Population-Level Impact and Cost-effectiveness of Continuous Glucose Monitoring and Intermittently Scanned Continuous Glucose Monitoring Technologies for Adults With Type 1 Diabetes in Canada: A Modeling Study

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Diabetes Care 2022;45:2012–2019 | https://doi.org/10.2337/dc21-2341

OBJECTIVE

Maintaining healthy glucose levels is critical for the management of type 1 diabetes (T1D), but the most efficacious and cost-effective approach (capillary self-monitoring of blood glucose [SMBG] or continuous [CGM] or intermittently scanned [isCGM] glucose monitoring) is not clear. We modeled the population-level impact of these three glucose monitoring systems on diabetes-related complications, mortality, and cost-effectiveness in adults with T1D in Canada.

RESEARCH DESIGN AND METHODS

We used a Markov cost-effectiveness model based on nine complication states for adults aged 18–64 years with T1D. We performed the cost-effectiveness analysis from a single-payer health care system perspective over a 20-year horizon, assuming a willingness-to-pay threshold of CAD 50,000 per quality-adjusted life-year (QALY). Primary outcomes were the number of complications and deaths and the incremental cost-effectiveness ratio (ICER) of CGM and isCGM relative to SMBG.

RESULTS

An initial cohort of 180,000 with baseline HbA_{1c} of 8.1% was used to represent all Canadians aged 18–64 years with T1D. Universal SMBG use was associated with ∼11,200 people (6.2%) living without complications and ∼89,400 (49.7%) deaths after 20 years. Universal CGM use was associated with an additional ∼7,400 (4.1%) people living complications free and ∼11,500 (6.4%) fewer deaths compared with SMBG, while universal isCGM use was associated with ∼3,400 (1.9%) more people living complications free and ∼4,600 (2.6%) fewer deaths. Relative to SMBG, CGM and isCGM had ICERs of CAD 35,017/QALY and 17,488/QALY, respectively.

CONCLUSIONS

Universal use of CGM or isCGM in the Canadian T1D population is anticipated to reduce diabetes-related complications and mortality at an acceptable cost-effectiveness threshold.

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Received 10 November 2021 and accepted 7 June 2022

This article contains supplementary material online at https://doi.org/10.2337/figshare.20173937.

Though the etiology is not known with certainty, type 1 diabetes (T1D) appears to be an autoimmune disease that destroys insulin-producing β-cells in the pancreas resulting in lifelong dependence on injected insulin therapy. Self-management of blood glucose levels is the cornerstone of T1D care. High levels of blood glucose can lead to acute events including diabetic ketoacidosis (DKA) and long-term micro- or macrovascular complications (1), while low blood glucose (hypoglycemia) puts patients at risk for immediate injury or death (2) and possibly a greater risk for developing cognitive impairment (3) and earlier cardiovascular mortality (4). To monitor glycemia and adjust insulin doses, most people with T1D use self-monitoring of blood glucose (SMBG) techniques, which requires lancing the fingertip to obtain a drop of capillary blood that is applied to a test strip and inserted into a glucose meter device. Recent development of innovative technological devices for T1D management has led to new strategies for monitoring glucose levels in interstitial fluid, including continuous glucose monitoring (CGM), such as the Dexcom G6 or Medtronic Guardian Connect, and intermittently scanned continuous glucose monitoring (isCGM) (previously known as flash glucose monitoring), such as the Abbott FreeStyle Libre systems. CGM systems provide measurement of glycemic levels throughout the day and night, which reduces the risk of undetected hypo- and hyperglycemic events, especially nocturnal hypoglycemic events (5). CGM systems are also equipped with alarms that alert users if glucose levels exceed or decline preset limits, enabling the user to take insulin or carbohydrates to avoid a dangerously high or low blood glucose. By comparison, while isCGM systems continuously monitor interstitial glucose levels, they only display glycemic levels when the sensor is scanned, and initial generations of these systems do not have alarms. CGM and isCGM may allow for better profiling of glucose management then SMBG or HbA_{1c} levels alone, since isCGM and CGM can more easily track the individual's percent time below, above, and within the recommended glycemic targets (6).

While randomized trials examining the efficacy of these new technologies are heterogeneous (7,8), on balance, these technologies have shown improved glycemic control (9,10), reduced hypoglycemia (11,12) and DKA (11,12) events, fewer hospital admissions (11), and improved quality of life (9,11) in a variety of real-world settings and study populations. In most Canadian provinces, people with diabetes over the age of 65 years (and $<$25 years old in some provinces) receive some support from their provincial health plan for these technologies, but the majority of adults require private insurance plans or stipends from public organizations like Diabetes Canada or incur these costs as personal expenses. Decision makers must determine whether these new technologies are appropriate for large-scale use and provide reasonable value in the context of limited health care resources. The purpose of this study is to estimate the impact on diabetes-related complications, mortality, and relative cost-effectiveness of SMBG, CGM, and isCGM for adults with T1D in Canada.

