Research Article

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Cost-utility of real-time continuous glucose monitoring versus self-monitoring of blood glucose in people with insulin-treated Type II diabetes in France

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Aim: Clinical trials and real-world data for Type II diabetes both show that glycated hemoglobin (HbA1c) levels and hypoglycemia occurrence can be reduced by real-time continuous glucose monitoring (rt-CGM) versus self-monitoring of blood glucose (SMBG). The present cost-utility study investigated the long-term health economic outcomes associated with using rt-CGM versus SMBG in people with insulin-treated Type II diabetes in France. **Materials & methods:** Effectiveness data were obtained from a real-world study, which showed rt-CGM reduced HbA1c by 0.56% (6.1 mmol/mol) versus sustained SMBG. Analyses were conducted using the IQVIA Core Diabetes Model. A French payer perspective was adopted over a lifetime horizon for a cohort aged 64.5 years with baseline HbA1c of 8.3% (67 mmol/mol). A willingness-to-pay threshold of €147,093 was used, and future costs and outcomes were discounted at 4% annually. **Results:** The analysis projected quality-adjusted life expectancy was 8.50 quality-adjusted life years (QALYs) for rt-CGM versus 8.03 QALYs for SMBG (difference: 0.47 QALYs), while total mean lifetime costs were €93,978 for rt-CGM versus €82,834 for SMBG (difference: €11,144). This yielded an incremental cost-utility ratio (ICUR) of €23,772 per QALY gained for rt-CGM versus SMBG. Results were particularly sensitive to changes in the treatment effect (i.e., change in HbA1c), annual price and quality of life benefit associated with rt-CGM, SMBG frequency, baseline patient age and complication costs. **Conclusion:** The use of rt-CGM is likely to be cost-effective versus SMBG for people with insulin-treated Type II diabetes in France.

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Keywords: cost-utility • health economics • quality of life • real-time continuous glucose monitoring • Type II diabetes

The prevalence of diabetes in France is estimated to be 6% [1], and the number of people living with the disease has doubled in the last 10 years [2]. Type II diabetes accounts for the vast majority of cases at 92% [3] and, as a progressive disease, patients often have to ultimately take active pharmacological treatments such as insulin to achieve or maintain glycemic control [4].

Given the increase in incidence rates of diabetes and the large number of people affected, the economic burden of the disease in France is substantial [5]. A recent study estimated the total direct cost of diagnosed Type II diabetes in France to be over 8.5 billion Euros (€) [5]. The mean reimbursement paid out by the general health scheme and local schemes for people with insulin-treated diabetes is €12,254, compared with €5234 for people with non-insulin-treated diabetes [6].

The economic burden of diabetes-related complications is significant, and such costs often comprise the majority of medical expenditure in patients with Type II diabetes. Cardiovascular disease is a very common complication [7],

affecting over one quarter of people with diabetes [6]. In addition to treating acute cardiovascular events, cardiovascular complications also lead to higher mean reimbursement for healthcare expenditure related to preventative hypertension and lipid-lowering therapies than for non-diabetic patients (i.e., excess reimbursements due to diabetes). Similarly, diabetes-related renal failure is associated with higher hospital-stay rates and subsequent excess reimbursements, estimated to be €279 million annually for end-stage renal disease in France [6]. Other complications include diabetic foot ulcers and amputations [8], which cost a reported €112 million annually in excess reimbursements, for people living with diabetes in France [6].

Given these substantial costs, there is a need for cost-effective management of diabetes that results in adequate glycemic control and reduces the risk of developing complications. Such management strategies can provide substantial benefits in terms of health-related quality of life (HRQoL) to those living with the disease, while also resulting in more efficient allocation of healthcare budgets. Real-time continuous glucose monitoring (rt-CGM) is one option that has been shown to improve glycemic control in people with insulin-treated diabetes in both randomized controlled trials (RCTs) and in real-world analyses. Specifically, the use of rt-CGM was associated with improvements in both glycated hemoglobin (HbA1c) levels and time in range compared with usual care in the DIAMOND Type II diabetes study and the MOBILE study (conducted in people using basal insulin only) [9,10].

A recent large-scale, US-based real-world study (n = 41,753) in people with insulin-treated type 1 or Type II diabetes examined outcomes in participants using rt-CGM versus those using self-monitoring of blood glucose (SMBG). At baseline, participants across both arms used a range of insulin delivery methods, including pens, pumps and multiple daily injections. Dexcom rt-CGM systems were the primary devices used within the rt-CGM arm. The results mirrored those reported in RCTs [11]; specifically, rt-CGM initiation was associated with a 0.56% (6.1 mmol/mol) reduction in HbA1c (from 8.20% [66 mmol/mol] to 7.64% [60 mmol/mol]) in people with Type II diabetes. Conversely, those individuals continuing on SMBG only experienced an HbA1c reduction of 0.09% (1.0 mmol/mol) during the study period (from 8.27% [67 mmol/mol] to 8.18% [66 mmol/mol]). Rt-CGM use was also linked with reduced hypoglycemia rates, hospitalizations and emergency department visits due to severe hypoglycemia versus SMBG [11]. A recent cost-utility analysis conducted in the UK found that the clinical benefits of rt-CGM translated to improved long-term outcomes for those with insulin-treated Type II diabetes. Additionally, the study found rt-CGM was likely to be cost-effective compared with SMBG [12]. A similar analysis set in Canada reported results that concurred with those from the UK-based study, further demonstrating how the cost–effectiveness associated with rt-CGM devices would likely apply across multiple patient demographics [13].

