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A Multicenter Prospective Evaluation of the Benefits of Two Advanced Hybrid Closed-Loop Systems in Glucose Control and Patient-Reported Outcomes in a Real-world Setting

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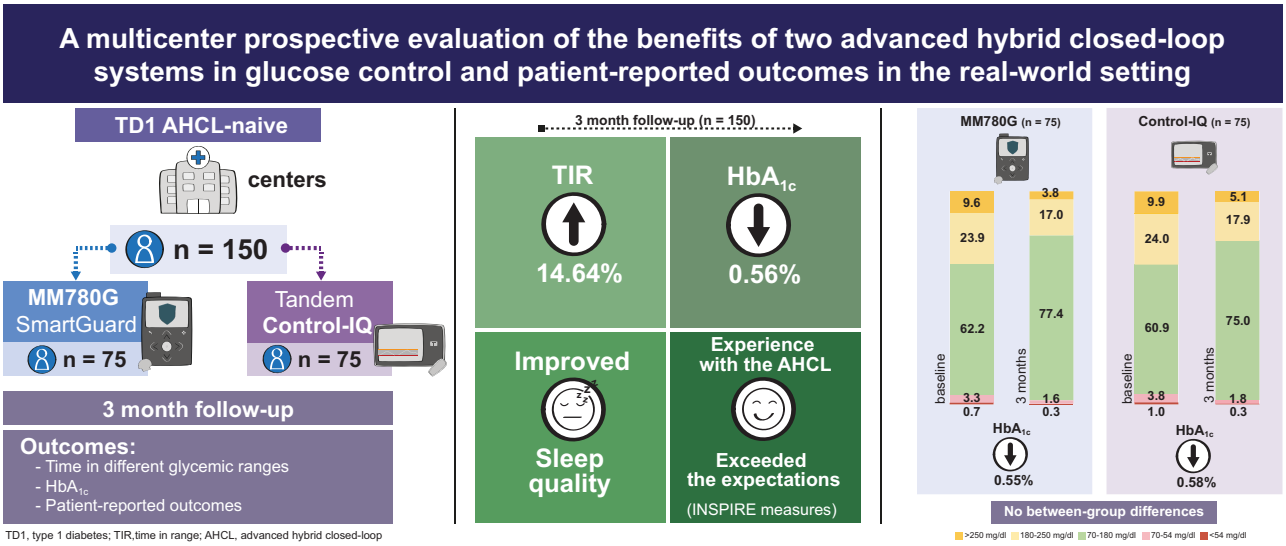

ARTICLE HIGHLIGHTS

- **Why did we undertake this study?**
  Advanced hybrid closed-loop (AHCL) therapy should be offered to all people living with type 1 diabetes. To date, information about direct comparison between different AHCL options is scarce.
- **What did we find?**
  Here, we describe the effect of MM780G with SmartGuard and the Tandem t:slimX2 with Control-IQ over glycemic control and patient-reported outcomes among adolescents and adults with type 1 diabetes.
- **What are the implications of our findings?**
  The two AHCL systems provide significant improvement in glucose control and satisfaction, with no superiority of one system over the other.

ORIGINAL ARTICLE

A Multicenter Prospective Evaluation of the Benefits of Two Advanced Hybrid Closed-Loop Systems in Glucose Control and Patient-Reported Outcomes in a Real-world Setting

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OBJECTIVE

Advanced hybrid closed-loop systems (AHCL) have been shown to improve glycemic control and patient-reported outcomes in type 1 diabetes. The aim was to analyze the outcomes of two commercially available AHCL in real life.

RESEARCH DESIGN AND METHODS

A prospective study was performed, including adolescents and adults with type 1 diabetes, AHCL naïve, from 14 centers, who initiated the use of MM780G with SmartGuard or Tandem t:slimX2 with Control-IQ. Baseline and 3-month evaluations were performed, assessing HbA_{1c}, time in different glycemic ranges, and patient-reported outcomes. The primary outcome was the between-group time in range 70–180 mg/dL difference from beginning to end of follow-up.

RESULTS

One hundred fifty participants were included, with 75 initiating each system (age: 39.9 ± 11.4 years [16–72]; 64% female; diabetes duration: 21.6 ± 11.9 years). Time in range increased from 61.53 ± 14.01% to 76.17 ± 9.48% ($P < 0.001$), with no between-group differences ($P = 0.591$). HbA_{1c} decreased by 0.56% (95% CI 0.44%, 0.68%) (6 mmol/mol, 95% CI 5, 7) ($P < 0.001$), from 7.43 ± 1.07% to 6.88 ± 0.60% (58 ± 12 to 52 ± 7 mmol/mol) in the MM780G group, and from 7.14 ± 0.70% to 6.56 ± 0.53% (55 ± 8 to 48 ± 6 mmol/mol) in the Control-IQ group (both $P < 0.001$ to baseline, $P = 0.819$ between groups). No superiority of one AHCL over the other regarding fear of hypoglycemia or quality of life was found. Improvement in diabetes-related distress was higher in Control-IQ users ($P = 0.012$). Sleep quality was improved (PSQI: from 6.94 ± 4.06 to 6.06 ± 4.05, $P = 0.004$), without differences between systems. Experience with AHCL, evaluated by the INSPIRE measures, exceeded the expectations.

