients were less effusive, they also emphasized the safety benefit. This was even more pronounced for those using the Nightscout feature. The overwhelming fear of a hypoglycemic event was mostly mitigated by continuous glucose monitoring; alarms would sound if the blood glucose decreased to a set level, alerting individuals to remedy the situation. This had a large impact on nighttime diabetes management.

This safety net brought incredible relief to a majority of those interviewed and was often described as life-changing. For children or adult patients with nocturnal (nighttime) hypoglycemia or hypoglycemia unawareness (inability to "feel" a low blood glucose), continuous glucose monitoring alleviated the fear of a sudden hypoglycemic event. Several patients had experienced an extreme blood glucose event and lamented the fact that they had not had access to continuous glucose monitoring at the time:

> *I mean, the first year before continuous glucose monitoring, I just didn't sleep. It was just constantly finger poking him and, really, this sense [that] I just had no control over this disease. I had absolutely no idea when he was going to go low. I didn't know when he was going to go high.*

> *He does not feel a low blood sugar. And that's dangerous and deadly, especially at night, when he will not wake up from a low blood sugar. This [continuous glucose monitoring device] has saved his life numerous times. If we don't have [continuous glucose monitoring], I'm poking him every hour just to see where his blood sugar is at.*

> *I wasn't wearing a sensor, because my money was going to [my daughter] for her to wear a sensor, because there's only so much money … And I was not wearing the sensor, and my pump got disconnected in the middle of the night and I went into diabetic ketoacidosis, and that is a life-threatening situation, and it was pretty horrendous and pretty awful. I mean, unfortunately, I know somebody who died in that situation. But all I was thinking of as I was vomiting the next morning is, "If I'd only had a sensor on, this wouldn't have happened, because the sensor would have woken me up when my blood sugar went high*."

For adult patients, the continuous glucose monitoring also provided safety by alerting them to potential hypoglycemic events when family or friends were not present:

> *Also, now I'm separated, so I live by myself, which is a big worry for me, because if you have someone there with you, especially a spouse that's in the same room, they can wake you or see signs of something going on. But when you're by yourself, it's a big worry.*

Concerns With the Use of Continuous Glucose Monitoring

A minority of patients and families expressed concerns about using continuous glucose monitoring, or reasons for not using it. These reasons included "alarm fatigue" and overwhelming data. Additionally, patients reported that older models were more inaccurate, potentially leading to a loss of trust in the displayed results. Some simply used continuous glucose monitoring as a targeted tool for a limited amount of time. Removing the device or choosing to not use continuous glucose monitoring was much more common among adults than among parents of children with type 1 diabetes, although numbers in both groups were relatively low in this study. Having managed diabetes for many years without continuous glucose monitoring, some adults were likely to contemplate ceasing to use the device:

> *There's been some times when I've actually taken the continuous glucose monitoring device off for a couple of weeks. I've just had enough, because you're trying to sleep, and it's telling you you're low and … it's about a 20-minute delay.*

> *So even though you may have brought your blood sugar up, it's still going, "You're low!" and it's like, "Oh, shut the hell up."*
>
> *But some of the drawbacks to it, too, were sometimes that information gave us more cause for anxiety. You know, like, you tend to micromanage things more.*
>
> *Yeah, well, because of the cost, really … and because I've been diabetic for so long, I kind of get into a routine, so I wasn't as quick to see the benefits.*

A few parents of children with type 1 diabetes spoke of an initial hesitation and the challenges of inserting the continuous glucose monitoring device and having their child accept it. It became a new device to carry and be responsible for, and occasionally this was seen to be too much of a burden. Some people got over such hesitation quickly, but for others it was a long-standing concern. Parents of teenagers were especially concerned about their child's dedication to managing their diabetes and whether continuous glucose monitoring was seen as a hassle:

> *For me, I needed a couple of months to kind of get over the fact that it'd be a thing on him all the time, which is pretty common. It's a common obstacle for parents to get over.*
>
> *So, it was a lot for him, and it was actually [my son] that asked to stop wearing it. Because he found it to be bulky, cumbersome, and all of the stuff that he had to carry for us to be able to see what his data was. We tried the Nightscout, and it was just too much stuff for him to have to carry around and be accountable for.*
>
> *We have a very delicate balance with these kids to keep them normal, and the last thing I want is a child rebelling against their [continuous glucose monitoring device] and diabetes diagnosis, because when they refuse to take insulin because they hate diabetes that much, it becomes very dangerous. You can't miss doses, you know what I mean?*

Discussion

Patient engagement surrounding the topic of continuous glucose monitoring was robust. We interviewed many adults with type 1 diabetes and parents of children with type 1 diabetes. Additionally, we held two focus groups, allowing for the discussion of themes and perspectives related to continuous glucose monitoring. Patients who had direct experience with a continuous glucose monitoring device were able to compare their experiences with those of usual care, such as finger pricks and a blood glucose meter.

Those interviewed were overwhelmingly supportive of continuous glucose monitoring and the many benefits it provides for the management of type 1 diabetes. Both adults and parents of children with type 1 diabetes reported the great impact the disease had on their daily activities and quality of life. They emphasized the positive effects of continuous glucose monitoring, including social, emotional, and medical and safety benefits.

We did not discuss the specific benefits of particular brands of devices as part of patient engagement for this topic. However, a number of patients spoke of the increased benefit they received from a particular device because of its unofficial feature known as Nightscout. This feature allowed wireless transmission of blood glucose data to multiple receivers, which patients and parents felt provided greater independence and increased safety.

While most of those interviewed were positively inclined toward continuous glucose monitoring, upon further probing some identified concerns or challenges related to using the devices. They reported hearing these concerns from friends or connections through social media or support groups. Such concerns included inaccurate readings (especially with older generations of devices), hesitation to adopt a new technology, difficulty understanding the data provided by the devices, and slow acceptance from the health care system.

However, nearly all of those interviewed felt that these concerns were minor and were overshadowed by the many benefits of continuous glucose monitoring. Many patients stated that continuous glucose monitoring was an essential part of their diabetes management, and they would not consider managing their diabetes without it.

Conclusions

Adult patients and parents of children with type 1 diabetes reported very positive experiences with continuous glucose monitoring. Patients perceived that these devices provided important social, emotional, and medical and safety benefits in managing type 1 diabetes, especially in children.

The high ongoing cost of continuous glucose monitoring devices was seen as the greatest barrier to their widespread use.

CONCLUSIONS OF THIS HEALTH TECHNOLOGY ASSESSMENT

Continuous glucose monitoring was more effective than self-monitoring of blood glucose in managing type 1 diabetes for some outcomes, such as time spent in target glucose range and time spent outside the target glucose range (quality of evidence: moderate). We obtained similar findings for severe hypoglycemic events, although the findings were less certain because the quality of the evidence was low.

Compared with self-monitoring of blood glucose, the costs of continuous glucose monitoring were higher, with relatively small increases in observed health benefits. Publicly funding continuous glucose monitoring for the type 1 diabetes population in Ontario would result in additional costs to the health system over the next 5 years.

Adult patients and parents of children with type 1 diabetes reported very positive experiences with continuous glucose monitoring. The high ongoing cost of continuous glucose monitoring devices was seen as the greatest barrier to their widespread use.

ABBREVIATIONS

A1C	Glycated hemoglobin
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
ICER	Incremental cost-effectiveness ratio
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
QALY	Quality-adjusted life-year
RoBANS	Risk of Bias Assessment Tool for Non-randomized Studies

APPENDICES

Appendix 1: Literature Search Strategies

Clinical Evidence Search

Clinical Literature Search—Continuous Glucose Monitoring

Search requested by: Stacey Vandersluis
Search date: January 24, 2017
Librarian: Corinne Holubowich
Databases searched: Ovid MEDLINE, Embase, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, CRD Health Technology Assessment Database, Cochrane Central Register of Controlled Trials, NHS Economic Evaluation Database, and CINAHL

Database: EBM Reviews - Cochrane Central Register of Controlled Trials <November 2016>, EBM Reviews - Cochrane Database of Systematic Reviews <2005 to January 18, 2017>, EBM Reviews - Database of Abstracts of Reviews of Effects <1st Quarter 2015>, EBM Reviews - Health Technology Assessment <4th Quarter 2016>, EBM Reviews - NHS Economic Evaluation Database <1st Quarter 2015>, Embase <1980 to 2017 Week 04>, Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present>
Search Strategy:
---
1 exp Diabetes Mellitus, Type 1/ (176236)
2 ((diabet* adj3 (typ* 1 or typ* i or type1 or typei or typ* one or brittl* or juvenil* or pediatric or paediatric or early or keto* or labil* or acidos* or autoimmun* or auto immun* or sudden onset or young onset)) or (insulin* adj2 depend*) or insulindepend* or dm1 or dm 1 or dmt1 or dm t1 or t1dm or t1 dm or t1d or iddm).ti,ab,kf. (232927)
3 Diabetic Ketoacidosis/ (15987)
4 (ketoacidosis or acidoketosis or keto acidosis or ketoacidemia or ketosis).ti,ab,kf. (20760)
5 Hypoglycemia/ (95050)
6 Diabetes Mellitus/ (672266)
7 5 and 6 (25348)
8 ((hypoglyc?em* or ((low or lower or decreas* or deficien* or insufficien* or reduce* or reduction* or fluctuat* or fallen or falling or threshold or safe) adj3 (glucose* or sugar* or hba1c or hb a1 or hba1 or a1c or h?emoglob* or glycoh?emoglob*))) adj5 (diabet* or IDDM or DM)).ti,ab,kf. (20611)
9 or/1-4,7-8 (326151)
10 Blood Glucose Self-Monitoring/ (21053)
11 (continu* or uninterrupt* or ongoing or looped or interminable).ti,ab,kf. (2393790)
12 10 and 11 (4475)
13 ((continu* or uninterrupt* or ongoing or looped or interminable) adj4 (blood glucose or blood sugar*) adj2 (self monitor* or home monitor*)).ti,ab,kf. (104)
14 ((continu* or uninterrupt* or ongoing or looped or interminable) adj4 SMBG).ti,ab,kf. (128)
15 (CGM or CGMS or continuous glucose monitor* or continuous glucose sensor*).ti,ab,kf. (9984)
16 ((medtronic adj3 (paradigm* or glucose monitor* or glucose sensor* or CGM or insulin pump* or LGS or 630G)) or veo or veotm or minimed or dexcom or g4 platinum or g5 platinum).ti,ab,kf. (1787)

17 ((flash or novel) adj2 glucose adj2 (monitor* or sensor or sensing)).ti,ab,kf. (182)
18 ((integrat* adj2 (pump or pumps or infusion*)) or (sensor adj3 (pump or pumps or therap* or infusion*)) or (sensor augment* adj2 pump*) or low glucose suspend*).ti,ab,kf. (1538)
19 (closed loop adj2 (pump* or deliver* or infus* or therap* or treatment* or system* or sensor* or control* or monitor* or hybrid*)).ti,ab,kf. (7164)
20 Pancreas, Artificial/ (2671)
21 (artificial adj3 (pancreas or beta cell*)).ti,ab,kf. (3436)
22 or/12-21 (22784)
23 9 and 22 (9180)
24 exp Animals/ not Humans/ (16218972)
25 23 not 24 (5561)
26 Case Reports/ or Comment.pt. or Editorial.pt. or Letter.pt. or Congresses.pt. (5047347)
27 25 not 26 (5308)
28 limit 27 to english language [Limit not valid in CDSR,DARE; records were retained] (4886)
29 limit 28 to yr="2010 -Current" [Limit not valid in DARE; records were retained] (2863)
30 29 use ppez,cctr,coch,dare,clhta,cleed (2282)
31 exp insulin dependent diabetes mellitus/ (176079)
32 ((diabet* adj3 (typ* 1 or typ* i or type1 or typei or typ* one or brittl* or juvenil* or pediatric or paediatric or early or keto* or labil* or acidos* or autoimmun* or auto immun* or sudden onset or young onset)) or (insulin* adj2 depend*) or insulindepend* or dm1 or dm 1 or dmt1 or dm t1 or t1dm or t1 dm or t1d or iddm).tw,kw. (239526)
33 diabetic ketoacidosis/ (15987)
34 (ketoacidosis or acidoketosis or keto acidosis or ketoacidemia or ketosis).tw,kw. (21100)
35 hypoglycemia/ (95050)
36 diabetes mellitus/ (672266)
37 35 and 36 (25348)
38 ((hypoglyc?em* or ((low or lower or decreas* or deficien* or insufficien* or reduce* or reduction* or fluctuat* or fallen or falling or threshold or safe) adj3 (glucose* or sugar* or hba1c or hb a1 or hba1 or a1c or h?emoglob* or glycoh?emoglob*))) adj5 (diabet* or IDDM or DM)).tw,kw. (21910)
39 or/31-34,37-38 (332387)
40 blood glucose monitoring/ (21276)
41 ((continu* or uninterrupt* or ongoing or looped or interminable) adj5 (self* or home*)).tw,kw,dv. (16003)
42 40 and 41 (116)
43 ((continu* or uninterrupt* or ongoing or looped or interminable) adj4 (blood glucose or blood sugar*) adj2 (self monitor* or home monitor*)).tw,kw,dv. (106)
44 ((continu* or uninterrupt* or ongoing or looped or interminable) adj4 SMBG).tw,kw,dv. (132)
45 (CGM or CGMS or continuous glucose monitor* or continuous glucose sensor*).tw,kw,dv. (10250)
46 ((medtronic adj3 (paradigm* or glucose monitor* or glucose sensor* or CGM or insulin pump* or LGS or 630G)) or veo or veotm or minimed or dexcom or g4 platinum or g5 platinum).tw,kw,dv. (2387)
47 ((flash or novel) adj2 glucose adj2 (monitor* or sensor or sensing)).tw,kw,dv. (184)
48 ((integrat* adj2 (pump or pumps or infusion*)) or (sensor adj3 (pump or pumps or therap* or infusion*)) or (sensor augment* adj2 pump*) or low glucose suspend*).tw,kw,dv. (1589)
49 (closed loop adj2 (pump* or deliver* or infus* or therap* or treatment* or system* or sensor* or control* or monitor* or hybrid*)).tw,kw,dv. (7269)
50 artificial pancreas/ (2671)
51 (artificial adj3 (pancreas or beta cell*)).tw,kw,dv. (3492)

52	or/42-51 (21829)
53	39 and 52 (8862)
54	(exp animal/ or nonhuman/) not exp human/ (10585394)
55	53 not 54 (8708)
56	Case Report/ or Comment/ or Editorial/ or Letter/ or conference abstract.pt. (9318976)
57	55 not 56 (6317)
58	limit 57 to english language [Limit not valid in CDSR,DARE; records were retained] (5819)
59	limit 58 to yr="2010 -Current" [Limit not valid in DARE; records were retained] (4070)
60	59 use emez (1754)
61	30 or 60 (4036)
62	61 use ppez (1766)
63	61 use emez (1754)
64	61 use coch (2)
65	61 use cctr (493)
66	61 use clhta (10)
67	61 use cleed (4)
68	61 use dare (7)
69	remove duplicates from 61 (2194)

