TANDEM
Diabetes Care

AUGUST 2022

The Who, What, When & Why:

The t:slim X2 insulin pump with Control-IQ technology

positively different

Over 375,000 t:slim X2 users worldwide

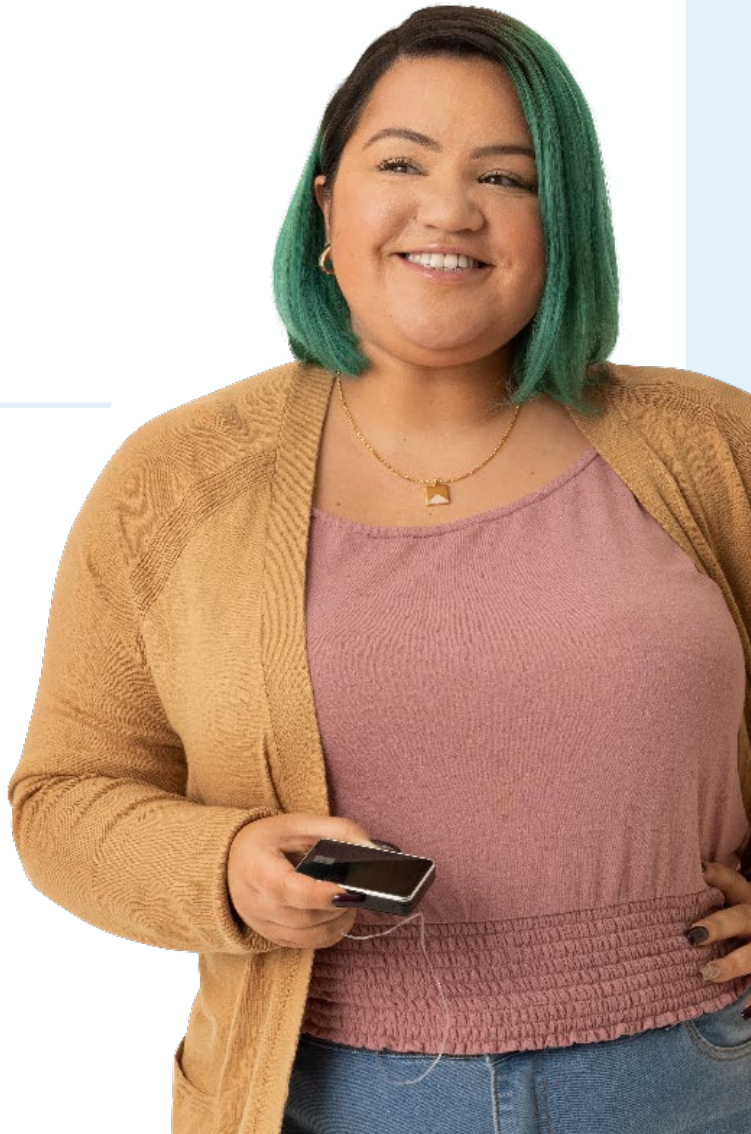
250,000
people using Control-IQ technology

#1
Advanced Hybrid Closed Loop system in the world

24 countries

65+ peer reviewed manuscripts and published abstracts on t:slim X2 insulin pump since 2019

More than **65,000,000** patient days of Control-IQ technology use data



Agenda

+ What makes Control-IQ technology so unique?
+ Who is a “candidate for pump therapy” in 2022?
+ When should MDI patients enable Control-IQ technology?
+ Why does overnight control matter? Does it improve sleep?
+ Moments that count

WHAT

What makes Control-IQ technology unique?

The Control-IQ Algorithm

Control-IQ technology is an **advanced hybrid closed-loop** system designed to help increase time in range (3.9-10.0 mmol/L) by:

- Adjusting basal insulin every 5 minutes based upon 30-minute predicted CGM values from Dexcom G6

- Delivering automatic correction boluses (up to one per hour) as needed

How can we as clinicians influence the algorithm's behavior?

