



Cost analysis of the flash monitoring system (FreeStyle Libre 2) in adults with type 1 diabetes mellitus

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ABSTRACT

Introduction Compare cost of the interstitial liquid glucose flash monitoring (FM) system (FreeStyle Libre 2) versus self-monitoring of blood glucose (SMBG) in adults with type 1 diabetes mellitus (T1DM) in Spain.

Research design and methods A model was developed to estimate, with the perspective of the Spanish health system, the annual costs associated with glucose monitoring and hypoglycemic events management in T1DM population, with multiple insulin daily doses (MDI). According to published evidence, rate of severe hypoglycemia (SHE) of 4.90 episodes per patient-year was applied. Reduction of SHE (58.6%) was modeled associated with FM use. Published rates of hospital care (20.2%) and subsequent admission (16%) were assumed for SHE. The daily consumption of strips and lancets was 9 in patients with SMBG (before and after 4 daily intakes and at bedtime) and 0.5 for FM users (according to IMPACT trial findings). Annual consumption of 26 FM sensors was considered (1 every 14 days). Unit costs (in € of 2019, excluding VAT) were obtained from literature and national databases. Sensitivity analyses (SA) were carried out to evaluate the model robustness.

Results The total annual cost/patient was €4437 for SMBG and €2526 for FM. The use of FM would be associated with an annual savings in the costs of monitoring and managing hypoglycemic events of €1911 per patient-year. In a hypothetical cohort of 1000 patients with T1DM MDI, FM could avoid in 1 year 4900 SHE, 93 hospitalizations for SHE. In addition, the use of FM would generate total savings of up to €1 910 000 per year. In the SA with alternative hypoglycemia events rates and use of strips and lancets, and including non-SHE episodes, savings from €370 000 to €1 760 000 were observed with FM.

Conclusions The use of the FM system to monitor glucose in adults with T1DM treated with MDI, would reduce hypoglycemic events and would result in cost savings for the health system.

INTRODUCTION

Diabetes mellitus (DM) is a chronic disease that according to WHO affects >422 million people worldwide.¹ In addition to its great and increasing clinical relevance, DM also has an important economic impact. In Spain,

Significance of this study

What is already known about this subject?

▶ Flash monitoring (FM) system for glucose monitoring in patients with diabetes mellitus has demonstrated to be effective and cost-savings in some healthcare settings.

What are the new findings?

▶ This analysis showed that due to the avoided hypoglycemic episodes, and cost neutrality in the monitoring consumables, the use of FM system in adult population with diabetes could be associated with annual savings for the Spanish National System.

How might these results change the focus of research or clinical practice?

▶ These results could be useful in the decision-making process related to the public reimbursement and the resource allocation in the diabetes mellitus field.
▶ Using FM system in T1DM population could avoid severe hypoglycemic episodes (up to 4900 in a 1000 patients cohort annually).
▶ In Spain, FM system could be associated with annual savings up to €1900 per patient for the National Health System.

it has been estimated that the direct costs associated with the disease may reach €5100 million, representing 8% of global public health expenditure.²

The clinical management of type 1 DM (T1DM) is oriented toward the individualization of therapy, including the promotion of an adequate lifestyle together with the use of insulin-based treatments³ adapted to the patient characteristics and preferences.

Health outcomes may be improved through interventions targeted to a triad of therapeutic goals: the reduction of glycated hemoglobin (HbA1c) levels, the limitation of glycemic variability and the reduction of hypoglycemic episodes.

The development of hypoglycemia is associated with increased complications and morbidity-mortality in patients with DM,⁴ and moreover has an impact on patient productivity and increases the overall associated costs.⁵

However, despite the pharmacotherapeutic advances of recent years, a proportion of patients are still unable to maintain their blood glucose levels within the recommended limits.^{6,7}

Blood glucose monitoring has been shown to be useful for controlling the HbA1c levels, and there is evidence that an increase in monitoring frequency contributes to achieve the aforementioned therapeutic objectives.⁸ However, current monitoring based on the self-monitoring of blood glucose (SMBG) has significant limitations,⁹ especially low patient adherence to the monitoring recommendations established by the national¹⁰ and international scientific societies.¹¹

The barriers complicating patient adherence to the SMBG recommendations include physical (related to pain and discomfort), psychological (fear, frustration), social (interference with lifestyle) and economic factors.^{12,13}

FreeStyle Libre 2 is an interstitial fluid glucose flash monitoring (FM) system with optional alarms, marketed and available in Spain, being fully reimbursed under the Basic Services Portfolio of the Spanish National Health System (Sistema Nacional de Salud) for T1DM population.¹⁴ FreeStyle Libre is fully or partially reimbursed in 36 markets. The FM system is accompanied by a digital ecosystem with free mobile applications (FreeStyle Libre Link and FreeStyle LibreLinkUp) and virtual software (LibreView) that simplify glucose monitoring, allowing better management of the disease and facilitating connection between professionals and patients.

