

# Supplemental Material

## Table of Contents

### Appendix A: Methods Details

A1: Initial Cohort and Model Structure.....	2
A2: Estimation of Efficacy of CGM and isCGM.....	5
A3: Intervention Costs and Model Parameters.....	10
A4: Rates of SH/DKA events from relevant studies .....	17

Appendix B: Sensitivity Analysis Details.....	22
---	----

Appendix C: Additional Results.....	23
-------------------------------------	----

References .....	26
------------------	----

CHEERS Checklist.....	30
-----------------------	----

Abbreviations	
CVD	Cardiovascular Disease
CGM	Continuous Glucose Monitoring
DCCT	Diabetes Control and Complications Trial
DKA	Diabetic Ketoacidosis
DM	Diabetes Mellitus
ESRD	End Stage Renal Disease
isCGM	Intermittently Scanned Continuous Glucose Monitoring
LEA	Lower Extremity Amputation
QALY	Quality-Adjusted Life-Year
OH	Ontario Health
RCT	Randomized Controlled Trial
RR	Relative Risk
SH	Severe Hypoglycemic
SBMG	Self-Monitoring of Blood Glucose
T1D	Type 1 Diabetes
TIR	Time in Range

**Note:** Reference numbers refer to the supplemental material and not the published manuscript.

# Appendix A: Methods details

## A1: Initial Cohort and Model Structure

### Initial cohort

The estimated mean prevalence of DM in Canada is calculated from various sources to be 8.4% (1-4). Approximately 9% (2) of Canadians with DM are diagnosed with T1D. Thus, the overall prevalence of T1D in Canada is approximately 0.76%, meaning approximately 287,000 people were diagnosed with T1D in Canada in 2021. As approximately 63.4% of people in Canada were aged 18 to 64 years in 2019 (5), the initial cohort of our model was calculated to be 180,000 people across Canada aged 18 to 64 years diagnosed with T1D.

Population-level age weights were derived from the Statistics Canada 2016 census (6), the most recent source available. Although individual population weights are used for each age in the model, a categorical summary of relative population weights is included in the interest of brevity. Note that they are all similar in magnitude, but individual weights range from 0.01851 (18 years of age) to 0.02487 (53 years of age). This corresponds to a 34% variation in weights by age at the population level.

Table A1: Demographic Distribution

Age (years)	Relative weight
18-19	0.01906
20-24	0.02084
25-29	0.02209
30-34	0.02191
35-39	0.02170
40-44	0.02037
45-49	0.02016
50-54	0.02105
55-59	0.02313
60-64	0.02113

## **Model Structure**

All participants begin in the no complications state. After the first year, participants can transition to a complication, remain in the no complications state, or die. Once in a complication state, participants can transition to a more severe complication (e.g., retinopathy to blindness), remain there, or die due to the increased risk of death from their complication or other causes.

Figure A1 illustrates our Markov cost-effectiveness model structure.

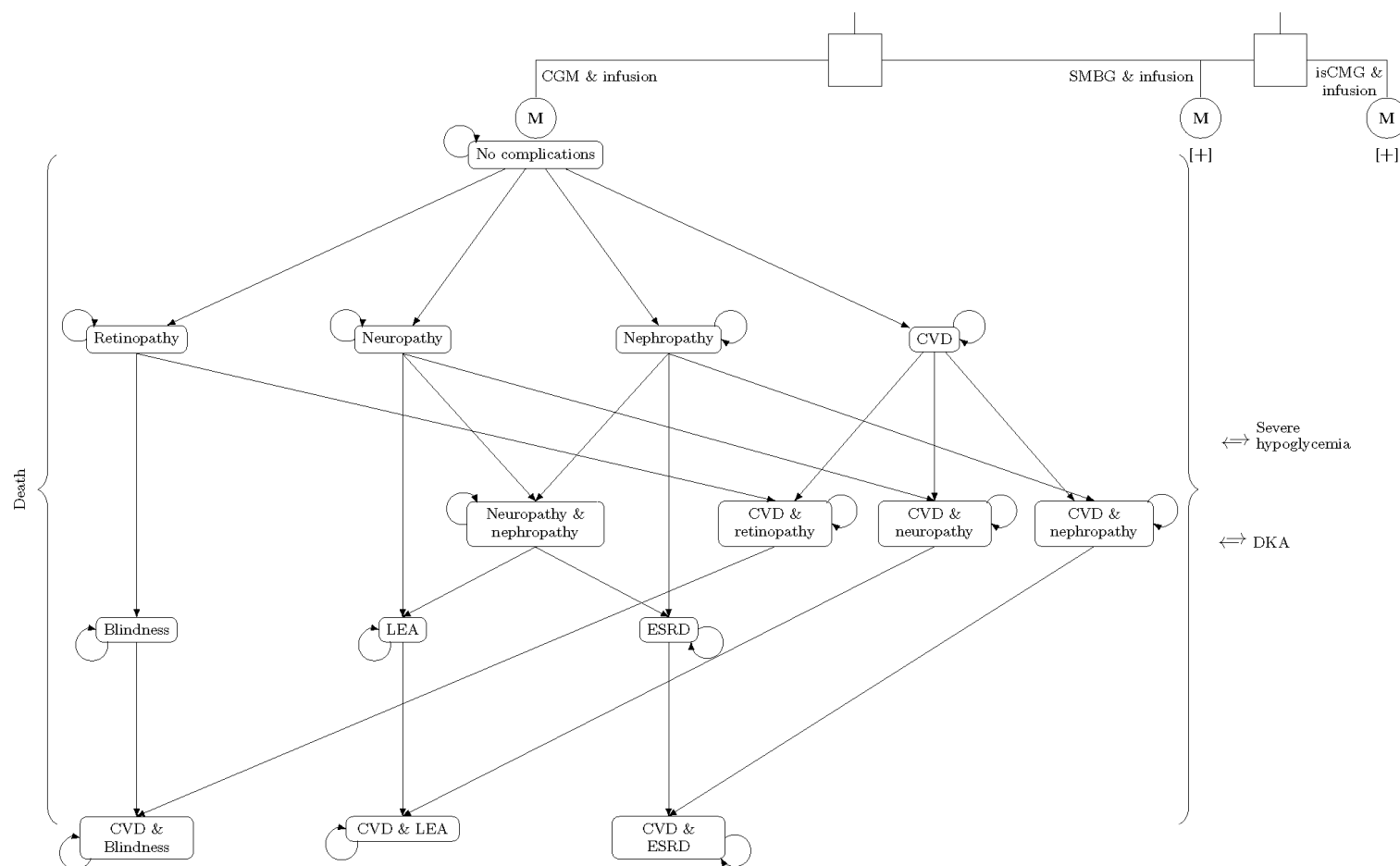


Figure A1: Diagram of Markov cost-effectiveness model structure

## A2: Estimation of Efficacy of CGM and isCGM

### Clinical Improvement of TIR due to CGM

Maiorino et al. (7) is the primary source for the evaluation of the clinical effectiveness of CGM and isCGM relative to SMBG for glycemic control. To ensure that no more recent studies have been published, a supplemental literature search was performed in June 2021 for relevant studies that represent our target population of adults between 18 to 64 years old. While other randomized trials in children and older adults were recently completed, they were not included in our analysis. Evaluation of the efficacy of CGM is based on the following subgroup of studies (adapted from Maiorino et al. (7), Supplemental Figure 2B), eliminating studies which include isCGM, sensor augmented pumps, pediatric patients, or patients with type 2 diabetes. Based on these criteria, the following five studies were retained:

Table A2: Study details

Study	Location	Follow-up (weeks)	Sample Size (treatment/control)	Mean Age (years, treatment/control)	Baseline HbA1c (% (treatment/control)	Mean Difference (95 % CI)	CGM sensor
JDRF (8)	United States	26	52/46	41.2/44.6	7.6/7.6	1.72 (0.69, 2.74)	Dexcom SEVEN
Little et al. (9)	United Kingdom	24	42/41	50.1/47.1	8.2/8.3	0.31 (-1.61, 2.23)	Medtronic
van Beers et al. (10)	Netherlands	16	26/26	48.6/48.6	7.5/7.5	2.30 (1.90, 2.70)	ENLITE
Beck et al. (11)	United States	24	105/53	46.0/51.0	8.6/8.6	1.50 (0.36, 2.64)	Dexcom G4
Heinemann et al. (12)	Germany	24	75/74	45.8/47.3	7.6/7.3	0.75 (0.00, 1.50)	Dexcom G5

A random effects meta-analysis produced a mean improvement in time in range of 1.48 hours (0.77 to 2.20), with an  $I^2$  of 69%, suggesting moderate to substantial heterogeneity (13). A graphical presentation of these results is included in Figure A2.

## Random Effects Meta-Analysis for CGM vs. SMBG

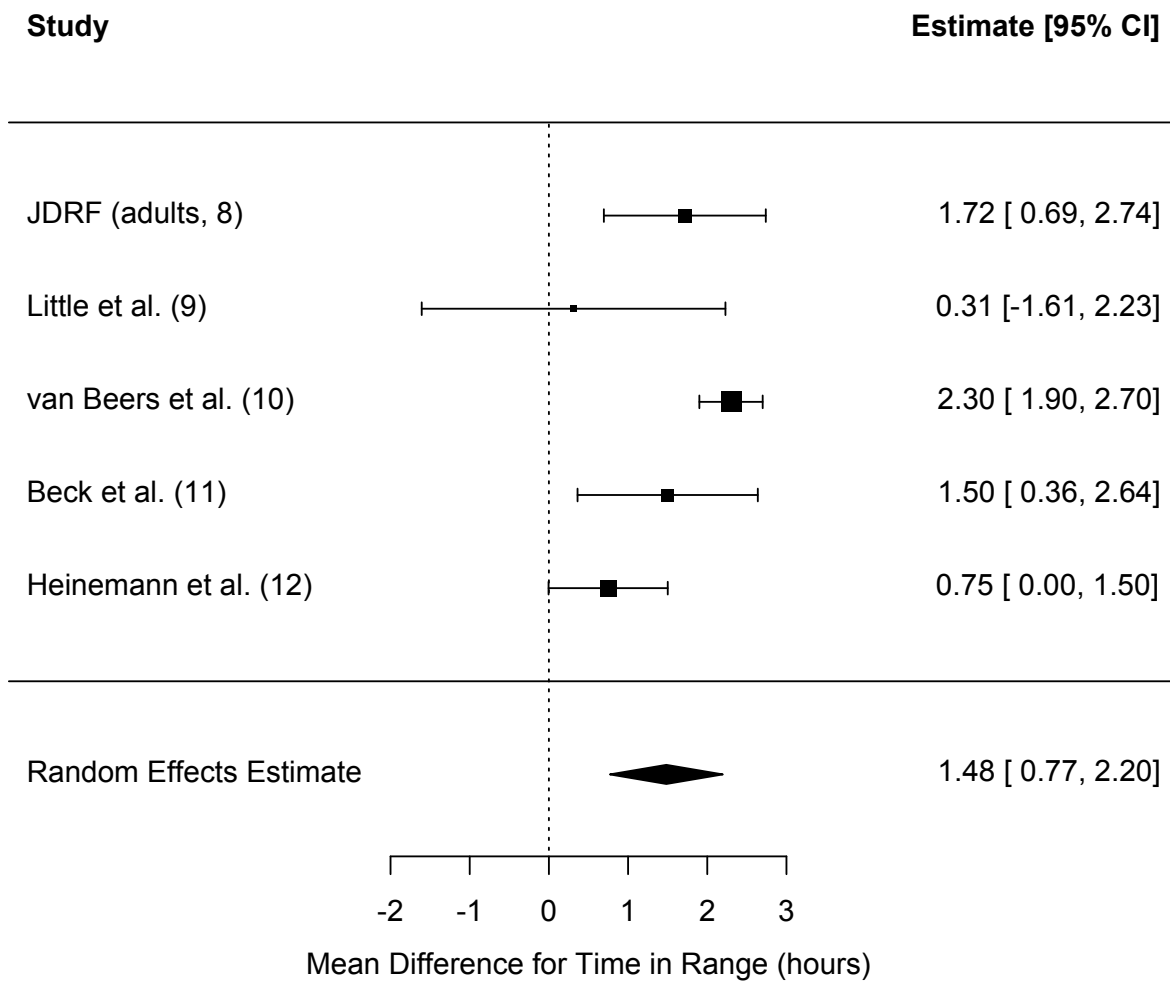


Figure A2: Random effects meta-analysis of mean TIR estimates presented in for CGM vs. SMBG.

### Clinical Improvement due to isCGM

Similarly, Maiorino et al. (7) provides an initial reference for evaluating the effectiveness of isCGM over SMBG for glycemic control. Upon examination of this report, one study was selected as relevant for our population. We note that while Maiorino et al. (7) reports a second study of isCGM (14), however as this is a subgroup of Bolinder et al. (15) it should not be included as a distinct study for meta-analysis purposes. Summary characteristics for Bolinder et al. (15) are included in Table A3.

Table A3: Study details

Study	Location	Follow-up (weeks)	Sample Size (treatment/ control)	Mean Age (years, treatment/ control)	Baseline HbA1c (%, treatment/ control)	Mean Difference (95 % CI)	CGM sensor
Bolinder et al. (15)	Europe (multiple locations)	24	119/120	42.0/45.0	6.8/6.8	1.00 (0.43, 1.57)	FreeStyle Libre

Based on these results, we estimate a mean improvement in TIR of 1.00 hours/day (0.43 to 1.57) when isCGM is used relative to SMBG. While we acknowledge that this is based only on one study, it represents the most relevant basis for our study population and the uncertainty is captured in the wide confidence interval and our conservative analysis strategy.

