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Clinical and Economic Impact of Hybrid Closed-Loop Systems for T1 Diabetes Management in Spain

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ABSTRACT

Objective: The main challenge in type 1 diabetes mellitus management is achieving and maintaining glycemic control. Hybrid closed-loop (HCL) systems offer patients the potential to safely achieve tight glycemic targets. This study analyzed the clinical and economic impact of HCL systems compared with intermittently scanned continuous glucose monitoring (is-CGM) and continuous subcutaneous insulin infusion (CSII) therapy from the Spanish health care system perspective.
Methods: IQVIA Core Diabetes Model v10.0 was used to simulate a cohort of 1000 individuals assigned to either the HCL or is-CGM+CSII therapy. Different time horizons were analyzed: 5, 15, 30, and 50 years. Cohort characteristics were extracted from published literature, and a 1.5% glycated hemoglobin A1C reduction was considered for the HCL group over is-CGM+CSII.
Results: In the HCL group, complications were averted or delayed across all time horizons whereas survival, quality of life, and cost savings were increased. At 50 years, HCL group survival was double than the comparator and 1.15 incremental quality-adjusted life years were gained. Cost savings were the highest at 50 years (28 704 922€/1000 individuals) mostly attributable to lower amputation, ulcer, and nephrological event rates. The current study is based on real-world evidence data with a median follow-up of 5.1 months. Thus, the long-term projections of clinical and economic outcomes may be affected by uncertainty. Additionally, the study did not include any hypoglycemia or diabetic ketoacidosis rates, which may lead to underestimation of the real impact of HCL systems.
Conclusion: HCL systems should be considered the primary treatment option compared with is-CGM+CSII therapy for people with type 1 diabetes mellitus in Spain.

Introduction

In 2021, an estimated 8.4 million individuals globally had type 1 diabetes mellitus (T1D), projected to double to 13.5 to 17.4 million by 2040.[1] In Spain, 46 455 adults were estimated to live with T1D in 2016.[2]

Variability in glucose levels is one of the biggest challenges for people living with T1D, resulting in suboptimal glucose

Abbreviations: BMI, body mass index; CDM, Core Diabetes Model; CGM, continuous glucose monitoring; CSII, continuous subcutaneous insulin infusion; DKA, diabetic ketoacidosis; HbA1c, glycated hemoglobin A1C; HCL, hybrid closed-loop; is-CGM, intermittently scanned continuous glucose monitoring; QALY, quality-adjusted life year; T1D, type 1 diabetes mellitus; T2D, type 2 diabetes mellitus.

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control,[3] physical and psychological implications.[4] The European Association for the Study of Diabetes recommends a targeted glycated hemoglobin A1C (HbA1c) goal of <7.0% (<53 mmol/mol) without significant hypoglycemia.[5] However, Gómez-Peralta et al[6] in a Spanish observational study reported that only <30% of the population was able to achieve this HbA1c target.[6] Clinical implications of unoptimized glycemic control include, among others, microvascular and macrovascular complications[7,8] and subsequent premature mortality.[9] Therefore, tight glycemic management is recommended for most people living with T1D.

Suboptimal glycemic control increases the burden of T1D not only for the individuals living with it, but also for the health care systems and society due to the costs of diabetes-related complications, productivity losses, and informal care costs.[10]

The clinical and economic burden associated with T1D and type 2 diabetes mellitus (T2D) is considerable. In 2012 diabetes costs accounted for 8.2% of the total Spanish national health system expenditure. Hospital care costs accounted for 33% of total diabetes expenditure; therefore, avoiding or delaying diabetes-related complications could considerably lower hospital costs and alleviate care burden.[11]

Kanavos et al[12] estimated that indirect costs of T1D or its complications due to absenteeism and early retirement exceed direct costs by a factor of 3.5 to 1 in Spain. Newer technologies such as hybrid closed-loop (HCL) systems for the management of T1D can contribute to the mitigation of long-term complications and increase the quality of life of people living with diabetes,[13] ultimately reducing the burden of disease.

HCL systems, also known as automated insulin delivery systems, combine a continuous glucose monitoring (CGM) system, a continuous subcutaneous insulin infusion (CSII) pump, and an algorithm that uses data from both the CGM and the pump to automatically adjust the amount of insulin delivered. In numerous studies, HCL systems have demonstrated to consistently improve glycemic control compared with any other treatment, currently being considered the most advanced therapy for T1D.[14-16]

Currently, only one study has analyzed the cost-effectiveness of advanced HCL systems in 6 European countries, including Spain.[17] This study compared an automated HCL insulin delivery system with intermittently scanned CGM (is-CGM) plus multiple daily insulin injections in adults with T1D with suboptimal glycemic control, using baseline cohort characteristics and treatment effect from the Adult Population with Type 1 Diabetes trial[18] and reported a cost-effectiveness ratio of 29 718€ per quality-adjusted life year (QALY).[17]

Therefore, to further increase the uptake of HCL therapy earlier in the T1D treatment pathway, it is crucial to further research the long-term clinical outcomes, as well as validate and actualize economic impact of such novel technology with additional studies such as this one.

The objective of the present study was to analyze and assess the long-term clinical and economic impact of HCL systems versus nonautomated systems in Spain for adults with T1D.[19] Short, mid-and long-term time horizons were considered to better reflect the treatment effect across different time frames. This analysis aims to support evidence-based decision making for health care professionals, health payers, and policy makers. Ultimately, providing additional clinical and economic data will support the adoption of HCL systems earlier in the treatment pathway to improve T1D people's length and quality of life, while striving for the economic sustainability of health care systems.