CINAHL

#	Query	Results
S1	(MH "Diabetes Mellitus, Type 1+")	17,154
S2	((diabet* N3 (typ* 1 or typ* i or type1 or typei or typ* one or brittl* or juvenil* or pediatric or paediatric or early or keto* or labil* or acidos* or autoimmun* or auto immun* or sudden onset or young onset)) or (insulin* N2 depend*) or insulindepend* or dm1 or dm 1 or dmt1 or dm t1 or t1dm or t1 dm or t1d or iddm)	26,754
S3	(MH "Diabetic Ketoacidosis")	1,653
S4	(ketoacidosis or acidoketosis or keto acidosis or ketoacidemia or ketosis)	2,266
S5	(MH "Hypoglycemia")	6,680
S6	(MH "Diabetes Mellitus")	46,253
S7	S5 AND S6	1,343
S8	((hypoglyc#em* or ((low or lower or decreas* or deficien* or insufficien* or reduce* or reduction* or fluctuat* or fallen or falling or threshold or safe) N3 (glucose* or sugar* or hba1c or hb a1 or hba1 or a1c or h#emoglob* or glycoh#emoglob*))) N5 (diabet* or IDDM or DM))	4,751
S9	S1 OR S2 OR S3 OR S4 OR S7 OR S8	30,991
S10	(MH "Blood Glucose Self-Monitoring")	2,779
S11	(continu* or uninterrupt* or ongoing or looped or interminable)	272,534
S12	S10 AND S11	537
S13	((continu* or uninterrupt* or ongoing or looped or interminable) N4 (blood	26

	glucose or blood sugar*) N2 (self monitor* or home monitor*))	
S14	((continu* or uninterrupt* or ongoing or looped or interminable) N4 SMBG)	25
S15	(CGM or CGMS or continuous glucose monitor* or continuous glucose sensor*)	1,176
S16	((medtronic N3 (paradigm* or glucose monitor* or glucose sensor* or CGM or insulin pump* or LGS or 630G)) or veo or veotm or minimed or dexcom or g4 platinum or g5 platinum)	205
S17	((flash or novel) N2 glucose N2 (monitor* or sensor or sensing))	17
S18	((integrat* N2 (pump or pumps or infusion*)) or (sensor N3 (pump or pumps or therap* or infusion*)) or (sensor augment* N2 pump*) or low glucose suspend*)	199
S19	(closed loop N2 (pump* or deliver* or infus* or therap* or treatment* or system* or sensor* or control* or monitor* or hybrid*))	393
S20	(artificial N3 (pancreas or beta cell*))	197
S21	S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20	1,971
S22	S9 AND S21	1,031
S23	(MH "Animals+") OR (MH "Rodents+")	123,580
S24	S22 NOT S23	1,021
S25	PT Case Study or Commentary or Editorial or Letter or Proceedings	389,044
S26	S24 NOT S25	982
S27	S24 NOT S25 Limiters - English Language	979
S28	S24 NOT S25 Limiters - Published Date: 20100101-20171231; English Language	681

Economic Evidence Search

Search requested by: Sandjar Djalalov
Librarians: Corinne Holubowich

Economic Evaluation and Cost Effectiveness Search
Search date: January 25, 2017
Databases searched: Ovid MEDLINE, Embase, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects (DARE), Centre for Reviews and Dissemination (CRD) Health Technology Assessment Database, National Health Service (NHS) Economic Evaluation Database and Cumulative Index to Nursing and Allied Health Literature (CINAHL)

Database: EBM Reviews - Cochrane Central Register of Controlled Trials <November 2016>, EBM Reviews - Cochrane Database of Systematic Reviews <2005 to January 18, 2017>, EBM Reviews - Database of Abstracts of Reviews of Effects <1st Quarter 2015>, EBM Reviews - Health Technology Assessment <4th Quarter 2016>, EBM Reviews - NHS Economic Evaluation Database <1st Quarter 2015>, Embase <1980 to 2017 Week 04>, Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present>
Search Strategy:
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1 exp Diabetes Mellitus, Type 1/ (176240)
2 ((diabet* adj3 (typ* 1 or typ* i or type1 or typei or typ* one or brittl* or juvenil* or pediatric or paediatric or early or keto* or labil* or acidos* or autoimmun* or auto immun* or sudden onset or young onset)) or (insulin* adj2 depend*) or insulindepend* or dm1 or dm 1 or dmt1 or dm t1 or t1dm or t1 dm or t1d or iddm).ti,ab,kf. (232943)
3 Diabetic Ketoacidosis/ (15987)
4 (ketoacidosis or acidoketosis or keto acidosis or ketoacidemia or ketosis).ti,ab,kf. (20764)
5 Hypoglycemia/ (95050)
6 Diabetes Mellitus/ (672276)
7 5 and 6 (25348)
8 ((hypoglyc?em* or ((low or lower or decreas* or deficien* or insufficien* or reduce* or reduction* or fluctuat* or fallen or falling or threshold or safe) adj3 (glucose* or sugar* or hba1c or hb a1 or hba1 or a1c or h?emoglob* or glycoh?emoglob*))) adj5 (diabet* or IDDM or DM)).ti,ab,kf. (20615)
9 or/1-4,7-8 (326173)
10 Blood Glucose Self-Monitoring/ (21053)
11 (continu* or uninterrupt* or ongoing or looped or interminable).ti,ab,kf. (2394149)
12 10 and 11 (4475)
13 ((continu* or uninterrupt* or ongoing or looped or interminable) adj4 (blood glucose or blood sugar*) adj2 (self monitor* or home monitor*)).ti,ab,kf. (103)
14 ((continu* or uninterrupt* or ongoing or looped or interminable) adj4 SMBG).ti,ab,kf. (127)
15 (CGM or CGMS or continuous glucose monitor* or continuous glucose sensor*).ti,ab,kf. (9984)
16 ((medtronic adj3 (paradigm* or glucose monitor* or glucose sensor* or CGM or insulin pump* or LGS or 630G)) or veo or veotm or minimed or dexcom or g4 platinum or g5 platinum).ti,ab,kf. (1788)
17 ((flash or novel) adj2 glucose adj2 (monitor* or sensor or sensing)).ti,ab,kf. (182)

18 ((integrat* adj2 (pump or pumps or infusion*)) or (sensor adj3 (pump or pumps or therap* or infusion*)) or (sensor augment* adj2 pump*) or low glucose suspend*).ti,ab,kf. (1538)
19 (closed loop adj2 (pump* or deliver* or infus* or therap* or treatment* or system* or sensor* or control* or monitor* or hybrid*)).ti,ab,kf. (7164)
20 Pancreas, Artificial/ (2671)
21 (artificial adj3 (pancreas or beta cell*)).ti,ab,kf. (3436)
22 or/12-21 (22784)
23 9 and 22 (9179)
24 economics/ (255645)
25 economics, medical/ or economics, pharmaceutical/ or exp economics, hospital/ or economics, nursing/ or economics, dental/ (787307)
26 economics.fs. (426430)
27 (econom* or price or prices or pricing or priced or discount* or expenditure* or budget* or pharmacoeconomic* or pharmaco-economic*).tw. (762124)
28 exp "costs and cost analysis"/ (555558)
29 cost*.ti. (255725)
30 cost effective*.tw. (277253)
31 (cost* adj2 (util* or efficacy* or benefit* or minimi* or analy* or saving* or estimate* or allocation or control or sharing or instrument* or technolog*)).ab. (174616)
32 models, economic/ (167652)
33 markov chains/ or monte carlo method/ (72304)
34 (decision adj1 (tree* or analy* or model*)).tw. (37669)
35 (markov or markow or monte carlo).tw. (113113)
36 quality-adjusted life years/ (34238)
37 (QOLY or QOLYs or HRQOL or HRQOLs or QALY or QALYs or QALE or QALEs).tw. (58790)
38 ((adjusted adj (quality or life)) or (willing* adj2 pay) or sensitivity analys*s).tw. (111268)
39 or/24-38 (2463705)
40 23 and 39 (636)
41 40 use ppez,cctr,coch,dare,clhta (186)
42 23 use cleed (4)
43 or/41-42 (190)
44 limit 43 to english language [Limit not valid in CDSR,DARE; records were retained] (187)
45 limit 44 to yr="2010 -Current" [Limit not valid in DARE; records were retained] (143)
46 exp insulin dependent diabetes mellitus/ (176083)
47 ((diabet* adj3 (typ* 1 or typ* i or type1 or typei or typ* one or brittl* or juvenil* or pediatric or paediatric or early or keto* or labil* or acidos* or autoimmun* or auto immun* or sudden onset or young onset)) or (insulin* adj2 depend*) or insulindepend* or dm1 or dm 1 or dmt1 or dm t1 or t1dm or t1 dm or t1d or iddm).tw,kw. (239545)
48 diabetic ketoacidosis/ (15987)
49 (ketoacidosis or acidoketosis or keto acidosis or ketoacidemia or ketosis).tw,kw. (21104)
50 hypoglycemia/ (95050)
51 diabetes mellitus/ (672276)
52 50 and 51 (25348)
53 ((hypoglyc?em* or ((low or lower or decreas* or deficien* or insufficien* or reduce* or reduction* or fluctuat* or fallen or falling or threshold or safe) adj3 (glucose* or sugar* or hba1c or hb a1 or hba1 or a1c or h?emoglob* or glycoh?emoglob*))) adj5 (diabet* or IDDM or DM)).tw,kw. (21914)
54 or/46-49,52-53 (332412)
55 blood glucose monitoring/ (21276)

56 ((continu* or uninterrupt* or ongoing or looped or interminable) adj5 (self* or home*)).tw,kw,dv. (16009)
57 55 and 56 (116)
58 ((continu* or uninterrupt* or ongoing or looped or interminable) adj4 (blood glucose or blood sugar*) adj2 (self monitor* or home monitor*)).tw,kw,dv. (105)
59 ((continu* or uninterrupt* or ongoing or looped or interminable) adj4 SMBG).tw,kw,dv. (131)
60 (CGM or CGMS or continuous glucose monitor* or continuous glucose sensor*).tw,kw,dv. (10250)
61 ((medtronic adj3 (paradigm* or glucose monitor* or glucose sensor* or CGM or insulin pump* or LGS or 630G)) or veo or veotm or minimed or dexcom or g4 platinum or g5 platinum).tw,kw,dv. (2388)
62 ((flash or novel) adj2 glucose adj2 (monitor* or sensor or sensing)).tw,kw,dv. (184)
63 ((integrat* adj2 (pump or pumps or infusion*)) or (sensor adj3 (pump or pumps or therap* or infusion*)) or (sensor augment* adj2 pump*) or low glucose suspend*).tw,kw,dv. (1589)
64 (closed loop adj2 (pump* or deliver* or infus* or therap* or treatment* or system* or sensor* or control* or monitor* or hybrid*)).tw,kw,dv. (7269)
65 artificial pancreas/ (2671)
66 (artificial adj3 (pancreas or beta cell*)).tw,kw,dv. (3492)
67 or/57-66 (21829)
68 54 and 67 (8861)
69 Economics/ (255645)
70 Health Economics/ or exp Pharmacoeconomics/ (223136)
71 Economic Aspect/ or exp Economic Evaluation/ (436072)
72 (econom* or price or prices or pricing or priced or discount* or expenditure* or budget* or pharmacoeconomic* or pharmaco-economic*).tw. (762124)
73 exp "Cost"/ (555558)
74 cost*.ti. (255725)
75 cost effective*.tw. (277253)
76 (cost* adj2 (util* or efficacy* or benefit* or minimi* or analy* or saving* or estimate* or allocation or control or sharing or instrument* or technolog*)).ab. (174616)
77 Monte Carlo Method/ (58378)
78 (decision adj1 (tree* or analy* or model*)).tw. (37669)
79 (markov or markow or monte carlo).tw. (113113)
80 Quality-Adjusted Life Years/ (34238)
81 (QOLY or QOLYs or HRQOL or HRQOLs or QALY or QALYs or QALE or QALEs).tw. (58790)
82 ((adjusted adj (quality or life)) or (willing* adj2 pay) or sensitivity analys*s).tw. (111268)
83 or/69-82 (2039296)
84 68 and 83 (475)
85 limit 84 to english language [Limit not valid in CDSR,DARE; records were retained] (461)
86 limit 85 to yr="2010 -Current" [Limit not valid in DARE; records were retained] (354)
87 86 use emez (220)
88 45 or 87 (363)
89 88 use ppez (110)
90 88 use emez (220)
91 88 use coch (2)
92 88 use cctr (23)
93 88 use clhta (1)
94 88 use cleed (4)
95 remove duplicates from 88 (253)

CINAHL

#	Query	Results
S1	(MH "Diabetes Mellitus, Type 1+")	17,153
S2	((diabet* N3 (typ* 1 or typ* i or type1 or typei or typ* one or brittl* or juvenil* or pediatric or paediatric or early or keto* or labil* or acidos* or autoimmun* or auto immun* or sudden onset or young onset)) or (insulin* N2 depend*) or insulindepend* or dm1 or dm 1 or dmt1 or dm t1 or t1dm or t1 dm or t1d or iddm)	26,773
S3	(MH "Diabetic Ketoacidosis")	1,653
S4	(ketoacidosis or acidoketosis or keto acidosis or ketoacidemia or ketosis)	2,266
S5	(MH "Hypoglycemia")	6,679
S6	(MH "Diabetes Mellitus")	46,256
S7	S5 AND S6	1,343
S8	((hypoglyc#em* or ((low or lower or decreas* or deficien* or insufficien* or reduce* or reduction* or fluctuat* or fallen or falling or threshold or safe) N3 (glucose* or sugar* or hba1c or hb a1 or hba1 or a1c or h#emoglob* or glycoh#emoglob*))) N5 (diabet* or IDDM or DM))	4,756
S9	S1 OR S2 OR S3 OR S4 OR S7 OR S8	31,012
S10	(MH "Blood Glucose Self-Monitoring")	2,778
S11	(continu* or uninterrupt* or ongoing or looped or interminable)	272,487
S12	S10 AND S11	537
S13	((continu* or uninterrupt* or ongoing or looped or interminable) N4 (blood glucose or blood sugar*) N2 (self monitor* or home monitor*))	27
S14	((continu* or uninterrupt* or ongoing or looped or interminable) N4 SMBG)	26
S15	(CGM or CGMS or continuous glucose monitor* or continuous glucose sensor*)	1,179
S16	((medtronic N3 (paradigm* or glucose monitor* or glucose sensor* or CGM or insulin pump* or LGS or 630G)) or veo or veotm or minimed or dexcom or g4 platinum or g5 platinum)	205
S17	((flash or novel) N2 glucose N2 (monitor* or sensor or sensing))	17
S18	((integrat* N2 (pump or pumps or infusion*)) or (sensor N3 (pump or pumps or therap* or infusion*)) or (sensor augment* N2 pump*) or low glucose suspend*)	199
S19	(closed loop N2 (pump* or deliver* or infus* or therap* or treatment* or system* or sensor* or control* or monitor* or hybrid*))	393
S20	(artificial N3 (pancreas or beta cell*))	197
S21	S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20	1,974
S22	S9 AND S21	1,034
S23	(MH "Economics")	10,992
S24	(MH "Economic Aspects of Illness")	6,584
S25	(MH "Economic Value of Life")	518
S26	MH "Economics, Dental"	104
S27	MH "Economics, Pharmaceutical"	1,760
S28	MW "ec"	140,414
S29	(econom* or price or prices or pricing or priced or discount* or expenditure* or budget* or pharmacoeconomic* or pharmaco-economic*)	210,045
S30	(MH "Costs and Cost Analysis+")	83,883
S31	TI cost*	39,344
S32	(cost effective*)	26,695
S33	AB (cost* N2 (util* or efficacy* or benefit* or minimi* or analy* or saving* or estimate* or allocation or control or sharing or instrument* or technolog*))	17,578
S34	(decision N1 (tree* or analy* or model*))	4,861
S35	(markov or markow or monte carlo)	3,005
S36	(MH "Quality-Adjusted Life Years")	2,571

