Title

Outcomes in Pump- and CGM-Baseline Use Subgroups in the International Diabetes Closed-Loop Trial.

Journal

DST, 17(4)

Authors

Ekhlaspour, Laya
Raghinaru, Dan
Forlenza, Gregory
et al.

Publication Date

2023-07-01

DOI

10.1177/19322968221089361

Peer reviewed

Journal of Diabetes Science and Technology
2023, Vol. 17(4) 935–942

DOI: 10.1177/19322968221089361
journals.sagepub.com/home/dst
SAGE

Outcomes in Pump- and CGM-Baseline Use Subgroups in the International Diabetes Closed-Loop Trial

Laya Ekhlaspour, MD[1], Dan Raghinaru, MS[2], Gregory P. Forlenza, MD[3], Elvira Isganaitis, MD, MPH[4,5], Yogish C. Kudva, MD[6], David W. Lam, MD[7], Camilla Levister, NP[7], Grenye O'Malley, MD[7], Mei Mei Church, NP, MS[8], John W. Lum, MS[2], Bruce Buckingham, MD[1], and Sue A. Brown, MD[9]

Abstract

Background: We investigated the potential benefits of automated insulin delivery (AID) among individuals with type 1 diabetes (T1D) in sub-populations of baseline device use determined by continuous glucose monitor (CGM) use status and insulin delivery via multiple daily injections (MDI) or insulin pump.

Materials and Methods: In a six-month randomized, multicenter trial, 168 individuals were assigned to closed-loop control (CLC, Control-IQ, Tandem Diabetes Care), or sensor-augmented pump (SAP) therapy. The trial included a two- to eight-week run-in phase to train participants on study devices. The participants were stratified into four subgroups: insulin pump and CGM (pump+CGM), pump-only, MDI and CGM (MDI+CGM), and MDI users without CGM (MDI-only) users. We compared glycemic outcomes among four subgroups.

Results: At baseline, 61% were pump+CGM users, 18% pump-only users, 10% MDI+CGM users, and 11% MDI-only users. Mean time in range 70-180 mg/dL (TIR) improved from baseline in the four subgroups using CLC: pump+CGM, 62% to 73%; pump-only, 61% to 70%; MDI+CGM, 54% to 68%; and MDI-only, 61% to 69%. The reduction in time below 70 mg/dL from baseline was comparable among the four subgroups. No interaction effect was detected with baseline device use for TIR ($P = .67$) or time below ($P = .77$). On the System Usability Questionnaire, scores were high at 26 weeks for all subgroups: pump+CGM: 87.2 ± 12.1, pump-only: 89.4 ± 8.2, MDI+CGM 87.2 ± 9.3, MDI: 78.1 ± 15.

Conclusions: There was a consistent benefit in patients with T1D when using CLC, regardless of baseline insulin delivery modality or CGM use. These data suggest that this CLC system can be considered across a wide range of patients.

Keywords

closed-loop control, continuous glucose monitoring, efficacy, insulin pump, multiple daily injection

Introduction

Poor glycemic control is associated with an increased risk of both life-threatening acute and chronic complications in patients with type 1 diabetes (T1D). Improving glycemic outcomes in patients with T1D remains challenging despite advances in diabetes care; moreover, only a small subset of patients meets the American Diabetes Association's recommended targets.[1] Recent technological innovations used in diabetes management include such systems as continuous glucose monitor (CGM), sensor-augmented insulin delivery, and associated automated insulin delivery (AID) systems. AID systems, or closed-loop systems, consist of three main components: a CGM, a control algorithm that makes automated insulin dosing decisions based on real-time CGM glucose values, and an insulin pump. Evidence shows that AID improves glycemic control, that is, increases time in range and decreases the risk of hypoglycemia.[2-4] These systems are expected to be the standard of care for patients with T1D in the near future and to decrease the burden of diabetes. Although the use of CGMs and pumps is increasing in the T1D population, there are many people with T1D who do not use these technologies for a variety of reasons including body image, compatibility with sports, the potential

complexity of the systems, and increased daily hassles with inserting devices and alarms. One of the additional barriers to the use of AID systems is not wanting to give up control of the diabetes management to an algorithm.[5] It is also known that not every user benefits equally from using these systems.[6] Therefore, the chosen technology must be individualized according to patients' needs and skill levels. The initiation and success of any technology is always contingent upon the patient's perception that the technology is safe, reliable, and effective.

