



ORIGINAL RESEARCH

Cost Analysis of FreeStyle Libre® 2 System in Type 2 Diabetes Mellitus Population

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ABSTRACT

Introduction: FreeStyle Libre® 2 system is a sensor-based flash-monitoring system that measures interstitial fluid glucose. The study aimed to compare cost of FreeStyle Libre 2 system and self-monitoring of blood glucose (SMBG) in the type 2 diabetes mellitus (T2DM) population from the Spanish Health System perspective.

Methods: On the basis of data collected from a literature review, the cost of glucose monitoring

was modelled for patients with T2DM on a basal-bolus insulin regimen. The cost estimate included annual consumption for glucose monitoring (strips, lancets and sensors) and severe hypoglycaemic events (SHE) management. A published rate of SHE (2.5 episodes/patient-year) was considered. A reduction of SHE (– 48.8%) associated with FreeStyle Libre 2 system, derived from the REPLACE trial, was applied. Hospital attendance for 20.5% of SHEs (with subsequent hospitalization in 16.0%) was applied. Consumption of strips and lancets was set at 6/day for SMBG (derived from national monitoring recommen-

The shape of the circle sensor unit, FreeStyle, Libre, and related brand marks are owned by Abbott.

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dations), and 0.2/day for FreeStyle Libre 2 system users, with 26 FreeStyle Libre 2 sensors/year. Unitary costs (€, year 2020 excluding VAT) were derived from literature (€0.28/strip; €0.09/lancet; €3.09/daily FM sensor; €3804/hospitalized SHE; €1794/hospital-attended non-admitted SHE; €389/community-attended SHE).

Results: Costs were €2700 and €2120/year/patient using SMBG or FreeStyle Libre 2 system, respectively. For 1000 patients with T2DM using basal-bolus insulin, 1220 SHEs/year (with 48 hospitalizations) could be prevented and FreeStyle Libre 2 system could generate cost savings of up to €580,953/year versus SMBG (− 21.5%).

Conclusion: FreeStyle Libre 2 system is a potential cost-saving strategy in patients with T2DM in Spain on a basal-bolus insulin regimen.

Keywords: Cost; Diabetes; Flash; FreeStyle Libre; Glucose monitoring

Key Summary Points

Why carry out this study?

A flash monitoring system for glucose monitoring in patients with diabetes mellitus has been demonstrated to be effective and cost savings in some healthcare settings.

The present analysis estimates the economic impact related to the use of a flash monitoring system, FreeStyle Libre 2, in an adult population with type 2 diabetes (T2DM) treated with basal-bolus insulin in Spain.

What was learned from the study?

Use of FreeStyle Libre 2 system in patients with T2DM treated with basal-bolus insulin could be associated with annual savings for the Spanish National System. Savings linked to avoided hypoglycaemic episodes are the main contributor to these savings.

Using the FreeStyle Libre 2 system in this population could avoid severe hypoglycaemic episodes (up to 1220 in a 1000 patients annually).

In Spain, the FreeStyle Libre 2 system could be associated with annual savings of up to €581 per patient for the National Health System.

These results could be useful in the decision-making process related to public reimbursement and resource allocation in the diabetes mellitus field.

DIGITAL FEATURES

This article is published with digital features, including a summary slide, to facilitate understanding of the article. To view digital features for this article go to <https://doi.org/10.6084/m9.figshare.14447457>.

INTRODUCTION

The latest report of the International Diabetes Federation (IDF) estimated that nearly 463 million adults are diagnosed with diabetes mellitus (DM) worldwide [1], and this figure is expected to rise to 578 million and 700 million in 2030 and 2045, respectively [1]. Type 2 DM (T2DM) accounts for the clear majority (around 90.0%) of diabetes cases [1]. The most recent update of a larger epidemiological study on DM (Di@bet.es study) [2] confirmed that known T2DM prevalence in Spain is at 7.8%.

In addition to the increasing clinical burden [3], DM and its complications are associated with an important economic impact. The cost of care for people with diabetes can be up to four times higher than in those without diabetes [4, 5]. Annual global health expenditure on diabetes is estimated to be USD 760 billion [1].