### Translating the efficacy of CGM and isCGM to rates of long-term T1D complications

To ensure that a conservative cost-effectiveness analysis, we used an improvement in TIR of 0.77 hours/day and 0.43 hours/day as our basis for CGM and isCGM efficacy, respectively. The DCCT (16) remains our best source of data for the impact of glycemic control on long-term complications, such as CVD (including stroke, heart failure, angina), retinopathy,

nephropathy and neuropathy. Recently, Beck et al. (17) validated TIR for retinopathy and microalbuminuria (which we apply to nephropathy). Based on their adjusted models, the hazard ratio of a 10% increase in daily TIR (i.e., 2.4 hours/day) corresponds to a reduction of 64% and 40% in risk of retinopathy and nephropathy, respectively. Assuming a linear relationship and that the hazard ratio approximates the RR, this corresponds to a 0.204 reduction in risk of retinopathy due to CGM and an approximate RR of 0.796. Similar calculations yield Table A4

Table A4: RRs based on TIR		
Model	Retinopathy	Nephropathy
CGM	0.796	0.872
isCGM	0.885	0.928

However, we are not aware of any other prospective analyses examining the risk of CVD and neuropathy based on TIR, thus we require a link to HbA1c to measure this reduction in risk. Note that Vigersky et al. (18) suggest that a 10% increase in TIR (i.e., 2.4 hours/day) corresponds to approximately a 0.80% decrease in HbA1c. This study was selected as our reference as it is based on a large number of studies from a variety of populations, the majority of which were from the T1D community. Thus, our estimates of relative efficacy of CGM and isCGM based on HbA1c are 0.257% and 0.143% of baseline (i.e., SMBG), respectively. Consistent with the OH (19) report and baseline cohort information of Aronson et al. (20), if we assume a baseline HbA1c of 8.1%, our relative improvements correspond to approximately a 3.2% and 1.8% long-term reduction of HbA1c for CGM and isCGM, respectively.

Table A5 is adapted from Table A7 in OH's (19) Appendix and contains the relative reductions in risk for neuropathy and CVD.



Table A5: Reduction of RRs of complications due to glycemic monitoring

Relative change in HbA1c (%) from baseline	Neuropathy (RR)	CVD (RR)
1	0.963	0.978
2	0.926	0.956
3	0.889	0.934
4	0.853	0.912
$\Delta_{RR}$	0.037	0.022

As an example, the baseline SMBG risk of moving from no complications to nephropathy is 0.072. Under CGM, this risk would reduce to 0.0628. Similarly, for isCGM the risk would reduce to 0.0668. Note that we assume that the probability of entering a more severe complication (e.g., ESRD, blindness, LEA) remains the same, independent of the monitoring strategy, and that only the rate of entering the first stage complication is reduced. To summarize, our conservative estimates of the reduction of risk associated CGM and isCGM are presented in Table A6.

Table A6: Overall summary of CGM and isCGM impact

Model	Retinopathy (RR)	Nephropathy (RR)	Neuropathy (RR)	CVD (RR)
CGM	0.795	0.872	0.882	0.930
isCGM	0.885	0.928	0.933	0.960

### **A3: Intervention Costs and Model Parameters**

#### **Intervention cost assumptions and calculation details**

**SMBG:** Our annual average cost estimate for SMBG is estimated as \$2,019 per year. This was estimated based on a review of the London Drugs and Amazon online stores for supplies. Costs were based on the purchase of a box of 100 strips for \$76.99 and 100 lancets for \$9.29. Assuming a recommended average testing rate of six tests per day (21), the annual cost is estimated as \$1,889 per year. Given the three-month expiration an additional \$120 is estimated for purchase of four bottles of solution. Purchase of a Contour Next glucose meter is also included for \$47.99, which is eligible for a warranty of five years pending registration. This yields a pro-rated cost of \$9.60 per year. To total annual cost is thus:  $\$1,889 + \$120 + \$10 = \$2,019$ .

**CGM:** Our annual average cost estimate for CGM is estimated as \$3,930 per year. This was estimated based on the following calculations and assumptions:

1. Based on 12-month subscription prices from manufacturer websites, a Dexcom G6 costs \$3,588 per year. This system does not require a receiver nor is any calibration required. Similarly, the Medtronic Guardian Connect costs \$3591 per year based on an annual subscription. No receiver is required, but this is currently only available for iOS. The Medtronic system also requires twice daily calibration (minimum). Thus, an additional \$681 is added to yield \$4,272 per year.
2. We assume an equal market share. Thus, an average cost for non-insulin pumps is:  $(\$3,588 + \$4,272)/2 = \$3,930$  per year.

**isCGM:** Our annual average cost estimate for isCGM is estimated as \$2,540 per year. As the FreeStyle Libre is the only isCGM that is approved for sale in Canada, we estimated the annual average cost from the FreeStyle Libre website. A reader can be purchased for \$54 (with a three-year warranty, pro-rated to \$18 per year). Bi-weekly sensors can be purchased for \$97 each, representing an annual cost of  $\$97 \times 26 + \$18 = \$2,540$ . Note that no calibration is necessary for these sensors.

### **Insulin Pump Usage**

Initial calculations assumed that approximately 15% of the T1D community use insulin pumps. While isCGM works similarly and is unaffected by diabetes pump use, CGM compatibility varies between Medtronic and Tandem pumps systems. However, based on our assumption of equal market share and recent cost reductions for the Medtronic Guardian Link 3 sensors, these do not impact our annual cost calculations. As a further note, our analysis only includes costs of glucose monitoring and does not include costs of insulin or delivery (e.g. pump or multiple daily injections).

## Transition Probabilities

Baseline transition probabilities for SMBG are included in Table A7:

Table A7: Baseline annual transition probabilities

Parameter	Baseline Probability	Min	Max	References
From no complications to:				
Retinopathy	0.011	0.006	0.017	McQueen et al. (22)
Neuropathy	0.0235	0.0218	0.0252	Nathan et al. (23), Nathan (24)
Nephropathy	0.072	0.041	0.112	McQueen et al. (22)
CVD	AD <sup>†</sup>	–	–	Livingstone et al. (25)
From retinopathy to:				
Blindness	0.0064	0.0062	0.0066	Hoerger et al. (26), McQueen et al. (22)
CVD	0.0155	0.0100	0.0430	Klein et al. (27), McQueen et al. (22)
From neuropathy to:				
Nephropathy	0.097	0.0550	0.1490	Wu et al. (28)
LEA	0.120	0.0620	0.1690	Hoerger et al. (26), Jonasson et al. (29), McQueen et al. (22)
SH event	0.052	0.012 <sup>‡</sup>	0.104 <sup>§</sup>	Pettus et al. (30)
DKA event	0.060	0.03 <sup>‡</sup>	0.12 <sup>§</sup>	Pettus et al. (30)
Other mortality	AD <sup>†</sup>	–	–	Livingstone et al. (25)
Additional probability of death				
Nephropathy	+0.0036	–	–	Orchard et al. (31)
LEA	+0.093	–	–	Vamos et al. (32)
ESRD	+0.164	–	–	Wolowacz et al. (33)
SH event	+0.0063	–	–	OH (19)
DKA event	+0.075	–	–	Fernando et al. (34)
CVD	AD <sup>†</sup>	–	–	Palmer et al. (35)

<sup>†</sup>AD = age-dependent. See Tables A8 to A10 for details.

<sup>‡</sup>Minimum rates of SH/DKA events from other relevant studies (see Table A13 in Appendix A)

<sup>§</sup>Maximum rates of SH/DKA events are estimated as double the baseline rate

## **Age-dependent other mortality and CVD risk**

### **Other mortality risk**

Mortality due to other causes was difficult to obtain as general mortality rates from the Canadian population do not generalize to those with T1D. Typically, individuals with T1D have significantly shorter lifespans due to many causes, including the direct pathways that we modelled (e.g., CVD and ESRD), but also other pathways that are not accounted for. Our age-specific risk of mortality is derived from the large-scale Scottish T1D registry (25) and combined with Canadian census data. This resource was chosen as it was based on 21,739 participants in the general population and represents the largest source of detailed information for mortality rates in T1D available. Moreover, Scotland uses a public health care system which supports its application to the Canadian context.