RESEARCH DESIGN AND METHODS

Model Overview and Initial Cohort

Our model is adapted from the Ontario Health (OH) (formerly Health Quality Ontario) (13) report and previous work by García-Lorenzo et al. (14) and McQueen et al. (15). The OH (13) study was a governmental report with investigation of the cost-effectiveness of publicly funding CGM for all residents of the province of Ontario with T1D. Their modeling study assumed a baseline average HbA_{1c} of 8.8% for the population and an SMBG testing regimen of an average of six tests per day. Primarily due to higher device costs at the time, the report did not support public funding of CGM at the willingness-to-pay threshold of CAD 50,000 per quality-adjusted life-year (QALY). Our model improves on these approaches, as it includes the key outcome of DKA events, focuses both on CGM and on isCGM, and includes the most recent costs of these devices. Our initial cohort was age weighted to represent the 180,000 Canadians with T1D between the ages of 18 and 64 years. This value was obtained by applying the overall estimates of rates of diabetes in Canada to recent Canadian census data (see Appendix A1). We assume that all 180,000 Canadians use each type of glucose monitoring (SMBG, CGM, isCGM) to obtain the population-level cost and QALY impact of universal use of these technologies. Our model is based on a Markov cost-effectiveness model with nine primary states: no complications, retinopathy, neuropathy, nephropathy, cardiovascular disease (CVD), end-stage renal disease, lower-extremity amputation, blindness, and death (Supplementary Fig. A1). Moreover, at any point in the model, a severe hypoglycemia (SH) or DKA event could occur. We compared the cost-effectiveness of SMBG, CGM, and isCGM in this T1D cohort over a 20-year period using the T1D complication rates, relative effects of CGM and isCGM, costs, and QALYs in Appendix A.

Estimates of Efficacy of isCGM and CGM

As a preliminary step, we required an estimate of clinical efficacy of isCGM and CGM vs. SMBG to estimate the clinical improvements that can be attributed to the national use of these advanced monitoring technologies. With this information and relevant epidemiological and economical information, we can evaluate our primary outcomes of the absolute number of complications and deaths that may be prevented and the cost-effectiveness of these interventions.

Identifying a summary measure for efficacy in clinical trials of glucose monitoring strategies and technologies presents a challenge. Some trials have been focused on recruitment of subjects with elevated HbA_{1c}, for which the primary outcome of interest is improvement in average glycemia (e.g., 16,17). In other trials investigators have recruited subjects with target HbA_{1c} and evaluated the outcome of reduction in risk of hypoglycemia (e.g., 18,19). While the effect of glucose monitoring approaches on HbA_{1c} levels remains an important predictor for complications of T1D (18), there is a demonstrated need to move beyond this metric, as it does not fully capture glycemic variability or risk of hypoglycemia (20). To this end, there has been an increased focus on time in range (TIR) as an alternative measure of glycemic control, particularly for CGM systems. The International Consensus on Time in Range defined TIR as the time spent in the optimal glycemic control range of 3.9–10.0 mmol/L

(70–180 mg/dL) in a 24-h period (6). It has been further suggested that a 10% increase in TIR corresponds to approximately a 0.5%–0.8% reduction in HbA_{1c}, depending on the baseline HbA_{1c} levels and population characteristics (6). Given the importance of TIR in CGM and isCGM systems, we selected TIR as our primary measure of efficacy.