In Spain, DM was ranked as the 15th most common cause of mortality in both sexes in 2016 [6], and the 9th most frequently treated

health problem in the public primary care health system [7], and it has been estimated that the direct costs associated with the disease may reach €5100 million, representing 8.0% of global public health expenditure [8].

The therapeutic cornerstone for patients with T2DM lies in the promotion of a healthy lifestyle including a balanced diet, regular physical activity, smoking cessation and maintenance of a healthy body weight. When attempts to change lifestyle are insufficient in controlling blood glucose levels, oral medication with metformin should be the first-line treatment. Beyond this, a range of combination therapy options are now available, but if oral medications are insufficient to maintain blood glucose within the recommended ranges, insulin-based regimens may be required.

Insulin concentration elevations in blood inevitably involve the risk of all types of hypoglycaemia so the use of insulin secretagogues and insulin-based regimens are risk factors for the development of hypoglycaemic episodes [9]. The incidence of hypoglycaemia is higher among insulin-treated patients with T2DM [10, 11], primarily those with complex insulin regimens following the use of basal insulin, who also required personalized treatment adjustments with several types of insulin.

Hypoglycaemia is a major contributing factor to long-term complications and reduced survival in patients with DM, in addition to its detrimental impact on health-related quality of life and increased overall associated costs [12].

Glucose monitoring is a useful tool for controlling glycosylated haemoglobin (HbA1c) levels; however, monitoring based on the self-monitoring of blood glucose (SMBG) has significant limitations [13], because it is cumbersome, painful and costly. Several barriers (physical, such as pain and discomfort; psychological, such as fear and frustration; social, such as interference with lifestyle) are directly related to low patient adherence to the monitoring recommendations established by national [14] and international scientific societies [15, 16].

Monitoring of glucose in interstitial fluid poses an alternative to the traditional SMBG, and is associated with better HbA1c levels, less

glucose variability, better quality of life and more lifestyle flexibility [17–19].

The FreeStyle Libre® 2 system is an interstitial fluid glucose flash monitoring system with optional alarms, marketed and available in Spain, fully reimbursed under the Basic Services Portfolio of the Spanish National Health System (Sistema Nacional de Salud [SNS]) for the type 1 DM population (T1DM) [20]. The FreeStyle Libre system is fully or partially reimbursed in 36 markets across the world for T1DM and T2DM; in most European countries (France, UK, Germany, Austria, Italy, Portugal, etc.), reimbursement for patients with T2DM has started with patients with T2DM treated with three or more insulin doses a day, including premixed and basal-bolus insulin regimens. The latter is considered a preferred subgroup in national [21] and international [22] guidelines.

The FreeStyle Libre 2 system is accompanied by a digital ecosystem with free mobile applications (FreeStyle Libre Link and FreeStyle LibreLinkUp) and virtual software (Libre View) that simplify glucose monitoring, allowing better management of the disease and facilitating communication between professionals and patients.

The clinical evidence of the FreeStyle Libre 2 system has been evaluated in many randomised clinical trials, like the IMPACT study [23, 24] for T1DM and the REPLACE trial [25, 26] in patients with T2DM and several real-world data studies. Treatment satisfaction with the FreeStyle Libre 2 system has been also tested in the T2DM population [27].

The findings in the REPLACE study showed that patients in the FreeStyle Libre 2 system arm experienced a decrease in the number and mean duration of hypoglycaemic episodes compared with those in the SMBG-only arm [25]. Moreover, the FreeStyle Libre 2 system users reduced their need for finger-prick blood glucose measurements by up to 95.0% versus SMBG.

The overall cost for management in patients with T2DM treated with insulin regimens is expected to be reduced following the lower consumption of SMBG supplies and the decreased need for healthcare resources due to the reduced incidence of hypoglycaemic

episodes associated with the use of the FreeStyle Libre 2 system.

