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ORIGINAL RESEARCH

Cost-Effectiveness of the FreeStyle Libre® System Versus Blood Glucose Self-Monitoring in Individuals with Type 2 Diabetes on Insulin Treatment in Sweden

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ABSTRACT

Introduction: Frequent glucose monitoring is essential to obtain glucose control. This is done by periodic self-monitoring of blood glucose (SMBG) using finger-prick testing, or by using continuous glucose monitoring devices, wherein a sensor records interstitial glucose data automatically. This study assessed the cost-effectiveness of using the FreeStyle Libre Flash Continuous Glucose Monitoring System (FSL) compared to SMBG in individuals with type 2 diabetes (T2D) treated with insulin from a Swedish societal perspective.

Methods: Cost-effectiveness analysis was conducted using the IQVIA Core Diabetes model v9.5, with demographic and clinical inputs from a real-world study using Swedish National Diabetes Register data. Two cohorts of individuals with T2D were considered based on baseline HbA1C (HbA1c: 8–9% [64–75 mmol/mol]; HbA1c: 9–12% [75–108 mmol/mol]). HbA1c reductions with FSL were − 0.41% (− 4 mmol/mol; SD: 0.94%-10 mmol/mol) and − 1.30% (− 14 mmol/mol; SD: 1.40%-15 mmol/mol) for the two cohorts, respectively. Utilities, treatment costs and diabetes-related complication costs were obtained from published sources. Analyses were conducted over a lifetime horizon, applying annual discounting of 3% on costs and effects. Scenario analyses and probabilistic sensitivity analyses were performed.

Results: Individuals with T2D who had a baseline HbA1c of 8–9% (64–75 mmol/mol) and 9–12% (75–108 mmol/mol) and used FSL gained 0.50 and 0.57 quality-adjusted life-years (QALYs), respectively, at an incremental cost of SEK109,957 and SEK82,170 compared to SMBG, generating an incremental cost-utility ratio of SEK219,127 and SEK144,412 per QALY gained.

Ann-Marie Svensson is deceased.

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Assuming a willingness-to-pay threshold of SEK300,000 per QALY gained, FSL use was considered cost-effective compared to SMBG for the majority of the individuals in both the lower and higher HbA1c cohorts. The key driver identified was the additional quality-of-life benefit that applied to FSL use.

Conclusion: The FreeStyle Libre Flash Continuous Glucose Monitoring System is a cost-effective glucose monitoring alternative to SMBG for individuals with T2D in Sweden who are treated with insulin but are not reaching their glycaemic goals.

Keywords: Continuous glucose monitoring; Cost-effectiveness; FreeStyle Libre flash continuous glucose monitoring system; Type 2 diabetes; Core diabetes model

Key Summary Points

Why carry out this study?

The economic burden of long-term diabetic complications in type 2 diabetes (T2D) is substantial, and Sweden bears one of the highest diabetes-related expenditures.

Frequent assessment of glucose levels is critical since poor glycaemic control is one of the key drivers of the total cost related to T2D.

The FreeStyle Libre® Flash Continuous Glucose Monitoring System (FSL) is a user-friendly sensor-based monitoring system that generates detailed glucose data needed for holistic glycaemic control.

The long-term cost-effectiveness of FSL in comparison to SMBG was assessed in individuals with T2D in Sweden who were treated with insulin but did not reach their glycaemic goals.

What was learned from the study?

Assuming a willingness to pay threshold of SEK300,000 per QALY gained, FSL has a more than 50% probability of being a cost-effective disease management option compared to SMBG.

Results were consistent irrespective of whether the patients had a baseline HbA1c of 8–9% (64–75 mmol/mol) or 9–12% (75–108 mmol/mol).

A key factor driving the cost-effectiveness in favour of FSL was the additional quality-of-life benefit that applied to FSL use compared to SMBG use.

INTRODUCTION

Type 2 diabetes (T2D) and its complications are a significant cause of mortality and disability. Globally, around 9.3% of adults aged 20–75 years are reported to have diabetes, of whom approximately 90% are diagnosed with T2D [1]. In Sweden, the prevalence of diabetes in adults has been reported to be 7.2% [1]. Poor glycaemic control can lead to an increased burden of long-term diabetes complications, which is considered to be the key driver of the total cost related to T2D [2–4]. In Sweden alone, diabetes complications amounted to €1,317 per individual with diabetes in 2016 [5].

To improve glycaemic control, frequent testing of glucose levels via glucometers, self-monitoring of blood glucose (SMBG) and continuous glucose monitoring have been shown to be critical in detecting and reducing the risk of hypoglycaemia and hyperglycaemia requiring hospitalisation or diabetic ketoacidosis [6–9]. However, SMBG only provides sporadic data and can be inconvenient to patients [10, 11]. SMBG provides glucose data for only a single time point, with no glucose information between measurements, making it difficult to interpret the data.