Risks for other mortality were obtained by combining the age-adjusted mortality rates due to malignant neoplasms, diabetes, respiratory disease, diseases of the digestive system, suicide/mental disorder, other external and other causes, averaged by gender, converted to annual probabilities and then weighted by the Canadian population. Risks of other mortality per age group are presented in Table A8.

Table A8: Other mortality risk by age

Age (years)	Probability of mortality
18-24	0.0018
25-29	0.0017
30-34	0.0025
35-39	0.0042
40-44	0.0050
45-49	0.0078
50-54	0.0063
55-59	0.0081
60-64	0.0120
65-69	0.0165
70-74	0.0310
75-79	0.0384
80+	0.0674

### CVD risk

The risk of CVD per age group was obtained from the large-scale Scottish T1D registry (25).

These are presented in Table A9.

Table A9: CVD risk by age

Age (years)	Probability of CVD
20-39	0.002245
40-49	0.00984
50-59	0.01789
60-69	0.03068
70+	0.05673

### CVD mortality risk

To simplify the model and ensure an increasing risk of mortality with age, annual CVD mortality risk was obtained by averaging the annual mortality risks for each of the four age groups across the first five years post-CVD event (19, 35). These are presented in Table A10.

Table A10: CVD mortality risk

Age (years)	Probability of death
18-59	0.117
60-69	0.157
70-79	0.197
80+	0.325

## QALY values

We used the largest decrement in QALYs as our model considered more severe cases of the included complications. For example, the QALY for CVD is obtained from the largest included disutility (i.e., stroke = -0.164) among the included conditions for this category (stroke, congestive heart failure, myocardial infarction, angina). In addition, note that disutilities are additive. For example, an individual with LEA (QALY = 0.536) who experiences a CVD event (disutility = -0.164) would have an overall utility of 0.372. Similarly, an individual with CVD and retinopathy (QALY = 0.666) would have a utility of 0.632 if they experience a DKA event. The QALYs used in the model are presented in Table A11.

Table A11: QALY values for included states

State	QALY
Single states	
No complications	0.900 <sup>a</sup>
Retinopathy	0.830
Neuropathy	0.816
Nephropathy	0.852
CVD	0.736
Blindness	0.756
LEA	0.536
ESRD	0.688
Death	0 <sup>b</sup>
Combined states	
Nephropathy & neuropathy	0.768
CVD & retinopathy	0.666
CVD & neuropathy	0.652
CVD & nephropathy	0.688
CVD & LEA	0.372
CVD & ESRD	0.524
CVD & blindness	0.592
Adverse events	
SH event	-0.021 <sup>§</sup>
DKA event	-0.034 <sup>§</sup>

Unless specified, QALYs were obtained from Beaudet et al. (36)

<sup>a</sup>Polonsky et al. (37)

<sup>b</sup>Definition

<sup>§</sup>Pettus et al. (30)

## Complication costs

Complication costs are presented in Table A12. Note that each individual's annual costs are additive and include the sum of the annual cost of the intervention, potential complications, and SH or DKA events.

Table A12: Added annual complication costs (2021 CAD)

State	First year cost	Subsequent year cost
No complications	—	—
Retinopathy	513	54
Neuropathy	200	200
Nephropathy	83	14
CVD	19,483	4,247
Blindness	3,632	2,588
LEA	45,871	6,282
ESRD	29,432	13,347
Death	0	0
SH event	3,937	3,937 <sup>a</sup>
DKA event	7,783	7,783 <sup>a</sup>

<sup>a</sup>Cost remains the same for all years



#### **A4: Rates of SH/DKA events from relevant studies**

Severe hypoglycemic (SH) events occur when blood sugar levels become extremely low. At the other extreme, DKA is a severe complication of T1D and is caused by insufficient insulin, resulting in high blood sugar levels and elevated levels of ketones in the bloodstream leading to ketoacidosis (38). A detailed literature review was performed to examine the overall prevalence of SH events and DKA that require hospitalization in the T1D population. The results are summarized in Table A13. RCTs are not a viable study design to measure these rates as they are generally low and require large sample sizes as well as potentially large follow-up times to observe enough events.

##### **SH events**

Based on the available data sources, we will use a baseline SH event rate of 5.2% per year (30). This source was selected as it is a large-scale U.S. study of adults with the vast majority (85%) in our target population age range of 18 to 64 years. When assessing the relative improvement due to CGM, we apply Parkin et al.'s (39) relative improvements in rates as they include both SMBG (1.2%) and CGM groups (0.7%) in the same cohort. This yields an RR of 0.583, which corresponds to an annual rate of 3.0% for CGM. While we have no direct study comparing isCGM to SMBG, Charleer et al. (40) provide a pre-post reduction of risk of SH events requiring hospital admission of 1.9% to 1.2% per year. Applying this result to our baseline rate yields an annual probability of 3.3% for isCGM. Costs (\$3,937), QALY (-0.021), and probability of mortality (0.0063) due to an SH event were obtained from OH (19) and adjusted for 2021 CAD as no additional Canadian sources were found.

##### **DKA events**

Similar to SH events, Pettus et al. (30) provide an annual rate of DKA events of 6.0%. Based on

the report by Parkin et al. (39), we have a very strong relative improvement of 0.133 due to CGM, which corresponds to a rate of 0.8%. Note that, while this appears very large, it is reasonable as this technology provides warnings of elevated glucose which helps ensure that high blood sugar does not remain untreated until DKA occurs. Similarly, using the pre-post rates of Charleer et al. (40) yields an annual RR of 0.714 for DKA in isCGM and an annual probability of 4.3%.

A recent report by Fernando et al. (34) in Ottawa, Canada shows that the average (non-ICU-based) hospital admission cost for a DKA event is \$6,484 while those requiring ICU admission cost approximately \$20,716. Based on this study, we have used an annual pooled DKA event cost of \$7,783 (in 2021 CAD) with a pooled mortality rate of approximately 7.75% due to a DKA event.

Given our population, the impact of DKA on QALY is best represented using a large study of 2,341 individuals with T1D in the U.K. Peasgood et al. (41) found a statistically significant disutility of -0.037 for experiencing a DKA event using a fixed effects model for the DQ-VAS QOL scale. This is also consistent with our value of reduction in QALY for SH events as we expect a DKA event to have a slightly larger impact on QOL because it often requires ICU admission and similarly, an extended loss of time at work/school.