CONCLUSIONS

The two AHCL provide significant improvement in glucose control and satisfaction, with no superiority of one AHCL over the other.

In recent years, the use of closed-loop systems for type 1 diabetes (T1D) management has increased exponentially. There is growing evidence of the benefit they offer in

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terms of glycemic control and user satisfaction, both in controlled and real-life evaluations (1–16). International guidelines have recommended that closed-loop systems should be offered to youth and adults with T1D who are capable of using the device (17–19). Different advanced hybrid closed-loop (AHCL) systems are available on the market. On the European market, the Medtronic MiniMed 780G system (MM780) and the Control-IQ system were launched at the end of 2020. The MM780G includes use of a model-based adaptative algorithm with a PID (Proportional-Integral-Derivative); the system delivers microboluses of insulin, to reach personalized glucose targets; also, auto-correction boluses are delivered (20). The Control-IQ system uses a Model Predictive Control (MPC) algorithm, which predicts glucose levels 30 min ahead and adjusts insulin delivery accordingly, including automatic correction boluses. Different treatment targets apply when Sleep or Exercise modes are enabled (10,21).

To date, no head-to-head randomized controlled trials have been published comparing the outcomes of AHCL systems. Some previous studies have compared different AHCL systems in real life. A prospective real-life evaluation of an Italian cohort of 31 children and adolescents showed no differences in time in range (TIR) between 70 and 180 mg/dL between MM780G and Control-IQ users after 1 month of use (22). Another Italian cohort series of children and adults, using MM780G or Control-IQ systems, were retrospectively evaluated, showing the superiority of the MM780G in TIR achieved (23,24). Also, Henry et al. (25) reported the superiority of the MM780G over Control-IQ after 3 months of use, in children and adults. The assessment of the differences in the performance of the systems could guide health care professionals in selecting which one should be prescribed in distinct clinical scenarios.

The current study was aimed at prospectively analyzing the effectiveness of two different commercially available AHCL systems in glycemic control and patient-reported outcomes in adolescents and adults with T1D in clinical practice.

RESEARCH DESIGN AND METHODS

Study Design and Ethics

The study protocol followed the Declaration of Helsinki principles and was approved by the Mutua de Terrassa University Hospital Ethics Committee (Barcelona, Spain; registration number: O22_047). All the participants were informed of the protocol and signed a consent form.

A multicenter prospective longitudinal study was designed. People with T1D were considered eligible for the study if aged ≥14 years and an indication for initiating an AHCL system had been established by the diabetologists, either the Medtronic MM780G system or the Control-IQ system, with Tandem t:slim ×2 and Dexcom G6. The devices were funded as part of routine care, and the choice of the AHCL system was made according to clinical judgment, or center reimbursement agreements if applicable, with no randomization of the participants. No specific requirements in previous monitoring system or insulin treatment were included. Exclusion criteria were ongoing pregnancy or planning of pregnancy in the following months, untreated psychiatric disease, and drug abuse. No HbA_{1c}, diabetic ketoacidosis, or severe hypoglycemia exclusions were considered.

Fourteen tertiary care centers in Spain participated in the study. A competitive enrollment system was implemented until sufficient participants were enrolled for each AHCL system. The study lasted from June 2022 to June 2023.

Initially, the inclusion of the Diabeloop AHCL system was planned. However, 25 days after the initiation of the enrollment period, the commercializing company announced that it would no longer be issuing new devices. Twelve participants had already been recruited. The investigators decided to stop the recruitment of Diabeloop users. The 12 participants completed the 3-month follow-up visit, and they experienced no serious adverse events during the study period. This group of participants was excluded from the final analysis.

The trial was designed to evaluate the noninferiority of any of the three AHCL systems in routine clinical practice. A between-group difference in the TIR of 10% (equivalent to a 0.5% [6 mmol/mol] HbA_{1c} difference) was chosen for the study (26). Fifty patients in each group had >90% power to detect a 10% TIR difference between groups at the 0.05 significance level. An SD of 10% has been assumed according to previously published data (27). After the announcement of the discontinuation of Diabeloop, an amendment was made to the protocol to redistribute the sample size while maintaining statistical power. Finally, 75 participants in each group (MM780G and Control-IQ) were included.

The primary outcomes were the differences in TIR within the groups and the whole cohort, from baseline to the end of the follow-up, and the difference in TIR between groups at the end of the follow-up. Secondary outcomes were the evaluation of differences in HbA_{1c}, time in hypoglycemia and hyperglycemia, continuous glucose monitoring metrics, and patient-reported outcomes, at the 3-month visit, compared with baseline.

Variables

Baseline and 3-month clinical visits were performed. The baseline was defined as the day the AHCL systems were initiated. Demographic variables, BMI, insulin requirements, and HbA_{1c} were collected. Data from the 14 days before the initiation of the systems and the 14 days after 3 months of use of the systems were downloaded from the available web-based software (Libreview, Clarity, Carelink, and Glooko). TIR, time in hypoglycemia <70 mg/dL and <54 mg/dL, and time in hyperglycemia >180 mg/dL and >250 mg/dL were analyzed, according to International Consensus on Time in Range (28). The glucose management indicator (GMI), mean, SD, and coefficient of variation (CV) of sensor glucose were recorded. Additionally, time in nocturnal hypoglycemia, <70 mg/dL and <54 mg/dL, from 12:00 A.M. to 6:00 A.M., was computed from the glucose sensor data in the comma-separated values files downloaded from each web-based software, at baseline and the end of the study.