The FreeStyle Libre® Flash Continuous Glucose Monitoring System (FSL; Abbott Diabetes Care, Witney, UK) is a sensor-based monitoring system that provides a user-friendly approach to generate the detailed glucose data needed for holistic glycaemic control. It uses a sensor that is worn by the individual and continuously monitors interstitial glucose levels. A reader or smartphone app scans the sensor to obtain the current glucose value, trends and variability and

to access data from the previous 8-h period. A meta-analysis assessing clinical trials and real-world studies has shown improvement in glycaemic levels with the use of flash glucose monitoring in individuals with type 1 diabetes (T1D) or T2D [12].

The FSL has been evaluated in comparison to SMBG in two pivotal trials, the IMPACT trial [13] in T1D and the REPLACE trial [14] in T2D. In the REPLACE trial, although there was no difference ($p = 0.8222$) in the primary outcome of change in HbA1c at 6 months between FSL and SMBG for the full analysis set, a significant reduction of 27.7% in hypoglycaemic episodes was observed in the FSL group compared to the SMBG group ($p = 0.0164$). Additionally, individuals aged under 65 years showed a significantly greater reduction in HbA1c in the FSL group compared to the SMBG group ($p = 0.0301$).

Several studies have demonstrated that people with diabetes have a better experience using FSL than they do with SMBG, since a scan using FSL is not only less stressful, painless and easier to understand [15], but it is also less time-consuming than traditional SMBG [16]. Further, a time trade-off analysis reported a significantly higher utility value for diabetes glucose monitoring using FSL compared with SMBG, suggesting that the use of FSL is associated with an improvement in health-related quality of life [17].

In addition, several real-world studies have demonstrated the effectiveness of flash glucose monitoring in individuals with T2D. A recently published prospective observational study found that it led to significant reductions in HbA1c, rate of hospitalisation and work absenteeism, and that it improved quality-of-life measures [18]. Findings from large retrospective studies have also reported similar clinical outcomes [19]. Recent analyses showed significant reductions in diabetes-related events and all-cause hospitalisations among adults with T2D using flash glucose monitoring [9, 19]. An assessment of hospitalisation for acute diabetes-related complications using the French national claims database showed a decrease in hospitalisation for hypoglycaemia (− 10.8%) as well as for hyperglycaemia (− 26.5%) among individuals with T2D. A recent real-world study using the Swedish National Diabetes Register (SweNDR) also demonstrated a significant reduction in HbA1c in individuals with T1D or T2D (−0.44 for T1D and −0.66 for T2D) who were using FSL [20, 21].

The economic burden of long-term diabetic complications in T2D is substantial. Sweden bears one of the highest diabetes-related expenditures, and was ranked fifth globally in mean health expenditure per adult (20–75 years) with diabetes in 2019 ($6643) [1]. A recent (2020) study by Andersson et al. also demonstrated that 75% of the total costs of hospital-based care are attributable to T2D [5]. Further, the costs of absences from work were found to be greater than those of hospital-based care, implying the need to consider treatment consequences from a societal perspective in Sweden [5]. Being an advanced technology, FSL is on the market at a higher cost than SMBG. Given the potential benefits associated with the device, the current study aimed to assess the long-term cost-effectiveness of FSL in comparison to SMBG in individuals with T2D who were treated with insulin but did not achieve their glycaemic goals.

METHODS

Modelling Approach

This study was performed using version 9.5 of the IQVIA Core Diabetes Model (IQVIA CDM). The IQVIA CDM is a non-product-specific diabetes policy analysis tool that was developed to determine the long-term health outcomes and economic consequences associated with interventions for T1D and T2D. The model includes a series of interdependent Markov sub-models that perform real-time simulations of the progression of diabetes-related complications and associated mortality. The model captures the cumulative incidence of complications, rates of clinical events, per-patient costs, life-years gained and quality-adjusted life-years (QALYs) gained over a lifelong time horizon. The model has been described previously and extensively

validated against clinical and epidemiological studies [22, 23].

The present analyses took a Swedish societal perspective, evaluating both direct and indirect costs and effects over a lifetime horizon (up to 40 years). Costs and effects were discounted at 3% according to Swedish guidance [24]. All analyses were run with 1000 individuals for 1000 iterations.

This cost-effectiveness analysis is based on a previously conducted real-world study for which the authors obtained ethical committee approval. This study was submitted to the Swedish Ethical Review Authority, Etikprovningsmyndigheten (ref. no. Dnr 2020-06565).

Model Inputs

Population

The target population comprised individuals with T2D receiving insulin as background therapy for a minimum of 6 months and naïve to FSL at study initiation [20, 21]. The present analysis included two different cohorts of individuals with T2D: one with HbA1c values of 8–9% (64–75 mmol/mol; average 8.5% or 69.4 mmol/mol) and the other with HbA1c values of 9–12% (75–108 mmol/mol). Baseline characteristics for the two cohorts used in the model were derived from a real-world study using SweNDR [20, 21], which included nationwide data on individuals with T2D who were treated with insulin (mainly by multiple daily injections, and a few by continuous subcutaneous insulin infusion) for a minimum of 6 months. Missing baseline characteristics were obtained from the REPLACE trial [14], and were already used in a previous cost-effectiveness analysis of FSL in Sweden [25]. Starting age was 57 years, average duration of diabetes was 13 years, and 67% of the population were males. A summary of the baseline characteristics of individuals in the model is provided in Supplementary Table S1.