In this study a cost analysis was conducted of the FreeStyle Libre 2 system compared to SMBG in adults with T2DM treated with basal-bolus insulin in Spain, which complements a previous analysis published for T1DM [28].

METHODS

A cost analysis model previously developed for T1DM [28] was used to estimate the economic impact associated with glucose monitoring and the management of hypoglycaemic events in a hypothetical cohort of 1000 adult (> 18 years) patients with T2DM treated with basal-bolus insulin regimen, using the FreeStyle Libre 2 system as compared to standard practice based on SMBG only. The FreeStyle Libre 2 system has been considered in the analysis, as this version of the FreeStyle Libre system will be available in Spain as of early 2020.

This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors. All the inputs for the model were derived from a literature review, so they were not directly collected from any study.

The perspective of the Spanish National Health System was used to estimate the annual costs derived from the consumption of resources associated with glucose monitoring (strips and lancets, plus FreeStyle Libre sensors in FreeStyle Libre 2 system users) and the management of severe hypoglycaemia.

The values of the parameters, obtained from the published literature, were validated by a panel of eight experts (three endocrinologists, two primary care physicians and three specialists in internal medicine) with expertise in the management of patients with diabetes.

A review of the scientific literature was performed to identify the available evidence on hypoglycaemia rates in the T2DM population.

In line with the widely accepted definition, severe hypoglycaemic episodes were regarded as those requiring help from another person [29, 30].

A wide variation of severe hypoglycaemia rates per patient-year was found during the literature review. The Hypoglycaemia Assessment Tool (HAT) study, an observational study conducted in 24 countries, was initially chosen in view of its robustness (sample size, multicentric nature and representativeness of the Spanish population) [31] to obtain base case results. In the aforementioned study an annual incidence of 2.5 severe hypoglycaemic episodes was reported per patient for the T2DM population [31].

The efficacy of the FreeStyle Libre system in T2DM was evaluated by the REPLACE study [25], a phase III, randomized, multicentre clinical trial that included 224 patients under intensive insulin therapy from 26 diabetes centres in three European countries (France, Germany and UK). A reduction in hypoglycaemia associated with the use of the FreeStyle Libre system (− 48.8% for episodes with glucose level < 2.5 mmol/L [45 mg/dL]) was reported [25].

A proposal for reporting hypoglycaemia events in clinical trials (based on three levels) has been issued by the International Hypoglycaemia Study Group [32]. However, in the REPLACE trial [25] severe hypoglycaemia episodes (requiring third-party assistance) were not specifically reported. For the purpose of this analysis, level 1 episodes according to the American Diabetes Association (ADA) proposed classification were equated to severe hypoglycaemic episodes with glucose level < 2.5 mmol/L (45 mg/dL) (Table 1).

For the management of hypoglycaemic events, the information source was the Emergency Care of the Person with Diabetes Project (PAUEPAD, for its initials in Spanish) [33]. This is a retrospective study of all registered hypoglycaemia-related emergency calls taken by the emergency medical services in Andalusia, Spain (8.5 million inhabitants). Hospital attendance was considered necessary in 20.5% of the episodes of severe hypoglycaemia. The rate of subsequent hospital admission (15.6% of them) comes from a survey in people with insulin-treated T2DM who have experienced severe hypoglycaemic events in Germany, Spain or the UK [34].

Table 1 Baseline characteristics of the patients and main results of the REPLACE study [25]

Parameter	SMBG (<i>N</i> = 75)	FreeStyle Libre system (<i>N</i> = 149)
Age, years	59.5 ± 11.0 (22–80)	59 ± 9.9 (33–81)
Duration of diabetes, years	18.0 ± 8.0 (11–31)	17.0 ± 8.0 (4–37)
Baseline HbA1c, %	8.9 ± 1.0 (7.5–11.7)	8.7 ± 1.0 (7.5–11.6)
Baseline daily frequency of SMBG	3.9 ± 1.3	3.6 ± 1.3
Number of episodes with glucose < 2.5 mmol/L (45 mg/dL)	Baseline: 0.1 ± 0.3	Baseline: 0.2 ± 0.4
	Final: 0.1 ± 0.2	Final: 0.1 ± 0.1
	Difference FreeStyle Libre vs SMBG: − 48.8%	
	Baseline: 0.6 ± 0.7	Baseline: 0.6 ± 0.6
Number of episodes with glucose < 3.9 mmol/L (70 mg/dL)	Final: 0.5 ± 0.6	Final: 0.4 ± 0.4
	Difference FreeStyle Libre vs SMBG: − 27.7%	