Highlights

- This is the first comprehensive clinical and economic impact Spanish study comparing hybrid closed-loop with intermittently scanned continuous glucose monitoring and continuous subcutaneous insulin infusion. The results indicate hybrid closed-loop systems as the optimal treatment for adults living with type 1 diabetes mellitus and have nonoptimal glycose levels
- €28.7M of cost savings per every 1000 treated patients were estimated for the Spanish health care system
- This study intends to inform clinicians and health care policy makers and assist with the better allocation of limited health care resources

Clinical Relevance

Hybrid closed-loop treatment demonstrated higher survival for type 1 diabetes mellitus adults over short- and long-term periods, with extended time alive and free of complications, especially for renal and eye complications. Hybrid closed-loop treatment can delay and reduce diabetes-related complications, leading to improved quality of life and considerable cost savings for the Spanish health care system.

Methods

Model Overview

For this study, the IQVIA Core Diabetes Model (CDM) version 10.0 was used. The IQVIA CDM is a widely adopted and validated model.[20] It enables the simulation of both short- and long-term clinical and economic outcomes when applying changes on key treatment effects (eg, change on HbA1c, hypoglycemia events, diabetic ketoacidosis [DKA] events, body mass index [BMI], etc.), delivering robust results in simulating both T1D and T2D disease progression. The IQVIA CDM consists of a series of submodels using Markov processes with yearly cycles and incorporates demographics, baseline risk factors, treatment effects and costs to simulate accurate lifelong clinical and economic outcomes.[21]

Cohort Characteristics

Baseline cohort characteristics entered in the IQVIA CDM model were sourced from the clinical study published by Crabtree et al[19] with a median follow-up of 5.1 months (IQR, 3.9-6.6).[19] These characteristics included age, proportion of male population, duration of diabetes, BMI, and baseline HbA1c. This prospective real-world observational single-arm study conducted in the UK included 570 adults with T1D with a baseline HbA1c of 8.5% or above who were already using an insulin pump plus is-CGM and who were willing to switch to an HCL system commercially available in the UK (specifically, Medtronic Minimed 780G [Medtronic], Tandem Control-IQ [Tandem Diabetes Care], CamAPS FX [CamDiab], Medtrum closed-loop system [Medtrum], Medtronic Minimed 670G [Medtronic]; and no brand name recorded for some individuals). The mean baseline HbA1c of the study population was 9.4 ± 0.9%, the median age was 40 ± 16.3 years, the median diabetes duration was 21 ± 11.1 years, and the mean BMI was 29 ± 6 kg/m^2. Since the IQVIA CDM model requires mean and SD values, the mean and the SD values were estimated by

Table 1
Baseline Cohort Characteristics by Crabtree et al[19] Were Used as an Input Within the IQVIA CDM

Characteristic	Value
Age (y), mean (SD)	40 (16.30)
Duration of diabetes (y), mean (SD)	22 (11.11)
Male, %	33
HbA1c %, mean (SD)	9.4 (0.9)
BMI, kg/m^2, mean (SD)	29 (6)
HbA1c %, reduction in HCL group	1.5

Abbreviations: BMI = body mass index; CDM = Core Diabetes Model; HbA1c = hemoglobin A1C, HCL = hybrid closed-loop.

assuming that the variables followed a normal distribution.[22] A summary of the model cohort inputs can be found in Table 1,[19] which are either sourced values for T1D population from the literature or default values of IQVIA CDM (Supplementary Table 1).

Clinical Inputs: Treatment Effect

The treatment effect for the HCL simulated cohort came from the reduction in HbA1c at the end of the follow-up period: HbA1c was reduced by 1.5% (95% CI 1.4, 1.6; $P < .001$; unadjusted change) (Table 1).

For all analyses 2 distinct groups were considered: one group which adopted the HCL as an intervention (intervention group) and another group which continued the is-CGM+CSII (comparator group). The treatment effect of HbA1c reduction was applied to the intervention group, presuming a static and sustained HbA1c reduction of 1.5% after the first year of HCL use, both over short and long-term time horizons. For the comparator group, HbA1c levels were assumed to remain static, with no HbA1c change applied at any time horizon (namely HbA1c baseline value). To assess the effect of the HbA1c reduction, for the rest of the physiologic parameters such as blood pressure, lipid levels, or BMI, no alterations were implemented to the baseline values, which were assumed to follow the default progression equations of the IQVIA CDM model. For BMI, the change from baseline was not considered significant ($P = .07$). Similarly, no statistically significant change in the rates of severe hypoglycemic events per 10 person-years was observed ($P = .483$) and for DKA episodes with hospital admission ($P = .458$). Therefore, the values for hypoglycemic and DKA events were assumed to be zero for both groups.

Costs and Time Horizon

All analyses were conducted from the perspective of the Spanish health system, with complication and management costs updated by health care inflation to 2024 values. Direct costs were sourced from the literature and included all health care utilization costs related to diabetes complications and management (Table 2).[23-34] All costs regarding the diabetes management devices and the insulin doses were assumed to be equal for the HCL system and is-CGM+CSII therapy.

A 3% discount rate per annum after the first year was applied to both costs and clinical outcomes.[35] To demonstrate the impact of using HCL or is-CGM+CSII systems, cohorts of population with T1D were simulated for the following times: 5-year, 15-year, 30-year, and 50-year (lifetime horizon).

Utilities

The model's default quality-of-life utility values were applied. For the QALYs estimation, the Michigan multiple linear regression-Self-Administered Quality of Well Being index approach was used. This approach uses different regressions for T1D and T2D,[36] subsequently using regressions for T1D in the current analyses.

Sensitivity Analysis

To assess the model robustness and account for the uncertainty of the individual characteristics and key parameters, first and second-order (probabilistic) sensitivity analysis were implemented in addition to the base case analysis. More specifically, the IQVIA CDM employs Monte Carlo simulations with nonparametric bootstrapping to account for parameter uncertainty, involving in each iteration the resampling of input parameters with replacement following their distributions. All analyses were run for 1000 individuals with T1D and 1000 iterations.