Clinical Inputs

Intervention Effect The data on the effect on HbA1c of using the FreeStyle Libre system was sourced from the SweNDR real-world study, which reported a reduction in HbA1c level of – 0.41% (−4 mmol/mol) and –1.30% (−14 mmol/mol) in individuals with HbA1c values of 8–9% (64–75 mmol/mol) and 9–12% (75–108 mmol/mol), respectively [20] (Table 1). Since it was a single-arm study, the immediate impact of SMBG on HbA1c was assumed to be zero, as it was considered a continuation of the previous therapy. It was assumed that there were no other changes in the other risk factors (lipids, blood pressure, body mass index, smoking habits), as they were not reported in the study. The progression over time of HbA1c in the base case was predicted using the United Kingdom Prospective Diabetes Study (UKPDS) 68 progression equation [26]. A scenario analysis was also run using the SweNDR progression equation. The progressions over time of blood pressure and lipid levels beyond year 1 were estimated using the UKPDS and Framingham derived equations available as defaults in the IQVIA CDM.

Adverse Events The main adverse event captured in the model is hypoglycaemia. Hypoglycaemic events were defined as either non-severe (they do not require third-party assistance) or severe (they require third-party medical or non-medical assistance). The rate for severe hypoglycaemic events was sourced from a published meta-analysis [27] and assumed to be the same for both the FSL and the SMBG arms. The estimates for the non-severe hypoglycaemia rate reported in the same meta-analysis were used for SMBG. To estimate the non-severe hypoglycaemic event (NSHE) rate for FSL, the SMBG event rate was reduced by 27.7%, based on the relative effect of FSL, as observed in the REPLACE trial [14]. A summary of intervention effects and adverse event data for the included intervention strategies is provided in Table 1.

Costs

As the societal perspective was taken, both direct costs and costs due to productivity loss were taken into account. Treatment-related costs differed between the two arms because the dose of insulin used and the number of SMBG tests varied. The lowest costs of pharmaceuticals, glucose monitor test strips and lancets

Table 1 Treatment effects

	Required values		Units/ range	Reference/notes
	FSL (SD)	SMBG		
Physiological parameters				
Change in baseline HbA1c in individuals with HbA1c 8–9% (64–75 mmol/mol)	− 0.41 (0.94)	0.00	%-points	Eeg-Olofsson et al. 2020 [20]
	−4 (10)		mmol/mol	
Change in baseline HbA1c in individuals with HbA1c 9–12% (75–108 mmol/mol)	− 1.30 (1.40)	0.00	%-points	Eeg-Olofsson et al. 2020 [20]
	−14 (15)		mmol/mol	
Adverse events				
Non-severe hypoglycaemic event rate	1685.00	2331.00	/100 pt. yrs	Calculated based on the REPLACE trial [14] and Edridge et al. 2015 [27]
Severe hypoglycaemia 1 event rate (req. non. med. assist.)	0.00	0.00	/100 pt. yrs	
Severe hypoglycaemia 2 event rate (req. med. assist.)	105.00	105.00	/100 pt. yrs	Calculated based on the REPLACE trial [14] and Edridge et al. 2015 [27]

HbA1c haemoglobin A1C, *FSL* FreeStyle Libre Flash Continuous Glucose Monitoring System, *Pt yrs* patient-years, *SMBG* self-monitoring of blood glucose, *SD* standard deviation

available from the Swedish Dental and Pharmaceutical Benefits Agency (TLV) were considered [28]. Table 2 summarises the unit costs and total annual costs of various interventions used in the model.

The cost of diabetes-related complications was sourced from the previously mentioned health economic analysis of FSL using the CDM [25] (Supplementary Table S2). The average salary for males and females and workdays lost due to complications and adverse events were also considered (Supplementary Table S3).

All costs were inflated to March 2020 using the consumer price index for Sweden from the Organisation for Economic Co-operation and Development [29].

Utility

The non-severe hypoglycaemia event disutility values for the FSL and SMBG arms were calculated using a previously published diminishing disutilities approach [30]. The literature shows that for the first few minor hypoglycaemic events, individuals experience relatively high disutilities; the disutility per event diminishes as the individual starts having more events. In addition, an intervention-related health utility benefit of 0.03 was applied to the FSL arm [17] (Supplementary Table S4).

Analytical Approach

Base Case Analysis

The base case analysis compared the cost-effectiveness of FSL with that of SMBG in two different cohorts of individuals with T2D who were on insulin, one with starting HbA1c values of 8–9% (64–75 mmol/mol; average 8.5% or 69.4 mmol/mol) and the other with starting HbA1c values of 9–12% (75–108 mmol/mol) for a lifetime horizon (40 years). To predict

