

Cost-Utility Analysis of FreeStyle Libre Systems in People with Type 2 Diabetes Mellitus on Treatment with Basal Insulin and Poor Glycemic Control in Spain

Mireya Robles-Plaza ¹; Fernando Gómez-Peralta ²; Virginia Bellido ³; Francisco Javier Ampudia-Blasco ^{4,5,6,7}; Juana Carretero-Gómez ⁸; Ana María Cebrián-Cuenca ^{9,10}; Alberto de la Cuadra-Grande ¹; Pedro Mezquita-Raya ¹¹

AFFILIATIONS:

¹ Pharmacoeconomics & Outcomes Research Iberia (PORIB), Paseo Joaquín Rodrigo 4 – Letter I, Pozuelo de Alarcón, 28224, Madrid, Spain.

² Endocrinology and Nutrition Unit, Hospital General de Segovia, Segovia, Spain.

³ Unidad de Gestión Clínica de Endocrinología y Nutrición, Instituto de Biomedicina de Sevilla (IBiS), Hospital Universitario Virgen del Rocío / CSIC / Universidad de Sevilla, Sevilla, Spain.

⁴ Endocrinology and Nutrition Department, Hospital Clínico Universitario de Valencia, Valencia, Spain.

⁵ Medicine Faculty, University of Valencia, Valencia, Spain.

⁶ Centro de Investigación Biomédica en Red de Diabetes y Enfermedades Metabólicas Asociadas (CIBERDEM), Instituto de Salud Carlos III, Madrid, Spain.

⁷ INCLIVA Biomedical Research Institute, Valencia, Spain.

⁸ Internal Medicine Service, Hospital Universitario de Badajoz, Badajoz, Spain.

⁹ Centro de Salud de Cartagena Casco, Cartagena (Murcia), Spain.

¹⁰ Instituto Murciano de Investigación Biomédica (IMIB) Murcia, Spain.

¹¹ Endocrinology and Nutrition Service, Hospital Universitario Torrecárdenas, Almería, Spain.

CORRESPONDING AUTHOR:

Francisco Javier Ampudia-Blasco.

Email: ampudia_fra@gva.es

– SUPPLEMENTARY MATERIAL –

SUPPLEMENTARY TABLES:

Supplementary Table 1. Evaluation of the study report by ISPOR checklist CHEERS 2022.

Supplementary Table 2. RECODE risk engine.

Supplementary Table 3. PSA inputs.

SUPPLEMENTARY MATERIAL REFERENCES:

1. Husereau D, Drummond M, Augustovski F, de Bekker-Grob E, Briggs AH, Carswell C, et al. Consolidated Health Economic Evaluation Reporting Standards (CHEERS) 2022 Explanation and Elaboration: A Report of the ISPOR CHEERS II Good Practices Task Force. *Value in Health*. 2022;25:10–31.
2. Basu S, Sussman JB, Berkowitz SA, Hayward RA, Yudkin JS. Development and validation of Risk Equations for Complications Of type 2 Diabetes (RECODE) using individual participant data from randomised trials. *Lancet Diabetes Endocrinol*. 2017;5:788–98.

Supplementary Table 1. Evaluation of the study report by ISPOR checklist CHEERS 2022.

Section		Items	Reported in section
Title	1	Identify the study as an economic evaluation and specify the interventions being compared	✓ (Title)
Abstract			
Abstract	2	Provide a structured summary that highlights context, key methods, results, and alternative analyses	✓ (Abstract)
Introduction			
Background and objectives	3	Give the context for the study, the study question, and its practical relevance for decision making in policy or practice	✓ (Introduction)
Methods			
Health economics analysis plan	4	Indicate whether a health economic analysis plan was developed and where available	✓ (Material and Methods)
Study population	5	Describe characteristics of the study population (such as age range, demographics, socioeconomic, or clinical characteristics).	✓ (Material and Methods – Study Population)
Setting and location	6	Provide relevant contextual information that may influence findings	✓ (Introduction/ Material and Methods – Clinical Inputs / Health Care Resource Consumption and Costs / Alternative Scenarios/ Discussion)
Comparators	7	Describe the interventions or strategies being compared and why chosen	✓ (Material and Methods)
Perspective	8	State the perspective(s) adopted by the study and why chosen	✓ (Material and Methods - Health Care Resource Consumption and Costs)
Time horizon	9	State the time horizon for the study and why appropriate	✓ (Material and Methods)
Discount rate	10	Report the discount rate(s) and reason chosen	✓ (Material and Methods - Health Care Resource Consumption and Costs)
Selection of outcomes	11	Describe what outcomes were used as the measure(s) of benefit(s) and harm(s)	✓ (Material and Methods – Clinical Inputs / Alternative Scenarios)
Measurement of outcomes	12	Describe how outcomes used to capture benefit(s) and harm(s) were measured	✓ (Material and Methods – Clinical Inputs / Alternative Scenarios)