In France, the national goal is to increase compliance to regular medical and biological monitoring of diabetes and its complications to 80% [14]. However, compliance rates are still well below the 80% regulatory objective for most follow-up examinations, and very low compliance rates persist for HbA1c testing, lipid profile, creatinine, urine albumin, resting EKG, ophthalmologist and dentist consultations in Type II diabetes [14]. Rt-CGM can help people with Type II diabetes achieve at least the metabolic monitoring goal through continuous monitoring of blood glucose; however, access to rt-CGM is currently limited. Therefore, this study aimed to examine the long-term health and economic outcomes associated with the use of rt-CGM relative to SMBG in people with insulin-treated Type II diabetes living in France. Our analysis was based on clinical input data from a US-based real-world study and utilizing relevant French cost data.

Methods

Model structure

A health economic analysis plan was not developed ahead of this study. The published and validated IQVIA CORE Diabetes Model (CDM; version 9.5+ E360) was used to perform the analysis. The CDM is a non-product-specific, patient-level, computer simulation model designed to estimate the cost–effectiveness of diabetes care interventions in people with type 1 or Type II diabetes. The model can be adapted to different countries and regional healthcare settings, with such adaptations made to ensure the model set-up was suitable and relevant, in order to effectively address the current study aims. Details of the model structure and validation have been described in previous publications [15,16]; briefly, the CDM comprises 17 Markovian complication sub-models that can interact with each other when appropriate, to predict long-term outcomes and costs associated with different diabetes treatments. These long-term outcomes comprise both microvascular (retinopathy, nephropathy and diabetic foot) and macrovascular (e.g., stroke and cardiovascular disease) complications, in addition to complication-specific mortality and "non-specific" mortality arising from causes not covered in the other sub-models. Clinical data that inform the probabilities of patients experiencing diabetes complications (e.g., hypoglycemia, renal disease,

Table 1. Baseline characteristics of the simulated patient cohort.

Characteristic	Baseline value		
	Rt-CGM cohort (n = 344)	SMBG cohort (n = 35,736)	Combined cohort (n = 36,080)
Mean (SD) age, years	59.1 (14.5)	64.6 (12.1)	64.5 (12.2)
Mean (SD) duration of diabetes, years	17.1 (11.1)	15.8 (8.8)	15.8 (8.8)
Proportion male, %	52.9	50.4	50.5
Mean HbA1c, mmol/mol	66	67	67
Mean (SD) HbA1c, %	8.20 (1.5)	8.27 (1.6)	8.27 (1.59)
BMI (kg/m^2)	30 (6.6)	33.4 (7.5)	33.4 (7.5)

HbA1c: Glycated hemoglobin; rt-CGM: Real-time continuous glucose monitoring; SD: Standard deviation; SMBG: Self-monitoring of blood glucose.
Sourced from Karter *et al.* [11].

amputation, cardiovascular events, etc.) are built into the model and probabilities can be modified by underlying risk factors including HbA1c, blood pressure and lipids. Key outcomes reported by the CDM included total lifetime direct costs, quality-adjusted life expectancy, projected incidence of complications, and the incremental cost-utility ratio (ICUR).

Baseline cohort characteristics & treatment effects

Baseline characteristics for the simulated patient cohort were obtained from a US-based retrospective cohort study in people with insulin-treated diabetes. The study included a total of 41,753 participants, comprising 36,080 individuals with Type II diabetes and 5673 individuals with Type 1 diabetes, all receiving care from a Northern California integrated healthcare delivery system between 2014 and 2019 [11]. Weighted averages were used to determine combined baseline characteristics for rt-CGM and SMBG users. Where data gaps were identified in the retrospective US study, missing data were sourced from other studies [17–24]. At baseline, the mean (standard deviation) age was 64.5 (12.2) years, mean duration of diabetes was 15.8 (8.8) years, mean HbA1c was 8.3% (1.6%) or 67 mmol/mol and mean BMI was 33.4 (7.5) kg/m^2. A full breakdown of baseline characteristics is presented in Table 1.