Several questionnaires were applied to the participants at baseline, before the AHCL was started, and after 3 months of use of the AHCL systems to evaluate multiple patient-reported outcomes, as follows: Hypoglycemia Fear Survey (HFS) to evaluate fear of hypoglycemia, Clarke score to evaluate hypoglycemia awareness, Diabetes Distress Scale (DDS) to assess distress related to diabetes, Diabetes Quality of Life questionnaire (DQoL) to assess the quality of life, Glucose Monitoring Experience Questionnaire (GME-Q) to analyze the satisfaction with the glucose monitoring system, and Pittsburgh Sleep Quality Index (PSQI) to evaluate sleep quality. Also, the INSPIRE measures, specifically designed to assess expectancies

and hopes of automated insulin delivery for users, were included (29–40). Detailed information on the scoring and interpretation of the questionnaires has been included as Supplementary Material. All questionnaires were validated for adults. Parental consent for participants under 18 years of age was obtained.

All the centers followed their routine training program. The primary indication for the system was selected from a multiple-choice question provided to the clinicians. The use of Guardian Sensor 3 was allowed in centers without the availability of Guardian Sensor 4. The initial settings and the adjustments during the study were decided by the clinical investigators, according to routine practice. The number of training sessions, follow-up intermediate visits, and setting adjustments recommended by the clinicians were recorded for each participant.

Data and Resource Availability

The data sets generated during the current study are available from the corresponding author upon reasonable request.

Statistical Analysis

Data analysis was performed using SPSS statistics software. A descriptive analysis of continuous variables was performed by calculating their mean and SD. Categorical variables were expressed as percentages. An assessment of the normality of data was performed through the Kolmogorov-Smirnov test. A paired Student *t* test or a Wilcoxon signed-rank test was used for the analysis of differences. For unpaired samples, the independent samples *t* test was used. A repeated-measures general linear model was used to evaluate the changes between baseline and end of follow-up. Comparisons between proportions were analyzed by a χ^2 test and the McNemar test. A multivariate linear regression model was performed. A P value < 0.05 was considered statistically significant.

RESULTS

A total of 150 participants with T1D were included in the analysis, 75 participants in the MM780G system group and 75 participants in the Control-IQ system group. All the participants completed the 3-month evaluation. Demographic characteristics are shown in Table 1. Age ranged from 16 to 72 years old, with a similar age distribution between AHCL groups. Minimum diabetes duration was 2 years.

Previous treatment was multiple daily insulin injections (MDI) in 62% (n = 93) of the individuals and pump therapy in 38% (n = 57). In the previous pump users, all the participants were AHCL naïve, 21 participants had a sensor-augmented pump (10 in the MM780G group and 11 in the Control-IQ group), and 8 participants were treated with the hybrid closed-loop system Medtronic MiniMed 670G (6 in the MM780G group and 2 in the Control-IQ group).

All the participants were using interstitial glucose monitoring before entering the study, as part of their routine treatment: flash glucose monitoring in 69% (n = 103)—48 in the MM780G group and 55 in the Control-IQ group—and real-time continuous glucose monitoring in 31% (n = 47) of the participants, and 98% (n = 147) of the participants had the sensor alarms activated.

Reasons for the initiation of the AHCL systems were HbA_{1c} >7% (53 mmol/mol) in 33% (n = 50) of the participants, high frequency of hypoglycemia in 31% (n = 46), high glycemic variability in 21% (n = 31), and the need for flexibility in daily activities and dawn phenomenon in the rest of the participants. The most frequent reason in the MM780G group was hypoglycemia, in 37% (n = 28) of individuals, and, in the Control-IQ group, high HbA_{1c}, in 31% (n = 23) of participants (P = 0.031 between groups).

Glycemic Control

In the total cohort, TIR increased from 61.53 ± 14.01% at baseline to 76.17 ± 9.48% after 3 months ($P < 0.0001$). In the MM780G group, TIR increased from 62.15 ± 14.96% to 77.38 ± 8.61% ($P < 0.0001$), and, in the Control-IQ group, from 60.93 ± 13.10% to 74.99 ± 10.17% ($P < 0.0001$). No differences at baseline or after 3 months between the two groups were found (P = 0.599 and P = 0.591, respectively). Change in TIR after 3 months, compared with baseline, was 15.2% (95% CI 12.12%, 18.3%,) in the MM780G users, compared with 14.1% (95% CI 10.95%, 17.15%) in the Control-IQ users (P = 0.591). The TIR, time in hypoglycemia, and time in hyperglycemia at baseline and after 3 months of use of the AHCL systems are represented in Fig. 1.