Terminology used for Control-IQ Technology

Target range (3.9-10.0 mmol/L):

International Consensus' Standard of Care as the ideal glucose range for people with diabetes.

Treatment values:

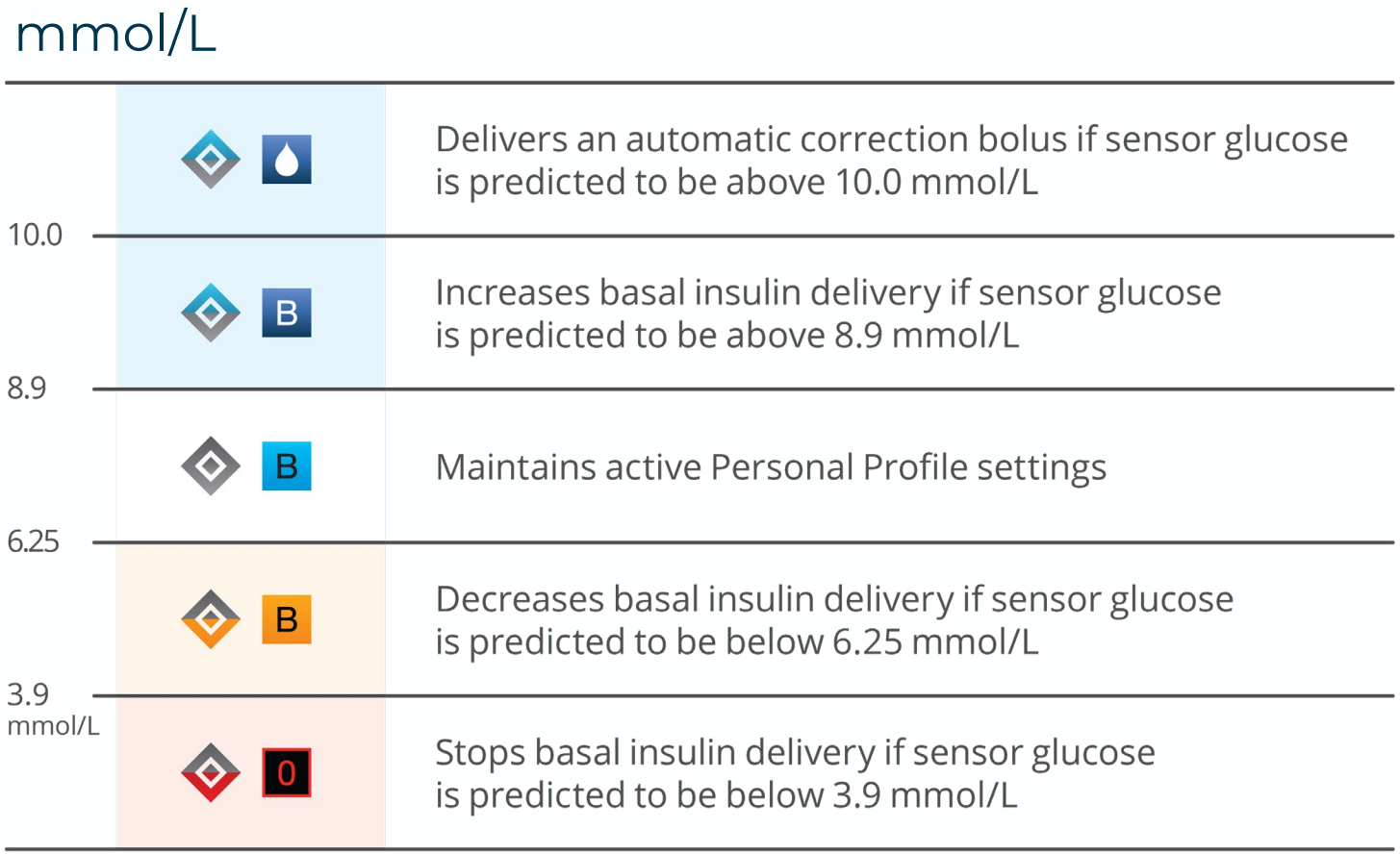
Predicted CGM values that trigger Control-IQ technology to act in order to maximize time spent in the target range.

