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Cost-Utility of Real-Time Continuous Glucose Monitoring versus Self-Monitoring of Blood Glucose in People with Insulin-Treated Type 2 Diabetes in Spain

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Objective: Management of advanced type 2 diabetes (T2D) typically involves daily insulin therapy alongside frequent blood glucose monitoring, as treatments such as oral antidiabetic agents are therapeutically insufficient. Real-time continuous glucose monitoring (rt-CGM) has been shown to facilitate greater reductions in glycated hemoglobin (HbA1c) levels and improvements in patient satisfaction relative to self-monitoring of blood glucose (SMBG). This study aimed to investigate the cost-utility of rt-CGM versus SMBG in Spanish patients with insulin-treated T2D..

Methods: The analysis was conducted using the IQVIA Core Diabetes Model (CDM V9.5). Baseline characteristics of the simulated patient cohort and treatment efficacy data were sourced from a large-scale, United States-based retrospective cohort study. Costs were obtained from Spanish sources and inflated to 2022 Euros (EUR) where required. A remaining lifetime horizon (maximum 50 years) was used, alongside an annual discount rate of 3% for future costs and health effects. A willingness-to-pay (WTP) threshold of EUR 30,000 per quality-adjusted life year (QALY) was adopted, based on precedent across previous cost–effectiveness studies set in Spain. A Spanish payer perspective was adopted.

Results: Over patient lifetimes, rt-CGM yielded 9.933 QALYs, versus 8.997 QALYs with SMBG, corresponding to a 0.937 QALY gain with rt-CGM. Total costs in the rt-CGM arm were EUR 2347 higher with rt-CGM versus SMBG (EUR 125,365 versus EUR 123,017). The base case incremental cost–utility ratio was therefore EUR 2506 per QALY gained, substantially lower than the WTP threshold of EUR 30,000 per QALY. The analysis also projected a reduction in cumulative incidence of ophthalmic, renal, neurological, and cardiovascular events in rt-CGM users, with reductions of 16.03%, 13.07%, 7.34%, and 9.09%, respectively.

Conclusion: Compared to SMBG, rt-CGM is highly likely to be a cost-effective intervention for patients living with insulin-treated T2D in Spain.

Keywords: continuous glucose monitoring, CGM, cost-effectiveness, hypoglycaemia, health economics, type 2 diabetes

Introduction

Type 2 diabetes (T2D) is a metabolic disorder that affects over 400 million people worldwide, with this number expected to rise to over 700 million by 2045.[1] In Spain, the prevalence of T2D is estimated to be 13.8% in the adult population,[2] although data on the current incidence of T2D in Spain is limited.[3,4] The impacts of the disease can vary, however available clinical evidence shows that patients living with T2D can have a reduced quality of life (QoL).[5] Furthermore, these patients are also likely to experience multiple related co-morbidities[6] and experience higher mortality risks than individuals without diabetes.[1,7] Clinical complications have been found to translate into higher costs, with a 2015 study

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set in Spain finding patients with T2D to have 72.4% higher annual average direct medical costs per patient than non-diabetic individuals (3110.1 Euros [EUR] versus EUR 1803.6, respectively).[8] The factors with the greatest impact on these costs were hospitalizations and medications, demonstrating that effective disease management can be paramount for minimizing the financial burden associated with T2D.[8]

For patients with insulin-treated T2D, regular monitoring of blood glucose levels and glycated hemoglobin (HbA1c) levels can be essential for ensuring optimal disease management.[9] Self-monitoring of blood glucose (SMBG) is a well-established and systematic approach to monitoring blood glucose levels that allows daily glycemic patterns to be identified.[10] The clinical outcomes associated with SMBG use have been investigated in multiple randomized trials involving T2D patients using insulin.[11,12] More recently, the emergence of continuous glucose monitoring (CGM) systems has helped alleviate the burden of repeated, manual monitoring (ie, using fingerstick testing) associated with SMBG. Real-time CGM (rt-CGM) is an advanced form of glucose monitoring that provides users with "real-time" (every 1–5 minutes) data on current blood glucose levels, as well as the direction of change relative to previous readings.[13,14] These devices can also issue high and low alarms that inform the user when their blood glucose levels lie outside of a present threshold.[15] Additionally, rt-CGM devices feature a graphical display of glucose trends showing whether blood glucose levels are steady, increasing or decreasing. A growing number of randomized controlled trials (RCTs) have investigated the clinical benefits of these new technologies versus SMBG. Specifically, results from the DIAMOND and MOBILE trials showed that CGM led to improved glycemic outcomes relative to SMBG for patients with T2D.[16,17]

The availability of data from large-scale, real-world studies investigating the clinical benefits of rt-CGM relative to SMBG is also growing. One such study (based in the United States [US]) included 36,080 patients with insulin-treated T2D and found that rt-CGM led to comparatively greater reductions in the HbA1c levels of participants compared to SMBG (−0.56% for rt-CGM and −0.09% for SMBG).[18] The same study found that rates of hypoglycemic events (ie, those events leading to emergency room visits or hospitalizations) were comparatively lower with rt-CGM use than with SMBG.