We recently published the results of the International Diabetes Closed-Loop (iDCL) trial, a randomized clinical trial testing the efficacy and safety of the Control-IQ system (Tandem Diabetes Care) compared with sensor-augmented pump (SAP) therapy.[7] Control-IQ is an advanced hybrid closed-loop system that adjusts basal insulin delivery based on 30-minute predicted glucose levels and includes a hypoglycemia safety module, as well as automated correction boluses. Premeal boluses remain a requirement for this hybrid system which was approved for clinical use by the FDA in December 2019.

The use of the closed-loop system in this six-month trial involving patients with T1D was associated with an overall significant improvement in glucose control compared with sensor-augmented insulin pump use. The benefits of using this technology in patients without previous knowledge of such devices have not been fully assessed. During enrollment, we intentionally recruited a proportion of subjects who were not currently using one or more components (prespecified 20% each CGM nonuse and pump nonuse, that is, multiple daily injections (MDI) with and without CGM) of an AID system. In this analysis, we assess the benefit of the closed-loop system, the acceptance of this technology, and the durability of use in these subgroups.

Research Design and Methods

Participants

For this secondary analysis, the aim was to assess the benefits of AID in baseline device use subpopulations enrolled into the six-month multicenter iDCL trial.[7] One hundred and sixty-eight individuals between 14 and 71 years of age with T1D participated in this study across seven clinical sites. All had T1D for ≥one year without a restriction on hemoglobin A1c (HbA1c). To collect baseline data, the trial began with a two- to eight-week run-in phase (with the duration dependent on baseline pump and CGM use status and comfort level with devices during the run-in). Insulin pump nonusers were defined as using MDI as their method of treatment prior to starting the study. CGM nonusers were defined as not using a CGM in the prior 14 days.

Participants were randomized 2:1 to closed-loop control (CLC) using Tandem Control-IQ or SAP. SAP participants used either their personal pump with the study Dexcom G6 CGM, or, if on MDI therapy, were trained on a Tandem pump without a low-glucose suspension feature and a Dexcom G6 CGM.[7] The participants who were already using a Dexcom CGM and an insulin pump could skip the run-in period. After randomization, each participant in the CLC group was trained on use of the Control-IQ system.

Closed-Loop System

The system consisted of an insulin pump (t:slim X2 insulin pump with Control-IQ Technology, Tandem Diabetes Care) and a CGM (Dexcom G6, Dexcom). Dexcom G6 does not require calibration. For participants randomized to the closed-loop arm who used MDI before the study (pump nonusers), use of the pump was initiated during the run-in phase with the pump connected to a Dexcom G6 CGM, but without a low-glucose suspension feature.

Human factor testing was evaluated by using the System Usability Scale, a ten-item technology-agnostic questionnaire that measures the perceived usability of a system,[8] as well as technology acceptance and expectations questionnaires. All the participants and the parents of adolescents completed the INSPIRE survey which measures user experience with AID technologies.[9]

Statistical Analysis

Given the study was not powered for this subanalysis, descriptive statistics are provided with no statistical tests to compare groups. For the purpose of this analysis, the

[1]Division of Pediatric Endocrinology and Diabetes, Department of Pediatrics, Stanford University School of Medicine, Stanford, CA, USA
[2]Jaeb Center for Health Research, Tampa, FL, USA
[3]Barbara Davis Center for Diabetes, Anschutz Medical Campus, University of Colorado, Aurora, CO, USA
[4]Research Division, Joslin Diabetes Center, Inc., Boston, MA, USA
[5]Department of Pediatrics, Harvard Medical School, Boston, MA, USA
[6]Division of Endocrinology, Diabetes, Metabolism and Nutrition, Department of Internal Medicine, Mayo Clinic, Rochester, MN, USA
[7]Division of Endocrinology, Icahn School of Medicine at Mount Sinai, New York, NY, USA
[8]Sansum Diabetes Research Institute, Santa Barbara, CA, USA
[9]University of Virginia Center for Diabetes Technology, Charlottesville, VA, USA

Corresponding Author:
John W. Lum, MS, Jaeb Center for Health Research, 15310 Amberly Dr, Suite 350, Tampa, FL 33647, USA.
Email: jl_manuscripts@jaeb.org

participants were stratified into four subgroups: those already using an insulin pump and CGM at enrollment (pump+CGM), pump-only users (pump-only), MDI and CGM users (MDI+CGM), and MDI users without CGM (MDI-only). Outcomes were summarized as mean ± standard deviation or median [interquartile range, IQR] depending on the distribution of data.