Table A13: Summary of studies for incidence of SH and DKA events

Study	Sample size	Population	Monitor type	Follow-up time	Annual SH events resulting in hospitalization	Annual DKA events resulting in hospitalization
SMBG						
Parkin et al. (39)	1,130 (565 SMBG)	Patients in the Optum Research Database with a diagnosis code for T1D, continuous enrolment in the health plan at least one claim for insulin during the study period (mean age in SMBG group = 38.02 years; mean age in CGM group = 36.22 years)	—	1 year	1.2%	3.0%
Foster et al. (42)	22,697	Patients from 2010 to 2012 and 2016 to 2018 (ages 1 to 93 years with 11,240 patients being $\geq 18$ years old, duration of T1D from $<1$ to 80 years) in the T1D Exchange clinic registry data collected from 81 U.S.-based pediatric and adult endocrinology practices in 35 states	—	5 years	—	3.0% <sup>a</sup>
Pettus et al. (30)	31,430	Patients from 2014 to 2016 in the T1PCO EHR database that contains data from hospitals and clinics in all census regions of the U.S. (age $\geq 18$ years with 85% aged 18 to 64 years, T1D duration of $\geq 24$ months)	—	12 months	5.2%	6.0%

Table A13: Summary of studies for incidence of SH and DKA events (continued)

Study	Sample size	Population	Monitor type	Follow-up time	Annual SH events resulting in hospitalization	Annual DKA events resulting in hospitalization
CGM						
Parkin et al. (39)	1,130 (565 CGM)	Patients in the Optum Research Database with a diagnosis code for T1D, continuous enrolment in the health plan at least one claim for insulin during the study period (mean age in SMBG group = 38.02 years; mean age in CGM group = 36.22 years)	Dexcom G4 Platinum	1 year	0.7%	0.4%
Foster et al. (42)	22,697	Patients from 2010 to 2012 and 2016 to 2018 (ages 1 to 93 years with 11,240 patients being $\geq 18$ years old, duration of T1D from $<1$ to 80 years) in the T1D Exchange clinic registry data collected from 81 U.S.-based pediatric and adult endocrinology practices in 35 states	Dexcom (version not specified)	5 years	—	1% <sup>a</sup>
isCGM						
Charleer et al. (40)	1,711	Patients living with T1D for $> 3$ months from University Hospitals Leuven, University Hospital Antwerp, and OLV Hospital Aalst in Belgium (mean $\pm$ SD length of T1D = $22.8 \pm 13.7$ years) mostly on multiple daily injections (78%), impaired awareness of	FreeStyle Libre software version 1.0 and LibreView	12 months	1.2%	1.0%

hypoglycemia in a minority of cases (16%), and suboptimal mean  $\pm$  SD baseline HbA1c of 7.8%  $\pm$  1.2%

Tsur et al. (43)	2,295	Patients aged $\geq 18$ years in the Clalit Health Services database with T1D in Israel	FreeStyle Libre	3 months	2.9 <sup>b</sup>	2.3 <sup>b</sup>
---------------------	-------	---	-----------------	----------	------------------	------------------

---

<sup>a</sup>Prevalence of at least one event in the 3 months prior to the questionnaire

<sup>b</sup>Number of events per 100 person-years

## Appendix B: Sensitivity Analysis Details

**Complication rates:** The minimum and maximum values for the complication rates examined in the sensitivity analysis were obtained from existing literature and are reported in Table A7 along with their respective sources.

**Complication RRs:** In order to remain conservative, our primary models used the lower bound of the 95% CIs of the pooled increase of TIR in CGM and isCGM users adapted from Maiorino et al. (7) and our own preliminary meta-analysis (see Figure A2). In the sensitivity analysis, we examined the impact of a less conservative model of CGM and isCGM efficacy by using the point estimate and upper bound of the pooled TIR 95% CIs to model how a larger effect of these technologies will affect our results.

**Cost and QALY discounts:** Our primary models used an annual discount rate of 1.5% for both costs and QALYs. We examined the impact of reducing the annual discount rate to 0% and increasing it to 5% on CGM and isCGM ICERs relative to SMBG.

**Frequency of glucose monitoring tests:** Higher frequencies of daily glucose tests are often linked to better glycemic control (44-47), though a higher testing frequency also results in higher cost. The 2021 National Institute for Health Care and Excellence guidelines (48) recommend up to 10 tests per day. We compared the American Diabetes Association's (21) recommendation of 6 tests per day to a higher frequency of tests to determine whether higher testing frequencies are still cost-effective for CGM and isCGM systems relative to SMBG. Thus, we examined the resulting ICERs from testing 8 (annual cost: \$2,649) or 10 (annual cost: \$3,324) times per day.

**Annual cost of CGM and isCGM:** In order to explore the impact of potential bulk purchase agreements by the government on CGM and isCGM ICERs, we reduced the annual cost of CGM and isCGM systems by 10% and 25%.

## Appendix C: Additional results

Figures C1 through C3 illustrate the modelled number of individuals in each state over the study.

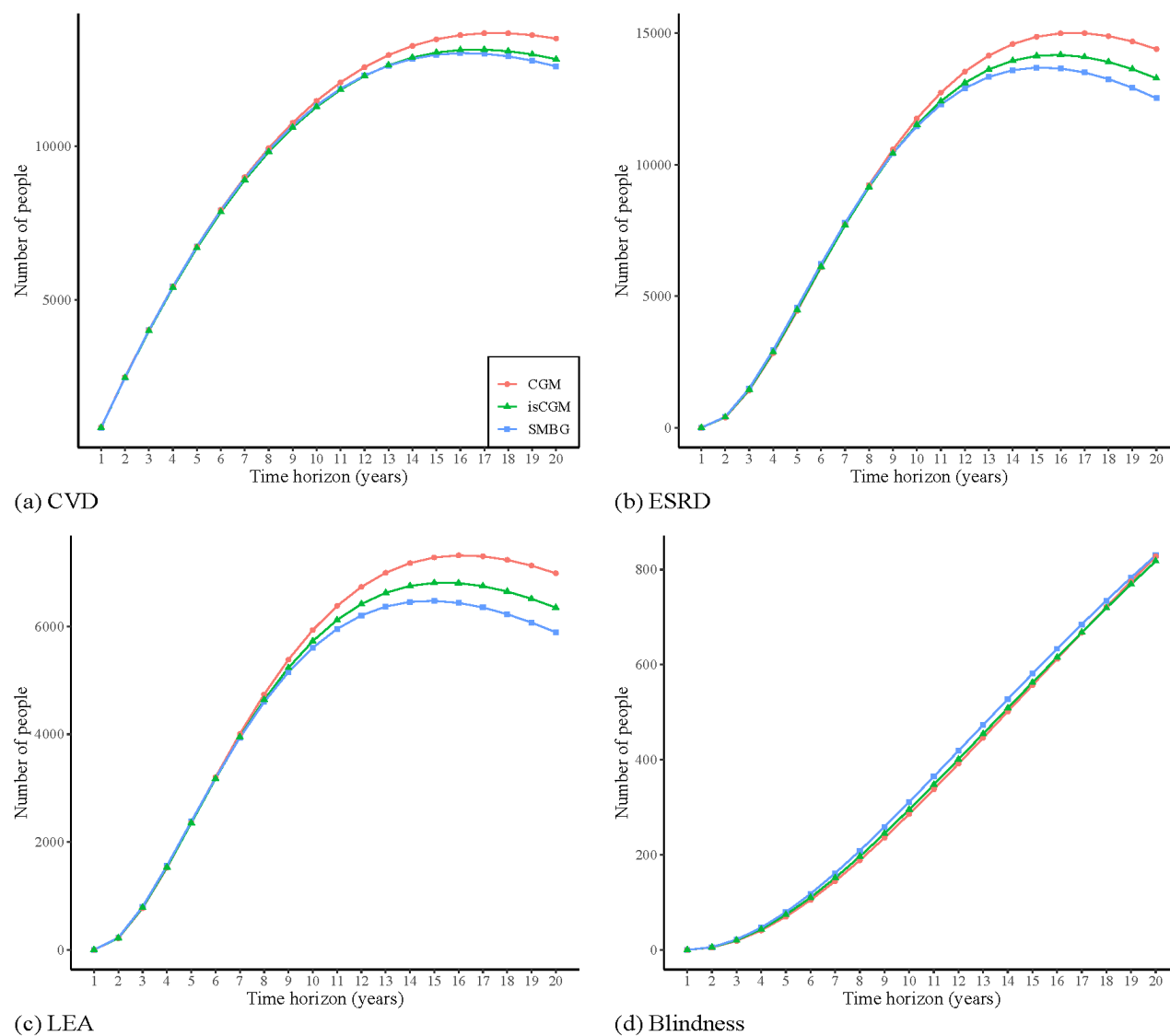
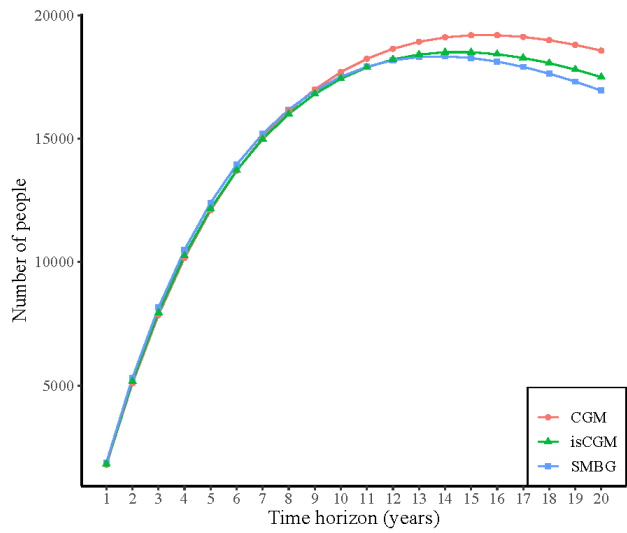
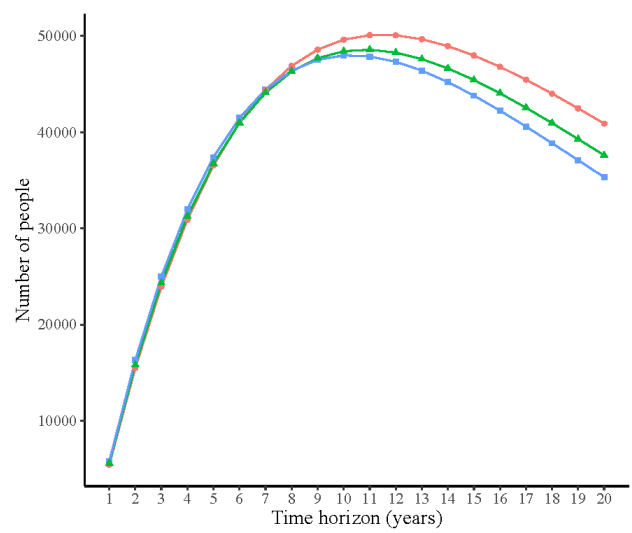