To estimate the efficacy of CGM and isCGM, we focused on randomized controlled trials (RCTs). A recent meta-analysis of RCTs (8) was published comparing the efficacy of CGM, including isCGM, with SMBG. An updated literature search in June 2021 did not reveal any additional randomized trials that were relevant for this analysis. To ensure generalizability of other study results to our study, we excluded studies based on isCGM, sensor-augmented pumps, pediatric patients, and patients with type 2 diabetes to estimate the efficacy of CGM versus SMBG (Supplementary Table A2). This yields an estimated improvement in TIR of 1.48 h/day (95% CI 0.77–2.20) based on five studies. As expected, due to the variety of patient characteristics, interventions, and study timelines, heterogeneity was moderate to substantial, with an I^2 (21) of 69% (Supplementary Fig. A2). Regarding isCGM, only one RCT (18) examining adults in Europe has been performed. Other isCGM studies were included in their review (8) but included people with type 2 diabetes and samples overlapping with Bolinder et al. (18) and are thus excluded. Bolinder et al. (18) show an increase in TIR of 1.00 h/day (0.43–1.57) (Supplementary Table A3). To ensure that our cost-effectiveness analysis is conservative, we used the lower bounds of the 95% CIs for TIR (i.e., an improvement in TIR of 0.77 and 0.43 h/day for CGM and isCGM, respectively) to estimate the impact of CGM and isCGM on our baseline complication rates. We note that long-term studies examining the relationships between glycemic control and micro- and macrovascular complications have traditionally relied on HbA_{1c}. Where required, we adopt the assumption that a 10% increase in TIR is approximately equal to a 0.8% absolute reduction in HbA_{1c} for our model to estimate the impact of CGM and isCGM on reducing these complication rates (Supplementary Tables A4–A6).

Epidemiologic Complications, Rates, Quality of Life, and Cost Parameters

Epidemiologic parameters were identified based on commonly reported T1D complications in literature and those used in the OH report (13). All participants began in the no complications state. After the first year, participants can transition to a complications state, remain in the no complications state, or die. Once in a complications state, participants can transition to a more severe complications state (e.g., from retinopathy to blindness), remain there, or die due to the increased risk of death from their complication or other causes. Up to two complications could also be combined and at any point in the model, an acute SH or DKA event could occur (Supplementary Fig. A1). Of particular note, while previous analyses included SH events, this cost-effectiveness study is the first with incorporation of the cost and QALY impact of DKA events. Costs for SH or DKA events are added to the individual's annual cost along with a corresponding reduction in QALY for that specific year. For simplicity, the occurrence of both an SH and DKA event in a single year was excluded from the model. Given the novel inclusion of DKA events in our model, a detailed literature search was performed to determine the most appropriate estimate of the rate of DKA events, costs, and reductions of QALY in our population. The baseline DKA and SH event rates were obtained from Pettus et al. (22), as their study was based on a large sample of 31,430 adults with T1D in the U.S., with ∼85% in our target age range of 18–64 years. Full details for both SH and DKA events can be found in Appendix A4. Baseline annual transition probabilities of these parameters, and associated references for the SMBG group, are included in Supplementary Table A7. Age-dependent CVD, CVD mortality, and other mortality rates are presented in Supplementary Tables A8–A10, respectively.

QALYs were obtained from the most recent available resources (Supplementary Table A11) and are consistent with values in the most recent cost-effectiveness analysis of CGM for T1D in the U.K. (23). Note that when an individual experiences multiple acute or chronic complications disutilities are additive. We obtained intervention costs using a combination of manufacturer resources and publicly available information on 12 August 2021. As the focus is on the cost-effectiveness of glucose monitoring and complications, costs of insulin delivery and treatment (e.g., pumps or daily injections) were not included. Note that our goal is not to compare individual monitoring technologies. Thus, to ensure an impartial evaluation of all competing monitoring systems, we apply an average cost of relevant technologies across models, and differences in sensor efficacy and reliability are not included. We assumed an annual cost of CAD 2,019, 3,930, and 2,540 for SMBG (average of six tests per day), CGM (based on the average annual cost of the Dexcom G6 and Medtronic Guardian Connect), and isCGM (based on the FreeStyle Libre), respectively. Full details can be found in Appendix A3. Complication costs were based on the sources presented by OH (13) in 2018 and inflated by 4.29% (24) to account for inflation in 2021 Canadian dollars (CAD) (Supplementary Table A12).

Outcomes

We examined two primary outcomes: *1*) the modeled absolute number of complications and deaths that may be prevented by national use of CGM and isCGM for adults with T1D and *2*) the cost-effectiveness of CGM and isCGM relative to SMBG. For cost-effectiveness, we calculated the incremental cost-effectiveness ratio (ICER) of CGM versus SMBG and isCGM versus SMBG. We used the traditional willingness-to-pay threshold of CAD 50,000/QALY as our cost-effectiveness threshold.