Change in time in hypoglycemia <70 mg/dL, compared with baseline, was −2.22% (95% CI −2.94%, −1.5%) in the MM780G users, compared with −2.65% (95% CI −3.71%, −1.6%) in the Control-IQ users (P = 0.499). Change in time in hyperglycemia >180 mg/dL was −12.73% (95% CI −15.88%, −9.57%) in the MM780G users, compared with −10.87% (95% CI −14.13%, −7.61%) in the Control-IQ users (P = 0.415). Similarly, there were no significant differences in changes in time in hypoglycemia <54 mg/dL or time in hyperglycemia >250 mg/dL between AHCL systems (P = 0.392 and P = 0.501, respectively). Additionally, no significant differences in TIR, time in hypoglycemia, or time in hyperglycemia at the end of follow-up were found when comparing previous pump users with MDI participants, in the whole cohort, and each AHCL group.

In a multivariate regression analysis, considering baseline HbA_{1c}, age, and diabetes duration as independent variables, baseline HbA_{1c} was the only significant predictor of change in TIR, with higher baseline HbA_{1c} predicting a greater increase in TIR (β = 0.338, $P < 0.001$).

The percentage of participants with TIR >70% increased from 25% (n = 38) at baseline to 80% (n = 120) after 3 months of use of the AHCL system ($P < 0.001$); in MM780G users, this percentage increased from 27% (n = 20) to 87% (n = 65), and, in Control-IQ users, it increased from 24% (n = 18) to 73% (n = 55) (both $P < 0.001$). The percentage of users with a TIR >70% at 3 months was significantly higher in the MM780G group compared with the Control-IQ group (87% vs. 73%) (P = 0.041), although there were no differences at baseline between the groups (P = 0.636).

The percentage of participants reaching all the International Consensus targets (28) (TIR >70%, time <70 mg/dL <4%, time >180 mg/dL <25%, and CV <36%) increased from 10% (n = 15) at baseline to 49% (n = 73) after 3 months of use of an AHCL system ($P < 0.001$); no between-group differences at baseline or the end of follow-up were observed (P = 0.414 and P = 0.624, respectively).

HbA_{1c} was reduced from 7.28 ± 0.92% at baseline to 6.73 ± 0.59% after 3 months of use of an AHCL system; mean reduction: 0.56% (95% CI 0.44%, 0.68%) (from 56 ± 10 to 50 ± 6 mmol/mol; mean reduction:

Table 1—Baseline demographic characteristics of participants included

	All	MM780G, *n* = 75	Control-IQ, *n* = 75	*P*
Age, years	39.9 ± 11.4	40 ± 11.8	39.7 ± 11.2	0.881
Young adults (≤25 years old), *n* (%)	19 (13)	10 (13)	9 (12)	0.806
Sex (female), *n* (%)	96 (64)	46 (61)	50 (67)	0.496
Diabetes duration, years	21.6 ± 11.9	22 ± 13.5	21.2 ± 10.1	0.687
Long-term diabetes (≥20 years)	79 (53)	39 (52)	40 (53)	0.870
HbA_{1c}, %	7.28 ± 0.92	7.43 ± 1.07	7.14 ± 0.70	0.153
HbA_{1c}, mmol/mol	56 ± 10	58 ± 12	55 ± 8	0.153
BMI, kg/m^2	26.3 ± 5.1	26.6 ± 4.7	25.8 ± 5.2	0.313
Impaired awareness of hypoglycemia (Clarke score >3), *n* (%)	31 (21)	11 (15)	20 (27)	0.07
Diabetes complications, *n* (%)	39 (26)	20 (27)	19 (25)	0.852
Level of education, *n* (%)				0.069
Primary education	34 (23)	23 (31)	11 (15)	
High school level	34 (23)	14 (19)	20 (28)	
University level	79 (54)	38 (50)	41 (57)	
Previous treatment, *n* (%)				0.239
MDI	93 (62)	43 (57)	50 (67)	
Insulin pump	57 (38)	32 (43)	25 (33)	
Previous glucose monitoring system, *n* (%)				0.218
Flash glucose monitoring	103 (69)	48 (64)	55 (73)	
Real-time continuous glucose monitoring	47 (31)	27 (36)	20 (27)	

Data are expressed as mean ± SD unless otherwise indicated; *n* = 150.

6 mmol/mL [95% CI 5, 7 mmol/mol]) ($P <$ 0.001). In the MM780G users, this reduction was from 7.43 ± 1.07% at baseline to 6.88 ± 0.60% after 3 months, with a mean reduction of 0.55% (95% CI 0.32%, 0.73%) (from 58 ± 12 to 52 ± 7 mmol/mol; mean reduction: 6 mmol/mL [95% CI 4, 8 mmol/mol) ($P <$ 0.001). In the Control-IQ users, HbA_{1c} was reduced from 7.14 ± 0.7% at baseline to 6.56 ± 0.53%, mean reduction: 0.58% (95% CI 0.44%, 0.71%) (from 55 ± 8 to 48 ± 6 mmol/mol, mean reduction: 6 mmol/mL (95% CI 5, 8 mmol/mol]) ($P <$ 0.001); no differences between groups were found in the mean HbA_{1c} reduction after 3 months of use of the AHCL systems (P = 0.819). Similarly, GMI was reduced significantly in the whole cohort, from 7.20 ± 0.77% to 6.81 ± 0.38% ($P <$ 0.001). There were no significant between-group differences in the mean reduction in GMI (P = 0.790) (Table 2).