Table 2 Intervention costs

Cost parameter	Required values (SEK)	Source
Intervention unit costs		
Insulin (Abasaglar Kwikpen, 10-pack) (per unit injection pen)	0.30	Tariff 2019-11-28
Metformin (per 500-mg tablet)	0.23	
FSL sensor	420	
Reader (reimbursed every 2 years)	599	
FSL (per test strip)	2.40	
SMBG (per test strip)	2.40	
Lancet	0.23	
Extra physician visits	1427	Sodra Regionvardsnamnden 2014 [37]
Total annual costs		
FSL intervention costs for first year	22,500	Sensors (26 × SEK420.00) + readers (SEK599.00/2) + insulin (85.2 units/day × SEK0.3/ per unit × 365.25) + 1500 mg metformin (SEK0.23 per 500 mg tablet × 3 × 365.25) + 0.3 strips per day (SEK2.4 × 0.3 × 365.25) + lancets (SEK0.23 × 0.3 × 365.25) + extra physician visit (SEK1426.59)
FSL intervention costs from second year onwards	21,074	Sensors (26 × SEK420.00) + readers (SEK599.00/2) + insulin (85.2 units/day × SEK0.3/ per unit × 365.25) + 1500 mg metformin (SEK0.23 per 500 mg tablet × 3 × 365.25) + 0.3 strips per day (SEK2.4 × 0.3 × 365.25) + lancets (SEK2.4 × 0.3 × 365.25)
SMBG comparator costs	12,503	Insulin (87.8 units/day × SEK0.3/per unit × 365.25) + 3 strips per day (SEK2.4 × 3 × 365.25) + lancets (SEK2.4 × 3 × 365.25) + 1500 mg metformin (SEK0.23 per 500 mg tablet × 3 × 365.25)

FSL FreeStyle Libre Flash Continuous Glucose Monitoring System, *OAD* oral antidiabetic drug, *SEK* Swedish Krona, *SMBG* self-monitoring of blood glucose

cardiovascular (CV) outcomes, the SweNDR T2D CV risk equation programmed into the IQVIA CDM was used in the base case analysis. Moreover, Sweden-specific life tables were used to predict non-specific mortality. These mortality rates represented the risk of death not covered in the complication and adverse event sub-models of the CDM.

For all simulations, the minimum approach method was applied to calculate the QALYs, wherein the utility value assigned was the lowest of the different comorbid conditions for individuals with multiple comorbidities. Thus, it was assumed that the disutility for comorbidities is not additive.

Uncertainty

Scenario Analyses As extrapolation of long-term clinical outcomes is associated with uncertainty, scenario analyses were conducted to evaluate how changes to key parameters in the modelling analyses impact the results of the base case analyses. Details of the scenarios are presented in Supplementary Table S5.

One of the scenarios explored the impact of using the SweNDR progression equation instead of UKPDS equation for HbA1c progression. In another scenario, inputs were varied based on the published study by Yaron et al. (2019) [31]. In this scenario, the baseline HbA1c and a lower annual insulin dose as reported by Yaron et al. (2019) [31] were applied. The change in HbA1c was –0.85% (0.45) for FSL and –0.32% (0.39) for SMBG, and NSHE rates with FSL (170/100 patient-years) and SMBG (197/100 patient-years) were used. Other scenario analyses included the impact of a decrease in the price of the FSL sensor from SEK420 (base case) to SEK405 with no FSL reader cost, altering discount rates to 0% and 5%, shortening the time horizon of the analyses to 5 years and 10 years, reducing treatment-related utility benefit to 0, reducing treatment-related change in HbA1c to 0%, changing the CV risk equation to UKPDS 82 [32] and including additional resource utilisation costs associated with SMBG only for the first year and for all years.

Probabilistic Sensitivity Analysis Probabilistic sensitivity analyses (PSA) were performed using Monte Carlo simulations together with a non-parametric bootstrapping approach to determine parameter uncertainty around cost-effectiveness outcomes. The parameters included in the PSA are the per individual characteristics, treatment efficacy, utility, and cost of complications. Log normal distributions and 10% variation were applied to sample the costs of complications. Treatment effects were sampled based on the estimated standard error (SE) detailed in Table 1. The utility data were varied according to the variability reported as standard deviation values in Supplementary Table S4. All were sampled following the beta distribution. To sample individuals' baseline characteristics, truncated normal distributions with the mean and SE reported in Supplementary Table S1 were used. Results are presented in the cost-effectiveness plane and as cost-effectiveness acceptability curves (CEAC).

RESULTS

Base Case Analysis

FreeStyle Libre Flash Continuous Glucose Monitoring System use provided additional life-years (LYs) (0.03) and higher QALYs (0.50) and total costs (SEK109,957) in individuals with T2D who had HbA1c values of 8–9% (64–75 mmol/mol), generating an estimated incremental cost-utility ratio (ICUR) of SEK219,127 per QALY gained. In individuals with HbA1c values of 9–12% (75–108 mmol/mol), the use of FSL resulted in higher LY (0.13), QALYs (0.57), and total costs (SEK82,170), generating an estimated ICUR of SEK144,412 per QALY gained. Assuming a willingness-to-pay (WTP)/accept threshold of SEK300,000 per QALY gained, the use of FSL can be considered cost-effective over a lifetime compared with SMBG. The results of the base case analysis are presented in Table 3.

For both cohorts, the base case analysis showed that higher direct and combined costs accrued for individuals using FSL over a lifetime compared with SMBG, which was mainly attributed to the higher treatment cost of FSL (Supplementary Fig. S1).