The interaction tests of percent time in target range 70-180 mg/dL (TIR), percent time above 180 mg/dL, HbA1c, mean glucose, and percent time below 70 mg/dL with the four subgroups were prespecified in the Protocol Statistical Analyses Plan, and the results generated prior to this study. Modification of the treatment effect by baseline subgroups was assessed by including an interaction term in a linear mixed effects regression model that compared the outcome between the two treatment groups while adjusting for the baseline level of the dependent variable, age, previous use of a CGM and pump, and clinical center (random effect). All *P* values are two-tailed. Analyses were performed using SAS 9.4.

Results

Participants' Characteristics

A total of 168 participants were randomly assigned to either the closed-loop group (112 participants) or the control group (56 participants) in a 2:1 randomization scheme.[7] All participants completed the trial. In the previously reported primary analysis, the mean TIR was higher in the CLC group compared with SAP with 2.6 more hours per day spent in target range with CLC. At enrollment there were 102 participants using pump+CGM, 31 using pump only, 16 using MDI and CGM, and 19 using MDI only therapy (Table 1). In the pump-only subgroup, seven of the 31 had no prior CGM use and 24 had previous (but not current) CGM use; in the MDI-only subgroup, seven of the 19 had no prior CGM use and 12 had previously used CGM. Baseline characteristics including age, gender, diabetes duration, income, race, and ethnicity were comparable among the subgroups.

Glycemic Outcomes

Table 2 summarizes the TIR at baseline and at the 26-week follow-up in the CLC and SAP arms for the four device subgroups. All subgroups had increased TIR in the CLC arm at 26 weeks compared with baseline, whereas TIR in the SAP arm was similar at baseline and 26 weeks. The improvements in TIR in the CLC group compared with the SAP group among all four subgroups are evident between 1 a.m. and 8 a.m. (Figure 1).

Additional glycemic outcomes including time spent in hyperglycemia and hypoglycemia, glycemic variability, and mean glucose were improved in the CLC group and generally were comparable among the four subgroups assigned to SAP. In the CLC group, HbA1c decreased from baseline to week 26 in all subgroups while showing mixed results in the subgroups assigned to SAP (Table 2).

There was no interaction effect with baseline device use for TIR (P=0.67), time above 180 mg/dL ($P = .50$), HbA1c ($P = .43$), mean glucose ($P = .21$), or time below 70 mg/dL ($P = .77$).

Glucose Monitoring, System Use, and Adverse Events

Median percentage of CGM use over the 26-week trial was similar among the four subgroups for both SAP and CLC: pump+CGM (96% and 98%), pump-only (94% and 98%), MDI+CGM (96% and 98%), and MDI-only (92% and 98%).

In the CLC group, all users attained high rates of closed-loop use. The median percentage of time the system was in closed-loop mode was 92% (IQR: 90%-94%) in the pump+CGM group, 91% (86%-95%) in the pump-only group, 94% (89%-95%) in the MDI+CGM group, and 91% (88%-95%) in the MDI-only group. Reported device issues were similar in all four subgroups. Among closed-loop users, seven participants out of 102 (7%) in the pump+CGM group reported a total of eight episodes involving hyperglycemia with ketosis, including one diabetic ketoacidosis (DKA). Three participants out of 31 (10%) reported an episode of hyperglycemia with ketosis in the pump-only group, none out of 16 in the MDI+CGM group, and two out of 19 (11%) in the MDI-only group.

The results of the Technology Expectation survey were similar in all four subgroups at baseline. The mean total scores were 145 ± 17 for pump+CGM, 152 ± 20 for pump-only, 149 ± 16 for MDI+CGM, and 143 ± 27 for MDI-only. There was an increase between baseline Technology Expectations scores and follow-up Technology Acceptance scores in the pump+CGM group (157 ± 18), pump-only group (159 ± 16), and MDI+CGM group (156 ± 21). However, the MDI-only group did not show an increase in their score (141 ± 22). On the System Usability Questionnaire, scores were high at 26 weeks for all subgroups: 87.2 ± 12.1 for pump+CGM, 89.4 ± 8.2 for pump-only, 87.2 ± 9.3 for MDI+CGM, and the lowest score of 78.1 ± 15 for the MDI-only subgroup. The results of the INSPIRE survey were similar in all four subgroups at baseline as well as the end of the study among adolescents, adults, and parents.

Discussion

This multicenter randomized control clinical trial (RCT) showed a consistent benefit in participants with T1D when using CLC, similar to the results of the overall RCT, regardless of baseline insulin delivery modality or CGM use. These data suggest that this CLC system can be considered across a wide range of patients. One of the strengths of this study is that it was designed to be broadly inclusive to represent the

Table 1. Baseline Characteristics.