Statistical Analysis

All analyses were performed with the heemod package (25) in R (26) and are from the perspective of a single-payer health care system. Note that cost estimates include direct publicly funded health diabetes monitoring and complication costs and do not include societal costs (e.g., lost income or productivity). Consistent with the parameters of the OH (13) report, we assumed a baseline average HbA_{1c} of 8.1% (27) and an annual discount rate of 1.5% for both costs and QALYs. These discount rates are based on the Canadian standards for cost-effectiveness models, which

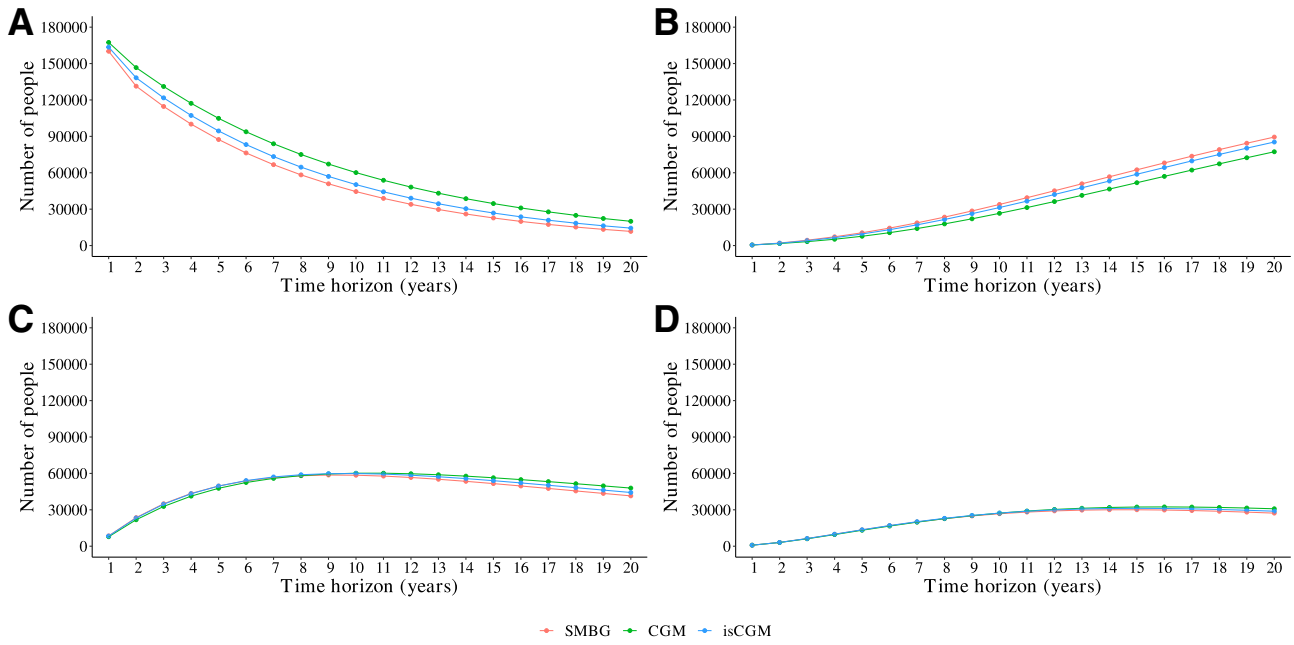

Figure 1—Number of people over a 20-year horizon with no complications (*A*), who died (*B*), with minor complications (*C*) or with major complications (*D*).

assume cost discounts equal to the approximate long-term borrowing costs for the Canadian government (28) and equal discount rates for QALYs.

Sensitivity Analyses

To ensure the robustness of our model, we performed a variety of one-way sensitivity analyses. They include variation in individual model parameters according to their plausible range (Supplementary Table A7), cost and QALY discounts of 0%–5%, incorporating a more liberal estimate of the efficacy of CGM and isCGM with use of the point estimates and upper bounds of the 95% CIs for TIR instead of our conservative estimate with use of the lower bound, comparing CGM and isCGM with a revised recommended SMBG regimen of 8 or 10 tests per day (vs. 6 tests per day), and reducing the annual cost of CGM and isCGM by 10% and 25% to represent potential bulk purchase agreements. Additional details regarding sensitivity analyses are included in Appendix B.

RESULTS

Modeled Number of Complications and Deaths

Figure 1 presents the general trends of no complications, minor complications (neuropathy, nephropathy, retinopathy), major complications (CVD, end-stage renal disease, lower-extremity amputation, blindness), and death. After 20 years, if the entire Canadian population uses CGM, ∼7,400 more people are living without complications compared with use of SMBG (Fig. 1*A*). Similarly, the number of deaths is reduced by ∼11,500 (Fig. 1*D*). In comparison with SMBG, isCGM keeps ∼3,400 more Canadians living without any complications of T1D (Fig. 1*A*) and prevents approximately 4,600 deaths (Fig. 1*D*). Figure 1*B* and *C* must be interpreted cautiously, as we predict a larger number of individuals living with minor complications with CGM and isCGM as individuals remain alive and live with fewer severe complications throughout the study period. Additional figures (Supplementary Figs. C1–C3) presenting the number of people in each individual complication state can be found in Appendix C.