Probabilistic sensitivity analysis at 5% was applied for direct costs, utilities, baseline characteristics, and efficacy of the intervention and comparator group. Additionally, by examining different time horizons, a univariate analysis of time was performed. Finally, sensitivity analysis varying the treatment effect by ±10% was performed (ΔHbA1c −1.35, ΔHbA1c −1.65).

Ethics

For this study, the input parameters were sourced from a previously conducted study involving human participants,[19] and thus no additional ethics approval was required.

Results

Overall, for people living with T1D with suboptimal glucose levels, the comparative analyses showed that HCL systems are associated with higher survival across all time horizons (Table 3). After 50 years of treatment, we observe a 5.1% survival rate on the HCL group, versus 2.4% in the comparator group. This means that at the end of the follow-up period, survival rates are double in the HCL group. These differences in the survival rates were maintained even when we applied a lower HbA1c treatment effect by 10% (HCL group: 4.8%, comparator group: 2.4%).

Additionally, HCL consistently reduced all major complications for T1D individuals across all evaluated periods. For the 5-year period, the 5 complications with the highest incidence reduction were proliferative diabetic retinopathy at 80%, macular edema and microalbuminuria at 71%, background diabetic retinopathy at 67%, neuropathy at 56%, and proteinuria at 46%. Over the lifetime 50-year period, the 5 complications with the highest incidence reduction were the following: proliferative diabetic retinopathy 68%, macular edema 55%, microalbuminuria 56%, gross proteinuria 55%, and end-stage renal disease 49%. Significant reductions in diabetes-related complications are observed even in the short- and mid-time horizons, indicating an early benefit of HCL systems (Table 4, Supplementary Tables 2 and 3).

Following, time alive free of complications was assessed for the 50-year time horizon (Fig). All diabetes-related complications were delayed for the intervention group compared with the comparator group. On average in the HCL group microalbuminuria is delayed by 8.4 years, macular edema by 8.2 years, neuropathy by 7.4 years, proliferative retinopathy by 7.1 years, gross proteinuria by 5.4 years, background retinopathy by 5.6 years, severe vision loss by 4.6 years, and all cardiovascular complications by at least 2.5 years. For the rest of the complications the delay is 2.8 years for end-stage renal disease and 2.3 years for foot ulcer.

Given the delay in onset of complications and the longer survival in the intervention group compared with the comparator group, there was an impact on both QALYs gained and total cost

Table 2
Direct Costs of Diabetes Complications and Management in Spain, Cost Values Inflated for 2024

Complication	Costs (€)	Reference
Cardiovascular complications		
Myocardial infarction first year	13 252	Barón Esquivias et al,[23] 2015
Myocardial infarction second+ years	2492	Barón Esquivias et al,[23] 2015
Angina first year	3953	Cosin Sales et al,[24] 2015
Angina second+ years	1064	Cosin Sales et al,[24] 2015
Congestive heart failure first year	6445	Delgado et al,[25] 2014
Congestive heart failure second+ years	3744	Escobar et al,[26] 2022
Stroke first year	12 831	Ribera et al,[27] 2022
Stroke second+ years	4631	Ribera et al,[27] 2022
Stroke death within 30 days	4794	Gaede et al,[28] 2003
Peripheral vascular disease first year	9119	Crespo et al,[29] 2013
Peripheral vascular disease second+ years	9119	Crespo et al,[29] 2013
Renal complications		
Hemodialysis first year	51 907	Villa et al,[30] 2011
Hemodialysis second+ years	48 035	Villa et al,[30] 2011
Peripheral dialysis first year	40 359	Villa et al,[30] 2011
Peripheral dialysis second+ years	37 718	Villa et al,[30] 2011
Renal transplant costs first year	55 955	Villa et al,[30] 2011
Renal transplant costs second+ years	9176	Villa et al,[30] 2011
Eye complications		
Laser treatment	745	Oblikue,[31]
Cataract operation	1664	Dilla et al,[32] 2017
Following cataract operation	465	Dilla et al,[32] 2017
Blindness year of onset	2800	Esvision,[33] 2022
Blindness following years	2800	Esvision,[33] 2022
Neuropathy/foot ulcer/amputation		
Neuropathy	4688	Crespo et al,[29] 2013
Neuropathy second+ years	4688	Crespo et al,[29] 2013
Ulcer treatment	2111	Linertová et al,[34] 2021
Amputation event	14 141	Linertová et al,[34] 2021
Management costs		
Statins	536	Gaede et al,[28] 2003
Aspirin	33	Gaede et al,[28] 2003
ACE-I/ARB	165	Gaede et al,[28] 2003
Screening for microalbuminuria	16	Gaede et al,[28] 2003
Screening for gross proteinuria	16	Gaede et al,[28] 2003
Stopping ACE-I /ARB due to adverse events	63	Gaede et al,[28] 2003
Eye screening	91	Gaede et al,[28] 2003

Abbreviations: ACE-I = angiotensin converting enzyme inhibitor; ARB = angiotensin II receptor blocker.

Table 3
Survival (in %) by Treatment Group and Time Horizon for the Base Case Analysis and for the Probabilistic Sensitivity Analysis

	Base case analysis					
	5 y	15 y	30 y	50 y	50 y +10% ΔHbA1c	50 y −10% ΔHbA1c
HCL	98.3%	89.9%	53.3%	5.1%	5.3%	4.8%
is-CGM and CSII	98.1%	87.9%	43.6%	2.4%	2.4%	2.4%
Relative difference	0.2%	2.4%	22.4%	113.1%	124.1%	102.1%
	Probabilistic sensitivity analysis					
	5 y	15 y	30 y	50 y	50 y +10% ΔHbA1c	50 y −10% ΔHbA1c
HCL	95.5%	81.1%	47.4%	13.9%	14.3%	13.6%
is-CGM and CSII	95.1%	78.3%	40.9%	10.0%	10.0%	10.0%
Relative difference	0.5%	3.6%	15.8%	39.0%	42.8%	35.7%