Data are presented as mean ± SD or mean ± SD (range)
SD standard deviation, SMBG self-monitoring of capillary
blood glucose

A daily consumption of six strips was considered for patients with T2DM treated with a basal-bolus insulin regimen, estimated as the average of national recommendations for glucose monitoring in these patients according to their level of blood glucose control [14], and in line with FL2 reimbursement criteria in Spain for patients with T1DM with the same insulin and glucose monitoring requirements. The use of one lancet per SMBG measurement was also assumed.

The REPLACE showed a frequency of 0.2 ± 0.6 tests a day in FreeStyle Libre users

[26], meaning a daily consumption of 0.2 strips and lancets which was used for calculations in the present analysis.

Considering the labelling requirements about sensor replacement [35] (one every 14 days), an annual consumption of 26 FreeStyle Libre 2 system sensors was applied in the cohort of patients with T2DM using the FreeStyle Libre 2 system.

The unit costs (in € year 2020 and excluding VAT) were obtained from the reviewed literature (€0.28 /strip [28], €0.09/lancet [28], €3.09/daily FreeStyle Libre 2 sensor [28], €3804.17/severe hypoglycaemic episode with hospital admission [36], €1793.74/severe hypoglycaemic episode with emergency hospital care but no admission [33], €388.83/severe hypoglycaemic episode without hospital care [37]).

Sensitivity Analysis

Sensitivity analyses (SAs) were conducted to assess the model's robustness by modifying the parameters with the greatest uncertainty. The following one-way SA were carried out: alternative severe hypoglycaemia rate (1.3 episodes per patient-year as indicated in the HAT study for the Northern European and Canadian population) [38] (SA1); reduction of consumption of strips and lancets in patients with SMBG to 3 daily (SA2); variation of consumption of strips and lancets in FreeStyle Libre 2 users to 0.66 per day based on recently published real-world data in Spain [39] (SA3); alternative daily consumption of strips and lancets (3 for SMBG only patients and 0.66 for FreeStyle Libre 2 users) (SA4); theoretical consumption of strips and lancets in patients with SMBG only estimated by assuming equivalence to the monitoring frequency with FreeStyle Libre system observed in a real-world study [39] (13 daily) (SA5).

An additional scenario was also tested, considering non-severe hypoglycaemia events (SA6), equated to those episodes with glucose level ≥ 2.5 mmol/L (45 mg/dL) and < 3.9 mmol/L (70 mg/dL). A rate of 17.02 non-severe hypoglycaemia episodes per patient-year reported on the HAT study [31] was considered. A reduction of 27.7% for episodes with a glucose

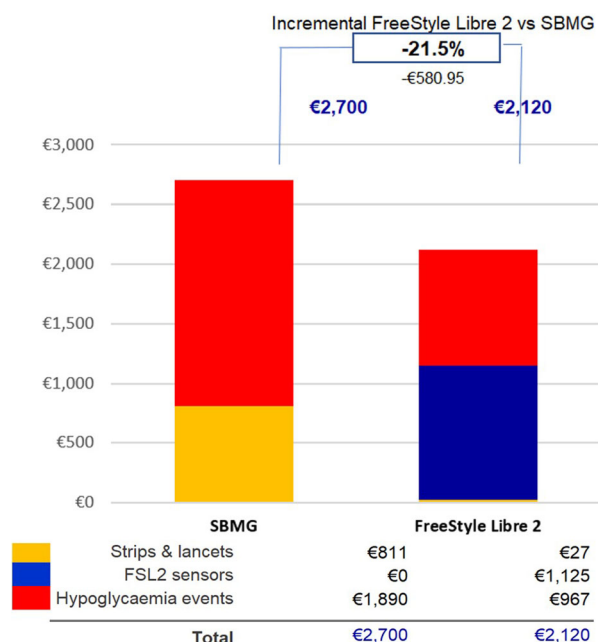


Fig. 1 Detailed annual costs per patient with T2DM receiving basal-bolus insulin therapy. FreeStyle Libre 2 system, SMBG self-monitoring of capillary blood glucose