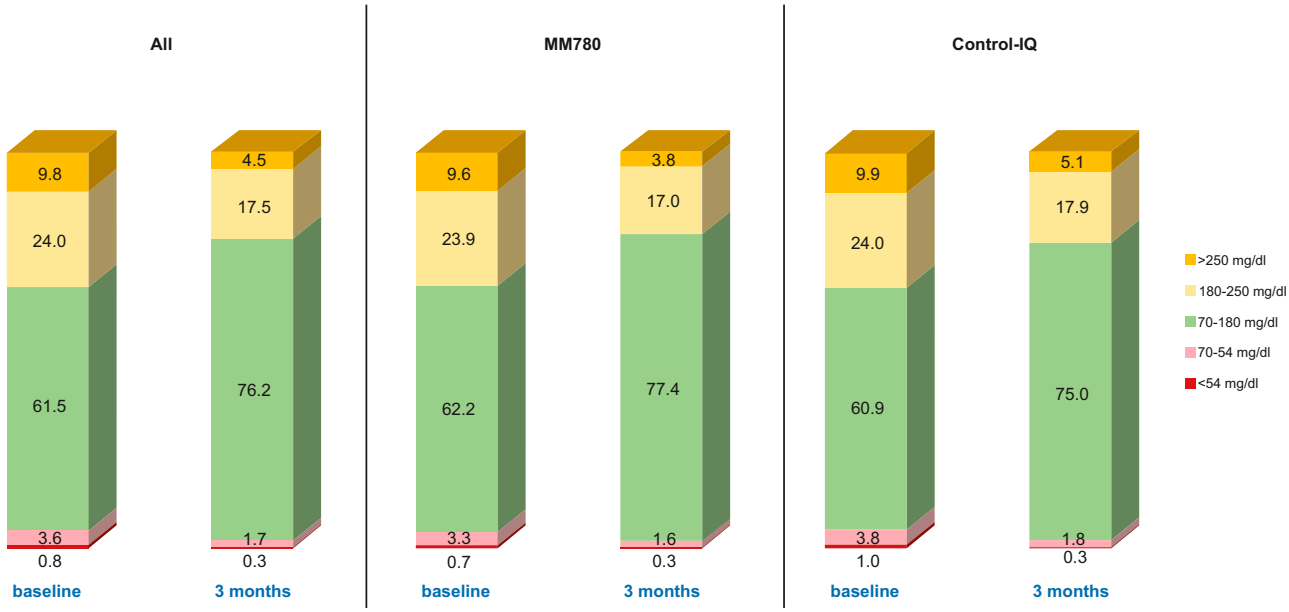

Figure 1—Percentage of time spent in different glycemic ranges. All $P <$ 0.001 baseline versus 3-month follow-up visit. There were no significant differences at baseline or after 3 months between both AHCL system groups (all $P >$ 0.05).

Table 2—Glucose control parameters and insulin requirements at baseline and after 3 months of use of the two AHCL systems

	All (n = 150)			MM780G (n = 75)			Control-IQ (n = 75)			
	Baseline	3 months	P	Baseline	3 months	P	Baseline	3 months	P	P‡
HbA_{1c} (%)	7.28 ± 0.92	6.73 ± 0.59	<0.001	7.43 ± 1.07	6.88 ± 0.60	<0.001	7.14 ± 0.70	6.56 ± 0.53	<0.001	0.819
HbA_{1c} (mmol/mol)	56 ± 10	50 ± 6	<0.001	58 ± 12	52 ± 7	<0.001	55 ± 8	48 ± 6	<0.001	0.819
GMI (%)	7.20 ± 0.77	6.81 ± 0.38	<0.001	7.19 ± 0.73	6.78 ± 0.34	<0.001	7.22 ± 0.82	6.84 ± 0.41	<0.001	0.790
Mean sensor glucose (mg/dL)	162.13 ± 30.43	146.25 ± 15.59	<0.001	161.48 ± 28.27	144.01 ± 14.67	<0.001	162.76 ± 32.57	148.43 ± 16.23	<0.001	0.481
SD (mg/dL)	59.86 ± 15.78	47.93 ± 9.86	<0.001	58.29 ± 14.15	46.76 ± 8.71	<0.001	61.38 ± 17.16	49.04 ± 10.79	<0.001	0.731
CV (%)	36.80 ± 6.53	32.37 ± 4.9	<0.001	36.01 ± 5.60	31.97 ± 4.35	<0.001	37.56 ± 7.26	32.75 ± 5.39	<0.001	0.475
Total insulin (units/kg/day)	0.61 ± 0.26	0.59 ± 0.24	0.279	0.63 ± 0.32	0.60 ± 0.26	0.816	0.59 ± 0.17	0.58 ± 0.20	0.154	0.736
Basal insulin (%)	51.08 ± 11.78	41.29 ± 12.08	<0.001	50.72 ± 11.37	37.98 ± 11.55	<0.001	51.47 ± 12.30	44.99 ± 11.66	<0.001	0.010
Bolus insulin (%)	48.92 ± 11.78	58.71 ± 12.08	<0.001	49.28 ± 11.37	62.02 ± 11.55	<0.001	48.53 ± 12.30	55.01 ± 11.66	<0.001	0.010

Data are expressed as mean ± SD; n = 150. There were no significant baseline differences between groups. ‡Three months of MM780G versus Control-IQ.