Abbreviations: CSII = continuous subcutaneous insulin infusion; HbA1c = glycated hemoglobin A1C; HCL = hybrid closed-loop; is-CGM = intermittently scanned continuous glucose monitoring.

savings. The QALYs increased across all time horizons. At 50 years, the analysis showed incremental QALY gains of 1.15 and incremental life expectancy of 1.03 years. The highest cost savings were observed for the 30 and the 50-year time horizons, with 28 076 070€ and 28 704 922€ per 1000 individuals with T1D, respectively. When the univariate sensitivity analysis with a decrease and an increase of 10% in the HbA1c effect was performed, respective cost savings of 26 613 125€ and 31 054 571€ per 1000 individuals with T1D were observed. The highest contribution to cost savings across all time horizons came from the reduction of foot ulcers and amputations, followed by nephrology-related and eye-related complications (Table 5).

Table 4
Relative Incidence Reduction of Complications (in %) by Time Horizon, and Additional Mean Time Alive and Free of Complications in the Hybrid Closed-Loop Treatment Group in Years at the 50-Year Period (Lifetime)

Complication	Incidence reduction 5 y	Incidence reduction 15 y	Incidence reduction 30 y	Incidence reduction 50 y	Time alive and free of complications (y) at 50 y
Eye complications					
Background diabetic retinopathy	−67%	−53%	−37%	−32%	5.6
Proliferative diabetic retinopathy	−80%	−80%	−73%	−68%	7.1
Macular edema	−71%	−66%	−59%	−55%	8.2
Severe vision loss	−11%	−29%	−32%	−28%	4.6
Renal complications					
Microalbuminuria	−72%	−67%	−60%	−56%	8.4
Gross proteinuria	−46%	−59%	−58%	−55%	5.4
End-stage renal disease	−18%	−42%	−49%	−49%	2.8
Neuropathy/foot ulcer/amputation					
Ulcer	−18%	−17%	−20%	−16%	2.3
First amputation	0%	−1%	−1%	−0%	2.3[a]
Second amputation	−14%	−10%	−4%	−2%	-
Neuropathy	−56%	−50%	−40%	−36%	7.4
Cardiovascular complications					
Congestive heart failure	−23%	−25%	−24%	−13%	2.5
Peripheral vascular disease onset	−27%	−26%	−22%	−13%	2.6
Angina	−21%	−22%	−20%	−9%	2.5
Stroke event	−15%	−24%	-−22%	−11%	2.5
MI event	−21%	−23%	−21%	−10%	2.5

Abbreviation: MI = myocardial infarction.
Results from the base case analysis.
[a] In the IQVIA Core Diabetes Model results, it is not specified whether the reported time alive and free of complications corresponds to first or second amputation.