level < 3.9 mmol/L (70 mg/dL) reported in the REPLACE trial [25] for FreeStyle Libre system users was applied to the non-severe hypoglycaemic events rate. A unitary cost of €15.07/non-severe hypoglycaemia episode [40] was used in calculations.

RESULTS

The total annual cost estimated in this analysis for the SMBG-only arm was €2700 per patient with T2DM receiving basal-bolus insulin. In the FreeStyle Libre 2 user arm, the total annual cost was €2120 per patient.

The costs associated with glucose monitoring in SMBG were €811 per patient. The glucose monitoring cost in patients using the FreeStyle Libre 2 system was €1125 per patient-year. Savings derived from the reduction in the use of daily strips and lancets were €783 (– 96.7%) per patient with T2DM receiving basal-bolus insulin, which offset the FreeStyle Libre 2 system sensor acquisition cost, estimated to be €1125 per patient-year.

Table 2 Hypoglycaemia episodes for a cohort of 1000 patients with T2DM

Parameter	SMBG	FSL2	Absolute difference FreeStyle Libre 2 system vs SMBG (percentage variation)
Severe hypoglycaemic episodes	2500	1280	– 1220 (– 48.8%)
SHE with hospital admission	98	50	– 48 (– 48.8%)
SHE with hospital care, no admission	416	213	– 203 (– 48.8%)
SHE without hospital care	1986	1017	– 969 (– 48.8%)

SHE severe hypoglycaemia episode, *SMBG* self-monitoring of capillary blood glucose, *T2DM* type 2 diabetes mellitus

The management of severe hypoglycaemic episodes represented an annual cost of €1890 per SMBG patient. In patients with FreeStyle Libre 2 system, the annual cost was €967 per patient. The hypoglycaemic episodes prevented annually with the FreeStyle Libre 2 system would result in a cost saving of €922 (– 48.8%).

The use of the FreeStyle Libre 2 system as compared to SMBG would be associated with an annual total cost saving of €581 (– 21.5%) per patient with basal-bolus insulin (Fig. 1).

In a cohort of 1000 patients with T2DM with intensive insulin therapy (basal-bolus regimen), a total of 2500 severe hypoglycaemic episodes would occur using SMBG versus 1280 with the FreeStyle Libre 2 system. Thus, the FreeStyle Libre 2 system would annually prevent 1220 severe hypoglycaemic episodes (48.8% reduction), and among them 48 cases of hospitalizations due to severe hypoglycaemia (Table 2).

The use of the FreeStyle Libre 2 system would generate total annual savings per 1000 patients of up to €580,953 compared with SMBG in patients with T2DM treated with basal-bolus

Table 3 Annual costs for a cohort of 1000 patients with T2DM receiving basal-bolus insulin therapy

Parameter	SMBG	FreeStyle Libre 2 system	Absolute difference FreeStyle Libre 2 system vs SMBG (percentage variation)
Patients with T2DM treated with basal-bolus insulin therapy			
Cost of SHE management	€1,889,644	€967,498	– €922,146 (– 48.8%)
Cost of glucose monitoring	€810,855	€1,152,048	€341,193 (42.1%)
Cost of strips and lancets	€810,855	€27,029	– €783,827 (– 96.7%)
Cost of FreeStyle Libre 2 system sensors	€0	€1,125,020	€1,125,020 (100.0%)
Total cost	€2,700,499	€2,119,546	– €580,953 (– 21.5%)

SHE severe hypoglycaemic episodes, *SMBG* self-monitoring of capillary glucose, *T2DM* type 2 diabetes mellitus

insulin (Table 3), thus representing a 21.5% reduction in overall costs.