	Pump + CGM		Pump Only		MDI+CGM		MDI Only	
	SAP (N = 33)	CLC (N = 69)	SAP (N = 10)	CLC (N = 21)	SAP (N = 7)	CLC (N = 9)	SAP (N = 6)	CLC (N = 13)
Mean age (years)	33 ± 17	34 ± 18	28 ± 10	32 ± 13	31 ± 21	28 ± 9	44 ± 18	29 ± 11
Age <18 years	12 (36%)	23 (33%)	1 (10%)	3 (14%)	4 (57%)	2 (22%)	0	3 (23%)
Age ≥18 years	21 (64%	46 (67%)	9 (90%)	18 (86%)	3 (43%)	7 (78%)	6 (100%)	10 (77%)
Median diabetes duration (years)	12 (5, 23)	18 (8, 33)	21 (13, 24)	19 (13, 25)	13 (3, 17)	15 (3, 23)	13 (8, 22)	8 (6, 15)
Gender, female	24 (73%)	32 (46%)	3 (30%)	12 (57%)	0	4 (44%)	3 (50%)	6 (46%)
Annual household income[a]								
<$50 000	0	3 (6%)	2 (22%)	3 (16%)	0	1 (13%)	0	3 (23%)
$50 000-$100 000	7 (23%)	11 (22%)	5 (56%)	8 (42%)	2 (29%)	1 (13%)	4 (100%)	4 (31%)
≥$100 000	23 (77%)	35 (71%)	2 (22%)	8 (42%)	5 (71%)	6 (71%)	0	6 (46%)
Race, white[b]	33 (100%)	61 (88%)	10 (100%)	17 (85%)	4 (57%)	7 (78%)	6 (100%)	9 (82%)
Ethnicity, Hispanic or Latino	1 (3%)	8 (12%)	1 (10%)	2 (10%)	2 (29%)	0	1 (17%)	3 (23%)
Median BMI, kg/m^2	24 (22, 28)	25 (23, 29)	26 (26, 28)	26 (22, 29)	22 (21, 28)	23 (23, 25)	25 (22, 26)	23 (22, 31)
Mean HbA1c at randomization, %	7.2 ± 0.7	7.3 ± 1.0	7.5 ± 0.6	7.4 ± 0.7	8.1 ± 0.8	7.7 ± 1.3	7.6 ± 0.9	7.7 ± 1.0
Median daily dose insulin, U/kg/d	0.6 (0.5, 0.7)	0.6 (0.5, 0.9)	0.7 (0.6, 0.8)	0.6 (0.5, 0.7)	0.8 (0.6, 0.9)	0.7 (0.4, 0.8)	0.6 (0.6, 0.6)	0.6 (0.5, 0.9)

Abbreviations: CGM, continuous glucose monitor; MDI, multiple daily injections; SAP, sensor-augmented pump; CLC, closed-loop control; BMI, body mass index.
Mean ± SD, median (IQR), or n (%).
[a]Twenty-three participants in the treatment group and six in the control group did not provide income information.
[b]Three participants in the treatment group did not provide race information.

Table 2. Glycemic and Other Outcomes.