Treatment effects and adverse event rates were also obtained from the same US retrospective cohort study [11]. Based on the adjusted mean difference between rt-CGM and SMBG, an HbA1c treatment effect of -0.56% (-6.1 mmol/mol) in favor of rt-CGM was assumed. The analysis assumed a conservative treatment effect duration, namely that the HbA1c effect took place in the first year within the rt-CGM arm, and then HbA1c progressed in both arms by 0.15 units per annum.

Severe hypoglycemic events (SHEs) were defined as those events needing emergency room visits or hospitalizations, and the rate was calculated to be 0 per 100 person-years (0%) in the rt-CGM arm versus 4 per 100 person-years (4%) in the SMBG arm [11]. The analysis also captured diabetic ketoacidosis (DKA) events requiring emergency room visits or hospitalizations; event rates were calculated to be 0 per 100 person-years (0%) with rt-CGM versus 2.5 per 100 person-years (2.5%) with SMBG [11].

Utilities

Patients who had Type II diabetes without complications were assumed to have a baseline utility value of 0.785, which was obtained from Beaudet *et al.* [25], and used as the default CDM value [26]. Quality of life utilities and disutilities associated with diabetes-related complications were obtained from Beaudet *et al.* [25] and Zhao *et al.* [27] (Supplementary Table 1). The disutility associated with DKA [27] (0.0367) was obtained from a study of people with Type 1 diabetes experiencing DKA, as data on DKA disutilities in people with Type II diabetes could not be identified. Based on the avoidance of daily and frequent fingerstick testing, an additional annual utility benefit of 0.03 (sourced from a time trade-off study [28]) was applied in the rt-CGM arm.

Costs

Direct costs of the treatment of diabetes-related complications and concomitant medications were obtained from published sources and inflated to 2021 Euros where necessary (Supplementary Table 2) [29]. The rt-CGM device used in the analysis was the Dexcom G6 rt-CGM device with a price (obtained from the manufacturer in France) of €2280 per year. This cost included a total of 36 sensors and 4 transmitters (as the latter accounted for battery replacement costs), with a breakdown presented in Supplementary Table 3. In the SMBG arm, it was assumed that

patients would take an average of 3.8 tests per day, based on data from the DIAMOND Type II diabetes study [10]. The cost of SMBG (€0.4451 per test) was obtained from a previously conducted health economic analysis set in France [30], with annual costs of SMBG totaling €617.35, again based on a mean assumption of 3.8 tests per day per patient.

Time horizon, perspective, & discounting

A lifetime horizon was used for this analysis (30 years for the base case). Given that the French payer perspective was adopted, only direct medical costs were incorporated. An annual discount rate of 4% was applied to future costs and clinical effects, which was in line with guidelines issued by the Haute Autorité de Santé (HAS) [31]. While no official WTP threshold is published in France, an informal range (€30,000–50,000 per QALY) has previously been proposed [32]. However, a recent study by Téhard *et al.* [33] sought to estimate the value of a statistical QALY (VSQ) in France, using the French value of statistical life (VSL) of €3,000,000. The final estimated VSQ was determined to lie within the range of €147,093 to €201,398. A willingness-to-pay (WTP) threshold of €147,093 per quality-adjusted life year (QALY) was therefore adopted for this study, as recent cost-effectiveness analyses in France frequently use the lower end of informal WTP range values [34–37].

Sensitivity analyses

The base case analysis was conducted using a two-stage Monte Carlo simulation process to enhance the robustness of the probabilistic sensitivity analysis. Initially, a first-order Monte Carlo simulation was employed to generate point estimates for each model parameter, reflecting the direct variability observed in patient data. These point estimates then served as inputs for a second-order Monte Carlo simulation, which was used to explore and quantify the uncertainty surrounding these parameters. This layered approach allowed for a thorough assessment of the impact of both individual variability and parameter uncertainty on the various model outcomes.

A range of one-way sensitivity analyses was also performed to determine key drivers of model outcomes. Parameters selected for sensitivity analyses included the utility benefit arising from reduced fingerstick testing applied to the rt-CGM arm, which was reduced by 50% and 100%, and increased by 50% relative to the base case. A further analysis was conducted in which a utility benefit associated with reduced fear of hypoglycemia (FoH) was captured, as reported in trials such as ALERTT1 [38] and DIAMOND [39] conducted in people with Type 1 diabetes. A FoH utility value was calculated using data from the DIAMOND trial and added to the baseline finger-stick utility value (0.03), yielding a final utility benefit of 0.055 with rt-CGM over SMBG. The influence of the HbA1c treatment effect was also examined in sensitivity analyses; in these analyses, the base case change in HbA1c with rt-CGM versus SMBG (-0.56% [-6.1 mmol/mol] in favor of rt-CGM) was varied by ±50% (to -0.84% [-9.0 mmol/mol] and -0.28% [-2.8 mmol/mol]). Analyses were also performed around the effect of SHE, with both 50% (2 events per 100 person-years) and 100% (4 events per 100 person-years) of the SHE rates in the SMBG arm captured in the rt-CGM arm. The time horizon, mean age of the simulated patient cohort, complication costs, annual rt-CGM prices, and number of SMBG tests performed per day, were also explored in sensitivity analyses.