In terms of clinical outcomes, use of FSL was associated with lower risks of renal disease, CV disease, eye disease, ulcer, amputation, neuropathy, and hypoglycaemia over a lifetime as compared to SMBG (Supplementary Table S6). The analysis also showed comparable survival over time for users of FSL and users of SMBG.

Scenario Analyses

Reducing the cost of FSL resulted in a lower ICUR value than in the base case (HbA1c 8–9% [64–75 mmol/mol]: SEK200,140; HbA1c 9–12% [75–108 mmol/mol]: SEK127,935). Altering the discount rate to 0% yielded higher ICUR values (HbA1c 8–9% [64–75 mmol/mol]: SEK222,616

Table 3 Cost-effectiveness results of the base case analysis

	HbA1c 8–9% (64–75 mmol/mol)		HbA1c 9–12% (75–108 mmol/mol)	
	FSL arm	SMBG arm	FSL arm	SMBG arm
LY (years)	13.24	13.20	13.01	12.88
QALY (years)	8.18	7.68	8.02	7.46
Total cost (SEK)	1,849,767	1,739,809	1,878,221	1,796,050
Comparison intervention vs. comparator				
Incremental LY	0.03		0.13	
Incremental QALY	0.50		0.57	
Incremental costs (SEK)	109,958		82,171	
ICER (SEK/LY gained)	3,342,179		645,489	
ICUR (SEK/QALY gained)	219,127		144,412	

FSL FreeStyle Libre Flash Continuous Glucose Monitoring System, *HbA1c* haemoglobin A1C, *ICER* incremental cost-effectiveness ratio, *ICUR* incremental cost-utility ratio, *LY* life-year, *QALY* quality-adjusted life-year, *SEK* Swedish Krona, *SMBG* self-monitoring of blood glucose

and HbA1c 9–12% [75–108 mmol/mol]: SEK151,823 per QALY gained) whereas altering the discount rate to 5% yielded lower ICUR values (HbA1c 8–9% [64–75 mmol/mol]: SEK217,142; HbA1c 9–12% [75–108 mmol/mol]: SEK139,805) in comparison to the base case in both cohorts. In the scenario where the impact of using the SweNDR progression equation instead of the UKPDS equation for HbA1c progression was explored, the LY and QALY increased marginally with a slightly lower cost, resulting in an increase in the ICUR value as compared to the base case (HbA1c 8–9% [64–75 mmol/mol]: SEK241,834; HbA1c 9–12% [75–108 mmol/mol]: SEK198,757). Reducing the time horizon to 5 years and 10 years, respectively, led to lower ICUR values as compared to the base case in both cohorts (5 years: HbA1c 8–9% [64–75 mmol/mol]: SEK205,579, HbA1c 9–12% [75–108 mmol/mol]: SEK98,481; 10 years: HbA1c 8–9% [64–75 mmol/mol]: SEK206,799, HbA1c 9–12% [75–108 mmol/mol]: SEK105,944).

The impact of removing the treatment utility benefit for FSL from the analysis was also tested. This generated a high ICUR in both cohorts (HbA1c 8–9% [64–75 mmol/mol]: SEK1,259,538; HbA1c 9–12% [75–108 mmol/mol]: SEK510,060); these ICURs were above the SEK300,000 threshold but within the identified potential threshold reported for Sweden (e.g. SEK208,000–827,000 per QALY in Persson (2010) [33]).

Removing the impact of FSL on HbA1c increased the ICUR to SEK252,576 and SEK252,639 for the two cohorts.

Applying a different CV risk equation (UKPDS 82) increased the ICUR to SEK220,508 and SEK158,846 in the HbA1c 8–9% (64–75 mmol/mol) and HbA1c 9–12% (75–108 mmol/mol) cohorts, respectively, in comparison to the base case. When the resource utilisation cost of SMBG for the first year of treatment was considered, it yielded lower ICUR values (HbA1c 8–9% [64–75 mmol/mol]: SEK194,571; HbA1c 9–12% [75–108 mmol/mol]: SEK121,735 per QALY gained) than in the base case. The results were consistent when the resource utilisation costs for the SMBG arm were extended beyond the first year.

Finally, the impact of varying the inputs based on the published study by Yaron et al. (2019) [31] (starting age 67 years, duration of diabetes 22 years, HbA1c 8.52% [70 mmol/mol])