There is a significant financial burden associated with the management of insulin-treated T2D in Spain.[3,19] Consequently, there is a pressing need to identify the most cost-effective interventions to ensure the optimal allocation of Spanish healthcare payers' financial resources. While rt-CGM may result in incremental clinical and health outcome benefits for patients living with insulin-treated T2D, these benefits must be weighed against any additional costs incurred relative to existing interventions (ie, SMBG). Previous studies have found rt-CGM to be cost-effective relative to SMBG in patients with T2D receiving insulin therapy across various settings, including Canada,[20] the United Kingdom (UK),[21] and France.[22] However, no such analysis has yet been conducted in the population of interest within the Spanish setting, although a comparative cost-only analysis of a flash glucose monitoring device (ie, the FreeStyle Libre 2) versus SMBG has been conducted.[23]

The objective of this study was therefore to conduct a cost-utility analysis of rt-CGM versus SMBG, in patients living with insulin-treated T2D in Spain.

Methods

Model Structure

This analysis was conducted using the IQVIA CORE Diabetes Model (CDM, V9.5) to evaluate the cost-utility of rt-CGM versus SMBG in patients with insulin-treated T2D in Spain. The CDM has been extensively validated and is designed to estimate the cost-effectiveness of various diabetes management strategies.[24–26] The model allows for adaptations to be made in order for various country and region-specific care settings to be adopted. The CDM has been used in numerous health technology appraisals conducted in the UK and subject to extensive scrutiny from the National Institute of Health and Care Excellence (NICE) in evaluating the cost-effectiveness of strategies for the management of type 1 diabetes (T1D)[27] and T2D.[28,29] The CDM structure comprises 17 inter-dependent Markov models that interact where and when appropriate in order to predict health outcomes and costs of diabetes care interventions over long-term time horizons.[30] Each sub-model consists of between two and nine different health states, with built-in equations used to predict progression of risk factors such as HbA1c, systolic and diastolic blood pressure, estimated glomerular filtration rate (eGFR) and total cholesterol levels. The cardiovascular risk prediction equations used for the

base case analysis were sourced from the United Kingdom Prospective Diabetes Study (UKPDS) Outcomes Model.[31] The model also contains clinical data that inform the probabilities of the onset of diabetes-related microvascular complications and event-specific mortalities. Further details on the CDM can be found in Palmer et al.[26]

In the present analysis, key outputs from the CDM included life expectancy (LE), quality-adjusted life years (QALYs),[32] direct and indirect costs, cumulative incidence of diabetes-related complications, and incremental cost-utility ratios (ICURs). The final ICURs were calculated by dividing the incremental costs by the incremental QALYs, to determine a "cost per QALY gained" with rt-CGM versus SMBG.[33]

Baseline Cohort Characteristics and Treatment Effects

For the simulated patient cohort, key baseline characteristics were obtained from a large-scale, US-based study that investigated the clinical outcomes of rt-CGM initiation in 41,753 participants with insulin-treated diabetes.[18] Of the 41,753 participants, 36,080 had T2D. A summary of patient cohort characteristics is outlined in Table 1, with a more detailed breakdown presented in Supplementary Table S1. Briefly however, at baseline, the patient cohort had a mean HbA1c level of 8.3% (±1.6%), a mean age of 64.5 years (±12.2 years) and a mean body mass index of 33.4 kg/m^2 (±7.5 kg/m^2). The cohort had lived with diabetes for a mean period of 16 years (±8.8 years), and 50.5% of simulated patients were male. Regarding racial and ethnic groups, 43% of the simulated patient cohort were White, 21.6% were Hispanic, 17.9% were Asian, and 10.5% were Black. The remaining 7% of modelled patients were Native American.[18] For any baseline characteristics that were not available from the US-based study, the default CDM values (based on the ACCORD trial) were used instead.[34,35]

A reduction in HbA1c of 0.56% (favoring rt-CGM) was adopted for the treatment effect based on the adjusted mean difference between rt-CGM and SMBG in the same US-based retrospective cohort study used to source cohort baseline characteristics.[18] This reduction was assumed to be sustained for two additional years after the first year in the rt-CGM arm, with the rationale for this assumption stemming from longitudinal study evidence, where glycemic improvements were shown to persist for up to 10 years.[36–38] The annual modeled increase of HbA1c in the SMBG arm after the first year and in the rt-CGM arm after the third year was identical *ie*, +0.15 units *per annum* (based on the CDM default clinical table).

Severe hypoglycemic event (SHE) rates and severe hyperglycemic event (assumed to be diabetic ketoacidosis [DKA]) rates were determined using emergency room visits or hospitalizations recorded by Karter et al.[18] For SHE, there were 0 and 4 events per 100 patient years calculated for RT-CGM and SMBG, respectively. For DKA, there were 0 and 2.5 events per 100 patient years calculated for RT-CGM and SMBG, respectively.

Costs

Where necessary, costs used for this analysis were inflated to EUR 2022 values using the Harmonized Index for Consumer Prices: Health for Spain.[39] Only direct medical costs associated with each intervention were incorporated within the model, with published sources used to identify costs related to concomitant therapies and screening. A recently conducted cost-effectiveness analysis of oral semaglutide set in Spain was used to identify the majority of diabetes-related complication costs,[40] with a full list of these costs outlined in Supplementary Table S2. A guidance document for

Table 1 Baseline Characteristics of the Simulated Patient Cohort

Characteristic	Baseline value
Mean (SD) age, years	64.5 (12.2)
Mean (SD) duration of diabetes, years	16 (8.8)
Proportion male, %	50.5
Mean (SD) HbA1c, %	8.3 (1.6)
Mean (SD) body mass index (kg/m^2)	33.4 (7.5)

Note: Data from Karter et al.[18]
Abbreviations: HbA1c, glycated hemoglobin; SD, standard deviation.