The clinical evidence of the FM system has been evaluated in randomized clinical trials in both the T1DM population of the IMPACT study^{15,16} and in patients with type 2 DM (T2DM) in the REPLACE trial.¹⁷

In the IMPACT study, the patients in the FM arm experienced a statistically significant decrease in the number and mean duration of hypoglycemic episodes compared with the patients in the SMBG arm.¹⁵ In addition, the users of the FM system reduced their need for finger-prick glycemia measurements by up to 91% vs SMBG. These results were also seen for the subgroup of patients with T1DM with multiple dose insulin (MDI) therapy.

The lesser consumption of healthcare resources associated with the FM system, resulting from fewer hypoglycemic episodes and a lesser consumption of SMBG supplies, could lower the overall cost of management in patients with T1DM subjected to intensive insulin therapy.¹⁷

The present study conducted a cost analysis of the FM system versus SMBG in adults with T1DM and MDI therapy in Spain.

RESEARCH DESIGN AND METHODS

A cost analysis model was developed to estimate the economic impact associated with glucose monitoring and the management of hypoglycemic events in patients using the FM system as compared with standard practice based on SMBG only. FreeStyle Libre 2 has been considered in the analysis, as this version of the FM system will be available in Spain since the beginning of 2020.

The analysis comprised a hypothetical cohort of 1000 adult patients (>18 years) with T1DM and treated with MDI.

Considering the perspective of the Spanish National Health System, an estimate was made of the annual costs derived from the consumption of resources associated with glucose monitoring (strips, lancets and FM sensors) and the management of severe hypoglycemia.

The values of the parameters, obtained from the published literature, were validated by a panel of six endocrinologists with expertise in the management of patients with diabetes.

A review of the scientific literature was made to identify the available evidence on hypoglycemia rates in the population with T1DM.

In line with the widely accepted definition, severe hypoglycemic episodes were regarded as those requiring help from another person.^{18,19}

A wide variation of severe hypoglycemia rates per patient-year were found during the literature review. For the base case, the Hypoglycaemia Assessment Tool (HAT) study, an observational study conducted in 24 countries, was chosen in view of its robustness (sample size, multicentric nature and representativeness of the Spanish population).²⁰ The mentioned study estimated an annual incidence of 4.90 severe hypoglycemic episodes per patient.²⁰

The efficacy of the FM system in T1DM was evaluated by the IMPACT study, a phase III, randomized, multicenter clinical trial that included 328 patients from 23 diabetes centers in 5 European countries (Austria, Germany, Spain, the Netherlands and Sweden).^{15,16} The results of the trial evidenced reductions in hypoglycemia associated with the use of the FM system (-58.6% for episodes with glucose level <2.2 mmol/L (40 mg/dL)).¹⁶ Despite that the International Hypoglycemia Study Group published a proposal for reporting hypoglycemia in clinical trials,²¹ based on three levels; in the IMPACT trial,¹⁶ severe hypoglycemic episodes (requiring third-party assistance) were not specifically reported. For the purposes of the present analysis, we analyzed level 1, according the American Diabetes Association (ADA) proposed classification equating severe hypoglycemia to episodes with glucose level <2.2 mmol/L (40 mg/dL) (table 1).