SA results confirmed the model robustness for the 1000 patients with T2DM receiving basal-bolus insulin.

The SA using the alternative severe hypoglycaemia rate (1.3 episodes per patient-year) [38] showed that FreeStyle Libre 2 system use

would be related to annual cost savings of €138,323 (– 7.7%), derived from the reduction of 634 severe hypoglycaemic episodes yearly (Table 4).

The modifications in daily use of strips and lancets also produced savings associated with the use of the FreeStyle Libre 2 system versus SMBG that ranged between €113,360 (– 4.9%)

Table 4 Results of the sensitivity analyses

	Total annual cost per 1000 patients with T2DM		
	SMBG	FreeStyle Libre 2 system	Absolute difference FreeStyle Libre 2 system vs SMBG (percentage variation)
Base case for T2DM with basal-bolus insulin	€2,700,499	€2,119,546	– €580,953 (– 21.5%)
SA1 (1.3 severe hypoglycaemic episodes/patient-year) [38]	€1,7938,470	€1,655,147	– €138,323 (– 7.7%)
SA2 (3 strips & lancets a day for SMBG)	€2,295,071	€2,119,546	– €175,525 (– 7.6%)
SA3 (0.66 strips & lancets a day for FreeStyle Libre 2 users) [39]	€2,700,499	€2,181,712	– €518,787 (– 19.2%)
SA4 (3 strips & lancets a day for SMBG, and 0.66 for FreeStyle Libre 2 users)	€2,295,071	€2,181,712	– €113,360 (– 4.9%)
SA5 (13 strips and lancets a day for SBMG, equivalent to daily scans in real-world studies)[39]	€3,646,496	€2,119,546	– €1,526,950 (– 41.9%)
SA6 (including severe and non-severe hypoglycaemic episodes)	€3,916,781	€3,501,680	– €415,101 (– 10.6%)

SA sensitivity analysis, *SMBG* self-monitoring of capillary blood glucose, *T2DM* type 2 diabetes mellitus

with a daily consumption of 3 strips and lancets in SMBG and 0.66 for FreeStyle Libre 2 users and €1,526,950 (– 41.9%) for 13 strips and 3 lancets a day in SBMG (Table 4).

In the additional scenario considering severe and non-severe hypoglycaemic episodes, the total annual cost reached €3,916,781 and €3,501,680 for the cohort with SMBG and the FreeStyle Libre 2 system, respectively. In this scenario it was shown that the use of the FreeStyle Libre 2 system would prevent 5407 hypoglycaemic episodes a year. Of these avoided hypoglycaemic events 1220 would correspond to severe episodes (– 48.8%), and 4187 to non-severe episodes (– 24.6%). Cost savings with the use of the FreeStyle Libre 2 system as compared to SMBG would be up to €415,101 per year (– 10.6%) (Table 4).

DISCUSSION

The efficacy of the FreeStyle Libre 2 system in the T2DM population has been proven in clinical trials [25, 26], and corroborated by real-world studies which have revealed reductions in hospitalizations due to DM complications, such as hypoglycaemic events [41] or ketoacidosis [42].

The present analysis proves the FreeStyle Libre 2 system to be a strategy that results in savings for the clinical management of patients with T2DM treated with basal-bolus insulin in Spain. On the basis of the assumptions described throughout the paper, the present model showed that the FreeStyle Libre 2 system would decrease the total annual cost by up to €580 (– 21.5%) per patient with T2DM treated with basal-bolus insulin, generating annual savings for the Spanish National Health System of more than half a million euros per cohort of 1000 treated patients.

The cost savings associated with the use of the FreeStyle Libre 2 system have also been observed in other settings such as the USA [43], where annual reductions of \$1682 per patient with T2DM receiving intensive insulin therapy were estimated in relation to the use of the FreeStyle Libre 2 system in comparison to SBMG (with a use of six strips and lancets per day), in

terms of glucose monitoring. Additionally, reductions in the cost of severe hypoglycaemia events management were also shown (– \$852 per patient/year).