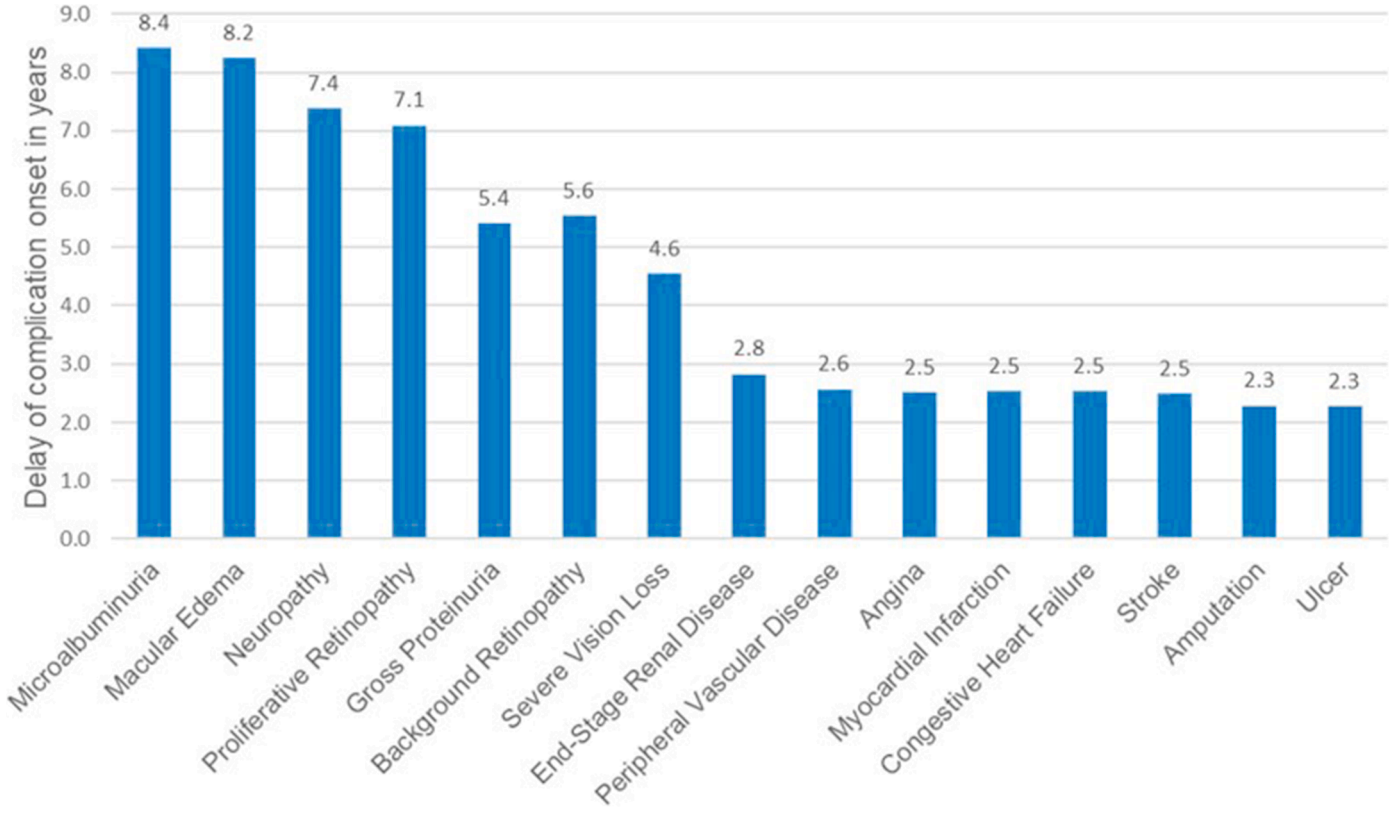

Fig. Complications onset delay for hybrid closed-loop versus is-CGM+CSII systems. Results of the base case analysis. *CSII* = continuous subcutaneous insulin infusion; is-*CGM* = intermittently scanned continuous glucose monitoring.

Discussion

In this study, the short- and long-term clinical and economic impact of HCL compared with is-CGM+CSII systems were assessed from the Spanish health care system perspective for people with T1D who have high glucose levels. Across all time horizons, the survival of people with T1D using HCL increased due to the reduction in the incidence of diabetes-related complications. The

Table 5
Cumulative Cost Reduction and Management Costs by Complication Category From the Adoption of HCL Instead of is-CGM and CSII Therapy, by Base Case Analysis and Probabilistic Sensitivity Analysis

	Base case analysis			
	5 y	15 y	30 y	50 y
Cardiovascular complications	123€	886€	2067€	1606€
Renal complications	89€	2130€	7831€	9067€
Eye complications	128€	1306€	3375€	3386€
Neuropathy/foot ulcer/amputation	1705€	8599€	14 828€	14 891€
Management costs	33€	106€	−25€	−245€
Total costs savings per HCL user	2079€	13 026€	28 076€	28 705€
Total costs savings per 1000 HCL users	2 078 660€	13 026 461€	28 076 070€	28 704 922€
	Probabilistic sensitivity analysis			
	5 y	15 y	30 y	50 y
Cardiovascular complications	194€	957€	1841€	1895€
Renal complications	298€	3426€	9888€	13 054€
Eye complications	145€	1202€	2683€	2871€
Neuropathy/foot ulcer/amputation	1766€	7811€	12 563€	13 247€
Management costs	35€	69€	−46€	−216€
Total costs savings per HCL user	2437€	13 465€	26 928€	30 850€
Total costs savings per 1000 HCL users	2 437 300€	13 465 148€	26 928 477€	30 850 297€

Abbreviations: CSII = continuous subcutaneous insulin infusion; HCL = hybrid closed-loop; is-CGM = intermittently scanned continuous glucose monitoring.
Values inflated to 2024 euros and represent mean cost per type 1 diabetes mellitus patient.

highest peak in survival difference was reached after 50 years of treatment, highlighting the increased benefits of a lifelong treatment with HCL. Cost savings mainly derived from ulcers, amputation, and nephrology treatment. Additionally, an incremental gain of 1.15 QALY was estimated for the 50-year period. Cost savings and QALY gains were solely based on HbA1c reduction; hence, results can be considered conservative.

Real-world studies[15,37-39] as well as randomized controlled trials[16,18] have shown the short-term benefits of HCL systems over conventional treatment, with a usual observation time of <1 year. The current study simulated both short- and long-term clinical and economic outcomes of HbA1c reduction based on real-world data focusing on adults with T1D and baseline HbA1c ≥8.5%. Such individuals are more likely to develop diabetes-related complications and require prompt therapy optimization.[40] Since lifelong disease progression was simulated, a detailed analysis of outcomes at different time horizons was possible. The long-term analysis of clinical and economic outcomes provided a comprehensive overview of potential benefits of HCL systems over conventional treatments, facilitating the understanding of the HCL systems full impact. As the study results suggest, there was a sizable reduction in diabetes-related complications incidence across all time horizons.

In addition, the results showed an association between HCL use and delayed onset of diabetes-related complications. Meaning that HCL-treated individuals will experience less complications and if they do, these will occur later in life. Complications delay ranged from a minimum of 2.3 to a maximum of 8.4 years. Having more people with T1D managed with HCL systems translates into healthier populations, living longer and with an overall quality of life. This was reflected by the additional year in perfect life gained (one QALY) and the increased survival rate on the HCL group, which was already evident at 5-year posttreatment.

Although the results of the current analyses are rather conservative, other studies have also reported increased time alive and free of complications,[41] increased incremental QALYs,[17,41-43] and life expectancy gains[44,45] with HCL systems. This aligns with existing literature[44,45] indicating anticipated gains in life expectancy of 0.78 and 0.16 years as well as QALYs of 1.45 and 1.95, respectively. Nevertheless, the abovementioned results indicate a higher QALY gain than the present study which reports a 1.15 lifelong QALY gain. This could be attributed to differences in study designs, clinical inputs, the inclusion of severe hypoglycemia and DKA events, or the comparison of HCL systems with either CGM plus multiple daily injection or CSII. Hypoglycemic events appear to have a significant impact on both quality of life and economic impact.[41,43]

The averted or delayed disease complications at any period shown in the current study unveil that improved glycemic control and tight T1D management may not only result in healthier populations, higher survival, and increased quality of life, but can also substantially reduce direct costs and health care burden. Although one study reports disease costs to be similar between HCL systems and standard of care over a longer time horizon of 60 years,[43] our results suggest cost savings for all major complications across all time horizons of 5, 15, 30, and 50 years. Lower costs associated with HCL systems use, either by delaying or averting complications, provide evidence to facilitate health policy decision making. Especially, the in-depth analyses of staggered time horizons allow for better planning and optimal allocation of health care resources and facilitate health payer decisions for technology adoption and reimbursement.