For the management of hypoglycemic events, hospital care was considered necessary in 20.2% of the cases of severe hypoglycemia, with subsequent hospital admission in 16% of the cases.²²

Table 1 Baseline characteristics of the patients and main results of the IMPACT study¹⁶

Parameter	SMBG (n=80)	FM system (n=81)
Age, years: mean (range)	44 (34–53)	42 (32–53)
Duration of diabetes, years: mean (range)	19 (11–31)	19 (14–25)
Baseline HbA1c, %: mean±SD	6.7±0.6	6.7±0.5
Baseline daily frequency of SMBG: mean±SD	5.6±1.9	5.5±2.0
Final daily frequency of SMBG: mean±SD	5.5±2.6	0.5±1.0
Number of episodes with glucose <2.2 mmol/L (40 mg/dL): mean±SD	Baseline: 0.49±0.52 Final: 0.52±0.63 Difference FM vs SMBG: –58.6%	Baseline: 0.44±0.48 Final: 0.20±0.32
Number of episodes with glucose <3.9 mmol/L (70 mg/dL): mean±SD	Baseline: 1.72±0.75 Final: 1.78±0.78 Difference FM vs SMBG: –32.8%	Baseline: 1.80±0.80 Final: 1.23±0.69

FM, flash monitoring; HbA1c, glycated hemoglobin; SMBG, self-monitoring of capillary blood glucose.

In line with the current recommendations for patients with T1DM referred to glucose monitoring before and after food intake and at bedtime,¹⁰ an optimum consumption of nine strips a day was considered in patients with SMBG (assuming four daily meals). The use of a lancet was assumed in each SMBG measurement, thereby representing nine lancets a day.

Based on the IMPACT study,¹⁶ at the end of the trial the users of the FM system performed only 0.5±1.0 SMBG test a day.

In the cohort of patients with T1DM with MDI that used the FM system, 26 FM system sensors were estimated to be used annually, considering the recommendations of the manufacturer to replace the sensor every 14 days.

The unit costs (in € of 2019 and excluding VAT) were obtained from the reviewed literature and national databases (€0.28/strip, €0.09/lancet, €43.27/FM sensor, €3773.98/severe hypoglycemic episode with hospital admission,²³ €1779.50/severe hypoglycemic episode with hospital care but no admission,²⁴ €293.23/severe hypoglycemic episode without hospital care.²⁵

Sensitivity analysis

Sensitivity analyses (SAs) were performed to evaluate the robustness of the model by modifying the parameters with the greatest uncertainty, with observation of the influence of these modifications on the results.

Given the uncertainty around the severe hypoglycemia rate per-patient-year, SA with alternatives values found in the literature were carried out: 3.4 severe hypoglycemic episodes referred to the population of northern Europe and Canada in the HAT study²⁶ (SA1); 3.2 severe hypoglycemic episodes according to a study of the UK Hypoglycaemia Group²⁷ (SA2); 1.05 severe hypoglycemic episodes according to available meta-analysis data²⁸ (SA3) and 0.9 severe hypoglycemic episodes recorded in a Spanish national study²⁹ (SA4).

An additional scenario was also tested, considering non-severe hypoglycemic events, equated to those episodes with glucose level ≥2.2 mmol/L (40 mg/dL)

and <3.9 mmol/L (70 mg/dL) (SA5). A rate of 68.62 non-severe hypoglycemic episodes per patient-year reported on the HAT study²⁰ was considered. Reduction of 32.8% for episodes with glucose level <3.9 mmol/L (70 mg/dL) reported in the IMPACT trial,¹⁶ for FM users was applied to non-severe hypoglycemic events. Unitary cost of €7.25/non-severe hypoglycemic episode³⁰ was used for the computations.

Different SAs were also performed regarding the daily consumption of strips and lancets in patients with SMBG only, with consideration of the following: six strips and lancets a day (coinciding with the criterion used to assess reimbursement of the FM system in Spain (children or adults with T1DM, MDI including patients with continuous subcutaneous insulin infusion and at least six glycemia controls a day)) (SA6); nine strips a day with half the lancets (4.5/day) (SA7) and six strips a day with half the lancets (3/day) (SA8). Lastly, an analysis was made without considering the unit costs associated with the use of strips (€0) and lancets (€0) (SA9).

RESULTS

The estimated total annual cost was €4437 per patient with SMBG and €2526 per patient with FM.

The costs per patient-year associated with glucose monitoring were €1216 with SMBG and €1193 with the FM system—this representing a decrease of €24 (–1.9%) per patient using the FM system. The saving from the reduction of strip and lancet consumption was €1149 (94.4% reduction), which compensated the FM system sensor acquisition cost, estimated to be €1125 per patient-year.

The management of severe hypoglycemic episodes represented an annual cost of €3220 per patient with SMBG. In patients with FM, the annual cost was €1333 per patient. The hypoglycemic episodes prevented with the FM system would result in a cost saving of €1887 (–58.6%).