S37 (QOLY or QOLYs or HRQOL or HRQOLs or QALY or QALYs or QALE or QALEs) 5,656
S38 ((adjusted N1 (quality or life)) or (willing* N2 pay) or sensitivity analys?s) 10,819
S39 S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 279,380
S40 S22 AND S39 66
S41 S22 AND S39
Limiters - English Language
66
S42 S22 AND S39
Limiters - Published Date: 20100101-20171231; English Language
44

Health State Utility Value Search
Search date: January 30, 2017

Database: Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present>
Search Strategy:
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1 exp Diabetes Mellitus, Type 1/ (67682)
2 ((diabet* adj3 (typ* 1 or typ* i or type1 or typei or typ* one or brittl* or juvenil* or pediatric or paediatric or early or keto* or labil* or acidos* or autoimmun* or auto immun* or sudden onset or young onset)) or (insulin* adj2 depend*) or insulindepend* or dm1 or dm 1 or dmt1 or dm t1 or t1dm or t1 dm or t1d or iddm).ti,ab,kf. (91144)
3 Diabetic Ketoacidosis/ (5695)
4 (ketoacidosis or acidoketosis or keto acidosis or ketoacidemia or ketosis).ti,ab,kf. (8451)
5 Hypoglycemia/ (24398)
6 Diabetes Mellitus/ (103774)
7 5 and 6 (2167)
8 ((hypoglyc?em* or ((low or lower or decreas* or deficien* or insufficien* or reduce* or reduction* or fluctuat* or fallen or falling or threshold or safe) adj3 (glucose* or sugar* or hba1c or hb a1 or hba1 or a1c or h?emoglob* or glycoh?emoglob*))) adj5 (diabet* or IDDM or DM)).ti,ab,kf. (7240)
9 or/1-4,7-8 (123756)
10 Blood Glucose Self-Monitoring/ (5246)
11 (continu* or uninterrupt* or ongoing or looped or interminable).ti,ab,kf. (963628)
12 10 and 11 (1335)
13 ((continu* or uninterrupt* or ongoing or looped or interminable) adj4 (blood glucose or blood sugar*) adj2 (self monitor* or home monitor*)).ti,ab,kf. (37)
14 ((continu* or uninterrupt* or ongoing or looped or interminable) adj4 SMBG).ti,ab,kf. (39)
15 (CGM or CGMS or continuous glucose monitor* or continuous glucose sensor*).ti,ab,kf. (3161)
16 ((medtronic adj3 (paradigm* or glucose monitor* or glucose sensor* or CGM or insulin pump* or LGS or 630G)) or veo or veotm or minimed or dexcom or g4 platinum or g5 platinum).ti,ab,kf. (459)
17 ((flash or novel) adj2 glucose adj2 (monitor* or sensor or sensing)).ti,ab,kf. (72)
18 ((integrat* adj2 (pump or pumps or infusion*)) or (sensor adj3 (pump or pumps or therap* or infusion*)) or (sensor augment* adj2 pump*) or low glucose suspend*).ti,ab,kf. (458)
19 (closed loop adj2 (pump* or deliver* or infus* or therap* or treatment* or system* or sensor* or control* or monitor* or hybrid*)).ti,ab,kf. (3028)

20 Pancreas, Artificial/ (556)
21 (artificial adj3 (pancreas or beta cell*)).ti,ab,kf. (1331)
22 or/12-21 (7943)
23 9 and 22 (2604)
24 Quality-Adjusted Life Years/ (9025)
25 (quality adjusted or adjusted life year*).tw. (11674)
26 (qaly* or qald* or qale* or qtime*).tw. (7579)
27 (illness state$1 or health state$1).tw. (5032)
28 (hui or hui1 or hui2 or hui3).tw. (1169)
29 (multiattribute* or multi attribute*).tw. (678)
30 (utility adj3 (score$1 or valu* or health* or cost* or measure* or disease* or mean or gain or gains or index*)).tw. (10653)
31 utilities.tw. (5404)
32 (eq-5d or eq5d or eq-5 or eq5 or euro qual or euroqual or euro qual5d or euroqual5d or euro qol or euroqol or euro qol5d or euroqol5d or euro quol or euroquol or euro quol5d or euroquol5d or eur qol or eurqol or eur qol5d or eurqol5d or euro?qul or eur?qul5d or euro* quality of life or European qol).tw. (7232)
33 (euro* adj3 (5 d or 5d or 5 dimension* or 5dimension* or 5 domain* or 5domain*)).tw. (2442)
34 (sf36* or sf 36* or sf thirtysix or sf thirty six).tw. (17901)
35 (time trade off$1 or time tradeoff$1 or tto or timetradeoff$1).tw. (1529)
36 ((qol or hrqol or quality of life).ti. or *quality of life/) and ((qol or hrqol* or quality of life) adj2 (increas* or decreas* or improve* or declin* or reduc* or high* or low* or effect or effects of worse or score or scores or change$1 or impact$1 or impacted or deteriorate$)).ab. (23194)
37 Cost-Benefit Analysis/ and (cost effectiveness ratio* and (perspective* or life expectanc*)).tw. (2420)
38 *quality of life/ and (quality of life or qol).ti. (42116)
39 quality of life/ and ((quality of life or qol) adj3 (improve* or chang*)).tw. (18236)
40 quality of life/ and ((quality of life or qol) adj (score$1 or measure$1)).tw. (9109)
41 quality of life/ and health-related quality of life.tw. (22860)
42 quality of life/ and ec.fs. (8369)
43 quality of life/ and (health adj3 status).tw. (7018)
44 (quality of life or qol).tw. and cost-benefit analysis/ (9308)
45 models, economic/ (7973)
46 or/24-45 (121614)
47 23 and 46 (51)
48 limit 47 to english language (50)

Grey Literature

Performed on:
January 12-27, 2017

Websites searched:
HTA Database Canadian Repository, Alberta Health Technologies Decision Process reviews, Canadian Agency for Drugs and Technologies in Health (CADTH), Institut national d'excellence en santé et en services sociaux (INESSS), Institute of Health Economics (IHE), McGill University Health Centre Health Technology Assessment Unit, National Institute for Health and Care Excellence (NICE), Agency for Healthcare Research and Quality (AHRQ) Evidence-based Practice Centers, Australian Government Medical Services Advisory Committee, Centers for Medicare & Medicaid Services Technology Assessments, Institute for Clinical and Economic

Review, Ireland Health Information and Quality Authority Health Technology Assessments, Washington State Health Care Authority Health Technology Reviews, ClinicalTrials.gov, Tuft's Cost-Effectiveness Analysis Registry

Keywords used: continuous glucose monitor, continuous glucose monitors, CGM, minimed, Medtronic, dexcom, platinum, paradigm, closed loop, artificial pancreas, integrated pump, sensor augment, sensor augmented

Results: 8
35 clinical trials not counted in PRISMA

Appendix 2: Clinical Evidence Quality Assessment

Table A1: GRADE Evidence Profile for Comparison of Continuous Glucose Monitoring and Usual Care

Number of Studies (Design)	Risk of Bias[a]	Inconsistency	Indirectness	Imprecision	Publication Bias	Upgrade Considerations	Quality
Time-Related Glucose Variability—Time Spent in Target Glycemic Range							
2 (RCTs, adults)[24,39]	Serious limitations (−1)	No serious limitations	No serious limitations	No serious limitations	Undetected	None	⊕⊕⊕ Moderate
1 (observational, adults)[43]	Serious limitations (−2)	No serious limitations	No serious limitations	Serious limitations[b] (−1)	Undetected	None	⊕ Very low
Time-Related Glucose Variability—Time Spent Outside of Target Glycemic Range							
4 (RCTs, adults)[24,27,33,39]	Serious limitations (−1)	No serious limitations[c]	No serious limitations	No serious limitations	Undetected	None	⊕⊕⊕ Moderate
Hypoglycemia							
4 (RCTs, adults)[25,27,30,38]	Serious limitations (−1)	Serious limitations (-1)	No serious limitations	No serious limitations	Undetected	None	⊕⊕ Low
2 (observational, adults)[42,43]	Serious limitations (−3)	No serious limitations	No serious limitations	No serious limitations[d]	Undetected	None	⊕ Very low
3 (RCTs, children)[25,26,37]	Serious limitations (−3)	No serious limitations[c]	No serious limitations	No serious limitations	Undetected	None	⊕ Very low
Hypoglycemia—Severe Hypoglycemic Events							
3 (RCTs, adults)[32,33,39]	Serious limitations (−1)	Serious limitations[e] (−1)	No serious limitations	No serious limitations[d]	Undetected	None	⊕⊕ Low
A1C Levels—Change From Baseline							
8 (RCTs, adults)[24,25,27,30,31,35,38,39]	Serious limitations (−1)	No serious limitations	No serious limitations	No serious limitations[d]	Undetected	None	⊕⊕⊕ Moderate
4 (observational, adults)[40-43]	Serious limitations (−2)	Serious limitations[f] (−1)	No serious limitations	No serious limitations[d]	Undetected	None	⊕ Very low
4 (RCTs, children)[25,26,29,34]	Serious limitations (−1)	Serious limitations[f] (−1)	No serious limitations	No serious limitations	Undetected	None	⊕⊕ Low
User Satisfaction							
7 (RCTs, adults)[24,27,28,30-32,36]	Serious limitations (−1)	Serious limitations[f] (−1)	No serious limitations	No serious limitations[d]	Undetected	None	⊕⊕ Low
1 (observational, adults)[42]	Serious limitations (−2)	No serious limitations	No serious limitations	Serious limitations[b] (−1)	Undetected	None	⊕ Very low

Number of Studies (Design)	Risk of Bias[a]	Inconsistency	Indirectness	Imprecision	Publication Bias	Upgrade Considerations	Quality
4 (RCTs, children)[28,29,34,36]	Serious limitations (−1)	Serious limitations[f] (−1)	No serious limitations	No limitations	Undetected	None	⊕⊕ Low

Abbreviations: RCT, randomized controlled trial.
[a]Details provided in Tables A2 and A3.
[b]Some studies had wide confidence intervals.
[c]Trend in results was inconsistent in favouring intervention or control groups; however, results were not statistically significant.
[d]Some studies did not find significant results or had large confidence intervals; however, this was likely owing to smaller sample sizes in individual studies. The body of evidence was substantive.
[e]Results were inconsistent in favouring intervention or control groups.
[f]Inconsistency in results; some studies favoured the intervention, and others favoured the control group.

Table A2: Risk of Bias Among Randomized Controlled Trials for Comparison of Continuous Glucose Monitoring and Usual Care[a]

	Selection Bias[b]	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Bias
Beck et al, 2017[24]	N	Y	Y	N	U	Y
Bergenstal et al, 2010[25]	N	Y	Y	N	N	Y[c]
Bukara-Radujkovic et al, 2011[26]	N	Y	Y	N	U	N
Hermanides et al, 2011[27]	N	Y	Y	N	U	N
Hommel et al, 2014[28]	Y	Y	Y	N	N	Y
Kordonouri et al, 2012[29]	N	Y	N	N	U	U
Langeland et al, 2012[30]	N	Y	Y	N	U	N
Lind et al, 2017[31]	N	Y	Y	N	N	N
Little et al, 2014[32]	N	Y	Y	N	N	Y[c]
Ly et al, 2013[33]	N	Y	Y	N	U	N
Olivier et al, 2014[34]	N	Y	U	Y	U	U[d]
Rosenlund et al, 2015[35]	N	Y	Y	N	U	N
Rubin and Peyrot, 2012[36]	N	Y	Y	N	U	Y
Slover et al, 2013[37]	N	Y	Y	N	U	Y[c]
Tumminia et al, 2015[38]	N	Y	Y	N	U	Y[c]
van Beers et al, 2016[39]	N	Y	Y	N	U	Y

Abbreviations: Y, yes or high risk of bias likely; N, no or low risk of bias detected; U, unclear risk of bias.
[a]Risk of bias assessed using the Cochrane Risk of Bias Tool.[22]
[b]The term selection bias refers to confounding in Table A3.
[c]Bias in the analytic approach.
[d]109 of 141 patients were excluded owing to preference for a different device from that included in the study.

Table A3: Risk of Bias Among Observational Studies for Comparison of Continuous Glucose Monitoring and Usual Care[a]

	Selection Bias	Performance Bias on Exposure	Detection Bias	Attrition Bias	Reporting Bias	Confounding	Other Biases
McQueen et al, 2014[40]	N	N	Y	N	U	Y	U
Quiros et al, 2015[41]	Y	N	Y	N	U	Y	U
Radermecker et al, 2010[42]	Y	N	Y	Y	U	Y	U
Soupal et al, 2016[43]	N	N	Y	N	U	Y	Y[b]

Abbreviations: Y, yes or high risk of bias likely; N, no or low risk of bias detected; U, unclear risk of bias.
[a]Using the Risk of Bias Assessment Tool for Non-randomized Studies (RoBANS) tool.[21]
[b]Bias in the analytic approach.

Appendix 3: Results of Applicability Checklist for Studies Included in the Economic Evidence Review

Table A4: Assessment of the Cost-Effectiveness of Continuous Glucose Monitoring

Objective: To assess the cost-effectiveness of continuous glucose monitoring					
Author, Year	**Is the study population similar to the question?**	**Are the interventions similar to the question?**	**Is the health care system in which the study was conducted sufficiently similar to the current Ontario context?**	**Was/were the perspective(s) clearly stated, and what were they?**	**Are estimates of relative treatment effect from the best available source?**
Huang et al, 2010[57]	Yes; adults aged ≥ 25 years	Partially; study did not consider insulin treatment	No; US health system	Yes	Yes
Kamble et al, 2012[52]	Partially; patient mean age 41.3 years; clinical experts suggest assessing younger patients with a shorter disease history	Yes	No; US health system	Yes	Yes
McQueen et al, 2011[51]	Partially; patient mean age 40; clinical experts suggest assessing younger patients	Partially; insulin infusion therapy not specified	No; US health system	Yes	Yes
Riemsma et al, 2016[58]	Partially; patients with a 27-year history of diabetes and a mean age of 42 years; clinical experts suggest assessing younger patients with a shorter disease history	Yes	Partially; UK health system	Yes	Yes
Roze et al, 2015[54]	Yes; patient mean age 27 years	Partially; comparator arm used SMPG	No; Sweden health system	Yes	Yes
Roze et al, 2016[53]	Yes; patient mean age 27 years	Yes	Partially; UK health system	Yes	Yes
Roze et al, 2016[55]	Yes; patient mean age 27 years	Yes	No; France health system	Yes	Yes
Roze et al, 2017[56]	No; patient population not specified	Yes	No; Denmark health system	Yes	Yes

Author, Year	Are all future costs and outcomes discounted? (If yes, at what rate?)	Is the value of health effects expressed in terms of quality-adjusted life-years?	Are costs and outcomes from other sectors fully and appropriately measured and valued?	Overall judgment (directly applicable/partially applicable/ not applicable)
Huang et al, 2010[57]	Yes; both costs and outcomes discounted at 3%	Yes	Yes	Partially applicable
Kamble et al, 2012[52]	Yes; both costs and outcomes discounted at 3%	Yes	Yes	Partially applicable
McQueen et al, 2011[51]	Yes; both costs and outcomes discounted at 3%	Yes	Yes	Partially applicable
Riemsma et al, 2016[58]	Yes; costs discounted at 1.5%, outcomes discounted at 3.5%	Yes	Yes	Partially applicable
Roze et al, 2015[54]	Yes; both costs and outcomes discounted at 3%	Yes	Yes	Partially applicable
Roze et al, 2016[53]	Yes; costs discounted at 1.5%, outcomes discounted at 3.5%	Yes	Yes	Partially applicable
Roze et al, 2016[55]	Yes; both costs and outcomes discounted at 4%	Yes	Yes	Partially applicable
Roze et al, 2017[56]	Yes; both costs and outcomes discounted at 3%	Yes	Yes	Partially applicable

Abbreviations: CGM, continuous glucose monitoring; SMBG, self-monitoring of blood glucose.