One of the strengths of this study is that the clinical inputs were leveraged from observational data under real-world settings, representing a large number of people with T1D from various diabetes centers. This allowed for the demonstration of individual-level outcomes in a diverse population, potentially with varied routine clinical practice and patient-physician interactions across a country.[46] Furthermore, all individuals switched to the HCL system and thus acted as their own controls. Thus, there was no confounding by indication, which enabled the estimation of the relative incidence and excess risk of complications across the various time horizons.[47] Another strength of this study was the simulation of clinical and economic impact over both short- and long-term periods. Rapid technology transformations require rigorous decisions, whereas depending on the age of the cohort and diabetes duration, the clinical and economic benefits may not be immediately apparent or be differentiated under longer observation periods. The analyses for various time periods act as univariate sensitivity analysis confirming the robust effect of

HbA1c reduction on clinical and economic outcomes. Furthermore, the sensitivity analysis fluctuating the HbA1c levels achieved with HCL demonstrated sustained clinical benefits, specifically regarding the incidence reduction of complications over the lifetime horizon. Finally, the first and second-order sensitivity analyses added accuracy and robustness to the study results and reduced uncertainty, whereas the employed IQVIA CDM is a robust and validated model.[21]

A limitation of this study is that the long-term clinical and subsequently economic results are based on short-term real-world data, inherently introducing an unavoidable uncertainty in the long-term predictions.[48] Another limitation is that baseline cohort characteristics and treatment effects were taken from a clinical study conducted in the UK, whereas the cost-effectiveness analysis was conducted for Spain. This approach was adopted due to the lack of regional data and is often used in cost-effectiveness analysis. For example, the clinical study of Choudhary[18] conducted in UK, Germany, and France was used as input for cost-effectiveness analysis for Austria, Greece, Italy, Netherlands, Sweden, and Spain[17] and for Singapore.[45] Another limitation is the lack of long-term and large cohort studies capturing the impact on hypoglycemia and DKA, which probably underestimates the results of the current study. Additionally, the assumption that the initial difference in HbA1c levels will be maintained over all examined time horizons, assuming prolonged adherence, is very strong[49] and may overestimate the long-term effect, whereas different spending dynamics might not be captured.[50] Finally, this study takes a health payer perspective, which considers the maximization of health care benefits in conjunction with a specific budget ignoring costs outside the health care sector such as productivity losses and family caregiver burden. There is ongoing debate as to whether such indirect costs should be included in decision making,[51,52] especially considering the emotional distress of diabetes management which highly impacts the person's quality of life and ability to work.

The global rise in T1D cases is anticipated to continue alongside technologic progress, leading to a higher population of older adults living with T1D and consequently a greater prevalence of complications. T1D can incur high costs, and negatively affect quality of life and life expectancy. This study adds evidence on the improved clinical and cost outcomes using HCL systems compared with nonautomated insulin pumps in Spain, advocating toward the replacement of the nonautomated insulin pumps by HCL systems, ultimately reducing the health care spending and burden of disease.

Future studies should have longer follow-up periods to observe the sustained tight glycemic targets, the surveillance of DKA, and hypoglycemia events, resulting in more robust and less underestimated clinical and economic outcomes.

Conclusion

HCL systems are associated with increased survival, improved clinical outcomes and cost savings for the health care system in both short and long term. Given these results, HCL systems should be considered as the primary treatment option for people with T1D in Spain, especially those whose glycemic levels are suboptimal.

Disclosure

A.C. reports consultant fees and speaker honoraria from Medtronic, Tandem, Dexcom, Abbott, Roche, Ypsomed, Novo Nordisk, Sanofi, Lilly. J.M.-F. reports consultant fees and speaker honoraria from Medtronic, Tandem, Dexcom, Abbott, Roche and Ypsomed. P.I.B.-V. has received speaking/consulting honoraria from Abbott, Novo Nordisk, Medtronic, Roche, Novalab and Lilly. A.K.M., G.B., and M.-E.S. are employees of Ypsomed Diabetes Care AG. M.N. is not an Ypsomed Diabetes Care AG employee but supported on this publication on behalf of Ypsomed Diabetes Care AG.

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Author Contributions

A.K.M.: Conceptualization. A.K.M., G.B., P.I.B.-V.: Study design & methodology. A.K.M., G.B., P.B.V., A.I.C.B.: Data collection and resources. A.K.M., M.E.S.: Formal analysis. A.K.M., M.E.S., G.B., P.I.B.-V., A.I.C.B.: Results interpretation. M.E.S., M.N.: Original draft writing. A.K.M., M.E.S, G.B., M.N., A.I.C.B., P.I.B.-V., J.M.-F.: Critical input and revision of the manuscript. P.I.B.-V.: Project supervision.

Data Availability

The data used in the current study are available from the corresponding author upon reasonable request.

Ethics Statement

No ethical approval was required for this study. This study used previously published study results and no additional human participants were included.