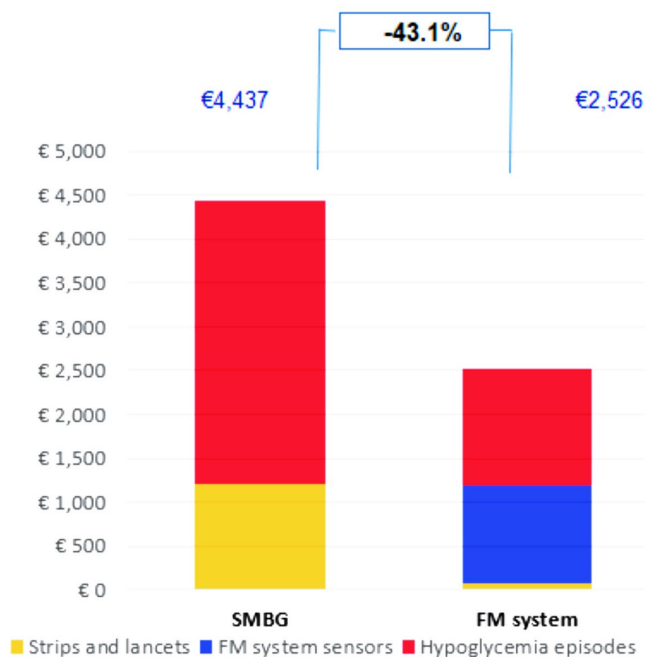


Figure 1 Detailed annual costs per patient. FM, flash monitoring; SMBG, self-monitoring of blood glucose.

Use of the FM system would be associated with an annual total cost saving of €1911 (–43.1%) as compared with SMBG (figure 1 and table 2).

In a cohort of 1000 patients with T1DM treated with MDI, a total of 4900 severe hypoglycemic episodes would occur using SMBG vs 2029 with the FM system. Thus, the FM system would avoid 2871 severe hypoglycemic episodes a year (58.6% reduction), among them 93 cases of hospitalizations by SHE (table 3).

The use of the FM system would generate total annual savings per 1000 patients of up to €1 910 764 compared with SMBG (table 3)—this representing a 43.1% reduction in overall costs.

For every 1000 patients with T1DM treated with MDI, the results of the SAs revealed annual savings associated with the FM system of €1 333 089 (–38.6%) on using the alternative severe hypoglycemia rate (3.4 episodes per patient-year),²⁶ derived from the reduction of 1992 severe hypoglycemic episodes. With the hypoglycemia rate per patient-year in the study of the UK Hypoglycaemia Group²⁷ (3.2 severe hypoglycemic episodes), the

FM system would allow savings of €1 256 065 in 1000 patients, that is, a decrease in overall cost of –37.8% as compared with the use of SMBG. The use of episode rates per patient-year of the meta-analysis²⁸ (1.05 severe hypoglycemic episodes) or the Spanish national study (0.9 severe episodes)²⁹ would continue to reveal savings with the FM system of €428 064 and €370 296, respectively, compared with use of SMBG alone, in a cohort of 1000 patients with T1DM and receiving MDI.

In the additional scenario considering also non-severe hypoglycemic episodes, total annual cost resulted €4 934 038 and €2 869 261 for the 1000 patient-cohort with SMBG and FM system, respectively. The use of FM system would avoid 24 115 hypoglycemic episodes a year. Of these avoided hypoglycemic episodes, 2871 would correspond to severe episodes (58.6% reduction), and 21 243 to non-severe episodes (31.0% reduction). Cost savings would be up to €2 064 777 per year with the use of FM systems in 1000 patients with T1DM treated with MDI, as compared with SMBG strategy.

The modifications in daily use of strips and lancets also produced a saving associated with the use of the FM system versus SMBG of €1 505 336 a year (37.3% reduction), considering six strips and six lancets a day. The analyses with 9 strips and 4.5 lancets a day and 6 strips and 3 lancets a day revealed savings of €1 761 358 and €1 405 733, respectively. In the last SA, considering that the strips and lancets would have no cost for the Spanish National Health System, the saving associated with the FM system versus SMBG was estimated to be €762 053 a year (23.7% reduction) (table 4).