At the European level, cost savings following the use of the FreeStyle Libre 2 system have been demonstrated for the UK setting in analyses comprising patients with T1DM [44], as well as in models focused on patients with T2DM [45]. The latter one showed annual savings of £191/patient associated with the use of the FreeStyle Libre 2 system in the T2DM population when considering three daily SMBG measurements.

One main limitation of this model involves the incidence of hypoglycaemia. There are a wide range of values available in the literature, very likely because of differences in the methodology and criteria used in the different studies. For the purpose of the present analysis, the expert panel selected a multicentre (2004 healthcare centres), multinational (24 countries), large-scale study (27,585 patients with diabetes; 19,563 patients with T2DM) [31] as the most robust data source. To reduce uncertainty about this parameter a SA was performed with an alternate hypoglycaemia rate, which also presented savings with the FreeStyle Libre 2 system. Additionally, a SA including non-severe hypoglycaemic events was also performed.

Reductions of biochemical hypoglycaemia episodes associated with use of the FreeStyle Libre 2 system reported in the REPLACE study [25] were applied to the incidence of clinical hypoglycaemia in this analysis. This is a controversial issue, because evidence on the relationship between low glucose levels and symptomatic hypoglycaemic episodes is limited, although a recent publication has concluded that the occurrence of biochemical hypoglycaemia (< 3.9 mmol/L or 3 mmol/L) is associated with an increased risk of severe hypoglycaemia [46].

To the better address the issue of hypoglycaemia risk, the International Hypoglycaemia Study Group issued a recommendation to the diabetes community to adopt common glucose levels when reporting outcomes about hypoglycaemic episodes in studies [32]. However,

since hypoglycaemic events were not specifically reported in the trial used in this analysis as efficacy source, an assumption was needed to equate those episodes with glucose levels < 2.5 mmol/L (45 mg/dL) to hypoglycaemic episodes requiring external care. Given the results of the REPLACE trial, this assumption represents a conservative scenario, as the proposed definition for severe hypoglycaemic episodes could also be applied to events with glucose levels ≥ 2.5 mmol/L (45 mg/dL).

As a result of the short time horizon of the cost analysis, the long-term benefits of FreeStyle Libre 2 system related to the prevention of other diabetes complications such as cardiovascular disease, renal failure, blindness, amputations, etc. owing to the improved glycaemic control were not included, so these results should be considered as representative of a conservative scenario in this sense.

This analysis assumed that the findings from the REPLACE study are fully transferable to FreeStyle Libre 2 system, but with FreeStyle Libre 2's optional alarms and the most recent improvements in accuracy, the use of the FreeStyle Libre 2 system could result in an even greater reduction of severe hypoglycaemia events, which could result in higher savings due to the prevention of hypoglycaemic events (especially in patients with hypoglycaemia unawareness).

In addition to the prevented hypoglycaemic episodes, the use of the FreeStyle Libre 2 system was associated with a decrease in the number of SMBG measurements required by the patients. Frequency of SMBG and therefore the daily consumption of strips and lancets is the second critical issue of the present model. The SA corroborated that even in scenarios with a lower number of SMBG measurements, the use of FreeStyle Libre 2 system would be associated with cost reductions of 7.6% as compared to the use of SMBG alone, generating direct cost savings of €175,525 per 1000 patients/year. In a theoretical scenario where the number of finger-prick blood glucose measurements would total 13 a day, which is the number of daily scans with the FreeStyle Libre 2 systems observed in a Spanish real-world study [39], the reduction of total cost would be 41.9%

(– €1,526,950 per 1000 patients with T2DM, yearly).

The value of glucose monitoring in the control of diabetes and the strong association between higher SMBG frequency and lower HbA1c levels are undeniable [47]; however, several scientific publications [17, 48] revealed poor adherence to the recommendations set out in the current clinical guidelines [14]. Considering possible low adherence to these monitoring recommendations, SAs with variations in optimum consumption were performed. Although the daily number of SMBG measurements in patients with T2DM was lower than recommended, the savings derived from the prevented hypoglycaemic episodes would offset the costs of purchasing FreeStyle Libre 2 sensors.