	Pump + CGM				Pump Only				MDI + CGM				MDI Only			
	SAP (N = 33)		CLC (N = 69)		SAP (N = 10)		CLC (N = 21)		SAP (N = 7)		CLC (N = 9)		SAP (N = 6)		CLC (N = 13)	
Glycemic outcomes																
	Base	26-Wk	Base	26-Wk	Base	26-Wk	Base	26-Wk	Base	26-Wk	Base	26-Wk	Base	26-Wk	Base	26-Wk
% CGM in range 70-180 mg/dL	61 ± 15	62 ± 14	62 ± 16	73 ± 10	56 ± 10	55 ± 10	61 ± 17	70 ± 11	50 ± 16	49 ± 21	54 ± 27	68 ± 19	62 ± 9	62 ± 13	61 ± 19	69 ± 15
Mean Glucose (mg/dL)	166 ± 26	166 ± 23	165 ± 29	154 ± 15	171 ± 16	173 ± 14	162 ± 31	156 ± 17	182 ± 34	189 ± 42	181 ± 52	164 ± 32	165 ± 14	168 ± 22	165 ± 33	162 ± 26
% below 70 mg/dL	2.4 (1.3, 4.5)	2.1 (1.7, 3.1)	2.8 (1.2, 5.5)	1.4 (0.7, 2.2)	2.0 (1.0, 3.7)	2.1 (1.6, 2.9)	3.9 (1.4, 7.9)	2.2 (1.2, 2.7)	1.2 (0.6, 3.6)	0.7 (0.7, 4.7)	1.0 (0.1, 1.6)	0.6 (0.4, 1.6)	1.6 (0.4, 3.4)	1.1 (1.0, 2.5)	2.2 (0.3, 3.7)	0.9 (0.5, 1.4)
% below 54 mg/dL	0.4 (0.2, 0.7)	0.3 (0.2, 0.5)	0.4 (0.1, 1.4)	0.2 (0.1, 0.4)	0.2 (0.0, 0.4)	0.3 (0.1, 0.4)	0.5 (0.3, 1.5)	0.3 (0.2, 0.5)	0.1 (0.0, 0.6)	0.2 (0.1, 0.9)	0.1 (0.0, 0.2)	0.1 (0.1, 0.2)	0.2 (0.0, 0.4)	0.2 (0.1, 0.3)	0.1 (0.0, 0.4)	0.1 (0.1, 0.2)
% above 180 mg/dL	36 ± 16	35 ± 14	35 ± 17	26 ± 10	41 ± 11	42 ± 10	35 ± 18	28 ± 12	47 ± 19	49 ± 22	44 ± 28	31 ± 20	36 ± 9	37 ± 13	36 ± 20	29 ± 15
% above 250 mg/dL	12 ± 11	11 ± 9	11 ± 11	6 ± 5	11 ± 6	11 ± 4	12 ± 12	8 ± 6	17 ± 11	21 ± 18	18 ± 24	10 ± 12	9 ± 6	11 ± 9	12 ± 12	10 ± 10
Other outcomes																
HbA_{1c} [a] (%)	7.2 ± 0.7	7.3 ± 0.8	7.3 ± 1.0	7.0 ± 0.7	7.5 ± 0.6	7.3 ± 0.8	7.4 ± 0.7	6.9 ± 0.8	8.1 ± 0.8	8.4 ± 1.2	7.7 ± 1.3	7.5 ± 0.8	7.6 ± 0. 9	7.3 ± 1.0	7.7 ± 1.0	7.3 ± 1.1
Insulin total daily dose (units/day)	43 (31, 59)	49 (33, 59)	48 (32, 69)	55 (37, 77)	57 (40, 79)	63 (37, 85)	43 (31, 59)	46 (33, 56)	43 (31, 59)	49 (33, 59)	48 (32, 69)	55 (37, 77)	57 (40, 79)	63 (37, 85)	43 (34, 56)	46 (33, 55)

Abbreviations: CGM, continuous glucose monitor; MDI, multiple daily injections; SAP, sensor-augmented pump; CLC, closed-loop control.
[a]One participant in SAP group and one participant in CLC group completed the 26-week visit outside the prespecified window and the 26-week values were excluded from analyses.
Mean ± SD or median (IQR).