Table 4 Cost-effectiveness results of scenario analyses

Scenarios	HbA1c 8–9% (64–75 mmol/mol)	HbA1c 9–12% (75–108 mmol/mol)
Scenario A: Decreased FSL cost		
Incremental cost (SEK)	100,430	72,795
ICUR (SEK/QALY gained)	200,140	127,935
Scenario B: Discount 0%		
Incremental cost (SEK)	156,165	120,244
ICUR (SEK/QALY gained)	222,616	151,823
Scenario B: Discount 5%		
Incremental cost (SEK)	90,006	65,764
ICUR (SEK/QALY gained)	217,142	139,805
Scenario C: Applying different HbA1c progression equation		
Incremental cost (SEK)	124,133	106,792
ICUR (SEK/QALY gained)	241,834	198,757
Scenario D: Time horizon: 5 years		
Incremental cost (SEK)	32,605	17,096
ICUR (SEK/QALY gained)	205,579	98,481
Scenario D: Time horizon: 10 years		
Incremental cost (SEK)	59,145	34,803
ICUR (SEK/QALY gained)	206,799	105,944
Scenario E: Treatment-related utility benefit in FSL arm		
Incremental cost (SEK)	109,958	82,171
ICUR (SEK/QALY gained)	1,259,538	510,060
Scenario F: Applying different CV risk equation		
Incremental cost (SEK)	128,071	102,058
ICUR (SEK/QALY gained)	220,508	158,846
Scenario G: Considering resource utilisation cost in SMBG for first year		
Incremental cost (SEK)	97,636	69,267
ICUR (SEK/QALY gained)	194,571	121,735
Scenario H: Considering impact of resource utilisation difference on all years		
Incremental cost (SEK)	−62,878	−87,339
ICUR (SEK/QALY gained)	Dominant	Dominant
Scenario I: Considering inputs from Yaron et al. [31]		
Incremental cost (SEK)	92,049	
ICUR (SEK/QALY gained)	254,912	

Table 4 continued

Scenarios	HbA1c 8–9% (64–75 mmol/mol)	HbA1c 9–12% (75–108 mmol/mol)
Scenario J: Assuming no HbA1C reduction with FSL		
Incremental cost (SEK)	119,544	116,870
ICUR (SEK/QALY gained)	252,576	252,639

CV cardiovascular, *FSL* FreeStyle Libre Flash Continuous Glucose Monitoring System, *HbA1c* haemoglobin A1C, *SEK* Swedish Krona, *SMBG* self-monitoring of blood glucose

generated an estimated ICUR of SEK254,912 per QALY gained.

Overall, in all scenario analyses (except for that in which the utility benefits of FSL were lowered to 0.00), FSL remained cost-effective as compared to standard SMBG at a threshold of SEK300,000 per QALY gained in individuals with T2D on insulin treatment. The results of the scenario analyses are detailed in Table 4.

Probabilistic Sensitivity Analysis

In the cohort with HbA1c values of 8–9% (64–75 mmol/mol), the probability of FSL being cost-effective at the defined WTP threshold of SEK300,000 per QALY gained was 54% (Fig. 1). In the cohort with HbA1c values of 9–12% (75–108 mmol/mol), the probability of the FreeStyle Libre system being cost-effective at the defined WTP threshold of SEK300,000 per QALY gained was 58% (Fig. 1).

DISCUSSION

The current health economic analysis evaluated the long-term economic and clinical outcomes of the FreeStyle Libre Flash Continuous Glucose Monitoring System in comparison to SMBG in Swedish individuals with T2D who were treated with insulin but could not achieve their glycaemic goals. The analyses were conducted using real-world data.

The base case analysis showed that the FSL led to better health outcomes than SMBG over a lifetime, albeit at a higher cost. In the cohort with HbA1c values of 8–9% (64–75 mmol/mol), use of FSL provided additional LYs (0.03) and QALYs (0.50) at an incremental cost of SEK109,957 compared to SMBG. Similarly, in the cohort with HbA1c values of 9–12% (75–108 mmol/mol), use of FSL resulted in gains in LY (0.13) and QALY (0.57) at an incremental cost of SEK82,170 compared to SMBG. Thus, the ICURs remained well within the identified potential threshold range for Sweden based on the literature (i.e. SEK330,000–827,000 per QALY in Persson (2010) [33]: SEK208,000–625,000 per QALY based on the World Health Organization recommendation [34]) when combined costs were considered. Therefore, the use of FSL can be considered cost-effective over a lifetime as compared to standard SMBG glucose monitoring. The current analyses confirm the previously published work in which the cost-effectiveness was studied based on the REPLACE randomised clinical trial [25].

When the UKPDS 68 HbA1c progression equation was used in the base case, there was a small decrease in HbA1c in the first year, even though no direct treatment effect was applied to SMBG; also, although the use of FSL was associated with a significant HbA1c reduction in the first year, both curves converged over time (Fig. 2). When the SweNDR HbA1c progression equation was used, HbA1c also decreased significantly in the SMBG arm. Nevertheless, the conclusions regarding cost-effectiveness remain similar. We also conducted an analysis removing the impact of FSL on HbA1c, and the cost-effectiveness was maintained.