References

1. Gregory GA, Robinson TIG, Linklater SE, et al. Global incidence, prevalence, and mortality of type 1 diabetes in 2021 with projection to 2040: a modelling study. *Lancet Diabetes Endocrinol*. 2022;10(10):741–760.
2. Gómez-Peralta F, Menéndez E, Conde S, Conget I, Novials A, SED and SED1 study investigators. Physical activity patterns in type 1 diabetes in Spain: the SED1 study. *BMC Sports Sci Med Rehabil*. 2023;15(1):92.
3. Prigge R, McKnight JA, Wild SH, et al. International comparison of glycaemic control in people with type 1 diabetes: an update and extension. *Diabet Med*. 2022;39(5):e14766.
4. Vanstone M, Rewegan A, Brundisini F, Dejean D, Giacomini M. Patient perspectives on quality of life with uncontrolled type 1 diabetes mellitus: a systematic review and qualitative meta-synthesis. *Ont Health Technol Assess Ser*. 2015;15(17):1–29.
5. Holt RIG, DeVries JH, Hess-Fischl A, et al. The management of type 1 diabetes in adults. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetologia*. 2021;64(12):2609–2652.
6. Gómez-Peralta F, Menéndez E, Conde S, Conget I, Novials A. investigators of the studies SED and SED1. Clinical characteristics and management of type 1 diabetes in Spain. The SED1 study. *Endocrinol Diabetes Nutr (Engl Ed)*. 2021;68(9):642–653.
7. Diabetes Control and Complications Trial Research Group, Nathan DM, Genuth S, et al. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med*. 1993;329(14):977–986.
8. Gubitosi-Klug RA, DCCT/EDIC Research Group. The diabetes control and complications trial/epidemiology of diabetes interventions and complications study at 30 years: summary and future directions. *Diabetes Care*. 2014;37(1):44–49.
9. Livingstone SJ, Levin D, Looker HC, et al. Estimated life expectancy in a Scottish cohort with type 1 diabetes, 2008-2010. *JAMA*. 2015;313(1):37–44.
10. Herman WH, Braffett BH, Kuo S, et al. What are the clinical, quality-of-life, and cost consequences of 30 years of excellent vs. poor glycemic control in type 1 diabetes? *J Diabetes Complications*. 2018;32(10):911–915.
11. Crespo C, Brosa M, Soria-Juan A, López-Alba A, López-Martínez N, Soria B. Direct cost of diabetes mellitus and its complications in Spain. Seccaid Study: Spain estimated cost Ciberdem-Cabimer in diabetes. *Value Health*. 2013;16(7):A436.
12. Kanavos P, van den Aardweg S, Schurer W. Diabetes expenditure, burden of disease and management in 5 EU countries (2012) [Internet]. London School of Economics. Accessed June 25, 2024. https://www.lse.ac.uk/business/