Appendix 4: Primary Economic Analysis, Included Interventions

Table A5: Reasons for Including Four Interventions in the Primary Economic Analysis

Case	Suggested Reference for Base Case	Reason for Inclusion
For A1C Change From Baseline		
SMBG plus multiple daily injections vs. standalone CGM plus multiple daily injections	Lind et al, 2017[31]	• Lower to average risk of bias compared with body of evidence • A more recent study • Estimate of effect was about in the middle of the observed results, with smaller confidence intervals owing to the larger sample size
SMBG plus multiple daily injections vs. sensor-augmented pump	Bergenstal et al, 2010[25]	• Lower to average risk of bias compared with body of evidence • Larger body of evidence • Estimate of effect is about in the middle of the observed results • Results presented for an adult population
SMBG + insulin pump vs. sensor-augmented pump	Quiros et al, 2015[41]	• Observational study, but so was the other option for this case (Soupal et al, 2016[43]). With no reason to prefer one study over another, this study offered a more conservative effect estimate
SMBG + insulin pump vs. standalone CGM plus insulin pump	Tumminia et al, 2015[38]	• Lower risk of bias compared with the other evidence for this case; it was a randomized controlled trial, and the other study (Radermecker et al, 2010[127]) was an observational study
For Severe Hypoglycemic Events		
All cases	Bergenstal et al, 2010[25]	• Low to average risk of bias compared with the rest of the body of evidence • Largest sample size, which was important because severe hypoglycemic events are rare

Abbreviations: A1C, glycated hemoglobin; CGM, continuous glucose monitoring; SMBG, self-monitoring of blood glucose.

Appendix 5: Primary Economic Analysis, Risk Reduction Estimation

We assumed that the reduction in glycated hemoglobin (A1C) levels resulting from continuous glucose monitoring would be similar to that resulting from intensive treatment. However, the Diabetes Control and Complications Trial reported absolute risk reduction, which "does not involve an explicit comparison to the control group as in the relative risk reduction and thus does not confound the effect size with the baseline risk."[128] We used relative risk reduction (RRR), which determines how much a treatment reduces the risk of incidence relative to a control group that does not receive treatment. We then determined relative risk (RR) and applied this to the model (Table A6). The formula for relative risk reduction was RRR = 1 – RR. The formula for risk reduction was RR = 1 − RRR.

Table A6: Relative Risk Associated With a 1% Reduction in A1C

		1% Reduction in A1C		
Complication	**RR**	**RR**	**RR (%)**	**Source**
Retinopathy	0.462	0.029	2.9	DCCT, 1993[64]
Nephropathy	0.611	0.038	3.8	DCCT, 1993[64]
Neuropathy	0.390	0.025	2.5	Martin et al, 2014[82]
Cardiovascular disease	0.643	0.040	4.0	DCCT, 2009[76]
Severe hypoglycemia[a]	1.13	0.061	6.1	DCCT, 2009[76]

Abbreviations: A1C, glycated hemoglobin; DCCT, Diabetes Control and Complications Trial; RR, relative risk.
[a]The risk of severe hypoglycemia increases as A1C is reduced.

The algorithm for calculating relative risk based on the Diabetes Control and Complications Trial data was as follows:

1. Obtain the relative change in A1C level (%) associated with continuous glucose monitoring. Use the change in A1C level associated with intensive treatment (15.9%; the difference between intensive versus conventional treatments after 6.5 years of follow-up from the 1993 Diabetes Control and Complications Trial[64]).
2. Obtain the relative risk for long-term complications (i.e., retinopathy, nephropathy, neuropathy, cardiovascular disease) from the 1993 Diabetes Control and Complications Trial,[64] the 2009 Diabetes Control and Complications Trial,[76] and the 2014 study conducted by Martin et al.[82] (RR = cumulative incidences of intensive arm divided by cumulative incidences of treatment arm).
3. Calculate relative risk reduction (RRR = 1 − RR; details in Tables A7, A8, and A9).
4. Calculate the relative risk reduction associated with a decrease in complications resulting from a 1% reduction in A1C level.
5. Calculate relative risk reduction (RRR = change in A1C level associated with continuous glucose monitoring multiplied by the relative risk reduction resulting from a 1% reduction in A1C).
6. Determine relative risk (RR = 1 – RRR) and apply it to the model. (A sample calculation of risk reduction resulting from changes in A1C level in the GOLD[31] and DIAMOND[24] trials is presented in Table A9.)

Table A7: Relationship Between Percentage Relative Change From Baseline A1C and Relative Risk of Diabetes Complications

% Relative Change From Baseline A1C	RR, Retinopathy	RR, Nephropathy	RR, Neuropathy	RR, Cardiovascular Disease
10	0.709	0.781	0.676	0.797
9	0.734	0.800	0.703	0.815
8	0.760	0.820	0.731	0.834
7	0.786	0.841	0.761	0.853
6	0.814	0.862	0.791	0.873
5	0.842	0.884	0.822	0.893
4	0.872	0.906	0.855	0.913
3	0.902	0.928	0.889	0.934
2	0.934	0.952	0.925	0.956
1	0.966	0.976	0.962	0.978

Abbreviation: A1C, glycated hemoglobin; RR, relative risk.

Table A8: Relative Risk Reduction and Relative Risk Associated With a 1% Reduction in A1C Level

			1% Reduction in A1C				
Complication	RR	RRR	RR	RRR	RR (%)	RRR (%)	Source
Retinopathy	0.462	0.538	0.025	0.029	2.5	2.9	DCCT, 1993[64]
Nephropathy	0.611	0.389	0.033	0.021	3.3	2.1	DCCT, 1993[64]
Neuropathy	0.390	0.610	0.021	0.033	2.1	3.3	DCCT, 1993[64]
Cardiovascular disease	0.643	0.357	0.034	0.019	3.4	1.9	Martin et al, 2014[82]
Severe hypoglycemia[a]	1.13	−0.13	0.061	−0.007	6.1	−0.7	DCCT, 2009[76]

Abbreviations: A1C, glycated hemoglobin; DCCT, Diabetes Control and Complications Trial; RR, relative risk; RRR, relative risk reduction.
[a]The risk of severe hypoglycemia increases as A1C is reduced.

Table A9: Calculation of Risk Reduction Owing to a Decrease in A1C Level

Intervention: CGM + MDI vs. SMBG + MDI	GOLD[a]		DIAMOND[b]	
Steps				
1. Calculate % change relative to baseline	5.15		10.47	
2. Obtain RR of complications from DCCT	Retinopathy: 0.462	Nephropathy: 0.611	Neuropathy: 0.390	CVD: 0.643
3. Calculate RRR from retinopathy (DCCT): RRR = 1 − RR	0.538	0.389	0.610	0.357
4. Calculate RRR change owing to 1% reduction in A1C level (15.9% A1C reduction from DCCT)	0.034	0.024	0.038	0.022
GOLD				
5. Calculate RRR for intervention	0.174	0.126	0.197	0.116
6. Calculate RR: RR = 1 − RRR	0.826	0.874	0.803	0.884
DIAMOND				
5. Calculate RRR for intervention	0.354	0.256	0.401	0.235
6. Calculate RR: RR = 1 − RRR	0.646	0.744	0.599	0.765
Average RR (GOLD and DIAMOND)	0.736	0.809	0.701	0.825

Abbreviations: A1C, glycated hemoglobin; CGM, continuous glucose monitoring; CVD, cardiovascular disease; DCCT, Diabetes Control and Complications Trial; MDI, multiple daily injections; SMBG, self-monitoring of blood glucose; RR, relative risk; RRR relative risk reduction.

[a]The GOLD study[31] was a randomized controlled trial conducted in Sweden with a 26-week duration. The mean age of study participants was 44 years, and the mean duration of diabetes duration was 22 years.

[b]The DIAMOND study[24] was randomized controlled trial conducted in the United States with a 24-week duration. The mean age of study participants was 48 years, and the mean duration of diabetes was 19 years.

Appendix 6: Primary Economic Analysis, Cost Parameters

Table A10: Time-Dependent Probability of Death Following the Onset of Congestive Heart Failure[a65]

	Age, y			
Year	27–59	60–69	70–79	80+
1	0.14	0.245	0.2	0.44
2	0.205	0.21	0.25	0.425
3	0.019	0.145	0.175	0.305
4	0.034	0.06	0.19	0.31
5	0.185	0.125	0.17	0.145
6	0.125	0.13	0.32	0.275
7	0.125	0.14	0.135	0.515
8	0.075	0.065	0.13	0.61
9	0.107	0.075	0.265	0.57
10	0.16	0.135	0.245	0.57

[a]Used for cardiovascular disease alone, and for cardiovascular disease combined with diabetes complications.

Table A11: Annual and Daily Cost of Multiple Daily Insulin Injections for Type 1 Diabetes—Canadian Clinical Practice

Treatment	Daily Treatment Cost Without Test Strips
Insulin NPH (insulin isophane)	$1.95
Biphasic human insulin	$3.81
Long-acting insulin analogue	$3.04
Biphasic insulin analogue	$4.34
Average daily cost	$3.29
Annual cost[a]	**$1,348**

[a]Annual costs inflated to 2017 Canadian dollars.
Source: McIntosh et al, 2011.[129]

Table A12: Annual Cost of Insulin Pump Therapy

We obtained an average daily insulin use of 42 units from 731 insulin pumps[130] People with diabetes using an insulin pump use 200-unit cartridges, so one insulin cartridge lasts approximately 4.5 days, or 81 cartridges (365/4.5 = 81) per year Humalog (insulin lispro) is provided in 3 × 5 mL = 15 mL packs (1 mL insulin = 100 units; 15 mL = 1,500 units). One pack of Humalog equals 7.5 cartridges (1,500/200) Humalog costs $67.99 per pack[131] The annual cost of Humalog with an insulin pump is $734 ([81/7.5] x $67.99).

Table A13: Daily and Annual Costs of Diabetes Treatment Supplies[a]

	Strips			Needles			Syringes			Total Daily Cost	Total Annual Cost
Technology	Quantity, units	Unit Price	Cost	Quantity, units	Unit Price	Cost	Quantity, units	Unit Price	Cost		
SAP (Dexcom G4 Platinum + Animas Vibe)	4	$0.73	$2.92							$2.92	$1,066
SAP (Dexcom G5 Mobile + Animas Vibe)	2	$0.73	$1.46							$1.46	$533
SAP with LGS (MiniMed Veo with LGS)	4	$0.73	$2.92							$2.92	$1,066
Standalone CGM + MDI (Dexcom G4 Platinum)	6	$0.73	$4.38	4	$0.10	$0.40	4	$0.40	$1.60	$6.38	$2,329
Standalone CGM + MDI (Dexcom G5 Mobile)	2	$0.73	$1.46	4	$0.10	$0.40	4	$0.40	$1.60	$3.46	$1,263
SMBG + insulin pump (Animas Vibe or MiniMed Veo)	6	$0.73	$4.38							$4.38	$1,599
SMBG + MDI	6	$0.73	$4.38	4	$0.10	$0.40	4	$0.40	$1.60	$6.38	$2,329

Abbreviations: CGM, continuous glucose monitoring; LGS, low-glucose suspend; MDI, multiple daily injections; SAP, sensor-augmented pump; SMBG, self-monitoring of blood glucose.
[a]All costs are presented in 2017 Canadian dollars.

Table A14: Annual Costs of Continuous Glucose Monitoring and Insulin Pump[a]

Product	Annual Cost	Description
Standalone CGM		
Dexcom G4 Platinum		
Receiver	$700	1 unit ($700 per unit)
Transmitters	$1,300	2 units ($650 per unit, replaced every 6 months)
Sensors	$4,420	52 units ($85 per unit, replaced every 7 days)
Total	**$6,420**	
Dexcom G5 Mobile		
Transmitters	$1,556	4 units ($389 per unit, replaced every 90 days)
Sensors	$4,420	52 units ($85 per unit, replaced every 7 days)
Total	**$5,976**	
Standalone Insulin Pump		
Insulin pump	$1,260	4-year warranty and 1-year extended warranty to meet Assistive Devices Program funding period of 5 years
Insulin pump infusion sets	$2,494	$20.50 per set every 3 days
Insulin pump reservoirs	$517	Assumed average use of reservoir: 4.5 days
Insulin pump batteries	$19	Energizer lithium AA battery
Total	**$4,290**	
CGM With Insulin Pump		
Insulin pump (Animas Vibe)	$4,290	
Transmitters	$1,300	2 units ($650 per unit, replaced every 6 months)
Sensors	$4,420	52 units ($85 per unit, replaced every 7 days)
Total: CGM (Dexcom G4 Platinum)	**$5,720**	
Total: Insulin pump and CGM	**$10,140**	
SAP With LGS		
Insulin pump (MiniMed Veo)	$4,290	
Sensors	$3,120	52 units ($60 per unit, replaced every 7 days)[b]
Total: CGM	**$3,120**	
Total: Insulin pump and CGM	**$7,410**	

Abbreviations: CGM, continuous glucose monitoring; MDI, multiple daily injections; SMBG, self-monitoring of blood glucose; LGS, low glucose suspend; SAP, sensor-augmented pump.

[a]All costs are presented in 2017 Canadian dollars.

[b]According to Medtronic, the average retail price for a CGM sensor is between $50 and $60. We have assumed a price of $60.

Table A15: Costs of Different Diabetes Treatment Technologies[a]

Intervention	Brands (Approved in Canada)	Diabetes Treatment Supplies	Insulin Treatment	CGM	Insulin Pump	Total Cost
SAP	Dexcom G4 Platinum + Animas Vibe	$1,066	$734	$5,720	$4,290	$11,811
SAP	Dexcom G5 Mobile + Animas Vibe *or* MiniMed VEO	$533	$734	$5,976	$4,290	$11,534
SAP with LGS	MiniMed Veo with LGS	$1,066	$734	$3,120	$4,290	$9,211
CGM + MDI	Dexcom G4 Platinum	$2,329	$1,348	$6,420	—	$10,097
CGM + MDI	Dexcom G5 Mobile	$1,263	$1,348	$5,976	—	$8,587
SMBG + insulin pump	Animas Vibe and MiniMed Veo	$1,599	$734	—	$4,484	$6,817
SMBG + MDI		$2,329	$1,348	—	—	$3,677

Abbreviations: CGM, continuous glucose monitoring; LGS, low-glucose suspend; MDI, multiple daily injections; SAP, sensor-augmented pump; SMBG, self-monitoring of blood glucose.

[a]All costs are presented in 2017 Canadian dollars.