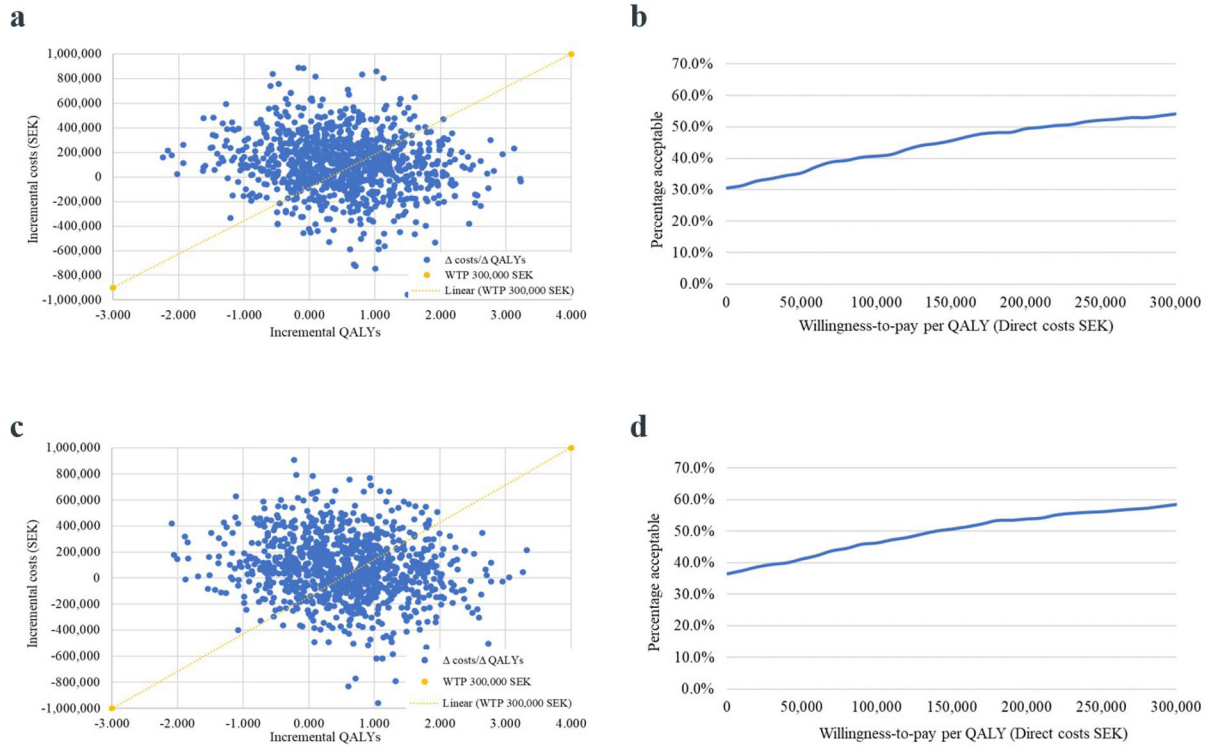

Fig. 1 Cost-effectiveness scatterplots and acceptability. **a** Cost-effectiveness plane for the base case analysis of the cohort with HbA1c values of 8–9% (64–75 mmol/mol) (QALY). **b** Cost-effectiveness acceptability curve for the base case analysis of the cohort with HbA1c values of 8–9% (64–75 mmol/mol) (QALY). **c** Cost-effectiveness plane for the base case analysis of the cohort with HbA1c values of 9–12% (75–108 mmol/mol) (QALY). **d** Cost-effectiveness acceptability curve for the base case analysis of the cohort with HbA1c values of 9–12% (75–108 mmol/mol) (QALY). *QALY* quality-adjusted life year, *SEK* Swedish Krona, *WTP* willingness to pay

To examine the impacts of key assumptions on the base case results, additional scenario analyses were conducted. The results remained robust to explorations of almost all the examined alternate inputs. In all scenario analyses (except when the utility benefits of FSL were lowered to 0.00), the FSL remained cost-effective as compared to standard SMBG glucose monitoring at a threshold of SEK300,000 per QALY gained. However, when the utility benefits of FSL were removed, the treatment was no longer cost-effective. Nevertheless, not having to finger-prick can make the treatment more convenient and less stressful/painful for the individual. Previous studies using CDM have found that the cost-effectiveness of interventions for T2D is driven primarily by HbA1c, although the impact of hypoglycaemia can also be significant [35, 36]. Here, we have shown that applying a utility increment is also impactful.

The PSA findings showed that FSL was cost-effective compared to SMBG in 54% of the simulations for the cohort of T2D individuals on insulin treatment with HbA1c values of 8–9% (64–75 mmol/mol), and in 58% of the simulations for the cohort with HbA1c values of 9–12% (75–108 mmol/mol).

There are certain limitations pertaining to the present analysis. Firstly, the analysis simplified the treatment pathway of individuals by assuming there is no step-up therapy in those individuals, and as such, glucose monitoring and insulin use do not change over time. Long-term real-world data are needed to clarify changes in glucose monitoring or medication