Target BG (6.1 mmol/L):

Fixed target glucose value used to calculate all correction dosing when Control-IQ technology is active.

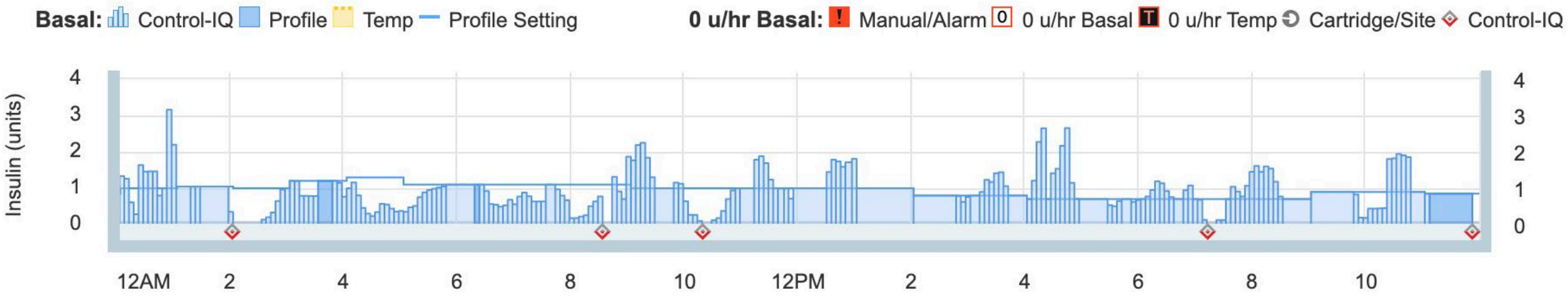
CONTROL-IQ TECHNOLOGY

How the Algorithm Works

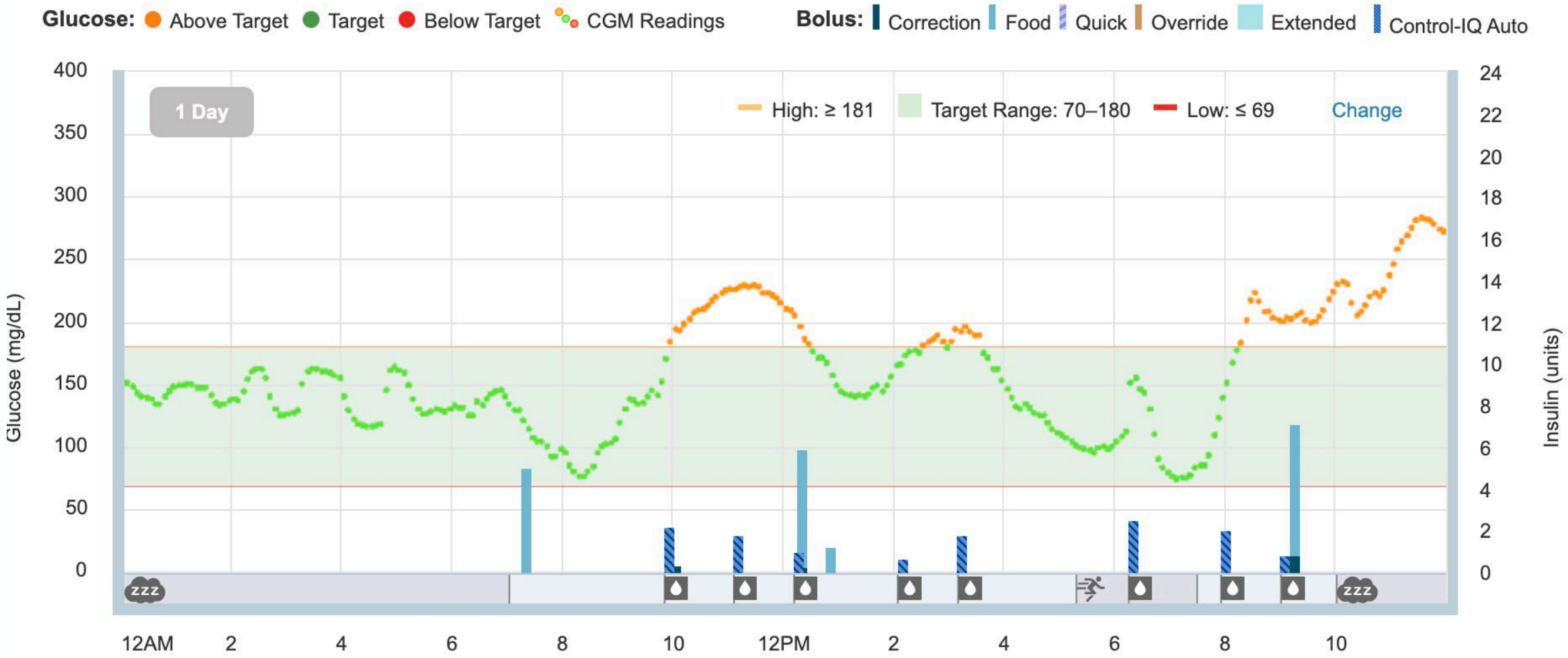


BASAL MODULATION

The system can vary the insulin infusion rate from zero to a maximum of ~4 times the user profile basal rate.