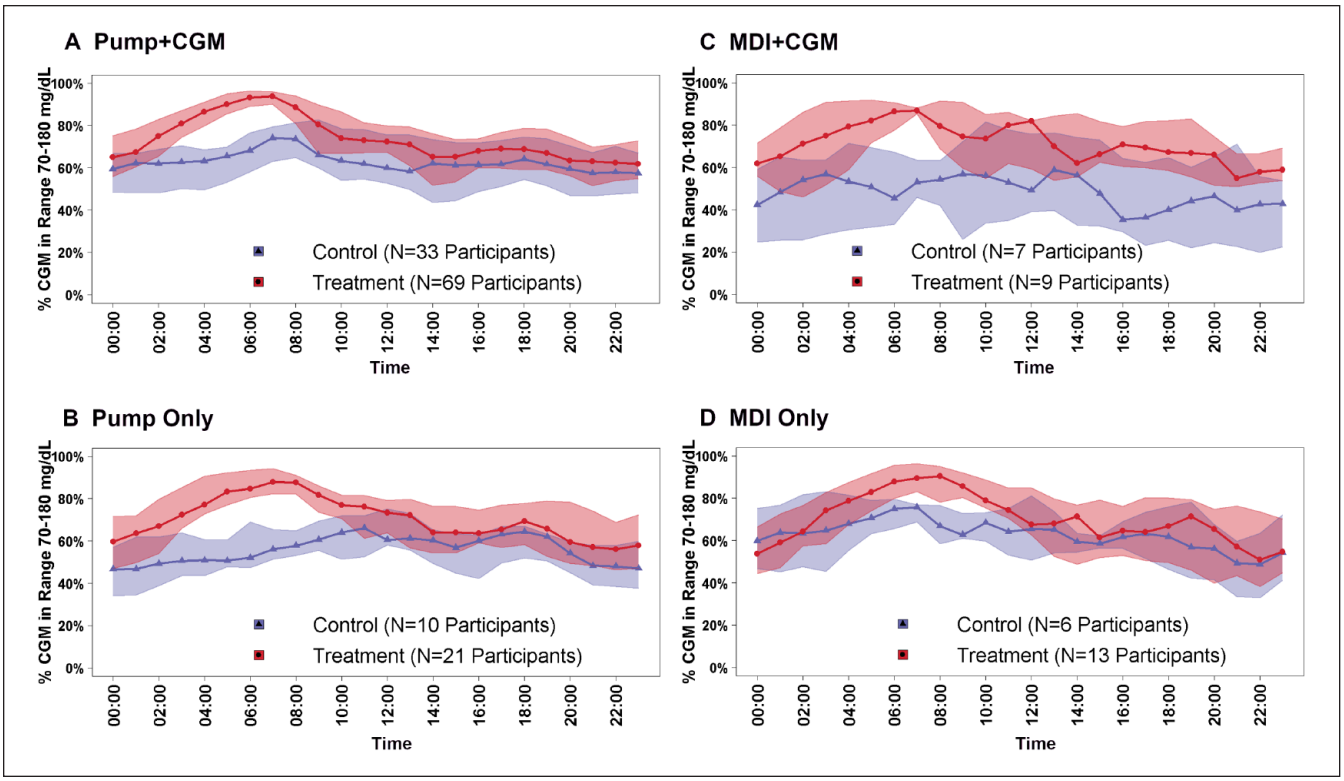

Figure 1. 24-hour TIR envelope plots for the four different subgroups based on their baseline technology use status: (a) pump+CGM, (b) pump-only, (C) MDI+CGM, and (d), MDI-only. Abbreviations: TIR, time in target range; CGM, continuous glucose monitor; MDI, multiple daily injections.

larger population living with T1D. Unlike other studies, we recruited a wide age range of participants without considering HbA1c or insulin delivery method. An additional objective of this study was to test the feasibility of a direct transition from MDI use to CLC therapy.

Most clinical trials recruit tech savvy participants and few trials include MDI participants; thus, it is difficult to establish an appropriate comparison with our study. More similarly inclusive studies, with more diverse populations are required to expand findings to a larger T1D patient population including those not currently using the devices being evaluated in the study. Based on the T1D Exchange registry report in 2019, about 62% of registry participants were using MDI as their insulin delivery modality,[1] which confirms the importance of including MDI users in these studies. A lower percentage (38%) were using a CGM.[1] These rates differ by age group, with young adults having the lowest rates of pump and CGM usage.

Overall, the Control-IQ system was found to be easy to use, reliable, and able to improve glycemic control across all subgroups of patients. The training only required short outpatient visits. Importantly, this trial was among the few trials that enrolled both insulin pump and MDI users. The successful direct transition of MDI to CLC users in this pivotal trial provides evidence to support quickly transitioning MDI patients to this commercially available CLC. The participants without experience using a CGM or an insulin pump had similar time in target range and time in CLC compared with those who used CGM and pump therapy at study baseline, and they were no more likely to report adverse events. The finding provides direct evidence of transitioning pump users not currently using CGM through CGM use to CLC use with two visits (two weeks of CGM run-in phase) and MDI patients not currently using CGM to CGM, and to CLC in about four to eight weeks (minimum of 14 days run-in for CGM and 14 days for insulin pump).

Prior to Control-IQ, the only commercially available closed-loop system was the MiniMed 670G HCL system which modulates basal insulin delivery (without automated boluses). The pivotal studies testing this system included only participants experienced with insulin pump therapy.[10] Following FDA approval, Petrovski et al tested a standardized protocol to initiate the HCL system in individuals on MDI. The transition to HCL lasted a total of 10 days including assessment, training, and manual mode and automode activation. TIR continuously improved over time from 46.9% ± 18.5% at baseline, reaching a plateau after one month of 75.6% ± 7.1% in the third month of Auto Mode.[11]

In our study, in addition to the glycemic outcomes we assessed whether the Control-IQ system would decrease the

diabetes burden similarly in all four subgroups. The technology acceptance survey showed support for benefit similarly regardless of their previous experience with technology. The INSPIRE questionnaires that assess the impact of AID systems on quality of life, and burden of disease in individuals with T1D and parents, as well as the System Usability Questionnaire all support the strong positive impact of this device on daily management of T1D.