In a multivariate regression analysis, including baseline HbA_{1c}, age, and diabetes duration as independent variables, baseline HbA_{1c} and age were the only significant predictors of HbA_{1c} at the end of follow-up, with older age and higher baseline HbA_{1c} predicting a greater HbA_{1c} at the end of follow-up ($\beta = 0.552$, $P < 0.001$, and $\beta = 0.163$, $P = 0.018$, respectively).

Time in nocturnal hypoglycemia <70 mg/dL, from 12:00 A.M. to 6:00 A.M., was reduced from 115 [17, 280] min per night to 45 [5, 120] min per night, and time <54 mg/dL from 2 [0, 45] min per night was reduced to 0 [0, 15] min per night (both $P < 0.001$), with no between-group differences at the 3-month evaluation ($P = 0.416$ and $P = 0.095$, respectively).

Use of the System

Most MM780G-treated participants used the Guardian Sensor 4 during the study, 87% (n = 65), while 13% (n = 10) of the participants used Guardian Sensor 3 as part of the MM780G system. All the participants in the Control-IQ group used the Dexcom G6 sensor.

At the end of the follow-up, in the MM780G group, sensor use was 94.1 ± 4.2% and automation time was 97.6 ± 3.1% of the time the sensor was worn. In the Control-IQ group, sensor use was 96 ± 3.5% and time in automation was 94.1 ± 8.4%. The sensor use was significantly higher in Control-IQ users ($P = 0.003$).

In the users of the MM780G system, at the 3-month follow-up visit, the glucose target was set at 100 mg/dL in 76% (n = 57) of the individuals, at 110 mg/dL in 16% (n = 12), and at 120 mg/dL in 8% (n = 6); active insulin time was set as 2 h in 49% (n = 37) of the participants; the percentage of autocorrection was 28.6 ± 13.8% of bolus insulin. The Temporary Target had been programmed at least once by 56% (n = 42) of the MM780G users.

In Control-IQ users, the Sleep mode was used by 96% (n = 69) of the participants, and the frequency of use of the Sleep mode, in those participants, was 31 ± 10% (7.2 ± 2.7 h/day). There was no correlation between TIR and frequency of use of the Sleep mode ($P = 0.808$). The Exercise mode was used by 49% (n = 35) of the participants, and the frequency of use was 4.7 ± 4.6% (0.6 ± 1.0 h/day).

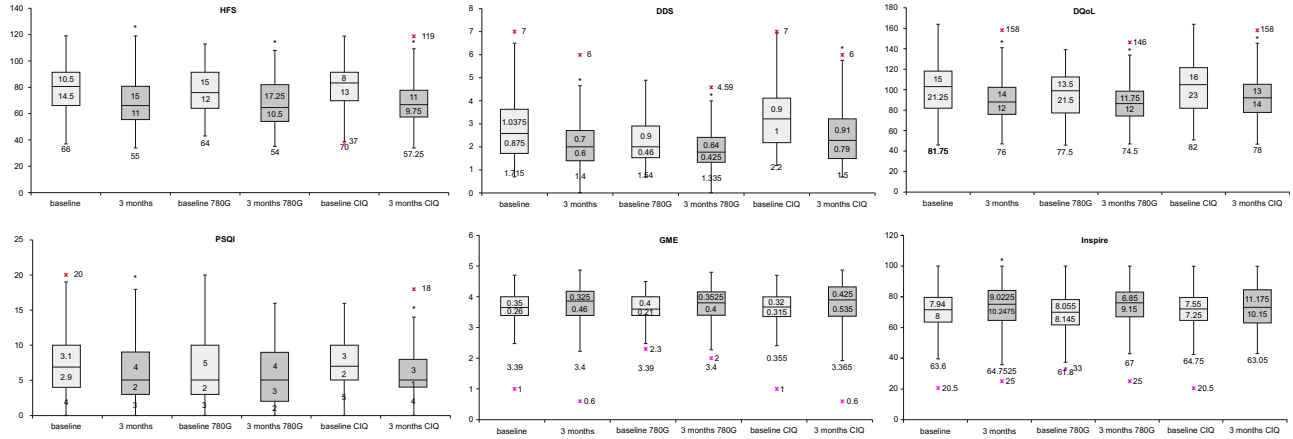

Figure 2—Questionnaire scores related to patient-reported outcomes at baseline and after 3 months of use of the AHCL system, for all the participants and for each AHCL system group. HFS: lower scores indicate less fear of hypoglycemia. DDS: lower scores indicate less diabetes-related distress. DQoL: lower scores indicate a better quality of life. PSQI: lower scores indicate better sleep quality. GME: lower scores indicate less satisfaction with the monitoring system. INSPIRE (INSPIRE measures): lower scores indicate lower expectancies. There was >90% questionnaire response. *$P < 0.05$ at 3 months compared with baseline. The total scores and different subscales scores, for each questionnaire, are detailed in Supplementary Table 1. CIQ (Control-IQ), 780G (MM780G).