Appendix 7: Primary Economic Analysis, Sensitivity Analyses

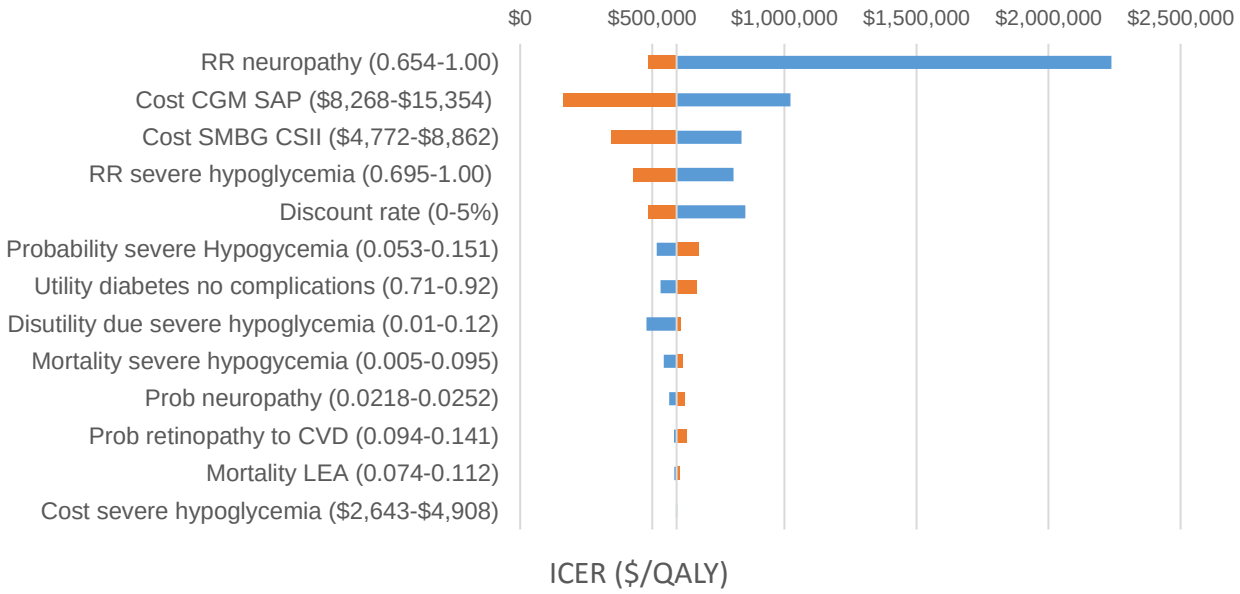


Figure A1: Continuous Glucose Monitoring With Sensor-Augmented Pump Versus Self-Monitoring of Blood Glucose Plus Insulin Pump

Abbreviations: CGM, continuous glucose monitoring; CSII, continuous subcutaneous insulin infusion (insulin pump); CVD, cardiovascular disease; ICER, incremental cost-effectiveness ratio; LEA, lower-extremity amputation; QALY, quality-adjusted life-year; RR, relative risk; SAP, sensor-augmented pump; SMBG, self-monitoring of blood glucose.

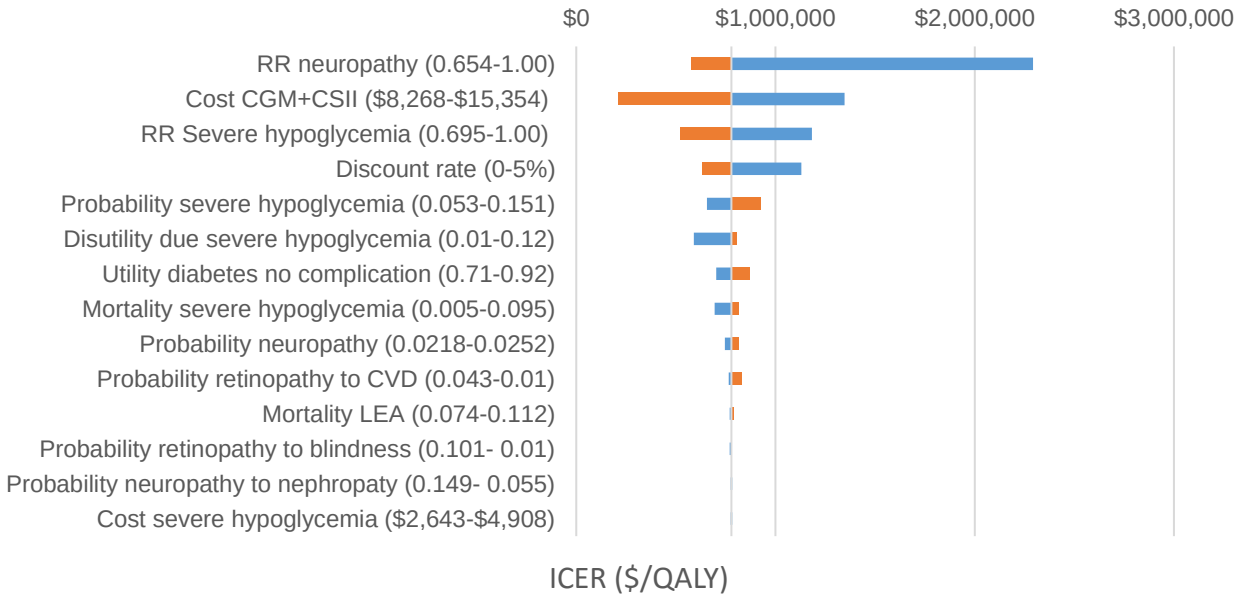


Figure A2: Continuous Glucose Monitoring Plus Insulin Pump Versus Self-Monitoring of Blood Glucose Plus Insulin Pump

Abbreviations: CGM, continuous glucose monitoring; CSII, continuous subcutaneous insulin infusion (insulin pump); CVD, cardiovascular disease; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year; LEA, lower-extremity amputation; RR, relative risk.

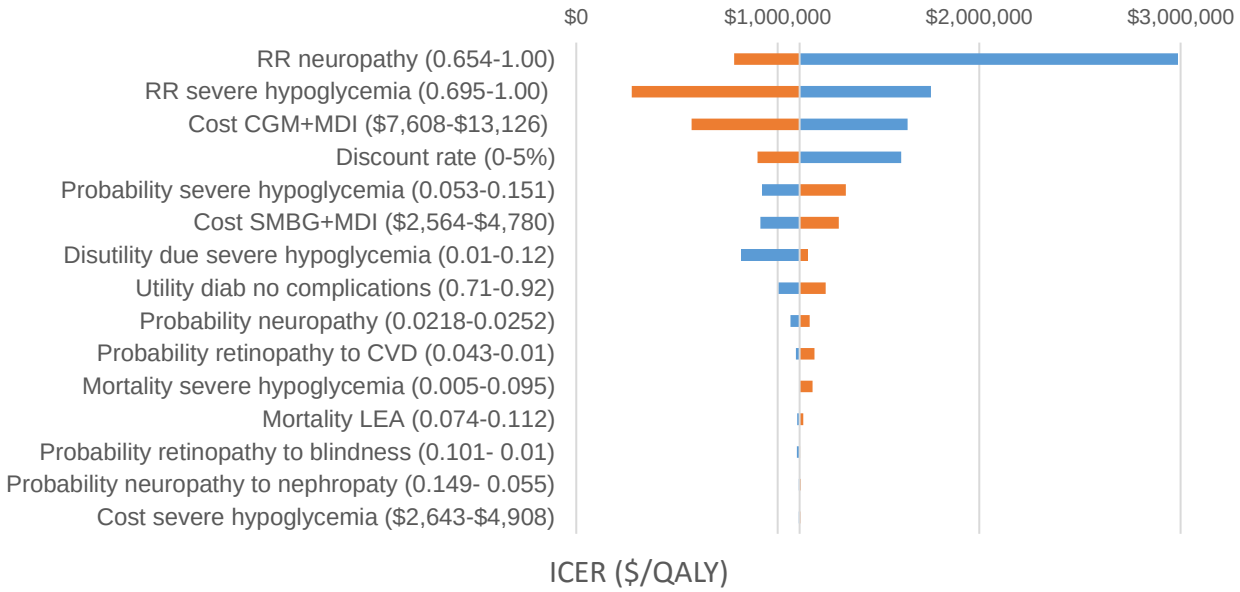


Figure A3: Continuous Glucose Monitoring With Sensor-Augmented Pump Versus Self-Monitoring of Blood Glucose With Multiple Daily Injections

Abbreviations: CGM, continuous glucose monitoring; CSII, continuous subcutaneous insulin infusion (insulin pump); CVD, cardiovascular disease; ICER, incremental cost-effectiveness ratio; LEA, lower-extremity amputation; MDI, multiple daily injections; QALY, quality-adjusted life-year; RR, relative risk; SAP, sensor-augmented pump; SMBG, self-monitoring of blood glucose.

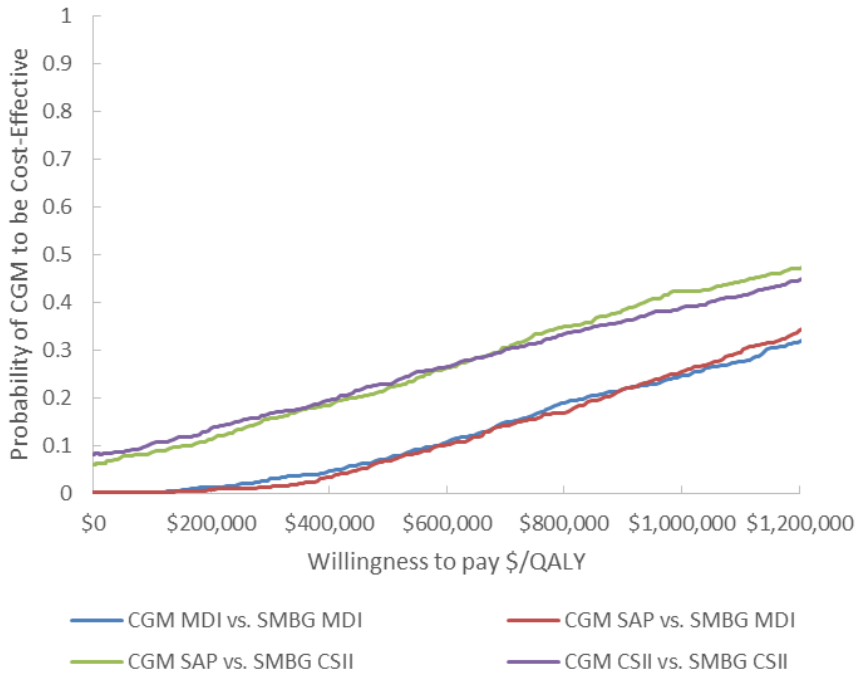


Figure A4: Cost-Effectiveness Acceptability Curves: Continuous Glucose Monitoring Interventions

Abbreviations: CGM, continuous glucose monitoring; CSII, continuous subcutaneous insulin infusion (insulin pump); MDI, multiple daily injections; QALY, quality-adjusted life-year; SAP, sensor-augmented pump; SMBG, self-monitoring of blood glucose.

Appendix 8: Budget Impact Analysis, Additional Calculations

Table A16: Government Expenses for the $170 Annual Grant to Purchase Needles and Syringes for People With Type 1 Diabetes Age 65 Years and Older in Ontario

	Year 1	Year 2	Year 3	Year 4	Year 5
Ontario Population With Type 1 Diabetes					
Number of people age 65+	16,196	17,201	18,271	19,371	20,527
Number of people using MDI (83%)	13,442	14,276	15,165	16,078	17,037
Total grant amount[a]	$2,285,201	$2,426,998	$2,578,000	$2,733,296	$2,896,324
Population With Hypoglycemia Unawareness					
Number of people age 65+	4,049	4,300	4,568	4,843	5,132
Number of people using MDI (83%)	3,361	3,569	3,791	4,020	4,259
Total grant amount[a]	$571,300	$606,749	$644,500	$683,324	$724,081
Population Using Continuous Glucose Monitoring					
Number of people age 65+	489	594	732	885	1011
Number of people using MDI (40%)	196	238	293	354	405
Total grant amount[a]	$33,259	$40,419	$49,774	$60,170	$68,767

Abbreviations: MDI, multiple daily injections.
[a]$170 per person per year.

Table A17: Government Expenses for the $920 Annual Grant to Purchase of Blood Glucose Test Strips Through the Ontario Monitoring for Health Program

	Year 1	Year 2	Year 3	Year 4	Year 5
Ontario Population With Type 1 Diabetes					
Number of people aged 25–64 years	50,937	52,487	53,987	55,437	56,779
Number of people without private or ODB funding for type 1 diabetes–related expenses (17%)	8,659	8,923	9,178	9,424	9,652
Cost of strips funded[a]	$7,966,607	$8,208,969	$8,443,618	$8,670,420	$8,880,254
Population With Hypoglycemia Unawareness					
Number of people aged 25–64 years	12,734	13,122	13,497	13,859	14,195
Number of people without private or ODB funding for type 1 diabetes–related expenses (17%)	2,165	2,231	2,294	2,356	2,413
Cost of strips funded[a]	$1,991,652	$2,052,242	$2,110,905	$2,167,605	$2,220,064
Population Using Continuous Glucose Monitoring					
Number of people aged 25–64 years	106	128	158	191	218
Number of people without private or ODB funding for type 1 diabetes–related expenses (17%)	18	22	27	32	37
Cost of strips funded[a]	$16,523	$20,080	$24,728	$29,892	$34,163

Abbreviation: ODB, Ontario Drug Benefit program.
[a]Funding for 75% of the cost of blood glucose test strips, to a maximum of $920.

Table A18: Estimated Number of Current Users of Continuous Glucose Monitoring in Ontario by Age Group

Age Group	Standalone CGM + MDI	Standalone CGM + Insulin Pump	Total Standalone CGM	SAP	SAP With LGS	Total SAP With or Without LGS	Total CGM Users
≤ 24 years, 28%	121	99	220	98	264	362	**581**
25–64 years, 54%	237	193	430	191	515	706	**1,135**
≥ 65 years, 18%	78	64	142	63	170	233	**375**

Abbreviations: CGM, continuous glucose monitoring; LGS, low-glucose suspend; MDI, multiple daily injections; SAP, sensor-augmented pump.

Table A19: Medtronic Projection of Sensor-Augmented Pump and Low-Glucose Suspend Use in People With Type 1 Diabetes in Ontario

	Assumption	2016	2017	2018	2019	2020	2021	2022
Ontario pump users	4% year-over-year increase	14,400	15,000	15,600	16,224	16,873	17,548	18,250
Ontario SAP users	4% year-over-year increase	9,600	10,000	10,400	10,816	11,249	11,699	12,167
Percentage of SAP users using a CGM sensor	Percentage use will plateau around 30% after a gradual increase over 5 years	13%	13%	17%	20%	24%	28%	30%
SAP users using a CGM sensor	—	1,248	1,300	1,768	2,163	2,700	3,276	3,650
SAP users with LGS functionality	90% of SAP users are using both SAP and LGS devices	8,640	9,000	9,360	9,734	10,124	10,529	10,950
Percentage of SAP and LGS users using a CGM sensor	Percentage use will plateau around 30% after a gradual increase over 5 years	13%	13%	17%	20%	24%	28%	30%
SAP and LGS users using a CGM sensor	—	1,123	1,170	1,591	1,947	2,430	2,948	3,285

Abbreviations: CGM, continuous glucose monitoring; LGS, low-glucose suspend; SAP, sensor-augmented pump.