Table 1—Cost and QALY projection and ICERs for an initial cohort of 180,000 adult Canadians using SMBG, CGM, and isCGM over a 20-year horizon

Strategy	Total cost (CAD)	Complications cost (CAD)	Interventions cost (CAD)	QALY	ICER[a]
SMBG	12,166,922,680	7,142,676,195	5,024,246,485	2,062,023	—
CGM	16,080,940,460	5,862,493,277	10,218,447,183	2,173,798	35,017
isCGM	12,981,653,727	6,548,934,955	6,432,718,772	2,108,612	17,488

[a]CAD/QALY (relative to SMBG).

Cost-effectiveness of CGM and isCGM

Table 1 contains the cost, number of QALYs, and ICERs for each of the three interventions. These results provide evidence that both CGM and isCGM are cost-effective interventions at the traditional willingness-to-pay threshold of CAD 50,000/QALY. We note that while the costs of funding CGM and isCGM are higher, they generate significant cost savings due to lower costs of complications of T1D. Finally, note that the government cost for these technologies in Canada would be much lower as some individuals already benefit from employer-sponsored health plans and national funding for these technologies would likely reduce costs due to bulk purchase agreements.

Sensitivity Analyses

The impact of departures from various model assumptions is presented in Figs. 2 and 3. Variation in the rate of DKA events has the largest impact on our observed ICERs, but this is due to the comparatively large degree of uncertainty in this parameter. Moreover, even considering the extreme case, the lowest rates of DKA events produce an ICER of approximately CAD 53,021/QALY for CGM, which nears our threshold of CAD 50,000/QALY (Fig. 2). Similarly, a QALY discount of 5% also produces a slightly elevated ICER of CAD 51,086 compared with our cost-effectiveness threshold for CGM. In all considered cases, isCGM meets our cost-effectiveness threshold (Fig. 3). Of particular note, if bulk government purchases decrease the cost of isCGM by 25%, this technology is cost-effective at any willingness-to-pay threshold, as the total cost of isCGM is lower than that of SMBG over a 20-year horizon while producing a higher total number of QALY. Similarly, if Canadians are assumed to be using a larger number of SMBG tests per day (i.e., 8 or 10), isCGM is cost-effective at any willingness-to-pay threshold, as the increased costs of the additional daily SMBG tests exceed the annual cost of isCGM and yield a lower total QALY. Based on these results, our model is reasonably robust against departures from our initial assumptions.

CONCLUSIONS

Our results show that compared with SMBG, universal adoption of CGM or isCGM is predicted to reduce diabetes-related complications and mortality over a 20-year time horizon, and they are cost-effective strategies for monitoring glycemia in Canadian adults living with T1D. Results are consistent across multiple assumptions including variation in plausible parameters, common cost and QALY discounts, and measures of efficacy. These results support use of public health resources to increase universal access to CGM and isCGM for the adult T1D population in Canada and emphasize the need for greater equity in technology adoption.

In the Canadian context, an earlier cost-effectiveness analysis in Ontario, that included data up to January 2017, did not find sufficient evidence for the public funding of CGM for people with T1D (13). However, this analysis was based on earlier estimates of efficacy and higher costs, prior to the reporting of updated evidence of effectiveness and the reduction in the absolute costs of these technologies. In a recent cost-effectiveness study (29) where investigators compared the Dexcom G6 with SMBG in Canada using the IQVIA Core Diabetes Model (IQVIA CDM) (30),