Patient-Reported Outcomes

The differences in the questionnaire scores at 3 months compared with baseline, for all the participants and for both AHCL systems groups, are shown in Fig. 2. The total scores and different subscales scores, for each questionnaire, are detailed in Supplementary Table 1.

Fear of hypoglycemia was improved in the total cohort of patients and for both AHCL systems, without differences between groups. Similarly, quality of life scores improved in the overall cohort and both groups, even when Control-IQ users reported significantly worse quality of life at baseline. Diabetes-related distress scores also improved significantly in the total population and each group; however, the improvement in the DDS score was significantly higher in the Control-IQ group, being that baseline DDS scores were also significantly higher in this group. Sleep quality was significantly improved after 3 months of use of the AHCL system in the whole cohort, where PSQI was reduced from 6.94 ± 4.06 to 6.06 ± 4.05, P = 0.004, and the Control-IQ system users, where PSQI was reduced from 7.35 ± 3.47 to 6.21 ± 3.78, P = 0.019, but no differences were observed specifically in the MM780G users, where PSQI was reduced from 6.52 ± 4.56 to 5.92 ± 4.32, P = 0.215 (P = 0.019 between groups at baseline; P = 0.361 between groups at 3 months), although the percentage of poor sleepers at baseline was higher in the Control-IQ group than in the MM780 group.

The INSPIRE measures showed that experience exceeded the expectations in the whole cohort, but not in each system specifically, and no differences were seen between groups. Regarding satisfaction with the glucose monitoring system, as shown by the GME-Q, no changes were seen in the whole cohort or for any of the AHCL systems.

There were no changes in the frequency of impaired awareness of hypoglycemia from baseline to the 3-month follow-up visit in the whole cohort (from 21% [n = 31] to 15% [n = 23], P = 0.096), or in any of the AHCL system groups or between groups at the 3-month evaluation, although a reduction in Clarke score was seen in both groups, and this reduction was significantly higher in the Control-IQ group (P = 0.044).

Safety

None of the participants had been hospitalized in the 3 months prior to the study or were hospitalized during the study, no diabetic ketoacidosis episodes occurred during follow-up, and none of the participants stopped using the system before the completion of the evaluation period. Five individuals (3% of the total), three in the Control-IQ group, developed ketosis that could be controlled in an outpatient setting.

Eight individuals had suffered from severe hypoglycemia episodes in the 3 months before the initiation of the study, two in the MM780G group and six in the Control-IQ group. One episode of severe hypoglycemia occurred during the study, in a participant using the Control-IQ system, who had reported five episodes in the 3 months before the recruitment.

Technical issues reported were infusion set occlusions, in 11% (n = 16) of the participants, 4 in the MM780G group and 12 in the Control-IQ group, and skin reactions to the sensor or infusion set adhesives in 5% (n = 7) of the participants, all in the Control-IQ group. Fourteen occlusions occurred with perpendicular cannulas, used by 88% of the participants, and two with angled cannulas, used by 11% of the participants.

Recruiting Centers and Education Process

Supplementary Table 2 shows the distribution of participants per center. Four hospitals were only allowed, according to reimbursement agreements, to initiate MM780G systems. The remaining hospitals were allowed to initiate both systems.

The number of training sessions before starting the system was 2.6 ± 1.2 in the MM780G group and 2.8 ± 1.1 in the Control-IQ group (P = 0.322).

The number of intermediate follow-up visits before the 3-month follow-up visit was 2.5 ± 2.2 in the MM780G group and 2.8 ± 1.8 in the Control-IQ group (P = 0.258).

The number of adjustments made between baseline and the 3-month follow-up visit was, in the MM780G group, as follows: none: 47% (n = 35); 1 to 3: 39% (n = 29); 4 or more: 15% (n = 11). In the Control-IQ group, the number was as follows: no adjustments: 7% (n = 5); 1 to 3: 67% (n = 50); 4 or more: 26% (n = 20)

($P < 0.001$ between groups). Most of the centers allowed the participants to make their own adjustments during the study.

CONCLUSIONS

Our study evaluates the performance of two different commercialized AHCL systems in clinical practice in adolescents and adults with T1D, focusing on glucose control, patient satisfaction, and impact on the quality of life, as well as differences in the use of the system. The results confirm the extensively proven improvement achieved in TIR, and also in time in hyperglycemia and hypoglycemia, and the clinically relevant reduction in HbA_{1c} provided by the two AHCL systems, with their different control algorithms. Also, the improvements in patient-reported outcomes are corroborated, with subtle differences between systems.

A consistent increase in TIR of 14–15% was observed in the whole cohort of participants and in users of both systems. Also, time in hypoglycemia, both mild and clinically relevant, and time in hyperglycemia, both moderate and severe, were significantly and similarly improved, without differences for any of the AHCL systems. The percentage of users who reached a TIR >70% at the end of the study was significantly higher in the Medtronic group, although this percentage was similar in both groups when considering all the International Consensus targets.