Table A20: Ontario Drug Benefit Plan Funding for People With Type 1 Diabetes

Age Group	Supplies Covered
People Taking Multiple Daily Injections	
Children and youth ≤ 24 years of age	Insulin and blood glucose test strips
Adults 25–64 years of age[a]	Blood glucose test strips to a maximum of $920 Insulin not funded
Adults ≥ 65 years of age	Most types of insulin and blood glucose test strips Annual grant of $170, paid once per year, for the purchase of needles and syringes used to inject insulin
People Using an Insulin Pump	
All ages	100% of the cost of an insulin pump listed with the program, which must be sold to the person at the Assistive Devices Program–approved price of $6,300 Funding for insulin pump can be renewed every 5 years if the pump is no longer in good working order Annual grant of $2,400 for related supplies, paid in 4 equal payments of $600 directly to the patient or their legal agent; grant to be used only for pump-related supplies and must be renewed yearly
Children and youth ≤ 24 years of age	Insulin and blood glucose test strips
Adults 25–64 years of age[a]	Most types of insulin and blood glucose test strips
Adults ≥ 65 years of age	Most types of insulin and blood glucose test strips

[a]Assuming 17% of population without private drug funding and who do not qualify for Ontario Drug Benefit Plan funding.
Source: Canadian Diabetes Association.[114]

Table A21: Net Budget Impact of Funding Continuous Glucose Monitoring in Ontario by Age Group—Reference Case, Conservative Projection of a 20% Annual Increase[a]

	Total Budget Impact				
Intervention	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
All Ages					
CGM	$14,192,322	$17,835,103	$22,441,206	$27,412,678	$31,857,150
SMBG	$5,701,743	$7,953,809	$10,498,720	$13,226,191	$15,621,231
NBI	**$8,490,579**	**$9,881,295**	**$11,942,486**	**$14,186,487**	**$16,235,919**
≤24 Years; Full Funding for Blood Glucose Test Strips (Annual Cost $1,243)					
CGM	$3,803,296	$4,794,113	$6,031,616	$7,372,929	$8,558,233
SMBG	$1,392,221	$1,976,076	$2,637,262	$3,339,882	$3,938,578
NBI	**$2,411,076**	**$2,818,038**	**$3,394,353**	**$4,033,047**	**$4,619,655**
25–64 Years; Blood Glucose Test Strips Covered to a Maximum of $920					
CGM	$7,946,862	$9,995,260	$12,536,319	$15,305,231	$17,800,809
SMBG	$3,235,553	$4,488,736	$5,903,659	$7,424,545	$8,773,875
NBI	**$4,711,309**	**$5,506,524**	**$6,632,660**	**$7,880,685**	**$9,026,934**
≥65 Years; Full Funding for Blood Glucose Test Strips + $170 Annual Grant for Syringes and Needles					
CGM	$2,442,164	$3,045,730	$3,873,271	$4,734,518	$5,498,108
SMBG	$1,073,970	$1,488,997	$1,957,798	$2,461,763	$2,908,778
NBI	**$1,368,194**	**$1,556,732**	**$1,915,473**	**$2,272,755**	**$2,589,330**

Abbreviations: CGM, continuous glucose monitoring; NBI, net budget impact; SMBG, self-monitoring of blood glucose.
[a]Assumes government funding for insulin, insulin pump, and blood glucose test strips.

Table A22: Net Budget Impact of Funding Continuous Glucose Monitoring in Ontario by Age Group—Reference Case, Entire Population With Hypoglycemia Unawareness[a]

	Total Budget Impact				
Intervention	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
All Ages					
CGM	$120,487,478	$131,981,755	$140,758,669	$147,524,997	$152,658,439
SMBG	$41,693,554	$51,518,633	$59,307,520	$65,546,416	$70,408,816
NBI	**$78,793,925**	**$80,463,123**	**$81,451,149**	**$81,978,581**	**$82,249,622**
≤24 Years; Full Funding for Blood Glucose Test Strips (Annual Cost $1,243)					
CGM	$31,013,678	$33,825,196	$35,827,008	$37,269,166	$38,302,048
SMBG	$7,537,092	$10,055,012	$11,965,768	$13,425,453	$14,500,223
NBI	**$23,476,586**	**$23,770,184**	**$23,861,240**	**$23,843,714**	**$23,801,825**
25–64 Years; Blood Glucose Test Strips Covered to a Maximum of $920					
CGM	$70,927,409	$77,170,104	$81,860,181	$85,381,041	$87,872,712
SMBG	$25,456,301	$30,761,244	$34,910,874	$38,175,589	$40,624,409
NBI	**$45,471,108**	**$46,408,861**	**$46,949,308**	**$47,205,451**	**$47,248,303**
≥65 Years; Full Funding for Blood Glucose Test Strips + $170 Annual Grant for Syringes and Needles					
CGM	$18,546,392	$20,986,455	$23,071,480	$24,874,790	$26,483,678
SMBG	$8,700,160	$10,702,377	$12,430,878	$13,945,374	$15,284,185
NBI	**$9,846,231**	**$10,284,078**	**$10,640,602**	**$10,929,416**	**$11,199,494**

Abbreviations: CGM, continuous glucose monitoring; NBI, net budget impact; SMBG, self-monitoring of blood glucose.
[a]Assumes government funding for insulin, insulin pump, and blood glucose test strips.

Table A23: Net Budget Impact of Funding Continuous Glucose Monitoring in Ontario by Age Group—Reference Case, Entire Type 1 Diabetes Population[a]

	Total Budget Impact				
Intervention	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
All Ages					
CGM	$481,949,914	$527,927,021	$563,034,675	$590,099,986	$610,633,755
SMBG	$166,774,215	$206,074,531	$237,230,078	$262,185,663	$281,753,568
NBI	**$315,175,698**	**$321,852,490**	**$325,804,597**	**$327,914,323**	**$328,880,187**
≤24 Years; Full Funding for Blood Glucose Test Strips (Annual Cost $1,243)					
CGM	$124,054,711	$135,300,783	$143,308,031	$149,076,666	$153,208,192
SMBG	$30,148,369	$40,220,049	$47,863,071	$53,701,811	$58,033,759
NBI	**$93,906,342**	**$95,080,735**	**$95,444,960**	**$95,374,854**	**$95,174,433**
25–64 Years; Blood Glucose Test Strips Covered to a Maximum of $920					
CGM	$283,709,635	$308,680,418	$327,440,726	$341,524,162	$351,490,850
SMBG	$101,825,204	$123,044,975	$139,643,495	$152,702,357	$162,561,861
NBI	**$181,884,430**	**$185,635,443**	**$187,797,231**	**$188,821,805**	**$188,928,989**
≥65 Years; Full Funding for Blood Glucose Test Strips + $170 Annual Grant for Syringes and Needles					
CGM	$74,185,567	$83,945,820	$92,285,919	$99,499,158	$105,934,714
SMBG	$34,800,642	$42,809,507	$49,723,513	$55,781,494	$61,157,948
NBI	**$39,384,926**	**$41,136,313**	**$42,562,406**	**$43,717,664**	**$44,776,765**

Abbreviations: CGM, continuous glucose monitoring; NBI, net budget impact; SMBG, self-monitoring of blood glucose.
[a]Assumes government funding for insulin, insulin pump, and blood glucose test strips.

Table A24: Net Budget Impact of Funding Continuous Glucose Monitoring in Ontario by Age Group—Scenario 2, Conservative Projection of a 20% Annual Increase[a]

	Total Budget Impact				
Intervention	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
All Ages					
CGM	$11,751,030	$14,879,176	$18,809,532	$23,072,200	$26,932,164
SMBG	$5,492,916	$7,666,296	$10,192,975	$12,859,486	$15,185,252
NBI	**$6,258,114**	**$7,212,880**	**$8,616,558**	**$10,212,713**	**$11,746,912**
≤24 Years; Full Funding for Blood Glucose Test Strips (Annual Cost $1,243)					
CGM	$3,130,910	$3,980,027	$5,031,197	$6,177,277	$7,202,217
SMBG	$1,392,221	$1,976,076	$2,637,262	$3,339,882	$3,938,578
NBI	**$1,738,689**	**$2,003,952**	**$2,393,935**	**$2,837,394**	**$3,263,640**
25–64 Years; Blood Glucose Test Strips Covered to a Maximum of $920					
CGM	$6,633,000	$8,404,513	$10,581,474	$12,968,892	$15,151,118
SMBG	$3,235,553	$4,488,736	$5,903,659	$7,424,545	$8,773,875
NBI	**$3,397,447**	**$3,915,777**	**$4,677,815**	**$5,544,347**	**$6,377,243**
≥65 Years; Full Funding for Blood Glucose Test Strips + $170 Annual Grant for Syringes and Needles					
CGM	$1,987,120	$2,494,636	$3,196,861	$3,926,031	$4,578,829
SMBG	$865,142	$1,201,485	$1,652,053	$2,095,059	$2,472,800
NBI	**$1,121,977**	**$1,293,151**	**$1,544,808**	**$1,830,972**	**$2,106,029**

Abbreviations: CGM, continuous glucose monitoring; NBI, net budget impact; SMBG, self-monitoring of blood glucose.
[a]Assumes full government funding for insulin, insulin pump, and blood glucose test strips, as well as 75% CGM sensor funding.

Table A25: Net Budget Impact of Funding Continuous Glucose Monitoring in Ontario by Age Group—Scenario 2, Entire Population With Hypoglycemia Unawareness[a]

	Total Budget Impact				
Intervention	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
All Ages					
CGM	$99,261,412	$110,217,741	$118,338,523	$124,780,315	$129,734,734
SMBG	$37,075,088	$46,587,198	$54,041,932	$59,937,590	$64,439,296
NBI	**$62,186,324**	**$63,630,543**	**$64,296,591**	**$64,842,725**	**$65,295,437**
≤24 Years; Full Funding for Blood Glucose Test Strips (Annual Cost $1,243)					
CGM	$25,036,832	$27,776,999	$29,654,330	$31,071,725	$32,113,835
SMBG	$7,537,092	$10,055,012	$11,965,768	$13,425,453	$14,500,223
NBI	**$17,499,740**	**$17,721,986**	**$17,688,562**	**$17,646,273**	**$17,613,612**
25–64 Years; Blood Glucose Test Strips Covered to a Maximum of $920					
CGM	$59,354,621	$65,362,015	$69,715,189	$73,109,997	$75,584,696
SMBG	$25,456,301	$30,761,244	$34,910,874	$38,175,589	$40,624,409
NBI	**$33,898,320**	**$34,600,771**	**$34,804,315**	**$34,934,408**	**$34,960,287**
≥65 Years; Full Funding for Blood Glucose Test Strips + $170 Annual Grant for Syringes and Needles					
CGM	$14,869,960	$17,078,727	$18,969,004	$20,598,593	$22,036,203
SMBG	$4,081,695	$5,770,942	$7,165,291	$8,336,548	$9,314,665
NBI	**$10,788,265**	**$11,307,785**	**$11,803,714**	**$12,262,045**	**$12,721,538**

Abbreviations: CGM, continuous glucose monitoring; NBI, net budget impact; SMBG, self-monitoring of blood glucose.
[a]Assumes full government funding for insulin, insulin pump, and blood glucose test strips, as well as 75% CGM sensor funding.

Table A26: Net Budget Impact of Funding Continuous Glucose Monitoring in Ontario by Age Group—Scenario 2, Entire Type 1 Diabetes Population[a]

	Total Budget Impact ($)				
Intervention	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
All Ages					
CGM	$397,045,650	$440,870,963	$473,354,092	$499,121,262	$518,938,935
SMBG	$148,300,352	$186,348,792	$216,167,728	$239,750,361	$257,875,488
NBI	**$248,745,298**	**$254,522,171**	**$257,186,365**	**$259,370,901**	**$261,063,447**
≤24 Years; Full Funding for Blood Glucose Test Strips (Annual Cost $1,243)					
CGM	$100,147,329	$111,107,994	$118,617,319	$124,286,902	$128,455,340
SMBG	$30,148,369	$40,220,049	$47,863,071	$53,701,811	$58,033,759
NBI	**$69,998,960**	**$70,887,946**	**$70,754,249**	**$70,585,090**	**$70,421,580**
25–64 Years; Blood Glucose Test Strips Covered to a Maximum of $920					
CGM	$237,418,483	$261,448,061	$278,860,755	$292,439,988	$302,338,784
SMBG	$101,825,204	$123,044,975	$139,643,495	$152,702,357	$162,561,861
NBI	**$135,593,278**	**$138,403,086**	**$139,217,260**	**$139,737,631**	**$139,776,924**
≥65 Years; Full Funding for Blood Glucose Test Strips + $170 Annual Grant for Syringes and Needles					
CGM	$59,479,838	$68,314,908	$75,876,018	$82,394,372	$88,144,811
SMBG	$16,326,778	$23,083,769	$28,661,162	$33,346,192	$37,279,868
NBI	**$43,153,060**	**$45,231,139**	**$47,214,856**	**$49,048,180**	**$50,864,943**

Abbreviations: CGM, continuous glucose monitoring; NBI, net budget impact; SMBG, self-monitoring of blood glucose.
[a]Assumes full government funding for insulin, insulin pump, and blood glucose test strips, as well as 75% CGM sensor funding.

Table A27: Net Budget Impact of Funding Continuous Glucose Monitoring in Ontario by Age Group—Scenario 2, Population With Hypoglycemia Unawareness Using a Conservative Projection[a]

	Total Budget Impact				
Intervention	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
All Ages					
CGM	$2,937,757	$3,719,794	$4,702,383	$5,768,050	$6,733,041
SMBG	$1,373,229	$1,916,574	$2,548,244	$3,214,872	$3,796,313
NBI	**$1,564,529**	**$1,803,220**	**$2,154,139**	**$2,553,178**	**$2,936,728**
≤24 Years; Full Funding for Blood Glucose Test Strips (Annual Cost $1,243)					
CGM	$782,727	$995,007	$1,257,799	$1,544,319	$1,800,554
SMBG	$348,055	$494,019	$659,316	$834,971	$984,644
NBI	**$434,672**	**$500,988**	**$598,484**	**$709,349**	**$815,910**
25–64 Years; Blood Glucose Test Strips Covered to a Maximum of $920					
CGM	$1,658,250	$2,101,128	$2,645,369	$3,242,223	$3,787,780
SMBG	$808,888	$1,122,184	$1,475,915	$1,856,136	$2,193,469
NBI	**$849,362**	**$978,944**	**$1,169,454**	**$1,386,087**	**$1,594,311**
≥65 Years; Full Funding for Blood Glucose Test Strips + $170 Annual Grant for Syringes and Needles					
CGM	$496,780	$623,659	$799,215	$981,508	$1,144,707
SMBG	$216,286	$300,371	$413,013	$523,765	$618,200
NBI	**$280,494**	**$323,288**	**$386,202**	**$457,743**	**$526,507**

Abbreviations: CGM, continuous glucose monitoring; NBI, net budget impact; SMBG, self-monitoring of blood glucose.

[a]Assumes full government funding for insulin, insulin pump, and blood glucose test strips, as well as 75% CGM sensor funding

Table A28: Continuous Glucose Monitoring Device Cost Reduction Scenarios

	CGM Device Cost					Diabetes Treatment				
Intervention	CGM Cost	CGM Cost (75% Sensor Funding)	10% Reduction	20% Reduction	30% Reduction	Base Case	75% Sensor Funding	10% CGM Cost Reduction	20% CGM Cost Reduction	30% CGM Cost Reduction
CGM + MDI (average)	$6,198	$4,743	$5,578	$4,958	$4,339	$9,342	$8,237	$8,408	$7,474	$6,539
CGM + insulin pump (average)	$5,848	$5,093	$5,263	$4,678	$4,094	$11,673	$10,567	$10,505	$9,338	$8,171
SAP (LGS)	$3,120	$2,340	$2,808	$2,496	$2,184	$9,211	$8,431	$8,290	$7,369	$6,448

Abbreviations: CGM, continuous glucose monitoring; LGS, low-glucose suspend; MDI, multiple daily injections; SAP, sensor-augmented pump.