T2D management published by the National Institute for Health and Care Excellence (NICE) was used to source data on drug therapies typically utilized for primary and secondary prevention of cardiovascular and microvascular disease.[41] This document was also used to identify screening rates for ocular and renal disease.

The summarized annual costs and equipment usage for each intervention can be found in Supplementary Table S3. Annual treatment costs specific to rt-CGM therapy were based on the Dexcom ONE system price in Spain, and comprised one receiver, four transmitters, and 36 sensors. No value added tax was factored into the final costs, which amounted to EUR 1100. For SMBG, a cost of EUR 0.29 per test strip was used (again based on the current price listings in Spain), which when considering an assumed 1387 tests *per annum*, resulted in a final annual cost of EUR 402. The 1387 annual test figure was calculated using data sourced from the DIAMOND T2D trial, wherein participants used an average of 3.8 tests per day.[16]

Utilities

All utility and disutility parameters are presented in Supplementary Table S4. For T2D without any associated complications, a utility value of 0.785 was modeled. This value (which is the default value used in the CDM) originated from a review of utility values for economic modelling in T2D, conducted by Beaudet et al.[42] The same study was used to source the majority of utilities and disutilities associated with diabetes-related complications as well as adverse events occurring due to diabetes treatment. A published cost-effectiveness analysis of flash glucose monitoring set in China was used to source one event-related disutility figure, namely a 0.0367 decrement associated with DKA in patients living with T1D.[43]

A utility benefit of 0.03 was assumed for patients modelled within the rt-CGM arm, based on the avoidance of frequent, daily fingerstick testing associated with SMBG. This figure was sourced from Matza et al,[44] a time trade-off study that investigated the difference in utilities associated with alternative blood glucose monitoring approaches. The present analysis additionally considered the avoidance of fear of hypoglycemia (FoH), and the subsequent impact this phenomenon could have on the QoL of the modeled patient cohort, as the prevalence of FoH in patients living with insulin-dependent T2D has been estimated to range between 27.7% and 34%.[45,46] An avoidance of FoH utility value of 0.02536 was therefore also assumed for the rt-CGM group, which when combined with the avoidance of fingerstick testing utility gain, yielded an overall rt-CGM specific utility benefit of 0.05536. This assumption was based on the inclusion of alarm features in rt-CGM devices that are expected to reduce hypoglycemia event occurrence (and therefore FoH) in patients. Briefly, the 0.02536 figure was determined by obtaining respondent scores from the Hypoglycemia Fear Survey conducted as part of the DIAMOND trial,[47] before mapping said data to the EQ-5D using modelling approaches outlined in Currie et al.[48]

Time Horizon, Perspective, and Discounting

The base case analysis was conducted over a remaining lifetime horizon (with a maximum of 50 years) and adopted a Spanish payer perspective. Future costs and effects were discounted annually at a rate of 3%, based on guidelines issued by the European network for Health technology Assessment (EUnetHTA).[49] No official willingness-to-pay (WTP) threshold currently exists in Spain, however EUR 30,000 per QALY is a commonly cited figure across numerous cost-effectiveness studies within this setting.[50,51] Therefore, this analysis also adopted a EUR 30,000 per QALY WTP threshold.

Sensitivity Analyses

The base case analysis was conducted as a probabilistic sensitivity analysis (Figure 1). A wide range of sensitivity analyses were also conducted to explore the impacts of potential variations across numerous model parameter values. These analyses would additionally identify which of the model parameters led to the largest variations in key model outputs, such as QALYs, costs, and subsequent ICUR values. The HbA1c treatment effect (modeled as −0.56% in favor of rt-CGM in the base case), was one such model parameter that was investigated. The chosen variations of ±30% (to −0.728% and −0.392%) and ±40% (−0.784% and −0.336%) were informed by treatment efficacies observed in T2D participant populations as part of the DIAMOND[16] and MOBILE trials.[17]

The base case values for parameters representing QoL benefits associated with the rt-CGM intervention (ie, the combined 0.05536 utility value comprising avoidance of fingerstick testing [AFS] and FoH) were also altered. The modeled scenarios

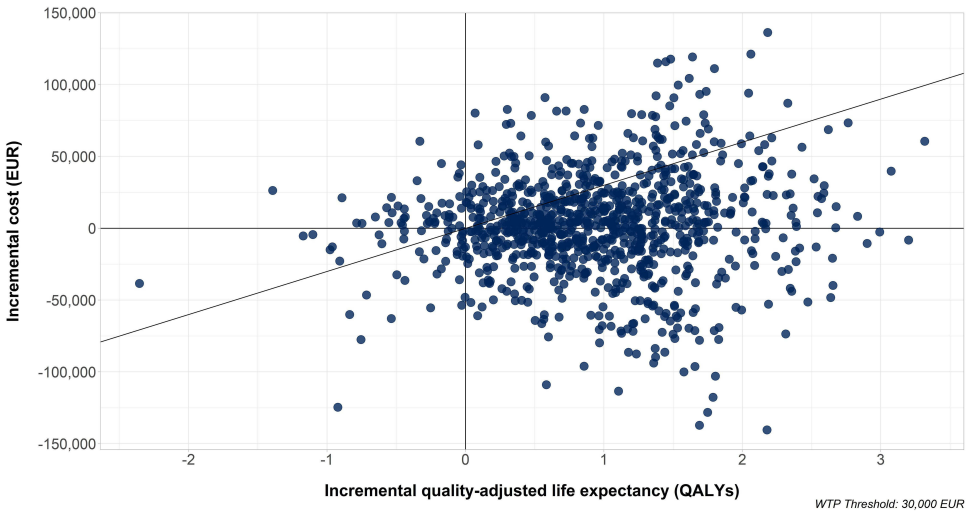

Figure 1 Cost-effectiveness scatterplot from the probabilistic base case analysis.
Abbreviations: EUR, Euro; WTP, willingness-to-pay.