Projected clinical outcomes

Finally, modeled clinical outcomes were used to calculate numbers needed to treat (NNT) and relative risks (RR) of each complication with rt-CGM versus SMBG. NNT values illustrate the expected number of patients who would need to receive rt-CGM rather than SMBG for one additional person to avoid the complication of interest over the specified study time frame [40]. Lower NNT values therefore reflect increased effectiveness of rt-CGM in reducing the incidence of the specified clinical outcome. RRs illustrate the relative likelihood of a complication occurring in patients receiving rt-CGM versus patients receiving SMBG, with values below 1 indicating the complication is less likely to occur in the rt-CGM group, and vice versa [41]. Both values were reported as RRs provide information about the relative reduction in risk, regardless of absolute incidence rates; conversely, NNTs are influenced by absolute incidence and may therefore be less instructive for changes in less common outcomes that may nevertheless effect major changes in cost and patient quality of life (QoL).

Results

The base case analysis comparing rt-CGM with SMBG showed that quality-adjusted life expectancy was estimated to be 8.50 QALYs with rt-CGM and 8.03 QALYs with SMBG, with rt-CMG resulting in an incremental gain of

Table 2. Summary of base case findings.

	rt-CGM	SMBG	Difference
Total mean lifetime costs, €	93,978	82,834	11,144
Treatment costs	25,345	6788	18,557
Management costs	1429	1404	25
Cardiovascular complications	14,448	14,566	-118
Renal complications	26,669	30,095	-3426
Ulcer/amputation/neuropathy complications	6751	6881	-130
Ophthalmic complications	19,337	20,038	-701
Severe hypoglycemia (requiring medical assistance)	0	1913	-1913
Adverse events (includes ketoacidosis)	0	1150	-1150
Mean quality-adjusted life expectancy, QALYs	8.50	8.03	0.47
ICUR, € per QALY gained	23,772		
Probability of rt-CGM being cost-effective vs SMBG at a WTP threshold of €147,093 per QALY gained	77.5%		

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.

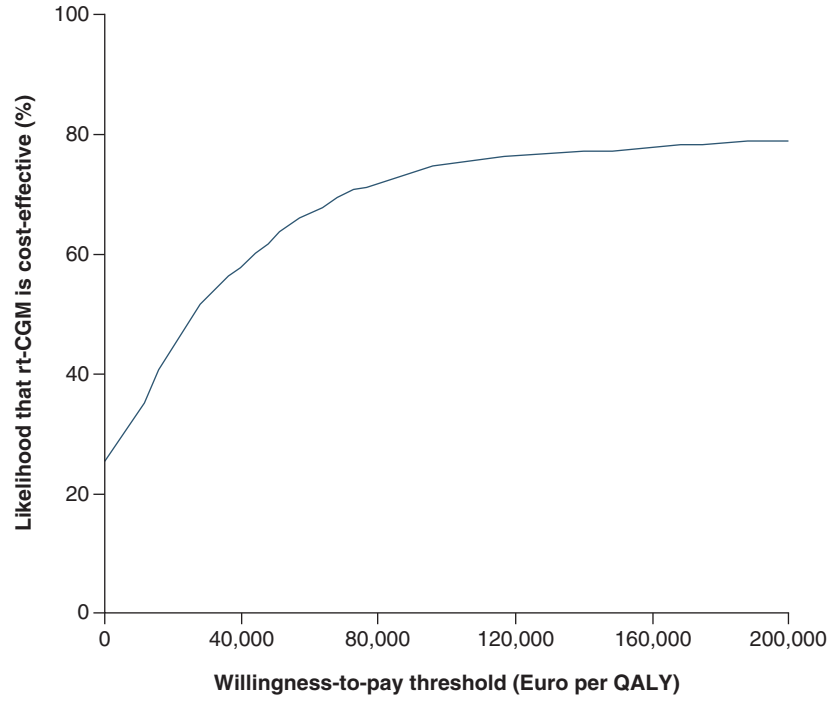

Figure 1. Cost-effectiveness scatterplot from the probabilistic base case analysis.
QALY: Quality-adjusted life year; rt-CGM: Real-time continuous glucose monitoring.