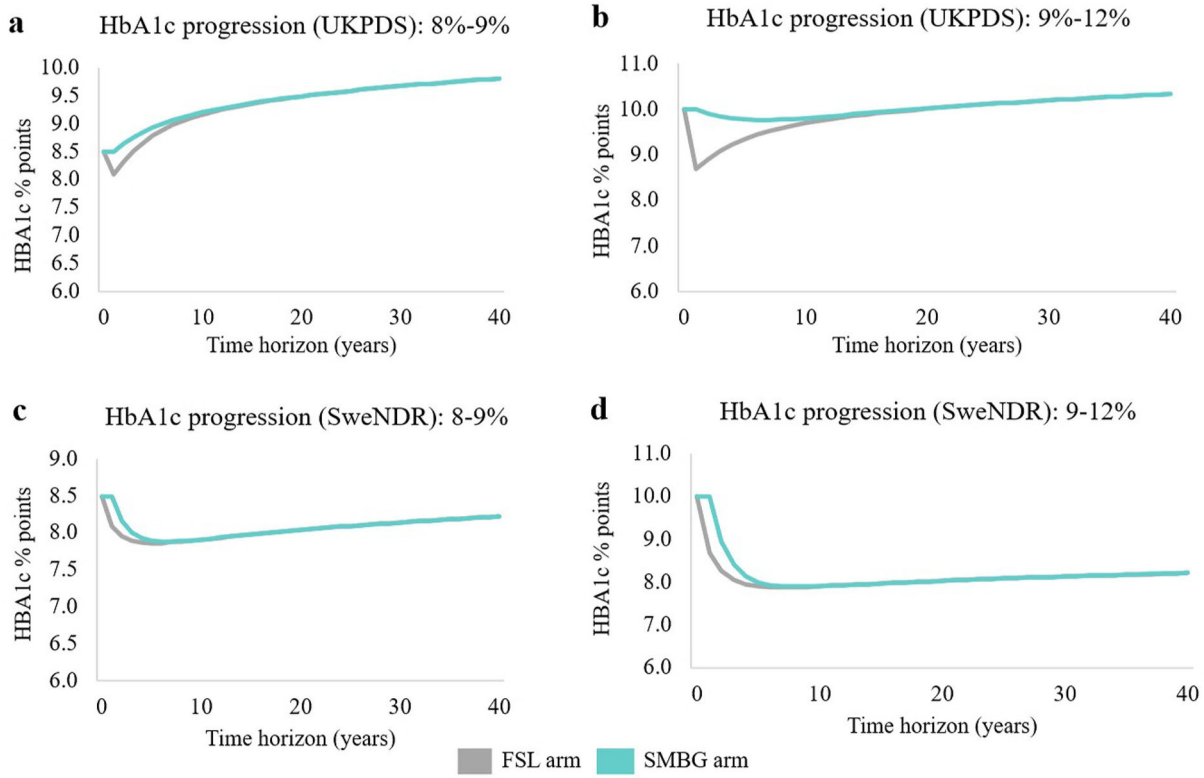

Fig. 2 Progression of HbA1c over time in the base case analysis. **a** Progression of HbA1c over time under UKPDS (base case) for the cohort with HbA1c values of 8–9% (64–75 mmol/mol). **b** Progression of HbA1c over time under UKPDS (base case) for the cohort with HbA1c values of 9–12% (75–108 mmol/mol). **c** Progression of HbA1c over time under SweNDR (scenario analysis) for the cohort with HbA1c values of 8–9% (64–75 mmol/mol). **d** Progression of HbA1c over time under SweNDR (scenario analysis) for the cohort with HbA1c values of 9–12% (75–108 mmol/mol). *FSL* FreeStyle Libre Flash Continuous Glucose Monitoring System, *HbA1c* haemoglobin A1C, *SMBG* self-monitoring of blood glucose, *SweNDR* Swedish National Diabetes Register, *UKPDS* United Kingdom Prospective Diabetes Study

based on the use of flash glucose monitoring and SMBG. For instance, the possible impacts of alternatives to the current algorithm on the precise lifetime costs and QALY of the model cohort are unknown. Secondly, this analysis assumed that NSHEs have no effect on the risk of subsequent severe hypoglycaemia as well as CV events and mortality, which may have led to a greater reduction in severe events with FSL than predicted. Another possible limitation was that the rate of use of strips and lancets with FSL was set at 0.3/d, which could be much more than what users are actually using. The same could be said about the three tests per day in the SMBG arm: it was less than that recommended by treatment guidelines, but it may be more than the number performed in a real-life setting. Thus, if the utilisation of strips and lancets was increased to meet the guidelines, the costs in the SMBG arm would further increase, improving the results in favour of FSL. Also, hypoglycaemic events were not captured in the real-life study, and as such, event rates were assumed to be the same as in the previous cost-effectiveness analyses. Lastly, it is also worth noting that the model inputs for a reduction in baseline HbA1c were based on a single-arm real-world study, and such observations are likely to overestimate the treatment effect in the absence of a control group. However, a scenario analysis

showed that the impact of this assumption was small.

Nevertheless, one of the main strengths of this study is that the current analysis utilized baseline characteristics and effects on HbA1c that are representative of the individuals using FSL in the real-world setting in Sweden. Moreover, a Swedish CV risk equation was used in the cost-effectiveness analysis.

CONCLUSION

The FreeStyle Libre Flash Continuous Glucose Monitoring System is associated with improvements in clinical outcomes for Sweden-based patients with T2D on insulin who are not reaching their glycaemic goals. Taking the model assumptions into consideration, FSL has a more than 50% probability of being a cost-effective disease management option compared to SMBG, based on a WTP threshold of SEK300,000 per QALY gained. Sensitivity and scenario analyses confirmed the robustness of the analysis.

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Compliance with Ethics Guidelines. This cost-effectiveness analysis is based on a previously conducted real world study for which the authors obtained ethical committee approval. This study was submitted to the Swedish Ethical Review Authority, Etikprovningsmyndigheten, (ref. no. Dnr 2020-06565).

Data Availability. All data generated or analysed during this study are included in this published article/as supplementary information files.

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