included: −50% AFS benefit (utility: 0.04), +50% AFS benefit (utility: 0.07), no FoH benefit (utility: 0.03), −50% FoH benefit (utility: 0.0425), and finally no FoH or AFS benefit (utility: 0.00).

For SHE in the SMBG arm (which considered 4 SHE per 100 patient years in the base case analysis), the rate was altered by ±50% (ie, 6 SHE and 2 SHE per 100 patient years). However, based on the rationale for the FoH utility incorporation, a 50% reduction in SHE in the SMBG arm would likely lead to an adjacent 50% reduction in FoH utility experienced in the rt-CGM arm. Therefore, the FoH utility value for rt-CGM was 0.0425 within the scenario where a 50% reduction in SHE in the SMBG arm was assumed.

The base case assumption of 3.8 finger-stick tests per day in the SMBG arm was also varied, alternately considering costs associated with 1, 2, 5 and 6 daily tests. Various time horizons were also explored in the sensitivity analyses, with separate analyses conducted over for 1-, 5-, 10-, 20- and 30-year time horizons. Other parameters investigated within the sensitivity analysis included the mean age of the modeled cohort and the duration of diabetes (with the latter also explored as a standalone parameter). Finally, the use of alternative cardiovascular risk prediction equations was also considered—namely the equations from the UKPDS Outcomes Model 82[52]—as well as varied prices for the rt-CGM system.

Projected Clinical Outcomes

The projected cumulative incidence of diabetes complications was used to derive various measures comparing rt-CGM with SMBG; specifically, the relative risk (RR) and number needed to treat (NNT) were calculated and reported. The NNT represents the number of patients who would need to use rt-CGM rather than SMBG in order for one patient to avoid experiencing the complication of interest over the study time frame.[53,54] RRs demonstrate the relative change in risk, irrespective of the absolute incidence. RRs greater than 1 would indicate that the given complication was more likely to occur in patients receiving rt-CGM than in patients receiving SMBG.[55,56] Conversely, RRs below 1 indicate that rt-CGM reduced the risk of patients experiencing the given complication.

Results

Over patient lifetimes, rt-CGM was associated with an additional 0.937 QALYs (9.933 QALYs compared to 8.997 QALYs with SMBG). Rt-CGM was also associated with incremental costs of EUR 2347 (EUR 125,365 versus EUR 123,017 with SMBG). The ICUR for rt-CGM versus SMBG was therefore EUR 2506 per QALY gained, falling well below the WTP threshold of EUR 30,000 per QALY. At this WTP threshold, rt-CGM was 75.9% likely to be cost-effective and 44.9% likely to be cost-saving compared with SMBG (see Table 2 and Figure 2).

Table 2 Summary of Base Case Findings

	rt-CGM	SMBG	Difference
Total mean lifetime costs, EUR	125,364.60	123,017.18	2,347.41
Treatment costs	14,018.73	5,024.77	8,993.96
Management costs	2,308.14	2,239.78	68.36
Cardiovascular complications	22,402.55	22,693.91	−291.36
Renal complications	16,954.14	20,592.42	−3,638.28
Ulcer/amputation/neuropathy complications	68,429.11	69,517.39	−1,088.28
Ophthalmic complications	1,251.94	1,377.16	−125.22
Severe hypoglycemia (requiring medical assistance)	0.00	564.55	−564.55
Adverse Events (including DKA)	0.00	1,007.20	−1,007.20
Mean quality-adjusted life expectancy, QALYs	9.933	8.997	0.937
ICUR, EUR per QALY gained	2,506		
Probability of rt-CGM being cost-effective versus SMBG at a WTP threshold of EUR 30,000 per QALY gained	75.9%		

Abbreviations: DKA, diabetic ketoacidosis; ICUR, incremental cost–utility ratio; QALY, quality-adjusted life year; rt-CGM, real-time continuous glucose monitoring; SMBG, self-monitoring of blood glucose; WTP, willingness-to-pay.

Clinical Outcomes

The cumulative incidence, RR and NNT for each projected diabetes complication is presented in Table 3. Neuropathy and microalbuminuria had the joint lowest NNTs (NNT: 19) followed by background diabetic retinopathy and macular edema (NNT for both: 21). All RRs for rt-CGM versus SMBG were below 1, demonstrating consistently favourable clinical outcomes with rt-CGM. Those complications with the lowest RRs included end-stage renal disease (RR: 0.77), proliferative diabetic retinopathy (RR: 0.78) and gross proteinuria (RR: 0.83). Overall, the analysis projected a reduction in cumulative incidence of ophthalmic, renal, neurological, and cardiovascular events by 16.03%, 13.07%, 7.34%, and 9.09%, respectively, for rt-CGM users.