0.47 QALYs versus SMBG (Table 2). Total lifetime costs were €93,978 for the rt-CGM arm and €82,834 for the SMBG arm. Although rt-CGM incurred higher total lifetime testing and treatment costs versus SMBG (€25,345 vs €6788), total mean lifetime complication costs were lower with rt-CGM (Table 2). The combination of higher lifetime costs with increased quality-adjusted life expectancy resulted in an ICUR of €23,772 per QALY gained for rt-CGM versus SMBG. Probabilistic sensitivity analysis results for the base case are outlined in Figure 1, and showed that at a WTP threshold of €147,093 per QALY gained, the likelihood of rt-CGM being considered cost-effective relative to SMBG was 77.5% (Figure 2). The probability of rt-CGM being cost-saving versus SMBG (irrespective of the adjacent effect on QALYs) at this threshold was 25.2%.

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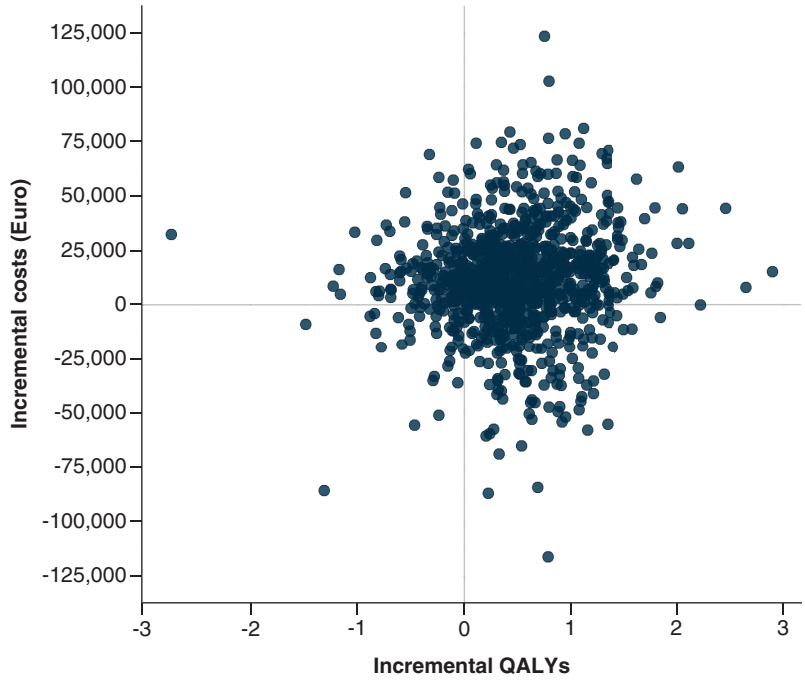

Figure 2. Cost-effectiveness acceptability curve from the probabilistic base case analysis.
QALYs: Quality-adjusted life years.

Clinical outcomes

The projected incidence of diabetes complications with rt-CGM and SMBG, alongside the respective NNT and RR figures can be found in Supplementary Table 4. Complications with the lowest NNTs included neuropathy (NNT: 26), background diabetic retinopathy (NNT: 28), macular edema (NNT: 30) and microalbuminuria (NNT: 30). All RR values were below 1.0, and complications with the lowest RR (i.e., most favorable to rt-CGM) included proliferative diabetic retinopathy (RR: 0.77), end-stage renal disease (RR: 0.81), gross proteinuria (RR: 0.86) and microalbuminuria (RR: 0.87).

Sensitivity analyses

Sensitivity analyses showed that base case results were most sensitive to changes in assumptions around the QoL benefits associated with the use of rt-CGM, the HbA1c treatment effect, the number of SMBG tests performed per day, baseline cohort age, time horizon, complication costs and the annual price of rt-CGM (Table 3). The utility benefit associated with the use of rt-CGM had the highest impact on the ICUR. Specifically, when this benefit was reduced by 50%, the incremental gain in quality-adjusted life expectancy with rt-CGM was reduced to 0.302 QALYs (versus 0.47 QALYs in the base case), resulting in an ICUR of €36,902 per QALY gained. When an additional QoL benefit associated with reduced FoH was incorporated into the analysis [39], the incremental quality-adjusted life expectancy gain with rt-CGM increased to 0.751 QALYs, which in turn resulted a lower ICUR of €14,845 per QALY gained.

Regarding the treatment effect, in the base case analysis, the use of rt-CGM was assumed to reduce HbA1c by -0.56% (-6.1 mmol/mol) relative to the use of SMBG. However, if this benefit was reduced by 50% to -0.28% (-2.8 mmol/mol), the ICUR increased to €31,552 per QALY gained. Similarly, if the benefit was increased by 50% to -0.84% (9.0 mmol/mol), the final ICUR decreased significantly to €18,065 per QALY gained. The ICUR was also sensitive to the frequency of daily SMBG in the comparator arm, where a mean frequency of one SMBG test per day led to an ICUR of €34,441 per QALY gained. The ICUR continued to decrease gradually as the number of SMBG tests was increased to a maximum of four, which yielded an ICUR of €23,010 per QALY gained. The mean age at baseline of the simulated patient cohort had a large influence on the results. Specifically, rt-CGM was found to be more cost-effective versus SMBG in younger cohorts; where mean baseline age was 30 years, the ICUR dropped to €3794 per QALY gained, increasing at 40 years of age (ICUR of €10,940 per QALY gained) and

Table 3. Summary findings of sensitivity analyses rt-CGM versus SMBG.