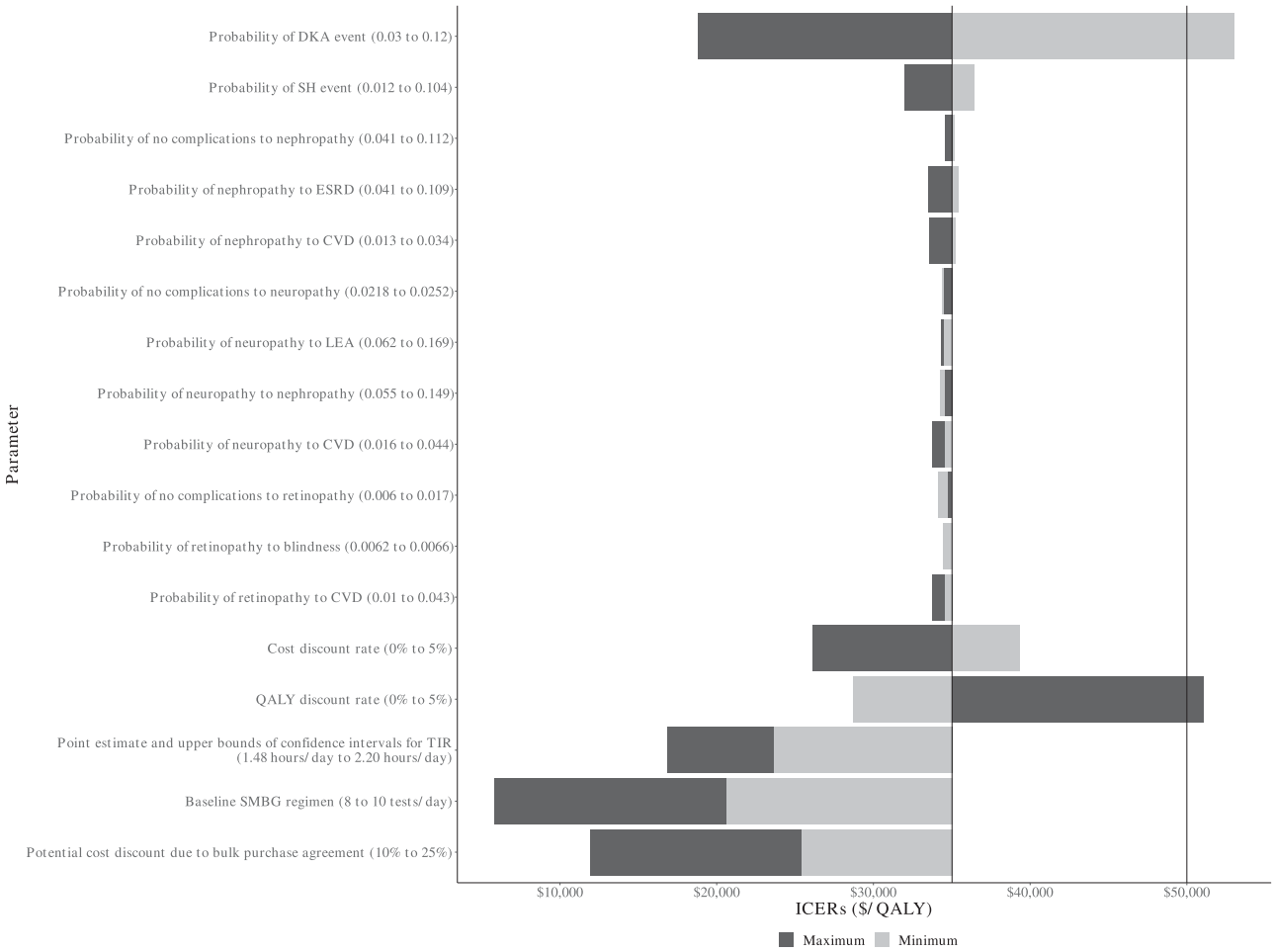

Figure 2—Sensitivity analyses examining the impact of various assumptions on ICERs for CGM. Baseline model of cost-effectiveness ICER of CAD 35,017/QALY and willingness-to-pay threshold of CAD 50,000/QALY are indicated. ESRD, end-stage renal disease; LEA, lower extremity amputation.