Regarding glucose control, both systems achieved similar outcomes, with a clinically significant reduction in HbA_{1c} of 0.6% (6.6 mmol/mol). There were no significant differences in the improvement achieved in HbA_{1c} with both systems.

Previous studies evaluating the performance of different systems have assessed glycemic outcomes. The only prospective evaluation was performed in 31 children and adolescents, finding no superiority of either of the systems, MM780G versus Control-IQ, in relation to the achieved TIR (22). A retrospective evaluation in a cohort of Italian adults and children found a superiority in TIR achieved in the MM780 users compared with Control-IQ users, both after 1 month and after 1 year of use. However, significant differences in age and diabetes duration were highlighted between the two groups of users (23,24). Also, a higher TIR was found after 3 months of use of the MM780G system, compared with Control-IQ, in another retrospective evaluation performed in a French population of 75 adults and children. However, again, the authors acknowledged significant differences in the baseline characteristics of the population, as Control-IQ users were younger, had shorter diabetes duration, lower HbA_{1c}, and lower BMI; nonetheless, baseline TIR levels were similar between groups (25).

The importance of specifically evaluating the patient-reported outcomes concerning the use of AHCL systems has increasingly been acknowledged (41). Ng et al. (42) evaluated prospectively the performance of different AHCL systems in children and young people, and patient-reported outcomes were also analyzed. The authors found no differences (scores not reported), but they highlighted that a comparison was not intended by the study. To the best of our knowledge, no other studies have compared patient-reported outcomes in users of different AHCL systems.

In our population, patient-reported outcomes were clearly and consistently improved, with subtle differences between AHCL systems. Fear of hypoglycemia was improved, both in total scores and worry and behavior subscales, demonstrating the greater safety the participants perceived when they experienced the automated insulin delivery, in comparison with their previous open-loop therapies. Similarly, quality of life scores improved in the whole cohort and both groups, without differences between groups, even when Control-IQ users reported worse quality of life at baseline.

In relation to diabetes-related distress evaluation, the scores improved significantly in the total population and each group of users. Nevertheless, the achieved improvement favored the Control-IQ users, although DDS scores were already higher at baseline in this group.

Sleep quality was significantly improved after 3 months of use of the AHCL system in the whole cohort and the Control-IQ system users, but no differences were observed specifically in the MM780G users. Wheeler et al. (43) showed a reduction in PSQI and increased satisfaction in 59 MM780G users.

The INSPIRE measures, designed to evaluate expectancies and hopes of an automated insulin delivery system, showed experience with AHCL exceeded the expectations, in the whole cohort, but not in each system specifically. To the best of our knowledge, no assessments of expectancies of the AHCL have been published, so far, specifically aimed at evaluating differences between commercialized AHCL systems.

Regarding severe hypoglycemia, severe hypoglycemia episodes in T1D patients can occur because of a variety of factors. Individuals must work closely with their health care team to develop a personalized management plan, considering carbohydrate counting, physical activity, and the use of less tight glucose targets to minimize the risk of severe hypoglycemia (44). Finally, no differences were seen in the frequency of hypoglycemia awareness, either in the whole population or in each AHCL group, although the Clarke score was significantly reduced in the whole population and in both AHCL systems. However, a previous study of a Spanish group demonstrated a significant reduction in both Clarke scores and frequency of impaired awareness of hypoglycemia in 46 adults after 6 months of use of the MM780G system, probably because of the longer study duration (45).

We acknowledge some limitations in our study. The real-life design allows for no randomization, as the decision of which system was prescribed for each user was based on clinical judgment or contractual agreements. Half of the MM780G systems were initiated in centers with no option to choose between systems, but the rest of the systems were prescribed according to clinical judgment or clinic protocol for each participant and indication, and this could mean a selection bias that might influence the outcomes. However, there were no significant differences in baseline characteristics between MM780G system users and Control-IQ system users; also, baseline glycemic control was similar between groups, so we might hypothesize that the mentioned bias should be minimal. However, the indications for the initiation of the system were not identical between groups, differences in some patient-reported outcomes at baseline were described, and baseline treatment was not homogeneous in all the participants. Additional limitations of the study are that data from different sensors were compared at baseline and the follow-up visits, and that a small number of participants used Guardian Sensor 3 instead of Guardian Sensor 4. Finally, the training process, initiation settings, and protocols for settings adjustments were decided by each center, and this

heterogeneity could represent a limitation to the interpretation of the results. For future research, a crossover design would allow for a better insight into patient-reported outcomes.

Several strengths of our study should be highlighted, such as its multicenter and prospective design; the large number of participants included, with a wide age range, from adolescents to elderly participants; and the 100% completion of the study. The real-life scenario could better reproduce the outcomes to be expected in clinical practice. Also, the inclusion of a significant number of questionnaires to comprehensively assess most patient-reported outcomes brings added value to our research.

In conclusion, to the best of our knowledge, this analysis represents the first prospective assessment of real-life outcomes with different AHCL systems, evaluating both glycemic control and patient-reported outcomes, in adolescents and adults with T1D. We showed that the two evaluated AHCL systems provide significant improvement in glycemic control and patient-reported outcomes, with no superiority of one system over the other.

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