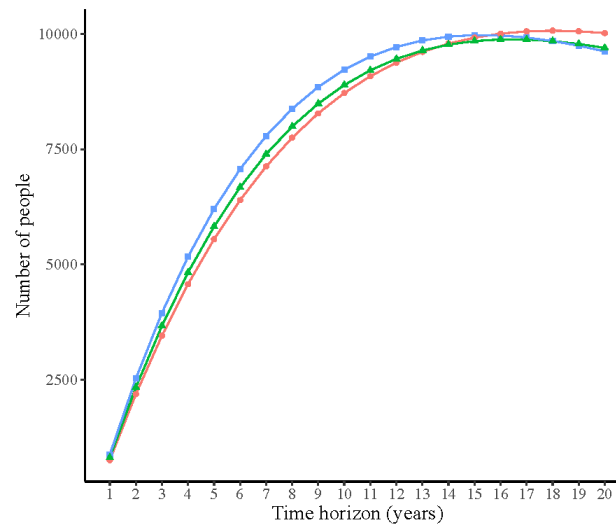
Figure C1: Number of people over a 20-year horizon with major complications: (a) CVD, (b) ESRD, (c) LEA, or (d) blindness



(a) Neuropathy



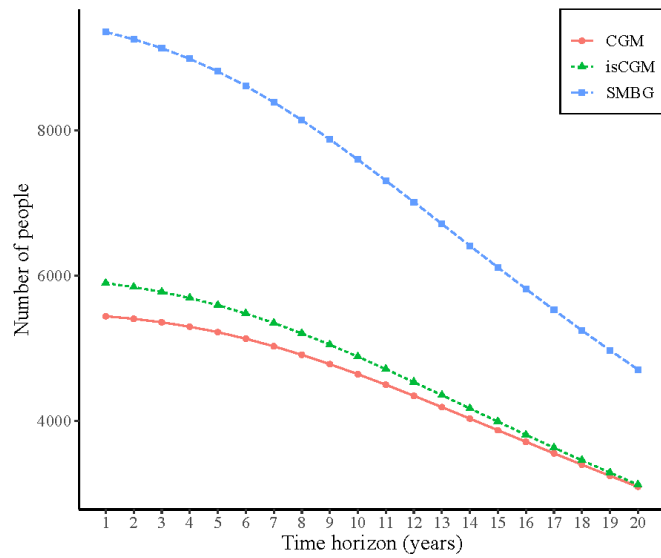
(b) Nephropathy



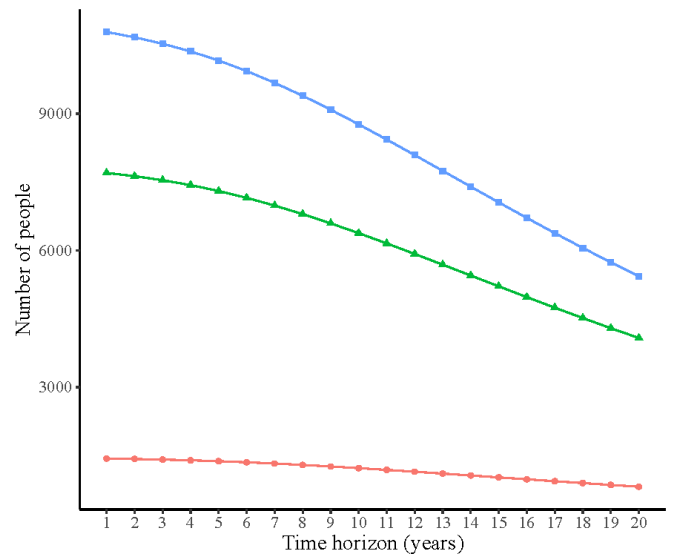
(c) Retinopathy

Figure C2: Number of people over a 20-year horizon with minor complications: (a) neuropathy, (b) nephropathy, or (c) retinopathy





(a) SH



(b) DKA

Figure C3: Number of people over a 20-year horizon with events of (a) SH or (b) DKA. Note that, since SH and DKA are independent events, annual counts are a function of the number of people alive in that year.