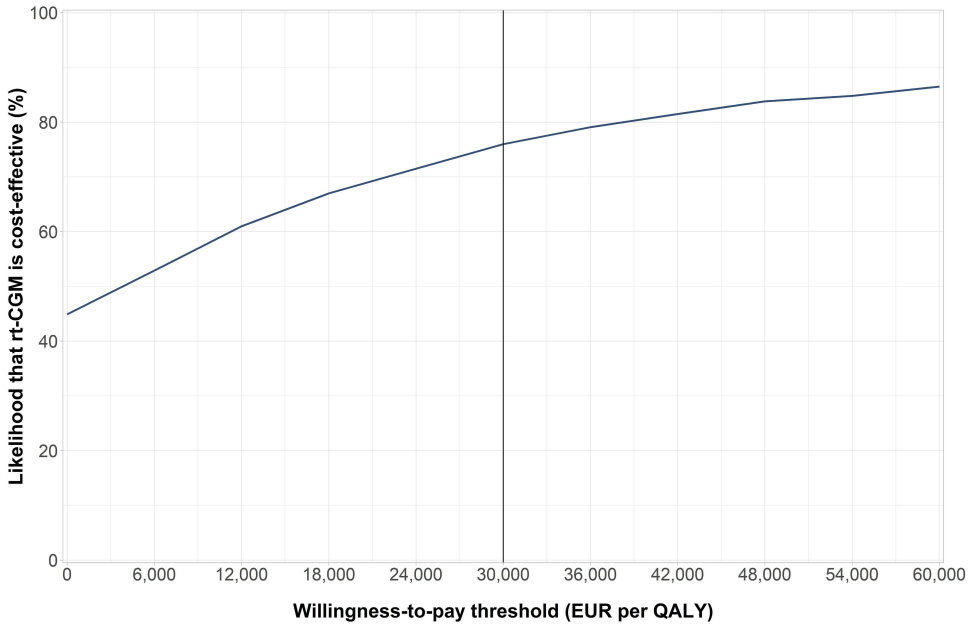

Figure 2 Cost-effectiveness acceptability curve from the probabilistic base case analysis.
Abbreviations: EUR, Euro; QALY, quality-adjusted life year; rt-CGM; real-time continuous glucose monitoring.

Table 3 Projected Diabetes Complications for Insulin-Treated Adult Type 2 Diabetes Patients in Spain: Rt-CGM Vs SMBG

Organ System	Complication	Cumulative Incidence ± SE (%)		Relative Risk (rt-CGM vs SMBG)	Number Needed to Treat (rt-CGM vs SMBG)
		rt-CGM	SMBG		
Ophthalmic	Background diabetic retinopathy	29.34±0.57	34.18±0.60	0.86	21
	Proliferative diabetic retinopathy	9.3±0.25	11.85±0.30	0.78	39
	Macular edema	27.1±0.54	31.8±0.58	0.85	21
	Severe vision loss	21.12±0.41	23.78±0.45	0.89	38
	Cataract	12.4±0.22	13.68±0.24	0.91	78
Renal	Microalbuminuria	29.06±0.58	34.39±0.62	0.85	19
	Gross proteinuria	22.17±0.49	26.7±0.54	0.83	22
	End-stage renal disease	10.66±0.34	13.87±0.40	0.77	31
Cardiovascular	Congestive heart failure	19.6±0.51	20.6±0.52	0.95	100
	Peripheral vascular disease onset	17.35±0.26	19.05±0.28	0.91	59
	Angina	10.63±0.23	11.43±0.24	0.93	125
	Stroke event	11.43±0.32	12.16±0.34	0.94	137
	Stroke fatality	22.08±0.37	24.56±0.39	0.90	40
	Myocardial infarction event	19.45±0.37	20.73±0.36	0.94	78
	Diabetes related mortality	19.02±0.37	20.12±0.40	0.95	91
Extremities	Ulcer	9.13±0.44	10±0.47	0.91	115
	Recurring foot ulcer	18.93±0.33	19.6±0.34	0.97	149
	Amputation from foot ulcer	6.81±0.26	7.13±0.27	0.96	313
	Amputation from recurring foot ulcer	5.97±0.18	6.32±0.20	0.94	286
	Neuropathy	59.17±0.68	64.3±0.65	0.92	19

Abbreviations: tr-CGM: real-time continuous glucose monitoring; SMBG: self-monitoring of blood glucose; SE, standard error.

Sensitivity Analyses

The findings of the analysis were sensitive to changes in assumptions around the following parameters: time horizon, number of SMBG tests per day, mean cohort age (and adjacent duration of diabetes), rt-CGM prices, clinical efficacy based on HbA1c changes and varying QoL utilities. Across all 35 scenarios that were explored, results unanimously showed that rt-CGM was either cost-effective or dominant versus SMBG (Table 4).

Each stepwise reduction in the time horizon from the baseline maximum of 50 years led to the final ICUR value increasing, with a minimum 1-year time horizon scenario yielding the second-highest positive ICUR across all sensitivity analyses conducted of EUR 9022 per QALY gained.

Changes in assumptions around the number of SMBG tests per day also led to significant changes in the ICUR. A testing frequency of 1 daily SMBG test resulted in the ICUR increasing to EUR 6458 per QALY gained. By contrast, when 6 daily SMBG tests were assumed per day, rt-CGM was cost-saving and therefore the dominant intervention.