Analysis	Total costs, €			Quality-adjusted life expectancy, QALYs			ICUR, € per QALY gained
	rt-CGM	SMBG	Difference	rt-CGM	SMBG	Difference	
Base case	93,978	82,834	11,144	8.50	8.03	0.47	23,772
QoL benefit with rt-CGM -50%	93,978	82,834	11,144	8.33	8.03	0.30	36,902
QoL benefit with rt-CGM +50%	93,978	82,834	11,144	8.70	8.03	0.67	17,536
Added QoL benefit for reduced FoH with rt-CGM	93,978	82,834	11,144	8.81	8.03	0.75	14,845
HbA1c treatment effect -50%	95,849	82,834	13,015	8.50	8.03	0.41	31,552
HbA1c treatment effect +50%	92,067	82,834	9,233	8.54	8.03	0.52	18,065
rt-CGM SHE rate 50% of SMBG rate	94,948	82,834	12,114	8.52	8.03	0.46	26,601
rt-CGM SHE rate 100% of SMBG rate	95,918	82,834	13,084	8.47	8.03	0.44	29,596
SMBG per day, n = 1	93,978	77,832	16,145	8.50	8.03	0.47	34,441
SMBG per day, n = 2	93,978	79,619	14,359	8.50	8.03	0.47	30,630
SMBG per day, n = 3	93,978	81,405	12,573	8.50	8.03	0.47	26,820
SMBG per day, n = 4	93,978	83,191	10,787	8.50	8.03	0.47	23,010
Time horizon = 10 years	48,026	39,774	8,252	5.39	5.13	0.26	31,937
Time horizon = 15 years	65,183	55,171	10,011	6.80	6.46	0.35	28,885
Time horizon = 20 years	78,159	67,666	10,493	7.68	7.28	0.40	26,050
Baseline mean age 30 years	271,928	269,000	2,928	14.73	13.96	0.77	3794
Baseline mean age 40 years	210,766	202,860	7,906	13.36	12.63	0.72	10,940
Baseline mean age 50 years	154,548	143,952	10,596	11.49	10.88	0.61	17,323
Complication costs -20%	80,250	67,505	12,745	8.50	8.03	0.47	27,187
Complication costs +20%	107,705	97,865	9,839	8.50	8.03	0.47	20,988
rt-CGM annual price -15%	90,176	82,834	7,342	8.50	8.03	0.47	15,663
rt-CGM annual price -25%	87,642	82,834	4,808	8.50	8.03	0.47	10,256
rt-CGM annual price -35%	85,107	82,834	2,273	8.50	8.03	0.47	4850
rt-CGM annual price -45%	82,573	82,834	-261	8.50	8.03	0.47	Dominant
rt-CGM annual price -55%	80,039	82,834	-2,795	8.50	8.03	0.47	Dominant
rt-CGM annual price -65%	77,504	82,834	-5,330	8.50	8.03	0.47	Dominant

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.

50 years of age (ICUR of €17,323 per QALY gained). A 20% reduction in complication costs led to an ICUR of €27,187 per QALY gained, while a 20% increase in costs led to an ICUR of €20,988 per QALY gained.

Finally, although the effects of increased SHE rates (50% and 100% of the SMBG arm rate, respectively) in the rt-CGM arm were explored, the impact on the final ICUR was relatively small versus other parameters. Specifically, an increase in the rt-CGM arm to 50% of the SMBG arm SHE rate resulted in an ICUR of €26,601 per QALY gained. Comparatively, an increase in the rt-CGM arm to 100% of the SHE rate in the SMBG arm (i.e., equivalent SHE rates) led to an ICUR of €29,596 per QALY gained.

Discussion

The present study showed that, for people with insulin-treated Type II diabetes meeting the criteria for the use of rt-CGM, the use of rt-CGM is likely to be cost-effective versus SMBG in France. The base case analysis showed that patients switching from SMBG to rt-CGM were likely to see an incremental gain in quality-adjusted life expectancy of 0.47 QALYs. Furthermore, these patients would also likely experience an increase in their lifetime treatment cost of €11,144. The final ICUR would therefore be €23,772 per QALY gained, significantly lower than the €147,093 per QALY gained WTP threshold. Indeed, even when considering a lower, more recently-determined (i.e., after this analysis was conducted) French WTP range of €27,847 and €112,586 per QALY, the base case ICUR still falls below this threshold [42]. However, the likelihood of rt-CGM being considered cost-effective relative to SMBG for this updated threshold is likely to be lower than the 77.5% reported in the base case analysis.