# References

1. Guariguata L, Whiting DR, Hambleton I, et al. Global estimates of diabetes prevalence for 2013 and projections for 2035. *Diabetes Res Clin Pract* 2014;103(2):137-49.
2. Public Health Agency of Canada. Diabetes in Canada. Ottawa, Canada: Government of Canada; 2017: HP35-94/2017E-PDF
3. Statistics Canada. Diabetes, 2017; 2018. Available from <https://www150.statcan.gc.ca/n1/pub/82-625-x/2018001/article/54982-eng.htm>
4. Yisahak SF, Beagley J, Hambleton IR, et al. Diabetes in North America and the Caribbean: An update. *Diabetes Res Clin Pract* 2014;103(2):223-30.
5. Statistics Canada. Population estimates, quarterly; 2020. Available from: <https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1710000901>
6. Statistics Canada. Statistics Canada data tables: Age; 2016. Available from: <https://www12.statcan.gc.ca/census-recensement/2016/dp-pd/dt-td/Rp-eng.cfm?Lang=e&apath=3&detail=0&dim=0&fl=a&free=0&gc=0&gid=0&gk=0&grp=1&pid=109525&priid=0&ptype=109445&s=0&showall=0&sub=0&temporal=2016&theme=115&vid=0&vnamee=&vnamef>
7. Maiorino MI, Signoriello S, Maio A, et al. Effects of continuous glucose monitoring on metrics of glycemic control in diabetes: A systematic review with meta-analysis of randomized controlled trials. *Diabetes Care* 2020;43(5):1146-56.
8. Tamborlane WV, Beck RW, Bode BW, et al. Continuous glucose monitoring and intensive treatment of type 1 diabetes. *N Engl J Med* 2008;359:1464-76.
9. Little SA, Leelarathna L, Walkinshaw E, et al. Recovery of hypoglycemia awareness in longstanding type 1 diabetes: A multicenter 2x2 factorial randomized controlled trial comparing insulin pump with multiple daily injections and continuous with conventional glucose self-monitoring (HypoCOMPaSS). *Diabetes Care* 2014;37(8):2114-22.
10. van Beers CA, DeVries JH, Kleijer, SJ et al. Continuous glucose monitoring for patients with type 1 diabetes and impaired awareness of hypoglycaemia (IN CONTROL): A randomized open-label, crossover trial. *Lancet Diabetes Endocrinol* 2016;4(11):893-902.
11. Beck RW, Riddlesworth T, Ruedy K, et al. Effect of continuous glucose monitoring on glycemic control in adults with type 1 diabetes using insulin injections: The DIAMOND randomized clinical trial. *JAMA* 2017;317(4):371-78.
12. Heinemann L, Freckmann G, Ehrmann D, et al. Real-time continuous glucose monitoring in adults with type 1 diabetes and impaired hypoglycaemia awareness or severe hypoglycaemia treated with multiple daily insulin injections (HypoDE): A multicenter, randomized controlled trial. *Lancet* 2018;391(10128):1367-77.
13. Deeks JJ, Higgins JPT, Altman D. Analysing data and undertaking meta-analyses. In: Higgins JPT, Thomas J, Chandler J, et al., editors. *Cochrane handbook for systematic reviews of interventions*. Chichester (SXW): John Wiley & Sons; 2019. Chapter 10.
14. Oskarsson P, Antuna R, Geelhoed-Duijvestijn P, et al. Impact of flash glucose monitoring on hypoglycaemia in adults with type 1 diabetes managed with multiple daily injection therapy: A pre-specified subgroup analysis of the IMPACT randomised controlled trial. *Diabetologia* 2018;61(3):539-50.

15. Bolinder J, Antuna R, Geelhoed-Duijvestijn P, et al. Novel glucose-sensing technology and hypoglycaemia in type 1 diabetes: A multicenter, non-masked, randomized controlled trial. *Lancet* 2016;388(10057):2254-63.
16. Nathan DM, Genuth S, Lachin J, et al. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med* 1993;329(14):977-86.
17. Beck RW, Bergenstal RM, Riddlesworth TD, et al. Validation of time in range as an outcome measure for diabetes clinical trials. *Diabetes Care* 2019;42(3):400-405.
18. Vigersky RA, McMahon C. The relationship of hemoglobin A1C to time-in-range in patients with diabetes. *Diabetes Technol Ther* 2019;21(2):81-5.
19. Health Quality Ontario. Continuous monitoring of glucose for type 1 diabetes: A health technology assessment. *Ont Health Technol Assess Ser* 2018;18(2):1-160.
20. Aronson R, Brown R, Abitbol A, et al. The Canadian LMC Diabetes Registry: A profile of the demographics, management, and outcomes of individuals with type 1 diabetes. *Diabetes Technol Ther* 2020;23(1):31-40.
21. American Diabetes Association. Diabetes technology: Standards of medical care in diabetes 2020. *Diabetes Care* 2020;43(Suppl 1):S77-88.
22. McQueen RB, Ellis SL, Campbell JD, et al. Cost-effectiveness of continuous glucose monitoring and intensive insulin therapy for type 1 diabetes. *Cost Eff Resour Alloc* 2011;9:13.
23. Nathan DM, Zinman B, Cleary PA, et al. Modern-day clinical course of type 1 diabetes mellitus after 30 years' duration: The diabetes control and complications trial/epidemiology of diabetes interventions and complications and Pittsburgh epidemiology of diabetes complications experience (1983-2005). *Arch Intern Med* 2009;169(14):1307-16.
24. Nathan DM. The diabetes control and complications trial/epidemiology of diabetes interventions and complications study at 30 years: Overview. *Diabetes Care* 2014;37(1):9-16.
25. Livingstone SJ, Looker HC, Hothersall EJ, et al. Risk of cardiovascular disease and total mortality in adults with type 1 diabetes: Scottish registry linkage study. *PLoS Med* 2012;9(10):e1001321.
26. Hoerger TJ, Harris R, Hicks KA, et al. Screening for type 2 diabetes mellitus: A cost-effectiveness analysis. *Ann Intern Med* 2004;140(9):689-99.
27. Klein BEK, Klein R, McBride PE, et al. Cardiovascular disease, mortality, and retinal microvascular characteristics in type 1 diabetes: Wisconsin epidemiologic study of diabetic retinopathy. *Arch Intern Med* 2004;164(17):1917-24.
28. Wu SY, Sainfort F, Tomar RH, et al. Development and application of a model to estimate the impact of type 1 diabetes on health-related quality of life. *Diabetes Care* 1998;21(5):725-31.
29. Jonasson JM, Weimin Y, Sparén P, et al. Risks of nontraumatic lower-extremity amputations in patients with type 1 diabetes. *Diabetes Care* 2008;31(8):1536-40.
30. Pettus JH, Zhou FL, Shepherd L, et al. Incidence of severe hypoglycemia and diabetic ketoacidosis and prevalence of microvascular complications stratified by age and glycemic control in U.S. adult patients with type 1 diabetes: A real-world study. *Diabetes Care* 2019;42(12):2220-27.