Reducing the mean baseline cohort age to 55 years, reduced the ICUR to EUR 602 per QALY gained; larger reductions in the ICUR were observed when the mean cohort age was further reduced to 45 years (ICUR: EUR −2066 per QALY gained) or 35 years (ICUR: EUR −4435 per QALY gained). Rt-CGM was associated with cost

Table 4 Summary Findings of Sensitivity Analyses: Rt-CGM versus SMBG

Analysis	Total costs, EUR			Quality-Adjusted Life expectancy, QALYs			ICUR, EUR per QALY Gained
	rt-CGM	SMBG	Difference	rt-CGM	SMBG	Difference	
Base case	125,364.60	123,017.18	2,347.41	9.933	8.997	0.937	2,506
−50% AFS	125,364.60	123,017.18	2,347.41	9.742	8.997	0.746	3,148
+50% AFS	125,364.60	123,017.18	2,347.41	10.125	8.997	1.128	2,081
−50% FoH	125,364.60	123,017.18	2,347.41	9.774	8.997	0.777	3,019
No FoH	125,364.60	123,017.18	2,347.41	9.615	8.997	0.618	3,797
No AFS+FoH	125,364.60	123,017.18	2,347.41	9.232	8.997	0.236	9,955
HbA1c treatment effect −30%	126,625.31	123,017.18	3,608.13	9.894	8.997	0.897	4,020
HbA1c treatment effect +30%	124,541.34	123,017.18	1,524.16	9.980	8.997	0.984	1,549
HbA1c treatment effect −40%	126,957.79	123,017.18	3,940.61	9.890	8.997	0.893	4,412
HbA1c treatment effect +40%	124,118.07	123,017.18	1,100.89	9.987	8.997	0.990	1,112
−50% SHE in SMBG arm and −50% FoH utility in rt-CGM arm	125,079.19	122,679.24	2,399.95	9.770	9.014	0.756	3,174
+50% SHE in SMBG arm	125,079.19	123,240.93	1,838.27	9.929	8.985	0.945	1,946
1-year time horizon	7,045.40	6,532.03	513.37	0.765	0.708	0.057	9,022
5-year time horizon	33,010.97	31,206.36	1,804.61	3.377	3.118	0.259	6,965
10-year time horizon	60,171.27	57,847.74	2,323.53	5.768	5.305	0.463	5,014
20-year time horizon	97,742.59	95,414.26	2,328.32	8.491	7.747	0.745	3,126
30-year time horizon	116,364.45	114,187.25	2,177.20	9.545	8.670	0.874	2,491
UKPDS82 cardiovascular risk equation	91,621.61	88,660.95	2,960.67	7.933	7.196	0.737	4,019
Number of SMBG per day = 1	125,364.60	119,314.72	6,049.88	9.933	8.997	0.937	6,458
Number of SMBG per day = 2	125,364.60	120,637.03	4,727.57	9.933	8.997	0.937	5,047
Number of SMBG per day = 5	125,364.60	124,603.95	760.65	9.933	8.997	0.937	812
Number of SMBG per day = 6	125,364.60	125,926.26	−561.66	9.933	8.997	0.937	−600
Baseline mean age of cohort = 35 years	256,844.36	263,508.66	−6,664.32	16.525	15.022	1.503	−4,435
Baseline mean age of cohort = 45 years	214,876.88	217,660.55	−2,783.66	14.746	13.399	1.347	−2,066
Baseline mean age of cohort = 55 years	168,472.78	167,771.02	701.77	12.457	11.291	1.166	602
1-year duration of diabetes	124,945.78	121,712.54	3,233.23	10.050	9.125	0.925	3,497
5-year duration of diabetes	124,426.57	121,945.66	2,480.91	9.957	9.041	0.916	2,708
10-year duration of diabetes	125,197.90	121,607.94	3,589.96	9.925	8.955	0.970	3,700
Baseline mean age of cohort = 45 years age and 1-year duration of diabetes	216,150.94	216,728.70	−577.76	14.938	13.598	1.339	−431
Baseline mean age of cohort = 55 years age and 10-year duration of diabetes	168,957.09	166,561.55	2,395.57	12.483	11.291	1.192	2,010
rt-CGM annual price +10%	126,766.48	123,017.18	3,749.30	9.933	8.997	0.937	4,001
rt-CGM annual price −10%	123,962.74	123,017.18	945.56	9.933	8.997	0.937	1,009
rt-CGM annual price +15%	127,467.42	123,017.18	4,450.24	9.933	8.997	0.937	4,749
rt-CGM annual price −15%	123,261.80	123,017.18	244.62	9.933	8.997	0.937	261
rt-CGM annual price +20%	128,168.36	123,017.18	5,151.18	9.933	8.997	0.937	5,498
rt-CGM annual price −20%	122,560.86	123,017.18	−456.32	9.933	8.997	0.937	487

Abbreviations: AFS, avoidance of fingerstick testing; EUR, Euro; FoH, fear of hypoglycemia; HbA1c, glycated hemoglobin; ICUR, incremental cost-utility ratio; QALY, quality-adjusted life year; QoL, quality of life; rt-CGM, real-time continuous glucose monitoring; SHE, severe hypoglycemic event; SMBG, self-monitoring of blood glucose; UKPDS, United Kingdom Prospective Diabetes Study.

savings versus SMBG in these younger cohorts, representing the dominant intervention. Rt-CGM remained dominant when a 1-year duration of diabetes was assumed in combination with the mean cohort age of 45 years.