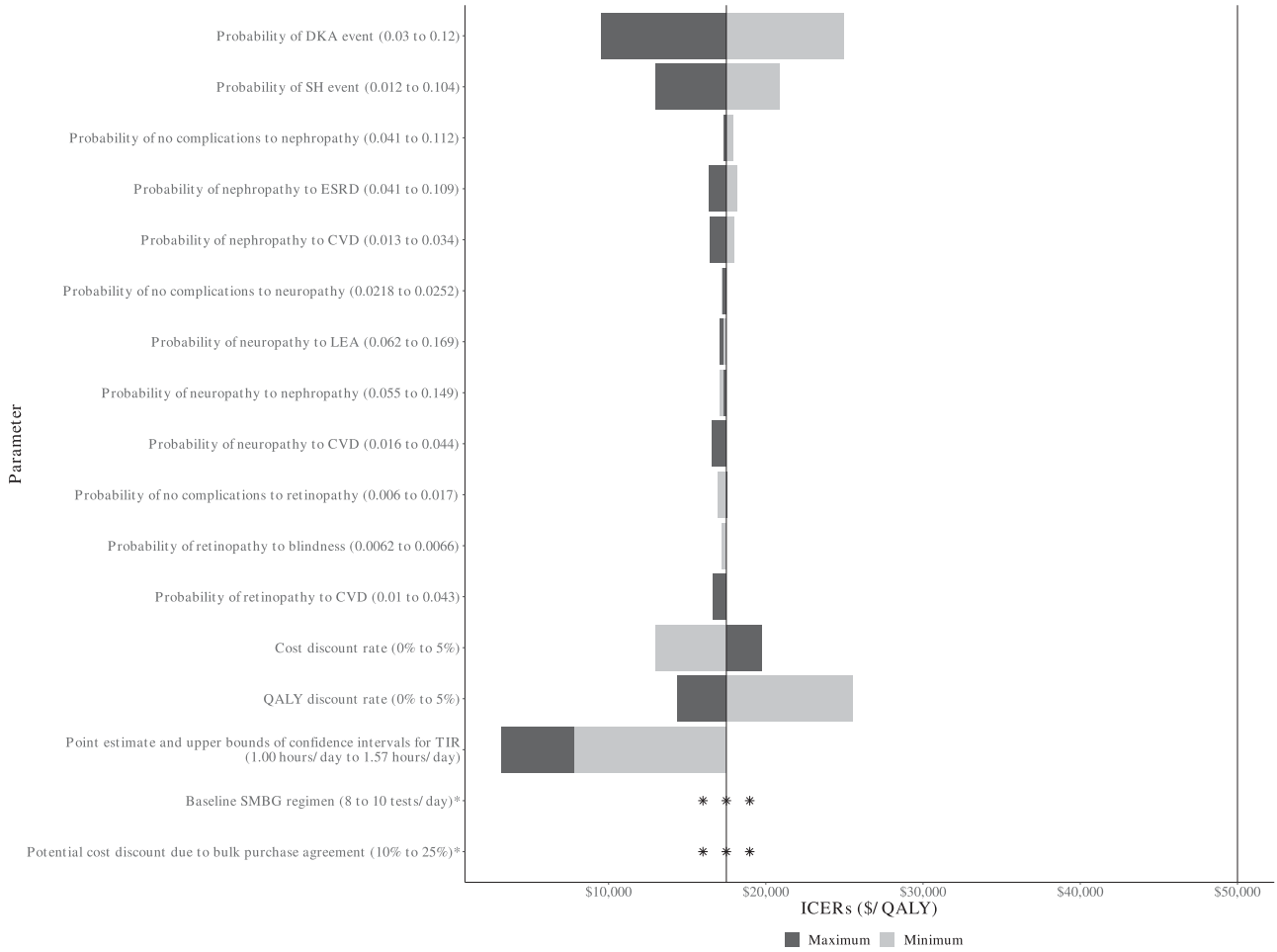

Figure 3—Sensitivity analyses examining the impact of various assumptions on ICERs for isCGM. Baseline model of cost-effectiveness ICER of CAD 17,488/QALY and willingness-to-pay threshold of CAD 50,000/QALY are indicated. ESRD, end-stage renal disease; LEA, lower extremity amputation. ***Model is cost-effective at any willingness-to-pay threshold.

results show that the Dexcom G6 is a cost-effective glucose monitoring system with an ICER of CAD 16,931/QALY. However, this study did not include consideration of isCGM and was financially supported by Dexcom, raising concerns of potential conflicts of interest. Similarly, while moderate cost-effectiveness has been shown for isCGM in Ontario (31) and Quebec (32), our updated results support their coverage across Canada. Canadian health care spending decisions are independently determined by the 10 provincial and 3 territorial governments; however, our results support cooperative and coordinated national approaches to health care spending, which could generate further cost savings due to bulk government purchases. This is best illustrated in our sensitivity analysis, where we showed that a 25% reduction in the cost of isCGM is cost-effective relative to SMBG at any willingness-to-pay threshold. In addition, we note that the costs for these devices for the health payer in Canada would be markedly lower, as many individuals already have isCGM or CGM devices funded by their employer-sponsored private benefits plans.

Internationally, a 2018 study on the cost-effectiveness of CGM in Spain did not show sufficient cost-effectiveness given the higher technology costs at the time (14). However, our findings are consistent with the most recent studies of CGM and isCGM use in the U.K (23), France (33), and the U.S (34), while isCGM alone has been shown to be a cost-effective intervention in a study based in Sweden (35). These more recent findings have led to the inclusion of these technologies in public health plans across the world, including Spain (36), France (33), Italy (37), and notably, in July 2021 the U.S. relaxed its qualification rules for CGM to encompass nearly all adults with T1D receiving Medicare benefits. Our results may also be of interest to private health insurers in the U.S. and other jurisdictions, as we have shown that isCGM is in fact a lower-cost glucose monitoring regimen compared with SMBG when individuals are averaging 8 or 10 tests per day, while improving health outcomes. However, it should also be stressed that only CGM technology, and not isCGM, can be used to inform sensor-augmented and hybrid closed loop insulin pump systems for more customized insulin delivery to help minimize both hyper- and hypoglycemia in T1D (38).