Table A29: Net Budget Impact of Funding Continuous Glucose Monitoring in Ontario—Scenario 3, Conservative Projection of a 20% Annual Increase, Device Cost Reduction by 30%, 20%, and 10%

	Total Budget Impact				
Intervention	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
CGM Device Cost					
CGM	$24,229,379	$29,075,255	$34,890,306	$41,868,368	$50,242,041
SMBG	$10,565,739	$12,678,887	$15,214,665	$18,257,598	$21,909,117
NBI	**$13,663,640**	**$16,396,368**	**$19,675,642**	**$23,610,770**	**$28,332,924**
CMG Device Cost + 75% Funding of Sensor Costs					
CGM	$21,962,668	$26,355,201	$31,626,241	$37,951,490	$45,541,787
SMBG	$10,565,739	$12,678,887	$15,214,665	$18,257,598	$21,909,117
NBI	**$11,396,928**	**$13,676,314**	**$16,411,577**	**$19,693,892**	**$23,632,670**
CGM Device Cost Reduction of 30%					
CGM	$16,960,566	$20,352,679	$24,423,214	$29,307,857	$35,169,429
SMBG	$10,565,739	$12,678,887	$15,214,665	$18,257,598	$21,909,117
NBI	**$6,394,826**	**$7,673,791**	**$9,208,550**	**$11,050,260**	**$13,260,312**
CGM Device Cost Reduction of 20%					
CGM	$19,383,504	$23,260,204	$27,912,245	$33,494,694	$40,193,633
SMBG	$10,565,739	$12,678,887	$15,214,665	$18,257,598	$21,909,117
NBI	**$8,817,764**	**$10,581,317**	**$12,697,580**	**$15,237,096**	**$18,284,516**
CGM Device Cost Reduction of 10%					
CGM	$21,806,441	$26,167,730	$31,401,276	$37,681,531	$45,217,837
SMBG	$10,565,739	$12,678,887	$15,214,665	$18,257,598	$21,909,117
NBI	**$11,240,702**	**$13,488,843**	**$16,186,611**	**$19,423,933**	**$23,308,720**

Abbreviations: CGM, continuous glucose monitoring; NBI, net budget impact; SMBG, self-monitoring of blood glucose.

Table A30: Net Budget Impact of Funding Continuous Glucose Monitoring in Ontario—Scenario 3, Entire Population With Hypoglycemia Unawareness, Device Cost Reduction by 30%, 20%, and 10%

	Total Budget Impact				
Intervention	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
CGM Device Cost					
CGM	$219,832,134	$227,215,875	$234,583,188	$241,925,675	$249,234,764
SMBG	$98,136,450	$101,511,186	$104,899,097	$108,297,686	$111,704,418
NBI	**$121,695,684**	**$125,704,689**	**$129,684,091**	**$133,627,989**	**$137,530,346**
CMG Device Cost + 75% Funding of Sensor Costs					
CGM	$198,111,455	$204,765,640	$211,405,020	$218,022,026	$224,608,936
SMBG	$98,136,450	$101,511,186	$104,899,097	$108,297,686	$111,704,418
NBI	**$99,975,005**	**$103,254,454**	**$106,505,923**	**$109,724,341**	**$112,904,518**
CGM Device Cost Reduction of 30%					
CGM	$153,882,494	$159,051,113	$164,208,231	$169,347,972	$174,464,335
SMBG	$98,136,450	$101,511,186	$104,899,097	$108,297,686	$111,704,418
NBI	**$55,746,044**	**$57,539,926**	**$59,309,134**	**$61,050,287**	**$62,759,917**
CGM Device Cost Reduction of 20%					
CGM	$175,865,707	$181,772,700	$187,666,550	$193,540,540	$199,387,811
SMBG	$98,136,450	$101,511,186	$104,899,097	$108,297,686	$111,704,418
NBI	**$77,729,257**	**$80,261,514**	**$82,767,453**	**$85,242,854**	**$87,683,393**
CGM Device Cost Reduction of 10%					
CGM	$197,848,921	$204,494,288	$211,124,869	$217,733,107	$224,311,288
SMBG	$98,136,450	$101,511,186	$104,899,097	$108,297,686	$111,704,418
NBI	**$99,712,471**	**$102,983,102**	**$106,225,772**	**$109,435,422**	**$112,606,870**

Abbreviations: CGM, continuous glucose monitoring; NBI, net budget impact; SMBG, self-monitoring of blood glucose.

Table A31: Net Budget Impact of Funding Continuous Glucose Monitoring in Ontario—Scenario 3, Entire Type 1 Diabetes Population, Device Cost Reduction by 30%, 20%, and 10%

	Total Budget Impact				
Intervention	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
CGM Device Cost					
CGM	$879,328,537	$908,863,502	$938,332,751	$967,702,698	$996,939,057
SMBG	$392,545,801	$406,044,745	$419,596,388	$433,190,742	$447,178,667
NBI	**$486,782,736**	**$502,818,757**	**$518,736,363**	**$534,511,956**	**$549,760,390**
CMG Device Cost + 75% Funding of Sensor Costs					
CGM	$792,445,820	$819,062,561	$845,620,078	$872,088,106	$898,435,744
SMBG	$392,545,801	$406,044,745	$419,596,388	$433,190,742	$447,178,667
NBI	**$399,900,019**	**$413,017,815**	**$426,023,690**	**$438,897,364**	**$451,257,077**
CGM Device Cost Reduction of 30%					
CGM	$615,529,976	$636,204,451	$656,832,926	$677,391,889	$697,857,340
SMBG	$392,545,801	$406,044,745	$419,596,388	$433,190,742	$447,178,667
NBI	**$222,984,175**	**$230,159,706**	**$237,236,538**	**$244,201,146**	**$250,678,673**
CGM Device Cost Reduction of 20%					
CGM	$703,462,830	$727,090,802	$750,666,201	$774,162,159	$797,551,245
SMBG	$392,545,801	$406,044,745	$419,596,388	$433,190,742	$447,178,667
NBI	**$310,917,029**	**$321,046,056**	**$331,069,813**	**$340,971,416**	**$350,372,578**
CGM Device Cost Reduction of 10%					
CGM	$791,395,683	$817,977,152	$844,499,476	$870,932,428	$897,245,151
SMBG	$392,545,801	$406,044,745	$419,596,388	$433,190,742	$447,178,667
NBI	**$398,849,882**	**$411,932,406**	**$424,903,088**	**$437,741,686**	**$450,066,484**

Abbreviations: CGM, continuous glucose monitoring; NBI, net budget impact; SMBG, self-monitoring of blood glucose.

Table A32: Net Budget Impact of Funding Continuous Glucose Monitoring in Ontario—Scenario 4, Device Cost Reduction by 30%, 20%, and 10%, Plus Government Funding[a]

	Total Budget Impact				
Intervention	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Conservative Projection of a 20% Annual Increase					
CGM Device Cost Reduction of 30%					
CGM	$7,463,670	$8,955,523	$10,744,428	$12,892,552	$15,477,008
SMBG	$5,531,782	$6,638,139	$7,965,767	$9,558,920	$11,470,704
NBI	**$1,931,887**	**$2,317,384**	**$2,778,662**	**$3,333,632**	**$4,006,304**
CMG Device Cost Reduction of 20%					
CGM	$8,591,500	$10,308,920	$12,368,505	$14,841,444	$17,815,678
SMBG	$5,531,782	$6,638,139	$7,965,767	$9,558,920	$11,470,704
NBI	**$3,059,718**	**$3,670,781**	**$4,402,738**	**$5,282,524**	**$6,344,974**
CGM Device Cost Reduction of 10%					
CGM	$9,719,331	$11,662,317	$13,992,581	$16,790,336	$20,154,348
SMBG	$5,531,782	$6,638,139	$7,965,767	$9,558,920	$11,470,704
NBI	**$4,187,549**	**$5,024,178**	**$6,026,815**	**$7,231,416**	**$8,683,644**
Entire Population With Hypoglycemia Unawareness					
CGM Device Cost Reduction of 30%					
CGM	$74,689,992	$77,196,635	$79,699,062	$82,195,855	$84,683,452
SMBG	$51,548,728	$53,261,896	$54,966,445	$56,660,112	$58,340,589
NBI	**$23,141,265**	**$23,934,738**	**$24,732,618**	**$25,535,742**	**$26,342,862**
CGM Device Cost Reduction of 20%					
CGM	$87,021,085	$89,941,905	$92,857,588	$95,766,244	$98,663,832
SMBG	$51,548,728	$53,261,896	$54,966,445	$56,660,112	$58,340,589
NBI	**$35,472,357**	**$36,680,008**	**$37,891,144**	**$39,106,132**	**$40,323,242**
CGM Device Cost Reduction of 10%					
CGM	$99,352,177	$102,687,175	$106,016,115	$109,336,634	$112,644,212
SMBG	$51,548,728	$53,261,896	$54,966,445	$56,660,112	$58,340,589
NBI	**$47,803,449**	**$49,425,278**	**$51,049,670**	**$52,676,522**	**$54,303,623**
Entire Type 1 Diabetes Population					
CGM Device Cost Reduction of 30%					
CGM	$298,759,970	$308,786,539	$318,796,249	$328,783,418	$338,733,806
SMBG	$206,194,912	$213,047,586	$219,865,778	$226,640,450	$233,447,017
NBI	**$92,565,058**	**$95,738,953**	**$98,930,471**	**$102,142,968**	**$105,286,789**
CGM Device Cost Reduction of 20%					
CGM	$348,084,338	$359,767,619	$371,430,354	$383,064,978	$394,655,327
SMBG	$206,194,912	$213,047,586	$219,865,778	$226,640,450	$233,447,017
NBI	**$141,889,427**	**$146,720,033**	**$151,564,575**	**$156,424,528**	**$161,208,310**
CGM Device Cost Reduction of 10%					
CGM	$397,408,707	$410,748,698	$424,064,458	$437,346,537	$450,576,848
SMBG	$206,194,912	$213,047,586	$219,865,778	$226,640,450	$233,447,017
NBI	**$191,213,795**	**$197,701,112**	**$204,198,680**	**$210,706,087**	**$217,129,831**

Abbreviations: CGM, continuous glucose monitoring; NBI, net budget impact; SMBG, self-monitoring of blood glucose.
[a]Assumes full government funding for insulin treatment, insulin pump, and blood glucose test strips, as well as 75% CGM sensor funding.

Table A33: Net Budget Impact of Funding Continuous Glucose Monitoring in Ontario—Scenario 5, Manufacturer's Scenario With an Annual Increase in Adoption of 40%

	Total Budget Impact				
Intervention	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Reference Case[a]					
CGM	$15,332,591	$20,637,518	$28,070,987	$37,349,650	$48,228,466
SMBG	$6,005,165	$8,767,523	$12,192,126	$16,294,145	$20,772,757
NBI	**$9,327,425**	**$11,869,995**	**$15,878,861**	**$21,055,505**	**$27,455,709**
All Direct Medical Costs					
CGM	$27,788,637	$37,017,152	$49,038,530	$63,905,655	$80,450,278
SMBG	$12,107,734	$16,675,345	$22,510,807	$29,610,087	$37,415,877
NBI	**$15,680,903**	**$20,341,806**	**$26,527,723**	**$34,295,568**	**$43,034,401**
Government Funding of Insulin, Insulin Pump, and Blood Glucose Test Strips + 75% of CGM Sensor Costs					
CGM	$12,714,256	$17,239,259	$23,557,815	$31,465,902	$40,777,115
SMBG	$5,767,077	$8,407,082	$11,740,884	$15,671,920	$19,917,114
NBI	**$6,947,180**	**$8,832,176**	**$11,816,931**	**$15,793,982**	**$20,860,001**
CGM Device Cost Reduction of 30%					
CGM	$19,452,046	$25,221,182	$33,189,610	$43,216,206	$54,468,371
SMBG	$12,107,734	$15,637,058	$20,507,344	$26,588,295	$33,282,780
NBI	**$7,344,312**	**$9,584,124**	**$12,682,266**	**$16,627,911**	**$21,185,591**
CGM Device Cost Reduction of 20%					
CGM	$22,230,910	$28,824,208	$37,930,983	$49,389,950	$62,249,567
SMBG	$12,107,734	$15,637,058	$20,507,344	$26,588,295	$33,282,780
NBI	**$10,123,176**	**$13,187,150**	**$17,423,639**	**$22,801,655**	**$28,966,786**
CGM Device Cost Reduction of 10%					
CGM	$25,009,774	$32,427,234	$42,672,356	$55,563,693	$70,030,762
SMBG	$12,107,734	$15,637,058	$20,507,344	$26,588,295	$33,282,780
NBI	**$12,902,039**	**$16,790,176**	**$22,165,012**	**$28,975,399**	**$36,747,982**
CGM Device Cost Reduction of 30% + Government Funding of Insulin, Insulin Pump, and Blood Glucose Test Strips + 75% of CGM Sensor Costs					
CGM	$8,526,961	$11,200,526	$14,903,805	$19,674,577	$25,333,014
SMBG	$5,779,420	$7,409,960	$9,656,020	$12,418,114	$15,341,921
NBI	**$2,747,541**	**$3,790,566**	**$5,247,785**	**$7,256,462**	**$9,991,093**
CGM Device Cost Reduction of 20% + Government Funding of Insulin, Insulin Pump, and Blood Glucose Test Strips + 75% of CGM Sensor Costs					
CGM	$9,825,054	$12,911,595	$17,187,316	$22,699,861	$29,249,668
SMBG	$6,339,107	$8,186,914	$10,736,794	$13,920,527	$17,425,481
NBI	**$3,485,947**	**$4,724,680**	**$6,450,522**	**$8,779,334**	**$11,824,186**
CGM Device Cost Reduction of 10% + Government Funding of Insulin, Insulin Pump, and Blood Glucose Test Strips + 75% of CGM Sensor Costs					
CGM	$11,123,147	$14,622,663	$19,470,827	$25,725,145	$33,166,321
SMBG	$6,339,107	$8,186,914	$10,736,794	$13,920,527	$17,425,481
NBI	**$4,784,040**	**$6,435,749**	**$8,734,034**	**$11,804,618**	**$15,740,840**

Abbreviations: CGM, continuous glucose monitoring; NBI, net budget impact; SMBG, self-monitoring of blood glucose.
[a]Government funding of insulin treatment, insulin pump and blood glucose test strips.