As rt-CGM prices were incrementally increased by 10%, 15% and 20%, the ICUR also gradually increased but rt-CGM remained cost-effective. Conversely, when rt-CGM prices were decreased, the ICUR also decreased, with rt-CGM becoming cost-saving and therefore dominant with a price reduction of 20% (ICUR: EUR −487.00 per QALY gained).

The ICUR increased to EUR 4020 per QALY gained when the HbA1c effect was reduced by 30%, with a 30% increase in the HbA1c effect leading to the ICUR decreasing to EUR 1549 per QALY gained. Similar effects were observed when the HbA1c effect was decreased or increased by 40%, yielding ICURs of EUR 4412 and EUR 1112 per QALY gained, respectively.

Changes to the rt-CGM-specific utility associated with AFS also led to notable changes in the final ICUR. When this utility benefit was reduced by 50%, the ICUR increased to EUR 3148 per QALY gained, whilst a 50% increase in the AFS utility benefit led to a the ICUR reducing to a value of EUR 2081 per QALY gained. A similar relationship was observed with the FoH utility benefit associated with rt-CGM. Specifically, when the FoH utility benefit was reduced by 50%, the ICUR increased to a value of EUR 3019 per QALY gained. Removing the FoH benefit entirely led to the ICUR further increasing to EUR 3797 per QALY gained. The largest ICUR all scenarios was observed when no utility benefits associated with either FoH or AFS were modeled, yielding an ICUR of EUR 9955 per QALY gained, with rt-CGM still representing a cost-effective intervention at the adopted WTP threshold.

Discussion

This analysis sought to determine the cost-utility of rt-CGM versus SMBG in patients living with insulin-treated T2D in Spain. The results showed that rt-CGM was highly likely to be a cost-effective option relative to SMBG, with the base case ICUR of EUR 2506 per QALY gained falling substantially below the WTP threshold of EUR 30,000 per QALY. The results presented here also align with those from previous analyses set in Canada,[20] the UK,[21] and France,[22] where rt-CGM was found to be cost-effective relative to SMBG.

When uncertainties surrounding clinical and cost parameter values were explored across a range of 35 scenarios, rt-CGM was consistently shown to be either cost-effective or dominant versus SMBG. One key finding showed that as the mean baseline age of the modelled cohort was reduced, the ICUR also decreased, with rt-CGM becoming cost-saving and therefore dominant when the mean age at baseline was either 35 years or 45 years. Assuming these modeled findings would transfer to a real-world setting, the results may have a meaningful effect on the future cost-effectiveness profile of rt-CGM versus SMBG, considering that T2D prevalence is estimated to rise considerably in the near future.[1] In particular, incidence and prevalence rates of T2D in young adults, adolescents and children have been observed to be increasing in recent decades, with this trend proving to be consistent across a wide range of patient demographics and ethnicities.[57–60] If current global epidemiological trends persist, the mean age of the worldwide T2D patient population will likely decrease over time, potentially further improving the health economic arguments favoring the use of rt-CGM over SMBG in routine practice. Indeed, results from the projected clinical outcomes also show that rt-CGM would likely play an increasingly significant role in helping to reduce the potentially substantial economic burden of T2D-related complications incurred over time for a younger patient cohort. These trends were also present when changes in assumptions regarding the time horizon of the study were explored; over longer time horizons, simulated patients are exposed to differences in glycemic control for longer periods, and therefore have incremental QoL benefits (with comparatively smaller adjacent gains in incremental cost), thus yielding a lower ICUR value and showing rt-CGM to be increasingly cost-effective.

Sensitivity analyses also revealed that the results were sensitive to changes in assumptions on other model parameters such as rt-CGM prices, HbA1c changes, QoL utilities and number of SMBG tests per day. For the SMBG testing frequency parameter, the base case analysis assumed patients would undergo a mean of 3.8 tests per day, based on findings from the DIAMOND trial.[16] This is a conservative estimate relative to a previous Spanish-based cost analysis of flash glucose monitoring, which considered a mean SMBG testing frequency of 6 tests per day.[23] As the mean number of daily tests in the present analysis was increased to a maximum of 6, rt-CGM became cost-saving and therefore the dominant strategy, owing to the increased total test strip costs associated with a higher testing frequency. However, this scenario (along with the wider exploration of various SMBG testing frequencies) did not account for the likely adjacent QoL impacts associated with changes to the number of daily tests. One such effect is that as patients conduct an increasing number of daily SMBG tests, glycemic control may improve (assuming consistent adherence), thereby ultimately improving QoL and QALY gains by reducing the long-term incidence of diabetes complications.[61] However, multiple studies across various settings have found that SMBG adherence in patients living with both T1D and T2D diabetes is suboptimal.[62–65] A further important caveat is that increased SMBG testing frequency could also

result in additional process disutilities (ie related to the increased testing itself), increased FoH, and potentially other impacts on patients' daily lives arising from the logistics of increased testing frequency. Therefore, any potential QoL gains arising from improvised glycemic control may be offset by the negative QoL impacts incurred due to increased SMBG testing.