Unique strengths of our analysis are the consideration of current device costs, the incorporation of DKA events in the Markov model, use of TIR as a measure of efficacy, and our examination of both

CGM and isCGM independently, without sponsorship from device manufacturers. However, there are potential limitations. First, cost estimates for the nine complication states may be underestimated, as health care costs have increased beyond typical rates of inflation (39). This may lead to an underestimation of comparative cost-effectiveness of CGM and isCGM. Secondly, cost estimates have been primarily based on Ontario data, and absolute costs may not generalize to all Canadian provinces. However, we expect that the estimation of relative cost-effectiveness between technologies will remain unbiased. Third, in implementing estimates of efficacy from randomized clinical trials, we assume that estimates are durable over the 20-year horizon. Fourth, we examined a hypothetical baseline population without consideration of population growth or new-onset T1D during the 20-year examination period. Fifth, we assumed that the efficacy of a new isCGM technology that includes alarms to indicate hyper- and hypoglycemia without a cost increase (FreeStyle Libre 2; Abbott) is comparable with that of its earlier version. As a result, our results may underestimate cost-effectiveness of newer isCGM technology. Additionally, we emphasize that our results are applicable to adults with T1D aged 18–64 years and that we cannot extrapolate these estimates of cost-effectiveness to children or older adults. Due to lack of population-level data, we could not include other clinical factors in our model, such as age of onset of T1D, which may affect risk of complications. Similarly, lack of long-term clinical data limits formal validation of our Markov cost-effectiveness model, but our detailed sensitivity analyses show that our conclusions remain robust against various departures from model assumptions. Moreover, our results are broadly consistent with the results of Roze et al. (29), who used the externally validated IQVIA CDM (40), providing additional confidence in our approach. Finally, we acknowledge that the evidence base of trials examining the impact of CGM do not include consideration of the additional benefits conferred by use of CGM in automated insulin delivery systems. We expect that the global impact of CGM will be amplified beyond the cost-effectiveness estimates reported here with greater adoption of automated insulin delivery systems. Future studies should focus on the evaluation of the cost-effectiveness of these technologies for children and youth, given their increased risk for poor glycemic control leading to acute SH or DKA events. In addition, in our review here we highlight the comparatively small body of evidence from RCTs for isCGM relative to the number of studies for CGM. More broadly, long-term clinical studies evaluating the risk of micro- and macrovascular complications based on TIR would also be of use to formally quantify the relationship between TIR and these adverse outcomes.

In conclusion, both CGM and isCGM are cost-effective tools for the management of T1D in the Canadian adult population. In addition to their ease of use and ability to improve day-to-day living with T1D, their widespread adoption is anticipated to lead to a significant reduction in risk of developing SH, DKA, and micro- or macrovascular complications and acceptable cost-effectiveness compared with SMBG. As these technologies further improve and costs continue to decrease, these results suggest that individuals with T1D should be strongly supported by public health programs and insurers to choose and implement either technology.

Funding. This study was funded through a fee-for-service consulting agreement between M.A.R. and JDRF Canada.

The funders had a role in the study design and provided feedback on the manuscript draft but had no role in data collection or data analysis or interpretation.

Duality of Interest. M.C.R. has received speaker honoraria from Medtronic Diabetes, Insulet Corporation, Ascensia Diabetes Care, Novo Nordisk (through JDRF T1D Performance in Exercise and Knowledge [PEAK] program), Xeris Pharmaceuticals, Lilly Diabetes, and Lilly Innovation. B.P. has received speaker honoraria from Abbott, Medtronic, Insulet, and Novo Nordisk and research support to his research institute from Boehringer Ingleheim, Novo Nordisk, and the Bank of Montreal. No other potential conflicts of interest relevant to this article were reported.

Author Contributions. M.A.R. developed the Markov cost-effectiveness model, performed analyses, and wrote the initial draft of the manuscript. O.W. supported the analysis methods, including model coding; performed preliminary literature searching for cost and effectiveness data; and wrote portions of *RESEARCH DESIGN AND METHODS* and appendices. M.R. provided substantial contributions to study design and revised the draft for critical content. B.P. provided valuable insight into model interpretation, framing the results within the literature and public health context, and revised the work for critical context and clarity. All authors contributed to critical revision of the first draft and all subsequent drafts of the manuscript. M.A.R. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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