Sensitivity analysis results showed that the final ICUR was sensitive to changes in a number of model parameters, including the QoL benefit associated with the use of rt-CGM, the HbA1c treatment effect, number of SMBG tests

per day, baseline cohort age, time horizon, complication costs and the annual price of rt-CGM. Results showed that rt-CGM was increasingly cost-effective as the assumed SMBG test frequency was increased. However, while the results showed rt-CGM to be cost-effective at a threshold of €147,093 per QALY assuming mean daily SMBG tests were 3.8 [10], routine clinical practice may affect the generalizability of these results. Specifically, while most experts recommend SMBG at least four-times a day for people with insulin-treated diabetes [43], adherence in a real-world setting may be significantly lower. One study in particular found that adherence to SMBG was 61.6% in a cohort of 2257 people on insulin therapy [44]. Reductions in adherence would likely result in smaller and less consistent HbA1c improvements in patients using SMBG, suggesting that the 0.47 QALY gain reported in the base case analysis may be a conservative estimate of the benefits of rt-CGM. Furthermore, the real-world SMBG adherence data highlight a key benefit of rt-CGM compared with SMBG with regards to achieving monitoring goals. Conversely, reduced adherence also reduces the (short-term) costs associated with SMBG testing; sensitivity analyses around the cost of SMBG testing showed that when the mean number of daily SMBG tests was reduced to two or lower, the resultant ICUR for rt-CGM versus SMBG was still lower than the WTP threshold of €147,093 per QALY. Additionally, these analyses did not capture the likely reduction in the long-term QALY outcomes that would likely be associated with reduced SMBG testing frequency. Even when capturing the lower costs associated with reduced SMBG testing frequency without any change in the QALY benefit, the final ICUR for rt-CGM versus SMBG was still well below a WTP of 147,093 (Table 3). One related limitation of the sensitivity analyses was that the link between more frequent SMBG testing and HbA1c level improvements was also not considered. Data from a multicenter study in Europe highlights the significance of the link between SMBG and HbA1c [45]. However, the potential utility gains arising from HbA1c improvements associated with increased SMBG testing frequency may be at least partially offset by the disutility incurred as a result of increased testing.

Results indicated that the lower the mean patient age, the more cost-effective rt-CGM was likely to be. The likely explanation for this was that more QoL benefits would be accumulated over a relatively longer time-horizon for younger people with Type II diabetes. This finding is relevant given that data from a 2014 French study determined that the incidence of diabetes is increasing, with cases doubling in 10 years [2]. Additionally, combined type 1 and Type II diabetes incidence was found to be 289 per 100,000 inhabitants in 2006 [46], corresponding to 178,000 new cases. Although a more recent study found results that suggest diabetes incidence is decreasing, prevalence data still showed an increase, with 12.1% of men and 8.4% of women having diabetes [47]. In concordance with these findings, the Manitoba Center for Health Policy found that the mean age of diabetes diagnosis has decreased by four years (59 to 55) from 1985 to 2017 [48]. This in turn strengthens the likelihood of rt-CGM being potentially more cost-effective than our results have outlined, particularly if current epidemiological trends persist in France.

While our analysis included disutilities associated with SHEs, the rates of SHEs were low. This was most likely due to the stringent definitions used, i.e., SHE was defined as an event requiring either an emergency room visit or hospitalization. Hypoglycemic events that require assistance from a patient's family member or friends can also possess significant costs and QoL impacts. However, the study used as the source for the SHE disutility defined SHE as an event requiring third-party assistance, and therefore this value is likely to encompass the wider scope required. Non-severe hypoglycemic events were also excluded from the analyses, but these account for 88–98% of all hypoglycemic events, and have been shown to affect functioning, QoL, healthcare resource use and work productivity [49–53]. The analyses also excluded indirect costs attributable to hypoglycemic events, as well as the quantification of the time spent in SMBG procedures, which would likely comprise a substantial economic burden to patients and the healthcare system. Given these exclusions, if a societal perspective were adopted, it is plausible that our findings would demonstrate an under-estimation of the likely cost–effectiveness of rt-CGM versus SMBG.

This study had some limitations and strengths. A major strength of our study was the use of real-world clinical data from a large sample of people with Type II diabetes. The use of real-world studies allow the incorporation of a wide variety of treatment-related aspects. These aspects in particular comprise adherence, efficacy, disease management, and concurrent health condition impacts. An important aspect to note is that the real-world study used was based in the US (Karter *et al.* [11]) whereas the present study was set in France. However, given the lack of similar real-world studies set in France, the use of a US-based study was deemed appropriate as it represented the best available evidence and also benefitted from a large study population. This was in part due to the fact that Karter *et al.* [11] represented a closed healthcare system with unified coverage criteria. Such a system resembles the French setting, which is predominantly state-funded and offers nearly universal coverage. Furthermore, glucose sensor technology measures glucose in interstitial fluid, while also integrating various features for effective diabetes management, and these core functionalities and physiological interactions remain consistent regardless of nationality or ethnicity.