A 2021 study similar in design to the present analysis (also set in Spain) focused on costs associated with flash glucose monitoring relative to SMBG, however this study only reported clinical benefits related to reductions in SHE rates.[23] The present analysis sought to evaluate cost-effectiveness based on a broader array of treatment effects, particularly by incorporating improvements in glycemic control that can arise with rt-CGM use versus SMBG, in addition to potential reductions in hypoglycemia incidence. These additional benefits, captured through improvements in HbA1c levels, translated to a reduction in the incidence of microvascular and macrovascular complications with rt-CGM. Specifically, rt-CGM led to a projected reduction in the cumulative incidence of ophthalmic, renal, neurological, and cardiovascular events by 16.03%, 13.07%, 7.34%, and 9.09%, respectively. These effects translated to direct and sustained QALY gains for patients, whilst reducing the substantial financial burden to the Spanish healthcare system arising from long-term management of complications.

Another recent Spanish study found that cardiovascular complications alone in patients with T2D led to longer stays in hospital and a higher mean cost per hospital discharge, compared to the same complications occurring in non-diabetes patients.[66] Productivity losses (for both patients and caregivers) associated with hospitalisation events elevate the costs further still from a societal perspective. Given that incidence trends indicate an ever-younger global cohort with T2D, the potential for rt-CGM to reduce complication incidence over patient lifetimes is likely to provide a continuously growing benefit.

A key strength of the present analysis was the use of clinical data sourced from a real-world study that investigated outcomes associated with the use of rt-CGM versus SMBG in a large subgroup of patients with insulin-treated T2D (n = 36,080).[18] Real-world data provide the potential to yield insights into effect size, which can demonstrate how meaningful observed differences in variables or outcomes between participants across different study groups (eg, rt-CGM users and non-rt -CGM users) can be, as opposed to simply determining whether an effect is present. Given the scale and real-world nature of the Karter et al[18] study that informed the treatment effects in the present analysis, the health economic findings are likely to have practical significance alongside a high degree of generalizability to the population of interest in routine clinical practice.

A second key strength was that all of the cost parameters used within the model were identified from Spanish sources, including a recently conducted Spanish cost–effectiveness study focusing on interventions for diabetes[40] and an official Spanish cost of procedures tariff document,[67] alongside NICE guidelines outlining management pathways for T2D.[41] In some cases, it proved necessary to inflate costs to 2022 EUR, which may have omitted effects of technological developments, economic forces, and legal developments such as loss of patent exclusivity on costs. Nevertheless, any such idiosyncratic price fluctuations not captured by the inflationary adjustments applied in the present analysis would likely only have a minimal effect given the relatively short time periods over which the costs were inflated.

The main limitations of the study were associated with a lack of publicly available and geographically specific data for all model parameters, with the latter specifically being an issue with regards to the patient cohort. One such example of this was the use of a disutility value associated with DKA events that was specific to a patient population living with T1D in China.[43] However, in all cases where proxy data inputs were sought, priority was placed on ensuring said data were as relevant to the study aims as possible, and any potential arising uncertainties were addressed as part of the sensitivity analysis. This limitation was also applicable to the real-world study (Karter et al[18]) that was used to source baseline patient characteristics and clinical efficacy data. The study was conducted within a large sample of patients living with insulin-treated T1D or T2D (N = 41,753), and measured outcomes based on participants' responses to the intervention of interest within this analysis (ie, rt-CGM initiation). Nevertheless, Karter et al[18] was based in the US, whilst the present analysis was conducted in a Spanish setting. The rationale for the use of this robustly conducted proxy-data is that there is currently a lack of similar real-world studies (with a comparably large sample size) set in Spain, or indeed other European countries. This exact approach has been used in a previous study investigating the cost-utility of rt-CGM versus SMBG in patients with insulin-treated T2D in France.[22] Regardless, potential differences between Spanish and US populations (particularly when considering the ethnic profile of the modeled cohort) would still need to be accounted for. The extensive sensitivity analyses conducted were designed with these differences in mind, and aimed to characterize and explore a range of hypothetical scenarios. The results of this study should

still, however, be interpreted with these population differences in mind, as the cost and health outcomes are likely most reflective of people with similar baseline characteristics to those used in the present analysis, with potentially limited generalizability beyond this scope. This limitation is also relevant when considering that the present analysis focused exclusively on patients with T2D receiving insulin therapy. Whilst our results are therefore likely limited to patients with a similar treatment profile, there is emerging evidence on the efficacy of CGM technologies in patients with T2D who are not receiving insulin therapy. However, further research is needed to explore the economic value of CGMs beyond insulin users, and this could be a potential focus for future cost–effectiveness studies.

Conclusion

The present analysis demonstrates that for patients living with insulin-treated T2D in Spain, rt-CGM is highly likely to be a cost-effective intervention relative to SMBG. These results can be used to inform the decision-making processes taken by the Spanish healthcare system, and to facilitate appropriate resource allocation for the optimal management of insulin-treated T2D.

Data Sharing Statement

The present study did not report original data. Data used for modeling were derived from public sources and have been reported in full in the paper and the accompanying online-only Supplemental Material.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

R.F.P. and W.A. are full-time employees, and R.F.P. is a director and shareholder in, Covalence Research Ltd., which has received consulting fees from Dexcom for this analysis and from Dexcom outside the submitted work. S.I., H.A. and G.J. N. are current employees of Dexcom. H.A. and G.N. hold stock or stock options in Dexcom. J.F.MT received consulting fees from Dexcom. The authors report no other conflicts of interest in this work.

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