Valuation of outcomes	13	Describe the population and methods used to measure and value outcomes	✓ (Material and Methods – Clinical Inputs / Health Care Resource Consumption and Costs / Alternative Scenarios)
Measurement and valuation of resources and costs	14	Describe how costs were valued	✓ (Material and Methods – Health Care Resource Consumption and Costs / Alternative Scenarios)
Currency, price date, and conversion	15	Report the dates of the estimated resource quantities and unit costs, plus the currency and year of conversion	✓ (Material and Methods – Health Care Resource Consumption and Costs)
Rationale and description of model	16	If modelling is used, describe in detail, and why used. Report if the model is publicly available and where it can be accessed	✓ (Material and Methods – Clinical Inputs / Health Care Resource Consumption and Costs / Alternative Scenarios)
Analytics and assumptions	17	Describe any methods for analysing or statistically transforming data, any extrapolation methods, and approaches for validating any model used	✓ (Material and Methods – Clinical Inputs / Health Care Resource Consumption and Costs / Alternative Scenarios)
Characterizing heterogeneity	18	Describe any methods used for estimating how the results of the study vary for subgroups	✓ (Material and Methods – Alternative Scenarios / Sensitivity Analyses)
Characterizing distributional effects	19	Describe how impacts are distributed across different individuals or adjustments made to reflect priority populations	✓ (Material and Methods – Alternative Scenarios / Sensitivity Analyses)
Characterizing uncertainty	20	Describe methods to characterize any sources of uncertainty in the analysis	✓ (Material and Methods – Alternative Scenarios / Sensitivity Analyses)
Approach to engagement with patients and others affected by the study	21	Describe any approaches to engage patients or service recipients, the general public, communities, or stakeholders (such as clinicians or payers) in the design of the study	✓ (Material and Methods)

Results

Study parameters	22	Report all analytic inputs (such as values, ranges, references) including uncertainty or distributional assumptions	✓ (Results – Base Case Results / Alternative Scenarios Results / Sensitivity Analyses Results)
Summary of main results	23	Report the mean values for the main categories of costs and outcomes of interest and summarize them in the most appropriate overall measure	✓ (Results – Base Case Results / Alternative Scenarios Results / Sensitivity Analyses Results)
Effect of uncertainty	24	Describe how uncertainty about analytic judgments, inputs, or projections affect findings. Report the effect of choice of	✓ (Results – Base Case Results / Alternative Scenarios Results / Sensitivity Analyses Results)

		discount rate and time horizon, if applicable	
Effect of engagements with patients and others affected by the study	25	Report on any difference patient/service recipient, general public, community, or stakeholder involvement made to the approach or findings of the study	✓ (Results – Sensitivity Analyses Results)
Discussion			
Study findings, limitations, generalizability, and current knowledge	26	Report key findings, limitations, ethical or equity considerations not captured, and how these could affect patients, policy, or practice	✓ (Discussion)
Other relevant information			
Source of funding	27	Describe how the study was funded and any role of the funder in the identification, design, conduct, and reporting of the analysis	✓ (Declarations)
Conflict of interest	28	Report authors conflicts of interest according to journal or International Committee of Medical Journal Editors requirements	✓ (Declarations)

CHEERS: Consolidated Health Economic Evaluation Reporting Standards; ISPOR: International Society for Pharmacoeconomics & Outcomes Research.

Source: ISPOR report of CHEERS 2022 checklist [1].

Supplementary Table 2. RECODE risk engine.

RECODE Parameters	Renal Failure	Blindness	CVD	MI	Stroke	CHF	CVD Death	All causes Death
Mean Beta (β_0)	0.23000	4.56000	3.65000	2.92000	6.96000	5.15000	3.97000	4.66000
Gamma (λ)	0.97300	0.92100	0.85000	0.93000	0.98000	0.96000	0.97000	0.93000
Beta Coefficients (β_i)	Age [years]	-0.01938	0.02285	0.03412	0.04363	0.02896	0.05501	0.06703
	Sex (Female)	-0.01129	0.22640	-0.16720	-0.20660	-0.00326	0.25290	-0.15290
	Ethnicity (Black)	0.08812	-0.16770	-0.11870	-0.11630	0.27160	-0.04969	-0.02393
	Ethnicity (Hispanic)	0.23380	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000
	Smoker (Yes)	0.14830	0.00000	0.15100	0.23580	0.16650	0.29050	0.53990
	SBP [mmHg]	0.00303	0.00824	0.00007	-0.00514	0.01659	0.00121	-0.00394
	History of CVD (Yes)	-0.02164	0.11270	0.77840	0.96180	0.41380	1.00700	0.58880
	Antihypertensives (Yes)	-0.07952	0.06393	0.05579	-0.12480	0.15980	0.63890	-0.15770
	Statins (Yes)	0.00000	0.00000	-0.03361	0.04699	-0.18870	-0.11750	-0.20450
	Oral antidiabetics (Yes)	-0.12560	-0.23490	0.00000	0.00000	0.00000	0.00000	0.00000
	Anticoagulants (Yes)	0.03199	0.00000	0.25240	0.54400	-0.13870	0.73650	0.69460
	HbA1c [%]	0.13690	0.14490	0.17160	0.21350	0.33650	0.20920	0.24540
	Total cholesterol [mg/dL]	-0.00111	-0.00017	0.00193	0.00019	0.00171	-0.00136	-0.00127
	HDL cholesterol [mg/dL]	0.00629	0.00545	-0.00837	-0.01358	-0.00639	-0.01758	-0.01081
	Serum creatinine [mg/dL]	0.86090	0.69470	0.43550	0.08027	0.59550	0.82140	0.45440
	UACR [mg/g]	0.00036	0.00020	0.00033	0.00042	0.00030	0.00041	0.00047

CHF: Congestive Heart Failure; CVD: Cardiovascular Disease; HDL: High Density Lipoprotein; MI: Myocardial Infarction; SBP: Systolic Blood Pressure; UACR: Urinary Albumin-Creatinine Ratio.