Patients' reasons for poor adherence to the monitoring vary greatly and include lack of time, invasiveness and needle phobia [48, 49]. The features of the FreeStyle Libre 2 system could eliminate some of these barriers [50], thereby increasing the daily number of glucose determinations as has been proven by all the clinical studies and real-world data on the FreeStyle Libre system (like the study from Spain that found a mean number of 13 daily scans) [39].

The savings identified in this cost study are a conservative estimate, as savings linked to hyperglycaemic events prevention by the FreeStyle Libre 2 system have not been included. A Spanish study calculated that the mean cost of a hospital admission for hyperglycaemic crisis was €3364.6 [36]. Another study found that the mean cost per episode involving emergency room care would add an additional cost of €1476.80 per episode [51]. Given that the FreeStyle Libre 2 system now has an optional alarm for high glucose values, the FreeStyle Libre 2's contribution to the prevention of hyperglycaemic events cannot be disregarded, with its associated savings owing to events prevented.

Furthermore, savings linked to the use of the FreeStyle Libre 2 system and LibreView as a telemedicine tool have not been considered in the present analysis. A literature review revealed a study in which patients in the telemedicine group showed a substantial reduction in their HbA1c levels compared to their counterparts in

conventional care, with patients with T2DM being the most favoured (Hedges $g = -0.48$) compared to T1DM (Hedges $g = -0.26$) [52]. Another meta-analysis [53] of randomized clinical trials identified that the telemedicine, compared to conventional care, reduces hypoglycaemia (odds ratio = 0.42%). Although not specifically referring to patients with DM, a local study has shown that telemedicine could save up to €15 per visit. Patients are the greatest beneficiaries of these savings (owing to shorter waiting time and travel costs) but it is also more efficient from the healthcare perspective [54]. The added benefits of telemedicine in the era of the COVID-19 crisis and lockdown, for patients, healthcare professional and the healthcare system, cannot be disregarded, even though they are not the focus of this analysis. This analysis showed savings from the National Health System perspective, but in addition to the direct medical resources, hypoglycaemic events often entail pain, suffering and work absenteeism which could also impact on the glucose monitoring cost. FreeStyle Libre 2 has been shown to improve quality of life and work productivity [55, 56]. The FreeStyle Libre 2 system has been positively evaluated in patients with T1DM and T2DM by health technology agencies in a number of countries and regions (France, Norway, Scotland, Sweden, England, Wales, etc.), and published cost-effectiveness analyses have shown the efficiency of the FreeStyle Libre 2 system in several settings [57–62].

Previous analysis in Spain showed annual cost savings of nearly €2 million (euros year 2019) per 1000 adults patients associated with the use of the FreeStyle Libre 2 system in T1DM populations treated with multiple daily doses of insulin [28].

The use of the FreeStyle Libre 2 system as a substitute for test strips in SMBG may result in savings for the National Health System, while simultaneously improving disease control and patient quality of life. It would be particularly interesting to conduct future studies and/or registries on the use of this technology in real life, with a view to obtaining information on the clinical, economic and quality of life repercussions for patients in our setting—particularly considering that the digital ecosystem

accompanying the FreeStyle Libre 2 system (LibreView, FreeStyle Libre Link, FreeStyle Libre LinkUp) can also have an impact on patients, their relatives and healthcare professionals.

CONCLUSIONS

The use of FreeStyle Libre 2 flash glucose monitoring system for patients with T2DM treated with basal-bolus insulin therapy is an efficient strategy for the Spanish National Health System thanks to the savings it can generate, owing to both the decrease in hypoglycaemia episodes and to the direct cost savings in blood glucose monitoring.

Considering the assumptions and costs described, in comparison with SMBG, the FreeStyle Libre 2 system would potentially allow cost savings of up to €580,953 per year in a cohort of 1000 patients with T2DM receiving basal-bolus insulin.

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This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

Data Availability. Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

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