CONCLUSIONS

The present analysis shows the FM system with optional alarms to be a strategy resulting in savings in terms of the consumption of glucose monitoring resources. The cost findings suggest that utilization of the FM system would lead to an overall reduction in associated costs in patients with T1DM treated with MDI. Based on the assumptions of this model, the use of the FM system would cut the total annual cost per patient by €1911 (43.1%), which could generate annual savings for the Spanish National Health System of more than €2 million per cohort of 1000 treated patients.

Table 2 Annual costs for patient with T1DM

Costs	SMBG	FM system	Difference FM system vs SMBG	
			Absolute	%
Cost of blood glucose monitoring	€1216	€1193	€–23.7	–1.9
Cost of strips and lancets	€1216	€68	€–1149	–94.4
Cost of FM system sensors	€0	€1125	€1125	
Cost of management of severe hypoglycemia episodes	€3220	€1333	€–1887	–55.1
Total cost	€4437	€2526	€–1911	–43.1

FM, flash monitoring; SMBG, self-monitoring of blood glucose; T1DM, type 1 diabetes mellitus.

Table 3 Hypoglycemia episodes and annual costs for a cohort of 1000 patients with T1DM with MDI

Parameter	SMBG	FM system	Absolute difference FM system vs SMBG (percentage variation)
Severe hypoglycemia episodes	4900	2029	-2871 (-58.6%)
SH with hospital admission	158	65	-93 (-58.6%)
SH with hospital care, no admission	830	344	-486 (-58.6%)
SH without hospital care	3912	1620	-2293 (-58.6%)
Cost of glucose monitoring	€1 216 283	€1 192 591	€-23 691 (-1.9%)
Cost of strips and lancets	€1 216 283	€65 571	€-1 148 711 (-94.4%)
Cost of FM system sensors	€0	€1 125 020	€1 125 020 (100.0%)
Cost of management of severe hypoglycemic episodes	€3 220 260	€1 333 188	€-1 887 073 (-58.6%)
Total cost	€4 436 543	€2 525 779	€-1 910 764 (-43.1%)

FM, flash monitoring; MDI, multiple dose insulin; SH, severe hypoglycemia; SMBG, self-monitoring of capillary glucose; T1DM, type 1 diabetes mellitus.

The cost savings associated with the FM system have also been observed in other settings such as the UK in patients with T1DM,³¹ and also in patients with T2DM.³² Utilization of the FM system in the population with T1DM was associated with annual savings of £234.28/patient³¹ in a scenario with 10 daily SMBG measurements as a reflection of the National Institute for Health and Care Excellence recommendations regarding patients with T1DM.¹¹

The reduction of hypoglycemic episodes is the parameter that contributes most to the estimated cost savings.

There are some limitations around this parameter. The first one is related to the uncertainty about the incidence of hypoglycemia. The broad range of values found in the literature is very likely due to the existence of differences in the methodology and criteria used in the different studies. In the present analysis, the expert panel selected a multicenter (2004 health-care centers), multinational (24 countries) and large

study (27 585 patients with diabetes; 8022 patients with T1DM)^{20 26} as the most robust data source. However, in all the SAs performed with alternative hypoglycemia rates, utilization of the FM system was always associated with savings in these patients ranging from €370 000 to €1 333 000 for a cohort of 1000 subjects. Even in the scenario characterized by no cost associated with blood glucose monitoring strips and lancets, the hypoglycemic events avoided would generate savings for the healthcare system up to €762 000 in 1000 patients.

The IMPACT trial¹⁶ reported reductions of biochemical hypoglycemia in association with FM system use that in the present analysis were applied to the incidence of clinical hypoglycemia. This is a controversial issue, because evidence about relationship between low glucose level and symptomatic hypoglycemic episodes is limited, although a recent publication has concluded that the occurrence of biochemical hypoglycemia (<3.9