Source: Basu *et al.* (2017) [2].

Supplementary Table 3. PSA inputs.

Baseline characteristic	Mean Value	SD	Probability Distribution
Time horizon [years, maximum 100]	50	10 *	Normal
Discount rate – Costs	0.03	0.006 *	Gamma
Discount rate – Events	0.03	0.006 *	Gamma
Number of patients	10,000	2,000 *	Normal
Age [years]	62.9	12.8	Normal
Percentage of women [%]	41.0%	-	-
Baseline level of glycated HbA1c [%]	9.2%	1.0%	Normal
SBP [mmHg]	139.9	28.4	Normal
HDL cholesterol [mg/dL]	46.8	9.6	Normal
Total cholesterol [mg/dL]	201.8	41.2	Normal
Serum creatinine [mg/dL]	0.86	0.2	Normal
UACR [mg/g]	99.2	359.4	Normal
Percentage of active smokers [%]	27.8%	-	-
Percentage of patients with CVD [%]	35.6%	-	-
Percentage of patients treated with statins [%]	36.6%	-	-
Percentage of patients treated with antihypertensives [%]	44.3%	-	-
Percentage of patients treated with anticoagulants [%]	39.5%	-	-
Percentage of patients treated with oral antidiabetics [%]	84.4%	-	-
Baseline health utility value (HRQoL)	0.7840	0.157 *	Beta
Hypoglycemic events/person-year (FSL)	7.148	1.430 *	Beta
Hypoglycemic events/person-year (SBGM)	17.02	3.404 *	Beta
Annual probability of SHEs (FSL)	0.037	0.007 *	Beta
Annual probability of SHEs (SBGM)	0.089	0.018 *	Beta
SHE mortality	0.003	0.001 *	Beta
Annual probability of DKA (FSL)	0.0008	0.0002 *	Beta
Annual probability of DKA (SBGM)	0.0025	0.0005 *	Beta
DKA mortality	0.004	0.001 *	Beta
Disutility of MI [Absolute value]	0.055	0.011 *	Beta
Disutility of chronic MI [Absolute value]	0.055	0.011 *	Beta
Disutility of CHF [Absolute value]	0.108	0.022 *	Beta
Disutility of chronic CHF [Absolute value]	0.108	0.022 *	Beta

Disutility of stroke [Absolute value]	0.164	0.033 *	Beta
Disutility of chronic stroke [Absolute value]	0.164	0.033 *	Beta
Disutility of blindness [Absolute value]	0.074	0.015 *	Beta
Disutility of chronic blindness [Absolute value]	0.074	0.015 *	Beta
Disutility of renal failure [Absolute value]	0.204	0.041 *	Beta
Disutility of chronic renal failure [Absolute value]	0.204	0.041 *	Beta
Fingerstick disutility [Absolute value]	0.031	0.006 *	Beta
One-time HbA1c reduction (FSL) [%]	1.10	0.1	Normal
Cost of acute MI [€]	31,013.22	6,202.64 *	Gamma
Annual cost of MI [€]	1,248.44	249.69 *	Gamma
Cost of acute CHF [€]	6,505.08	1,301.02 *	Gamma
Annual cost of CHF [€]	1,523.14	304.63 *	Gamma
Cost of acute stroke [€]	7,849.48	1,569.90 *	Gamma
Annual cost of stroke [€]	3,187.92	637.58 *	Gamma
Cost of acute blindness [€]	2,943.37	588.67 *	Gamma
Annual cost of blindness [€]	2,943.37	588.67 *	Gamma
Cost of acute renal failure [€]	4,057.053	811.41 *	Gamma
Annual cost of renal failure [€]	42,757.39	8,551.48 *	Gamma
Annual cost of glucose monitoring (FSL) [€]	1,207.43	241.49 *	Gamma
Annual cost of glucose monitoring (SBGM) [€]	650.51	130.10 *	Gamma

CHF: Congestive Heart Failure; CVD: Cardiovascular Disease; DKA: Diabetic Ketoacidosis; FSL: FreeStyle Libre systems; HDL: High-Density Lipoprotein; HRQoL: Health-Related Quality of Life; MI: Myocardial Infarction; PSA: Probabilistic Sensitivity Analysis; SBP: Systolic Blood Pressure; SD: Standard Deviation; SBGM: Self-Blood Glucose Monitoring; SHE: Severe Hypoglycemic Event; UACR: Urinary Albumin-Creatinine Ratio.

* SD estimated as $\pm 20\%$ of the mean value.