Table A34: Net Budget Impact of Funding Continuous Glucose Monitoring in Ontario—Scenario 5, Manufacturer's Scenario With an Annual Increase in CGM Adoption of 40%, Entire Type 1 Diabetes Population and Population With Hypoglycemia Unawareness

	Total Budget Impact				
Intervention	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Reference Case					
Funding Continuous Glucose Monitoring in the Entire Type 1 Diabetes Population					
CGM	$481,949,914	$527,927,021	$563,034,675	$590,099,986	$610,633,755
SMBG	$166,774,215	$206,074,531	$237,230,078	$262,185,663	$281,753,568
NBI	**$315,175,698**	**$321,852,490**	**$325,804,597**	**$327,914,323**	**$328,880,187**
Funding Continuous Glucose Monitoring in the Entire Population With Hypoglycemia Unawareness					
CGM	$120,487,478	$131,981,755	$140,758,669	$147,524,997	$152,658,439
SMBG	$41,693,554	$51,518,633	$59,307,520	$65,546,416	$70,408,816
NBI	**$78,793,925**	**$80,463,123**	**$81,451,149**	**$81,978,581**	**$82,249,622**
All Direct Medical Cost					
Funding Continuous Glucose Monitoring in the Entire Type 1 Diabetes Population					
CGM	$879,328,537	$940,384,046	$982,740,880	$1,015,543,322	$1,040,991,872
SMBG	$392,545,801	$439,784,653	$476,011,572	$504,717,816	$527,683,516
NBI	**$486,782,736**	**$500,599,393**	**$506,729,308**	**$510,825,506**	**$513,308,356**
Funding Continuous Glucose Monitoring in the Entire Population With Hypoglycemia Unawareness					
CGM	$219,832,134	$235,096,011	$245,685,220	$253,885,830	$260,247,968
SMBG	$98,136,450	$109,946,163	$119,002,893	$126,179,454	$131,823,378
NBI	**$121,695,684**	**$125,149,848**	**$126,682,327**	**$127,706,376**	**$128,424,590**
Government Funding of Insulin, Insulin Pump, and Blood Glucose Test Strips + 75% of CGM Sensor Costs					
Funding Continuous Glucose Monitoring in the Entire Type 1 Diabetes Population					
CGM	$397,045,650	$440,870,963	$473,354,092	$499,121,262	$518,940,535
SMBG	$148,300,352	$186,348,792	$216,167,728	$239,750,361	$257,875,960
NBI	**$248,745,298**	**$254,522,171**	**$257,186,365**	**$259,370,901**	**$261,064,575**
Funding Continuous Glucose Monitoring in the Entire Population With Hypoglycemia Unawareness					
CGM	$99,261,412	$110,217,741	$118,338,523	$124,780,315	$129,735,134
SMBG	$37,075,088	$46,587,198	$54,041,932	$59,937,590	$64,439,414
NBI	**$62,186,324**	**$63,630,543**	**$64,296,591**	**$64,842,725**	**$65,295,719**
CGM Device Cost Reduction of 30%					
Funding Continuous Glucose Monitoring in the Entire Type 1 Diabetes Population					
CGM	$615,529,976	$636,204,451	$656,832,926	$677,391,889	$697,857,340
SMBG	$392,545,801	$406,044,745	$419,596,388	$433,190,742	$447,178,667
NBI	**$222,984,175**	**$230,159,706**	**$237,236,538**	**$244,201,146**	**$250,678,673**
Funding Continuous Glucose Monitoring in the Entire Population With Hypoglycemia Unawareness					
CGM	$153,882,494	$159,051,113	$164,208,231	$169,347,972	$174,464,335
SMBG	$98,136,450	$101,511,186	$104,899,097	$108,297,686	$111,704,418
NBI	**$55,746,044**	**$57,539,926**	**$59,309,134**	**$61,050,287**	**$62,759,917**

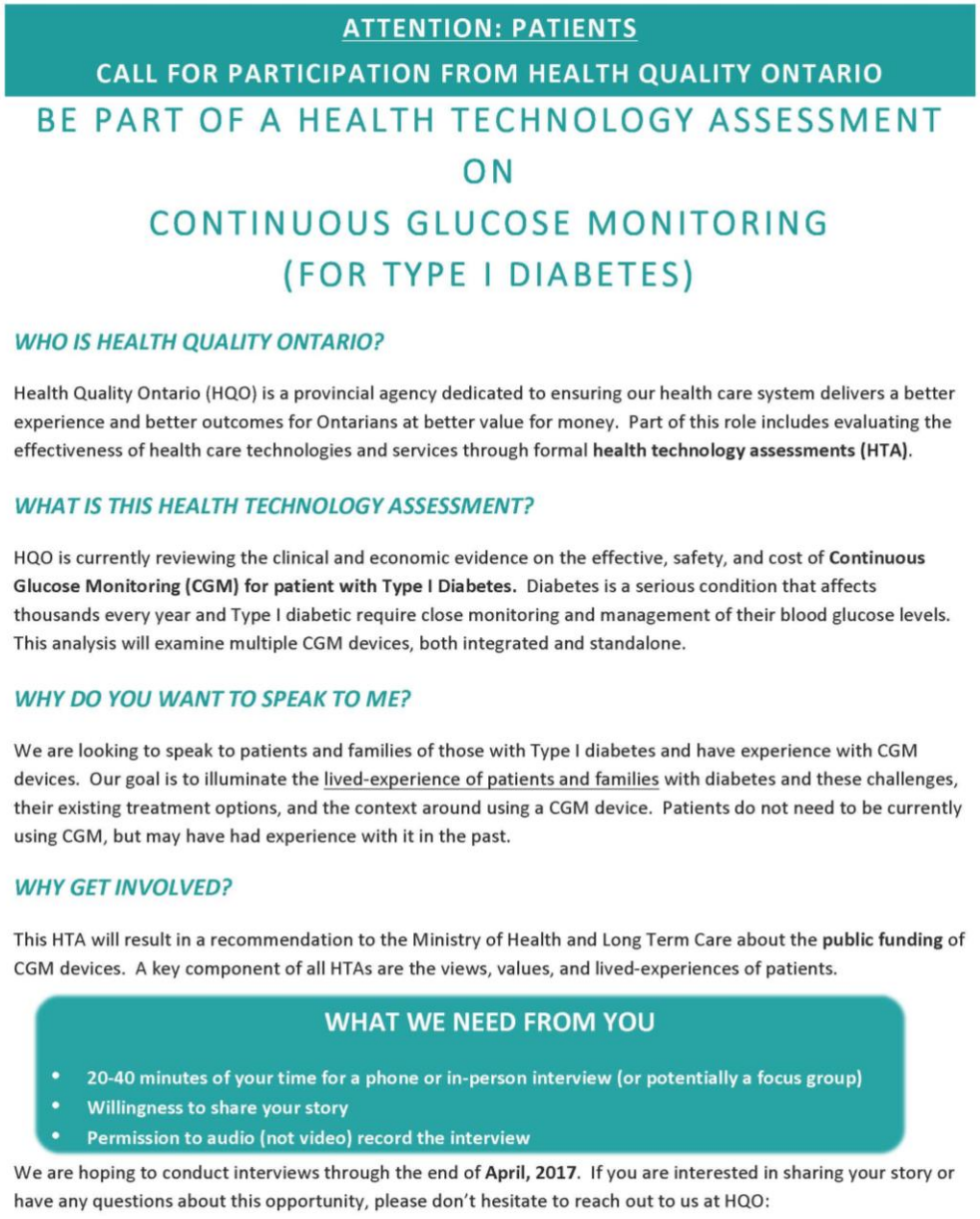
CGM Device Cost Reduction of 20%					
Funding Continuous Glucose Monitoring in the Entire Type 1 Diabetes Population					
CGM	$703,462,830	$727,090,802	$750,666,201	$774,162,159	$797,551,245
SMBG	$392,545,801	$406,044,745	$419,596,388	$433,190,742	$447,178,667
NBI	**$310,917,029**	**$321,046,056**	**$331,069,813**	**$340,971,416**	**$350,372,578**
Funding Continuous Glucose Monitoring in the Entire Population With Hypoglycemia Unawareness					
CGM	$175,865,707	$181,772,700	$187,666,550	$193,540,540	$199,387,811
SMBG	$98,136,450	$101,511,186	$104,899,097	$108,297,686	$111,704,418
NBI	**$77,729,257**	**$80,261,514**	**$82,767,453**	**$85,242,854**	**$87,683,393**
CGM Device Cost Reduction of 10%					
Funding Continuous Glucose Monitoring in the Entire Type 1 Diabetes Population					
CGM	$791,395,683	$817,977,152	$844,499,476	$870,932,428	$897,245,151
SMBG	$392,545,801	$406,044,745	$419,596,388	$433,190,742	$447,178,667
NBI	**$398,849,882**	**$411,932,406**	**$424,903,088**	**$437,741,686**	**$450,066,484**
Funding Continuous Glucose Monitoring in the Entire Population With Hypoglycemia Unawareness					
CGM	$197,848,921	$204,494,288	$211,124,869	$217,733,107	$224,311,288
SMBG	$98,136,450	$101,511,186	$104,899,097	$108,297,686	$111,704,418
NBI	**$99,712,471**	**$102,983,102**	**$106,225,772**	**$109,435,422**	**$112,606,870**
CGM Device Cost Reduction of 30% + Government Funding of Insulin, Insulin Pump, and Blood Glucose Test Strips + 75% of CGM Sensor Costs					
Funding Continuous Glucose Monitoring in the Entire Type 1 Diabetes Population					
CGM	$298,759,970	$308,786,539	$318,796,249	$328,783,418	$338,733,806
SMBG	$159,684,304	$164,966,568	$170,223,295	$175,452,951	$180,730,177
NBI	**$139,075,666**	**$143,819,971**	**$148,572,954**	**$153,330,467**	**$158,003,629**
Funding Continuous Glucose Monitoring in the Entire Population With Hypoglycemia Unawareness					
CGM	$74,689,992	$77,196,635	$79,699,062	$82,195,855	$84,683,452
SMBG	$39,921,076	$41,241,642	$42,555,824	$43,863,238	$45,161,379
NBI	**$34,768,917**	**$35,954,993**	**$37,143,238**	**$38,332,617**	**$39,522,072**
CGM Device Cost Reduction of 20% + Government Funding of Insulin, Insulin Pump, and Blood Glucose Test Strips + 75% of CGM Sensor Costs					
Funding Continuous Glucose Monitoring in the Entire Type 1 Diabetes Population					
CGM	$348,084,338	$359,767,619	$371,430,354	$383,064,978	$394,655,327
SMBG	$206,194,912	$213,047,586	$219,865,778	$226,640,450	$233,447,017
NBI	**$141,889,427**	**$146,720,033**	**$151,564,575**	**$156,424,528**	**$161,208,310**
Funding Continuous Glucose Monitoring in the Entire Population With Hypoglycemia Unawareness					
CGM	$87,021,085	$89,941,905	$92,857,588	$95,766,244	$98,663,832
SMBG	$51,548,728	$53,261,896	$54,966,445	$56,660,112	$58,340,589
NBI	**$35,472,357**	**$36,680,008**	**$37,891,144**	**$39,106,132**	**$40,323,242**
CGM Device Cost Reduction of 10% + Government Funding of Insulin, Insulin Pump, and Blood Glucose Test Strips + 75% of CGM Sensor Costs					
Funding Continuous Glucose Monitoring in the Entire Type 1 Diabetes Population					
CGM	$397,408,707	$410,748,698	$424,064,458	$437,346,537	$450,576,848
SMBG	$206,194,912	$213,047,586	$219,865,778	$226,640,450	$233,447,017
NBI	**$191,213,795**	**$197,701,112**	**$204,198,680**	**$210,706,087**	**$217,129,831**

Funding Continuous Glucose Monitoring in the Entire Population With Hypoglycemia Unawareness					
CGM	$99,352,177	$102,687,175	$106,016,115	$109,336,634	$112,644,212
SMBG	$51,548,728	$53,261,896	$54,966,445	$56,660,112	$58,340,589
NBI	**$47,803,449**	**$49,425,278**	**$51,049,670**	**$52,676,522**	**$54,303,623**

Abbreviations: CGM, continuous glucose monitoring; SMBG, self-monitoring of blood glucose; NBI, net budget impact.

Appendix 9: Public and Patient Engagement—Interview Materials

Figure A5: Call for Participation



ATTENTION: PATIENTS

CALL FOR PARTICIPATION FROM HEALTH QUALITY ONTARIO

BE PART OF A HEALTH TECHNOLOGY ASSESSMENT ON CONTINUOUS GLUCOSE MONITORING (FOR TYPE I DIABETES)

WHO IS HEALTH QUALITY ONTARIO?

Health Quality Ontario (HQO) is a provincial agency dedicated to ensuring our health care system delivers a better experience and better outcomes for Ontarians at better value for money. Part of this role includes evaluating the effectiveness of health care technologies and services through formal **health technology assessments (HTA)**.

WHAT IS THIS HEALTH TECHNOLOGY ASSESSMENT?

HQO is currently reviewing the clinical and economic evidence on the effective, safety, and cost of **Continuous Glucose Monitoring (CGM) for patient with Type I Diabetes.** Diabetes is a serious condition that affects thousands every year and Type I diabetic require close monitoring and management of their blood glucose levels. This analysis will examine multiple CGM devices, both integrated and standalone.

WHY DO YOU WANT TO SPEAK TO ME?

We are looking to speak to patients and families of those with Type I diabetes and have experience with CGM devices. Our goal is to illuminate the lived-experience of patients and families with diabetes and these challenges, their existing treatment options, and the context around using a CGM device. Patients do not need to be currently using CGM, but may have had experience with it in the past.

WHY GET INVOLVED?

This HTA will result in a recommendation to the Ministry of Health and Long Term Care about the **public funding** of CGM devices. A key component of all HTAs are the views, values, and lived-experiences of patients.

WHAT WE NEED FROM YOU

- 20-40 minutes of your time for a phone or in-person interview (or potentially a focus group)
- Willingness to share your story
- Permission to audio (not video) record the interview

We are hoping to conduct interviews through the end of **April, 2017**. If you are interested in sharing your story or have any questions about this opportunity, please don't hesitate to reach out to us at HQO:

Figure A6: Interview Guide

Ontario
Health Quality Ontario

Interview for Continuous Glucose Monitoring HTA

Intro
Explain HQO purpose, HTA process, and purpose of interview
History of Type I Diabetes diagnosis and various treatments (general only)

Lived- Experience
Day-to-day routine
What is the impact on family? Adverse events?
Impact on parent if child with Type I diabetes (if applicable)

CGM Devices
Experience with glucose monitoring devices, past v present
Current CGM – equity issues
- Cost? Access? Health Literacy (ie training to be comfortable)
- Safety?
- "Why do you think there is not a greater uptake of CGMs in market?"

Decision-Making
What options are available?
(any equity issues in regards to treatment options? Cost/inconveniences?)
How to choose among treatment options? Factors that influence those decisions?
(how to choose for you child, if applicable?)

Role of family in decision-making? Physician? Other sources of information (Internet)?

Contrast emotion (anxiety, worry) vs logic? As this applies to risk and side-effects?

Was it difficult to weigh up potential benefits and risks when deciding on which therapies to go with?

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About Health Quality Ontario

Health Quality Ontario is the provincial advisor on the quality of health care. We are motivated by a single-minded purpose: **Better health for all Ontarians.**

Who We Are.

We are a scientifically rigorous group with diverse areas of expertise. We strive for complete objectivity, and look at things from a vantage point that allows us to see the forest and the trees. We work in partnership with health care providers and organizations across the system, and engage with patients themselves, to help initiate substantial and sustainable change to the province's complex health system.

What We Do.

We define the meaning of quality as it pertains to health care, and provide strategic advice so all the parts of the system can improve. We also analyze virtually all aspects of Ontario's health care. This includes looking at the overall health of Ontarians, how well different areas of the system are working together, and most importantly, patient experience. We then produce comprehensive, objective reports based on data, facts and the voice of patients, caregivers and those who work each day in the health system. As well, we make recommendations on how to improve care using the best evidence. Finally, we support large scale quality improvements by working with our partners to facilitate ways for health care providers to learn from each other and share innovative approaches.

Why It Matters.

We recognize that, as a system, we have much to be proud of, but also that it often falls short of being the best it can be. Plus certain vulnerable segments of the population are not receiving acceptable levels of attention. Our intent at Health Quality Ontario is to continuously improve the quality of health care in this province regardless of who you are or where you live. We are driven by the desire to make the system better, and by the inarguable fact that better has no limit.

About the Ontario Health Technology Advisory Committee (OHTAC)

About OHTAS

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