Table 4 Results of the sensitivity analyses

	Total annual cost for 1000 patients with T1DM with MDI		
	SMBG	FM system	Absolute difference FM system vs SMBG (percentage variation)
Base case	€4 436 543	€2 525 779	€-1 910 764 (-43.1%)
SA1 (3.4 severe hypoglycemic episodes/patient-year)	€3 450 749	€2 117 660	€-1 333 089 (-38.6%)
SA2 (3.2 severe hypoglycemic episodes/patient-year)	€3 319 310	€2 063 244	€-1 256 065 (-37.8%)
SA3 (1.05 severe hypoglycemia episodes/patient-year)	€1 906 338	€1 478 274	€-428 064 (-22.5%)
SA4 (0.9 severe hypoglycemia episodes/patient-year)	€1 807 759	€1 437 462	€-370 296 (-20.5%)
SA5 (including severe and non-severe hypoglycemia)	€4 934 038	€2 869 261	€-2 064 777 (-41.85%)
SA6 (6 strips and lancets a day for SMBG)	€4 031 115	€2 525 779	€-1 505 336 (-37.3%)
SA7 (9 strips and 4.5 lancets a day for SMBG)	€4 287 137	€2 525 779	€-1 761 358 (-41.1%)
SA8 (6 strips and 3 lancets a day for SMBG)	€3 931 512	€2 525 779	€-1 405 733 (-35.8%)
SA9 (no cost associated with strips and lancets)	€3 220 260	€2 458 208	€-762 053 (-23.7%)

FM, flash monitoring; MDI, multiple dose insulin; SA, sensitivity analysis; SMBG, self-monitoring of capillary glucose; T1DM, type 1 diabetes mellitus.

or 3 mmol/L) is associated with an increased risk of severe hypoglycemic events.³³

For the better addressing of the issue of hypoglycemic risk, the International Hypoglycemia Study Group recommended to the diabetes community the adoption of common glucose levels when reporting outcomes about hypoglycemia in studies.²¹ However, since in the trial used in this analysis as efficacy source, hypoglycemic events were not specifically reported, an assumption was needed equating those episodes with glucose levels <2.0 mmol/L (40 mg/dL) to hypoglycemic episodes requiring external assistance. Given the results of the IMPACT trial, this assumption represents a conservative scenario, because the proposed definition for severe hypoglycemic episodes could also be applied to events with glucose levels \geq 2.0 mmol/L (40 mg/dL). Given the lack of additional evidence, the present analysis assumes that findings of the IMPACT trial¹⁶ are generalizable to the population of patients with T1DM with MDI, although the eligible population of the IMPACT¹⁶ was restricted to patients with HbA1c level of 7.5% or lower. Further development of randomized controlled studies including patients with HbA1c level >7.5% would be required to confirm that and being the source for updating the analysis. We have also assumed that the IMPACT results are fully transferable to FreeStyle Libre 2, but with FreeStyle Libre 2 optional alarms and the improved accuracy performance, the use of FreeStyle Libre 2 could result in a higher reduction of severe hypoglycemia.

Regardless of the avoided hypoglycemic episodes, use of the FM system was associated with a decrease in the number of SMBG measurements required by the patients, and this alone generated cost reductions of -1.9% as compared with the use of SMBG alone. This resulted in direct cost savings for the Spanish National Health System of €24 000 per 1000 patient-year.

There is not discussion about the value of the glucose monitoring on the diabetes control, and the strong association between higher SMBG frequency and lower HbA1c levels,³⁴ however several scientific publications^{12 35} revealed a poor follow-up of the recommendations stated in the current clinical guidelines.^{10 11} 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 T1DM with MDI was lower than the nine recommended daily measurements, the savings derived from the avoided hypoglycemic episodes would compensate for the costs of acquiring the sensors of the FM system.

The low adherence of patients to the monitoring recommendations is justified by a wide variety of reasons among which lack of time, invasiveness and needle phobia are included.^{35 36} The features of FM system could overcome some of these barriers,³⁷ contributing to increase the daily number of glucose determinations.

The FM system has been positively evaluated in application to patients with T1DM and T2DM by health assessment agencies in a number of countries and regions (France, Norway, Scotland, Sweden, UK, Wales, etc), and published cost-effectiveness analysis have shown the efficiency of the FM system in several settings.^{38–43}

The use of the FM system as a substitute for test strips in SMBG may result in savings for the National Health system, while also 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 the patients, their relatives and the healthcare professionals.

In conclusion, the use of the glucose FM system (FreeStyle Libre 2) represents an efficient strategy for the Spanish National Health System, thanks to the savings it can generate, linked to both the decrease in hypoglycemic episodes and to the direct cost savings in blood glucose monitoring.

Considering the assumptions and costs described, in comparison with SMBG, the FM system would potentially allow cost savings of up to €1 910 000 per year in a cohort of 1000 patients with T1DM treated with MDI in Spain.

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