consulting/reports/diabetes-expenditure-burden-of-disease-and-management-in-5-eu-countries.
13. Elian V, Popovici V, Ozon E-A, et al. Current technologies for managing type 1 diabetes mellitus and their impact on quality of life-a narrative review. *Life (Basel)*. 2023;13(8):1663.
14. Beato-Víbora PI, Gallego-Gamero F, Lázaro-Martín L, Romero-Pérez MDM, Arroyo-Díez FJ. Prospective analysis of the impact of commercialized hybrid closed-loop system on glycemic control, glycemic variability, and patient-related outcomes in children and adults: a focus on superiority over predictive low-glucose suspend technology. *Diabetes Technol Ther*. 2020;22(12):912–919.
15. Alwan H, Wilinska ME, Ruan Y, Da Silva J, Hovorka R. Real-world evidence analysis of a hybrid closed-loop system. *J Diabetes Sci Technol*. 2025;19(2):385–389.
16. Boughton CK, Hartnell S, Thabit H, et al. Hybrid closed-loop glucose control compared with sensor augmented pump therapy in older adults with type 1 diabetes: an open-label multicentre, multinational, randomised, crossover study. *Lancet Healthy Longev*. 2022;3(3):e135–e142.
17. Jendle J, Buompensiere MI, Ozdemir Saltik AZ, et al. A European cost-utility analysis of the MiniMed™ 780G advanced hybrid closed-loop system versus intermittently scanned continuous glucose monitoring with multiple daily insulin injections in people living with type 1 diabetes. *Diabetes Technol Ther*. 2023;25(12):864–876.
18. Choudhary P, Kolassa R, Keuthage W, et al. Advanced hybrid closed loop therapy versus conventional treatment in adults with type 1 diabetes (ADAPT): a randomised controlled study. *Lancet Diabetes Endocrinol*. 2022;10(10):720–731.
19. Crabtree TSJ, Griffin TP, Yap YW, et al. Hybrid closed-loop therapy in adults with type 1 diabetes and above-target HbA1c: a real-world observational study. *Diabetes Care*. 2023;46(10):1831–1838.
20. McEwan P, Foos V, Palmer JL, Lamotte M, Lloyd A, Grant D. Validation of the IMS CORE Diabetes Model. *Value Health*. 2014;17(6):714–724.
21. Palmer AJ, Roze S, Valentine WJ, et al. Validation of the CORE Diabetes Model against epidemiological and clinical studies. *Curr Med Res Opin*. 2004;20(suppl 1):S27–S40.
22. Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. *BMC Med Res Methodol*. 2014;14(1):135.
23. Barón Esquivias G, Escolar Albaladejo G, Zamorano JL, et al. Cost-effectiveness analysis comparing apixaban and acenocoumarol in the prevention of stroke in patients with nonvalvular atrial fibrillation in Spain. *Rev Esp Cardiol (Engl Ed)*. 2015;68(8):680–690.
24. Cosin Sales J, Fuentes Jiménez FJ, Mantilla Morató T, et al. Coste-efectividad de rosuvastatina frente a simvastatina, atorvastatina y pitavastatina en pacientes con riesgo cardiovascular alto y muy alto en España. *Clin Investig Arterioscler*. 2015;27(5):228–238.
25. Delgado JF, Oliva J, Llano M, et al. Health care and nonhealth care costs in the treatment of patients with symptomatic chronic heart failure in Spain. *Rev Esp Cardiol (Engl Ed)*. 2014;67(8):643–650.
26. Escobar C, Palacios B, Varela L, et al. Healthcare resource utilization and costs among patients with heart failure with preserved, mildly reduced, and reduced ejection fraction in Spain. *BMC Health Serv Res*. 2022;22(1):1241.
27. Ribera A, Vela E, García-Altés A, et al. Trends in healthcare resource use and expenditure before and after ischaemic stroke. *A population-based study. Neurologia (Engl Ed)*. 2022;37(1):21–30.
28. Gaede P, Vedel P, Larsen N, Jensen GV, Parving HH, Pedersen O. Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. *N Engl J Med*. 2003;348(5):383–393.
29. Crespo C, Brosa M, Soria-Juan A, et al. Costes directos de la diabetes mellitus y de sus complicaciones en España (Estudio SECCAID: Spain estimated cost Ciberdem-Cabimer in diabetes). *Av Diabetol*. 2013;29(6):182–189.
30. Villa G, Rodríguez-Carmona A, Fernández-Ortiz L, et al. Cost analysis of the Spanish renal replacement therapy programme. *Nephrol Dial Transplant*. 2011;26(11):3709–3714.
31. Oblikue. Información económica del sector sanitario. Accessed March 4, 2024. http://www.oblikue.com/bddcostes; Published February 2024.
32. Dilla T, Alexiou D, Chatzitheofilou I, Ayyub R, Lowin J, Norrbacka K. The cost-effectiveness of dulaglutide versus liraglutide for the treatment of type 2 diabetes mellitus in Spain in patients with BMI $\geq$30 kg/m^2. *J Med Econ*. 2017;20(5):443–452.
33. 2022- Informe sobre la ceguera en España. Accessed March 4, 2024. https://www.esvision.es/wp-content/uploads/2019/11/Informe_Ceguera.pdf; Published February 2024.
34. Linertová R, Del Pino-Sedeño T, Pérez L-G, et al. Cost-effectiveness of platelet-rich plasma for diabetic foot ulcer in Spain. *Int J Low Extrem Wounds*. 2021;20(2):119–127.
35. López-Bastida J, Oliva J, Antoñanzas F, et al. Spanish recommendations on economic evaluation of health technologies. *Eur J Health Econ*. 2010;11(5):513–520.
36. Coffey JT, Brandle M, Zhou H, et al. Valuing health-related quality of life in diabetes. *Diabetes Care*. 2002;25(12):2238–2243.
37. Beato-Víbora PI, Gallego-Gamero F, Ambrojo-López A. Real-world outcomes with different technology modalities in type 1 diabetes. *Nutr Metab Cardiovasc Dis*. 2021;31(6):1845–1850.
38. Chico A, Navas de Solís S, Lainez M, Rius F, Cuesta M. Efficacy, safety, and satisfaction with the Accu-Chek insight with diabeloop closed-loop system in subjects with type 1 diabetes: a multicenter real-world study. *Diabetes Technol Ther*. 2023;25(4):242–249.
39. Nigi L, Iraci Sareri G, Cataldo D, Dotta F. 12-month efficacy of advanced hybrid closed-loop system in adult type 1 diabetes patients. *Diabetes Technol Ther*. 2024;26(2):130–135.
40. Holt RIG, DeVries JH, Hess-Fischl A, et al. The management of type 1 diabetes in adults. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetes Care*. 2021;44(11):2589–2625.
41. Serné EH, Roze S, Buompensiere MI, Valentine WJ, De Portu S, de Valk HW. Cost-effectiveness of hybrid closed loop insulin pumps versus multiple daily injections plus intermittently scanned glucose monitoring in people with type 1 diabetes in the Netherlands. *Adv Ther*. 2022;39(4):1844–1856.
42. Roze S, Buompensiere MI, Ozdemir Z, De Portu S, Cohen O. Cost-effectiveness of a novel hybrid closed-loop system compared with continuous subcutaneous insulin infusion in people with type 1 diabetes in the UK. *J Med Econ*. 2021;24(1):883–890.
43. Biskupiak JE, Ramos M, Levy CJ, et al. Cost-effectiveness of the tubeless automated insulin delivery system vs standard of care in the management of type 1 diabetes in the United States. *J Manag Care Spec Pharm*. 2023;29(7):807–817.
44. Jendle J, Buompensiere MI, Holm AL, De Portu S, Malkin SJP, Cohen O. The cost-effectiveness of an advanced hybrid closed-loop system in people with type 1 diabetes: a health economic analysis in Sweden. *Diabetes Ther*. 2021;12(11):2977–2991.
45. Gardner D, Lakkad M, Qiu Z, Inoue Y, Rama Chandran S, Wherry K. The cost-effectiveness of an advanced hybrid closed-loop system compared to standard management of type 1 diabetes in a Singapore setting. *Diabetes Technol Ther*. 2024;26(5):324–334.
46. Blonde L, Dendy JA, Skolnik N, White JR. From randomized controlled trials to the real world: putting evidence into context. *J Fam Pract*. 2018;67(8 suppl):S55–S60.
47. Winterstein AG, Ehrenstein V, Brown JS, Stürmer T, Smith MY. A road map for peer review of real-world evidence studies on safety and effectiveness of treatments. *Diabetes Care*. 2023;46(8):1448–1454.
48. Graham VG, Lucas M, Ciarán G-L. Estimating long-term causal effects from short-term experiments and long-term observational data with unobserved confounding. In: *Proceedings of Machine Learning Research*; 2023:2 [Internet] Accessed June 4, 2024. https://proceedings.mlr.press/v213/goffrier23a/goffrier23a.pdf
49. Franklin JM, Shrank WH, Lii J, et al. Observing versus predicting: initial patterns of filling predict long-term adherence more accurately than high-dimensional modeling techniques. *Health Serv Res*. 2016;51(1):220–239.
50. Lauffenburger JC, Mahesri M, Choudhry NK. Use of data-driven methods to predict long-term patterns of health care spending for medicare patients. *JAMA Netw Open*. 2020;3(10):e2020291.
51. de Vries LM, van Baal PHM, Brouwer WBF. Future costs in cost-effectiveness analyses: past, present, future. *Pharmacoeconomics*. 2019;37(2):119–130.
52. Sittimart M, Rattanavipapong W, Mirelman AJ, et al. An overview of the perspectives used in health economic evaluations. *Cost Eff Resour Alloc*. 2024;22(1):41.