Several studies tracked the hurdles to using the only other FDA-approved closed-loop system (MiniMed 670G) system in real life, all of them reinforcing the importance of the human factor in usability and acceptability of the technology.[12,13] The key obstacles to consistent use of the devices included their compatibility with sports, burdensome management requirements, the frequency of user input (sensor calibrations, the number of alarms), and fear of hypoglycemia.

We compared our findings with those of another closed-loop study testing the safety and performance of the Omnipod hybrid closed-loop system with T1D participants six years and older.[14] Similar to our study, the glycemic outcomes were comparable for those who entered the study using insulin pump or MDI. Time in range was similar in pump users compared with MDI users in all age groups (adults: 74.7 ± 8.5 vs 71 ± 3.7, adolescents: 79.5 ± 11.2 vs 77.8 ± 18.3 children 66.9 ± 13.9 vs 78.4 ± 7.3). The time below 70 mg/dL was also similar in all groups—adults:1.9% (1.0%-3.1%) vs 0.8% (0.6-2.6), adolescent: 2.6% (0.8-3.0) vs 1.7% (0.2%-4.3%), children 1.6% (0.6%-3.4%) vs 1.9% (1.2%-2.8%).[14] However, the closed-loop system in this study was an investigational device that used a modified version of the Omnipod Insulin Management System (Insulet Corp., Acton, MA), consisting of a tubeless insulin pump (Pod), a modified Personal Diabetes Manager, the Dexcom G4, and the Omnipod personalized MPC algorithm running on a Windows 10 tablet configured with the portable AP System.

Similar to our study, in the FLAIR study (Fuzzy Logic Automated Insulin Regulation), 20% of the participants were not current pump users, 38% were not current CGM users, and 12% were neither a pump nor a CGM user. The percent time above 180 mg/dL and time below 54 mg/dL were similar in four subgroups using the advanced hybrid closed-loop system (percent time above 180 mg/dL in participants who used CGM with MDI: 35%, CGM with pump: 41%, non-CGM with MDI: 34%, non-CGM with pump 31%; percent time below 54 mg/dL in participants who used CGM with MDI: 0.31%, CGM with pump: 0.42%, non-CGM with MDI: 0.21%, non-CGM with pump: 0.40%).[15]

Our study has several limitations. First, the sample size of each subgroup is small. Moreover, our participants consisted mainly of white individuals with annual household income above $100 000. Furthermore, the participants were a self-selected group who were interested in joining a clinical trial and motivated to follow the study protocol and be adherent to study requirements and might be different from the general population. In addition, the baseline HbA1c was lower than general population with T1D regardless of their baseline method of management. Thus, our findings may not be fully generalizable to the broader population of individuals with T1D.

Conclusions

This iDCL study demonstrated that adults and adolescents with T1D benefited from using Control-IQ, regardless of their baseline insulin delivery modality or CGM use. Previous studies have shown that diabetes devices, including insulin pumps, CGM, and closed-loop systems, reduce glucose variability and improve glycemic control as well as overall quality of life for individuals with T1D as they provide increased glycemic information and greater flexibility with insulin dosing. Our study findings support the successful use of CLC across subgroups with different baseline device usage profiles, and therefore attention should be paid to limiting barriers to access for individuals to realize the benefits from these types of devices. It will also be important to obtain long-term follow-up in the general population with T1D to better understand the risks, benefits, and adherence of using diabetes technology in patients of all ages regardless of their previous experience of using diabetes technology.

Abbreviations

AID, automated insulin delivery; T1D, type 1 diabetes; MDI, multiple daily injections; CGM, continuous glucose monitoring; CLC, closed-loop control; SAP, sensor-augmented pump; HbA1c, hemoglobin A1c; TIR, time in target range 70-180 mg/dL.