Nevertheless, several sensitivity analyses were conducted to evaluate a range of baseline cohort characteristics and treatment effects, which were designed to characterize any differences between the French and US populations. Our results may still, however, be limited in their generalizability beyond people with similar baseline characteristics as those used in the present analyses. A final note with regards to the use of Karter *et al.* [11] data is that the observational nature of said retrospective cohort study meant that some findings could be still susceptible to selection bias, due to residual confounders that could not be accounted for by the robust methods incorporated (such as overlap weighting). The results of our study should therefore be interpreted with this in mind.

Another limitation was the lack of recently-published data, particularly concerning costs. While all costs were inflated to 2021 values, recent innovations in diagnostic or treatment technology may mean that newer costs relating to these procedures may not have been captured.

Due to lack of available clinical data, a range of relevant studies were used to source adequate proxy inputs for the economic analysis. One such example was the use of the -0.0367 disutility value for ketoacidosis, which was derived from a Type 1 diabetes patient cohort. However, in cases where clinical data pertaining exactly to our simulated cohort were unavailable, the study team sourced suitable, robustly-conducted studies using relevant patient groups (i.e., patients with Type 1 diabetes) to retrieve proxy data.

Finally, this analysis assumed a 100% usage and success rate for the rt-CGM intervention. While in routine practice these devices may be associated with issues stemming from sensor failures, removals or injuries [54], these issues are likely to be transient in nature as they can be rectified with relative ease, with the manufacturer (not the payer) bearing the burden of replacement costs. Therefore, the inclusion of costs associated with said failures would likely result in minimal changes to the final results (and subsequent conclusions) presented here.

Conclusion

Further work investigating the cost–effectiveness of rt-CGM relative to SMBG in broader patient populations could be conducted, with a particular view to confirming the finding of sensitivity analyses which showed that rt-CGM would likely be more cost-effective in younger people with insulin-treated Type II diabetes. Regardless, the present findings should be applicable to populations with similar baseline characteristics, demonstrating that, as in the UK [12], rt-CGM is likely to represent a cost-effective use of healthcare expenditure versus SMBG in people with insulin-treated Type II diabetes in France.

Summary points

- A cost-utility analysis was conducted to examine the cost–effectiveness of real-time continuous glucose monitoring (rt-CGM) versus self-monitoring of blood glucose (SMBG) in people with insulin-treated Type II diabetes living in France.
- The extensively validated IQVIA CORE Diabetes Model (CDM; version 9.5+ E360) was used to conduct the relevant analyses.
- Clinical data used for the model was primarily sourced from a US-based real world study.
- Costs were measured in 2021 Euros, and a willingness-to-pay (WTP) threshold of €147,093 per quality-adjusted life year (QALY) was used.
- Future costs and effects were discounted at 4% per annum, and a lifetime horizon of 30 years was used for the base case analysis.
- Rt-CGM was associated with 0.47 incremental QALY gains, as well as incremental cost gains of €11,144.
- This yielded an incremental cost-utility ratio (ICUR) of €23,772 per QALY gained for rt-CGM versus SMBG, which was below the WTP threshold of €147,093 per QALY.
- The use of rt-CGM is therefore likely to be cost-effective versus SMBG for people with insulin-treated Type II diabetes in France.

Supplementary data

To view the supplementary data that accompany this paper please visit the journal website at: https://bpl-prod.literatumonline.com/doi/10.57264/cer-2023-0174

Author contributions

H Alshannaq, PM Lynch and GJ Norman conceived of the study. S Roze designed the analyses and conducted the analyses. W Ahmed and RF Pollock drafted the manuscript. All authors contributed to data interpretation and all authors reviewed and edited the manuscript. All authors approved the final version of the manuscript.

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Competing interests disclosure

S Roze is a current employee of Vyoo Agency, which has received consulting fees from Dexcom for this analysis and from Dexcom outside the submitted work. RF Pollock and W Ahmed are full-time employees, and RF Pollock 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. H Alshannaq, PM Lynch and GJ Norman are current employees of Dexcom. GJ Norman and PM Lynch hold stock or stock options in Dexcom. M Joubert has performed clinical trials and/or has provided advisory/speaking services and/or has received research grants from Abbott, Air Liquide Santé International, Amgen, Astrazeneca, Bayer, BMS, Boehringer-Ingelheim, Dexcom, Glooko, Lifescan, Lilly, LVL, Medtronic, MSD, Nestle Home Care, NovoNordisk, Orkyn, Roche Diabetes, Sanofi, Vitalaire, Voluntis. The authors have no other competing interests or relevant affiliations with any organization or entity with the subject matter or materials discussed in the manuscript apart from those disclosed.

Writing disclosure

No writing assistance was utilized in the production of this manuscript.

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.

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