31. Orchard TJ, Nathan DM, Zinman B, et al. Association between 7 years of intensive treatment of type 1 diabetes and long-term mortality. *JAMA* 2015;313(1):45-53.
32. Vamos EP, Bottle A, Majeed A, et al. Trends in lower extremity amputations in people with and without diabetes in England, 1996-2005. *Diabetes Res Clin Pract* 2010;87(92):275-82.
33. Wolowacz S, Pearson I, Shannon P, et al. Development and validation of a cost-utility model for type 1 diabetes mellitus. *Diabet Med* 2015;32(8):1023-35.
34. Fernando SM, Bagshaw SM, Rochwerg B, et al. Comparison of outcomes and costs between adult diabetic ketoacidosis patients admitted to the ICU and step-down unit. *J Crit Care* 2019;50:257-61.
35. Palmer AJ, Roze S, Valentine WJ, et al. The CORE Diabetes Model: Projecting long-term clinical outcomes, costs and cost-effectiveness of interventions in diabetes mellitus (types 1 and 2) to support clinical and reimbursement decision-making. *Curr Med Res Opin* 2004;20(Suppl 1):S5-26.
36. Beaudet A, Clegg J, Thuresson P, et al. Review of utility values for economic modeling in type 2 diabetes. *Value Health* 2014;17(4):462-70.
37. Polonsky WH, Hessler D, Ruedy KJ, et al. The impact of continuous glucose monitoring on markers of quality of life in adults with type 1 diabetes: Further findings from the DIAMOND randomized clinical trial. *Diabetes Care* 2017;40(6):736-41.
38. Chiasson J, Aris-Jilwan N, Bélanger R, et al. Diagnosis and treatment of diabetic ketoacidosis and the hyperglycemic hyperosmolar state. *CMAJ* 2003;168(7):859-66.
39. Parkin CG, Graham C, Smokis J. Continuous glucose monitoring use in type 1 diabetes: Longitudinal analysis demonstrates meaningful improvements in HbA1c and reductions in health care utilization. *J Diabetes Sci Technol* 2017;11(3):522-8.
40. Charleer S, De Block C, Van Huffel L, et al. Quality of life and glucose control after 1 year of nationwide reimbursement of intermittently scanned continuous glucose monitoring in adults living with type 1 diabetes (FUTURE): A prospective observational real-world cohort study. *Diabetes Care* 2020;43(2):389-97.
41. Peasgood T, Brennan A, Mansell P, et al. The impact of diabetes-related complications on preference-based measures of health-related quality of life in adults with type 1 diabetes. *Med Decis Making* 2016;36(8):1020-33.
42. Foster NC, Beck RW, Miller KM, et al. State of type 1 diabetes management and outcomes from the T1D Exchange in 2016-2018. *Diabetes Technol Ther* 2019;21(2):66-72.
43. Tsur A, Cahn A, Israel M, et al. Impact of flash glucose monitoring on glucose control and hospitalization in type 1 diabetes: A nationwide cohort study. *Diabetes Metab Res Rev* 2021;37(1):e3355.
44. Aleppo G. Role of continuous glucose monitoring in diabetes treatment. Arlington (VA): American Diabetes Association; 2018. Chapter 6, Approaches for successful outcomes with continuous glucose monitoring.
45. Laurenzi A, Careto A, Barrasso M, et al. Frequency of flash glucose monitoring scans and hemoglobin A1c in real life. *Diabetes* 2018;67(Suppl 1):898-P.
46. Dunn TC, Xu Y, Hayter G, et al. Real-world flash glucose monitoring patterns and associations between self-monitoring frequency and glycaemic measures: A European analysis of over 60 million glucose tests. *Diabetes Res Clin Pract* 2018;137:37-46.

47. Calliari LEP, Krakauer M, Vianna AGD, et al. Real-world flash glucose monitoring in Brazil: Can sensors make a difference in diabetes management in developing countries? *Diabetol Metab Syndr* 2020;12:3.
48. National Institute for Health and Care Excellence. Type 1 diabetes in adults: Diagnosis and management. 2021. Available from: <https://www.nice.org.uk/guidance/ng17>

## Consolidated Health Economic Evaluation Reporting Standards (CHEERS) 2022 Checklist

The CHEERS 2022 statement replaces the 2013 CHEERS statement, which should no longer be used. The CHEERS 2022 checklist contains 28 items with accompanying descriptions. Checklist users should indicate the section of the manuscript where relevant information can be found. The authors recommend using a section heading with a paragraph number. If an item does not apply to a particular economic evaluation, checklist users are encouraged to report “Not Applicable.” If information is otherwise not reported, checklist users are encouraged to write, “Not Reported.” Users should avoid the term “Not Conducted” as CHEERS is intended to guide and capture reporting. Additional information on CHEERS 2022 can be found [here](#).

### Title

#### 1. Title

Identify the study as an economic evaluation and specify the interventions being compared.

---

### Abstract

#### 2. Abstract

Provide a structured summary that highlights context, key methods, results, and alternative analyses.

---

### Introduction

#### 3. Introduction: Background and Objectives

Give the context for the study, the study question, and its practical relevance for decision making in policy or practice.

---

### Methods

#### 4. Health economic analysis plan

Indicate whether a health economic analysis plan was developed and where available.

---

## **5. Study population**

Describe characteristics of the study population (such as age range, demographics, socioeconomic, or clinical characteristics).

---

## **6. Setting and location**

Provide relevant contextual information that may influence findings.

---

## **7. Comparators**

Describe the interventions or strategies being compared and why chosen.

---

## **8. Perspective**

State the perspective(s) adopted by the study and why chosen.

---

## **9. Time horizon**

State the time horizon for the study and why appropriate.

---

## **10. Discount rate**

Report the discount rate(s) and reason chosen.

---

---

## **11. Selection of outcomes**

Describe what outcomes were used as the measure(s) of benefit(s) and harm(s).

---

## **12. Measurement of outcomes**

Describe how outcomes used to capture benefit(s) and harm(s) were measured.

---

### 13. Valuation of outcomes

Describe the population and methods used to measure and value outcomes.

---

### 14. Measurement and valuation of resources and costs

Describe how costs were valued.

---

### 15. Currency, price date, and conversion

Report the dates of the estimated resource quantities and unit costs, plus the currency and year of conversion.

---

### 16. Rationale and description of model

If modeling is used, describe in detail and why used. Report if the model is publicly available and where it can be accessed.

---

### 17. Analytics and assumptions

Describe any methods for analyzing or statistically transforming data, any extrapolation methods, and approaches for validating any model used.

---

### 18. Characterizing heterogeneity

Describe any methods used for estimating how the results of the study vary for subgroups.

---

### 19. Characterizing distributional effects

Describe how impacts are distributed across different individuals or adjustments made to reflect priority populations.

---

### 20. Characterizing uncertainty

Describe methods to characterize any sources of uncertainty in the analysis.

---

21.

### 21. Approach to engagement with patients and others affected by the study

---



Describe any approaches to engage patients or service recipients, the general public, communities, or stakeholders (eg, clinicians or payers) in the design of the study.

NA

---

## Results

### 22. Study parameters

Report all analytic inputs (eg, values, ranges, references) including uncertainty or distributional assumptions.

Supplemental Information Tables A7; Age dependent transitions included in Tables A8, A9 and A10

---

### 23. Summary of main results

Report the mean values for the main categories of costs and outcomes of interest and summarize them in the most appropriate overall measure.

---

### 24. Effect of uncertainty

Describe how uncertainty about analytic judgments, inputs, or projections affects findings. Report the effect of choice of discount rate and time horizon, if applicable.

---

### 25. Effect of engagement with patients and others affected by the study

Report on any difference patient/service recipient, general public, community, or stakeholder involvement made to the approach or findings of the study.

---

## Discussion

### 26. Study findings, limitations, generalizability, and current knowledge

Report key findings, limitations, ethical, or equity considerations not captured and how these could impact patients, policy, or practice.

---

## Other Relevant Information

### 27. Source of funding

Describe how the study was funded and any role of the funder in the identification, design, conduct, and reporting of the analysis.

---

### 28. Conflicts of interest

Report authors' conflicts of interest according to journal or International Committee of Medical Journal Editors requirements.

---