Author Contributions

LE researched data and wrote/edited the manuscript. DR performed statistical analyses and wrote/edited the manuscript. GPF, EI, YCK, DWL, CL, GOM, MMC, JWL, BB, and SAB research data, contributed to discussion, and reviewed/edited the manuscript.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: LE has received consulting fees from Tandem Diabetes and Ypsomed. DR reports receiving grant support and supplies, paid to his institution from Tandem Diabetes. GPF reports receiving grant support and lecture fees from Medtronic MiniMed and Insulet, grant support from Abbott, grant support and consulting fees from Lilly, and grant support and lecture fees from Dexcom. YCK has received product support from Dexcom Inc, Roche Diabetes, and Tandem Diabetes. DWL has no disclosures to report. CL has no disclosures to report. GO receives research support from Tandem Diabetes, Insulet, Dexcom, and Abbott. MMC has no disclosures to report. JWL reports receiving consulting fees, paid to his institution, from Animas Corporation, Bigfoot Biomedical, Tandem Diabetes Care, and Eli Lilly and Company. BB has received research support from Medtronic, Insulet, Tandem, Dexcom, and Convatec. SAB has received research support from Tandem Diabetes Care, Insulet, Dexcom, Roche, and Tolerion.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by NIDDK grant UC4 DK 108483, as well as material support from Tandem. We thank research participants and their families.

ORCID iDs

Laya Ekhlaspour https://orcid.org/0000-0002-3263-1419
Mei Mei Church https://orcid.org/0000-0003-3393-2042
John W. Lum https://orcid.org/0000-0002-0006-4376
Bruce Buckingham https://orcid.org/0000-0003-4581-4887

References

1. Foster NC, Beck RW, Miller KM, et al. State of type 1 diabetes management and outcomes from the T1D exchange in 2016-2018. *Diabetes Technol Ther*. 2019;21:66-72.
2. Bekiari E, Kitsios K, Thabit H, et al. Artificial pancreas treatment for outpatients with type 1 diabetes: systematic review and meta-analysis. *BMJ*. 2018;361:k1310.
3. Karageorgiou V, Papaioannou TG, Bellos I, et al. Effectiveness of artificial pancreas in the non-adult population: a systematic review and network meta-analysis. *Metabolism*. 2019;90:20-30.
4. Weisman A, Bai JW, Cardinez M, Kramer CK, Perkins BA. Effect of artificial pancreas systems on glycaemic control in patients with type 1 diabetes: a systematic review and meta-analysis of outpatient randomised controlled trials. *Lancet Diabetes Endocrinol*. 2017;5:501-512.
5. Naranjo D, Tanenbaum ML, Iturralde E, Hood KK. Diabetes technology: uptake, outcomes, barriers, and the intersection with distress. *J Diabetes Sci Technol*. 2016;10:852-858.
6. Liberman A, Barnard K. Diabetes technology and the human factor. *Diabetes Technol Ther*. 2019;21:S138-S147.
7. Brown SA, Kovatchev BP, Raghinaru D, et al. Six-month randomized, multicenter trial of closed-loop control in type 1 diabetes. *N Engl J Med*. 2019;381:1707-1717.
8. Bangor A, Kortum P, Miller J. Determining what individual SUS scores mean: adding an adjective rating scale. *J Usability Stud*. 2009;4:114-123.
9. Weissberg-Benchell J, Shapiro JB, Hood K, Laffel LM, Naranjo D, Miller K, Barnard K. Assessing patient-reported outcomes for automated insulin delivery systems: the psychometric properties of the INSPIRE measures. *Diabet Med*. 2019;36:644-652.
10. Garg SK, Weinzimer SA, Tamborlane WV, et al. Glucose outcomes with the in-home use of a hybrid closed-loop insulin delivery system in adolescents and adults with type 1 diabetes. *Diabetes Technol Ther*. 2017;19:155-163.
11. Petrovski G, Al Khalaf F, Campbell J, Fisher H, Umer F, Hussain K. From multiple daily injections to hybrid closed-loop system in ten days, utilizing a structured initiation protocol. *J Diabetes Sci Technol*. 2020;14:689-690.
12. Lal RA, Basina M, Maahs DM, Hood K, Buckingham B, Wilson DM. One year clinical experience of the first commercial hybrid closed-loop system. *Diabetes Care*. 2019;42:2190-2196.
13. Messer LH, Berget C, Vigers T, et al. Real world hybrid closed-loop discontinuation: predictors and perceptions of youth discontinuing the 670G system in the first 6 months. *Pediatr Diabetes*. 2020;21:319-327.
14. Sherr JL, Buckingham BA, Forlenza GP, et al. Safety and performance of the Omnipod hybrid closed-loop system in adults, adolescents, and children with type 1 diabetes over 5 days under free-living conditions. *Diabetes Technol Ther*. 2020;22:174-184.
15. Bergenstal RM, Nimri R, Beck RW, et al. A comparison of two hybrid closed-loop systems in adolescents and young adults with type 1 diabetes (FLAIR): a multicentre, randomised, crossover trial. *Lancet*. 2021;397:208-219.