AUTOMATIC CORRECTION BOLUSES

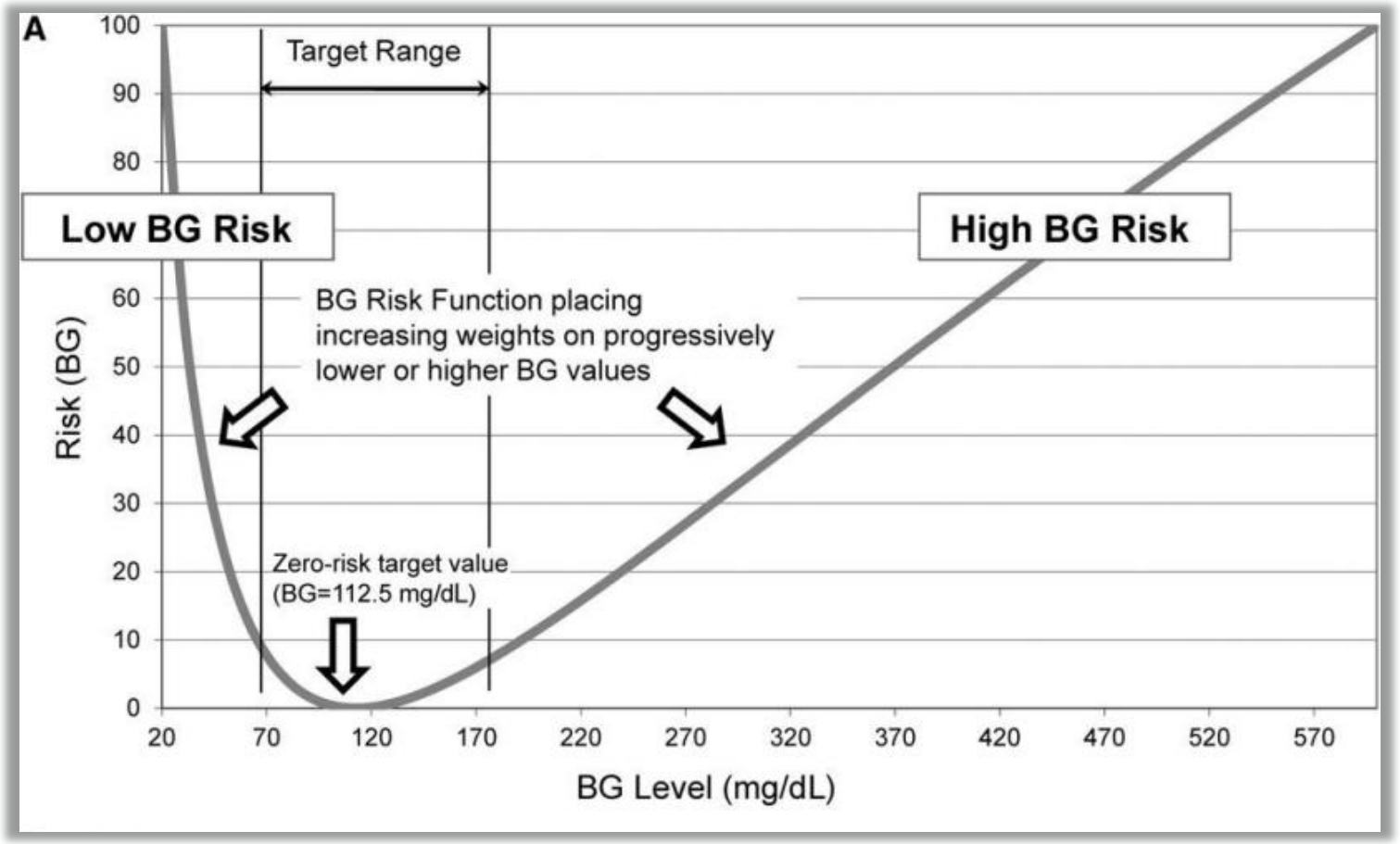


Starting Control-IQ technology

- Turning on Control-IQ requires a current weight, a Total Daily Dose, and a Personal Profile (current basal rates, Carb Ratio, and Correction Factor)
- There are no “modes”
- The only time Control-IQ is not in closed-loop is when CGM data are not available for over 20 minutes. Resumes automatically when CGM values are available.

Why 6.25 mmol/L treatment value?

Minimizing diabetes' disproportionate risk



Kovatchev BP. Measures of Risk and Glucose Variability in Adults Versus Youths. *Diabetes Technol Ther*. 2015;17(11):766-769. doi:10.1089/dia.2015.0276

Does Control-IQ technology adapt?

Control-IQ technology is a complex metabolic and predictive algorithm that uses many factors to determine next steps to maintain time in range.

You may hear people say that the algorithm adapts from total daily dose, but what does that mean?

A smart summary of TDD:

+ Rolling 6-day average updated every 5 minutes
+ Helps determine the safety parameters of the automatic basal rate modulation
+ Built in rules of 83 - 100 ensure this will not exceed safe dosing limits
+ Basal rate modulation bounded by these constraints

Settings Changes – How often? When?

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DOI: 10.1089/dia.2020.0472

DTT

ORIGINAL ARTICLE

Clinical Management and Pump Parameter Adjustment of the Control-IQ Closed-Loop Control System: Results from a 6-Month, Multicenter, Randomized Clinical Trial

Grenye O'Malley, MD,[1] Laurel H. Messer, PhD, RN,[2] Carol J. Levy, MD,[1] Jordan E. Pinsker, MD,[3] Gregory P. Forlenza, MD,[2] Elvira Isganaitis, MD, MPH,[4] Yogish C. Kudva, MD,[5] Laya Ekhlaspour, MD,[6] Dan Raghinaru, MS,[7] John Lum, MS,[7] and Sue A. Brown, MD[8] for the iDCL Trial Research Group

benefits of pump setting optimization with automated insulin a closed-loop control (CLC) system and its relationship to

arameter adjustments in 168 participants in a 6-month mul- ensor-augmented pump (SAP) therapy. Preset parameters bohydrate ratios) were optimized at randomization, 2 and 13 initiation by participants' usual diabetes care team. Time in week before and after parameter changes.

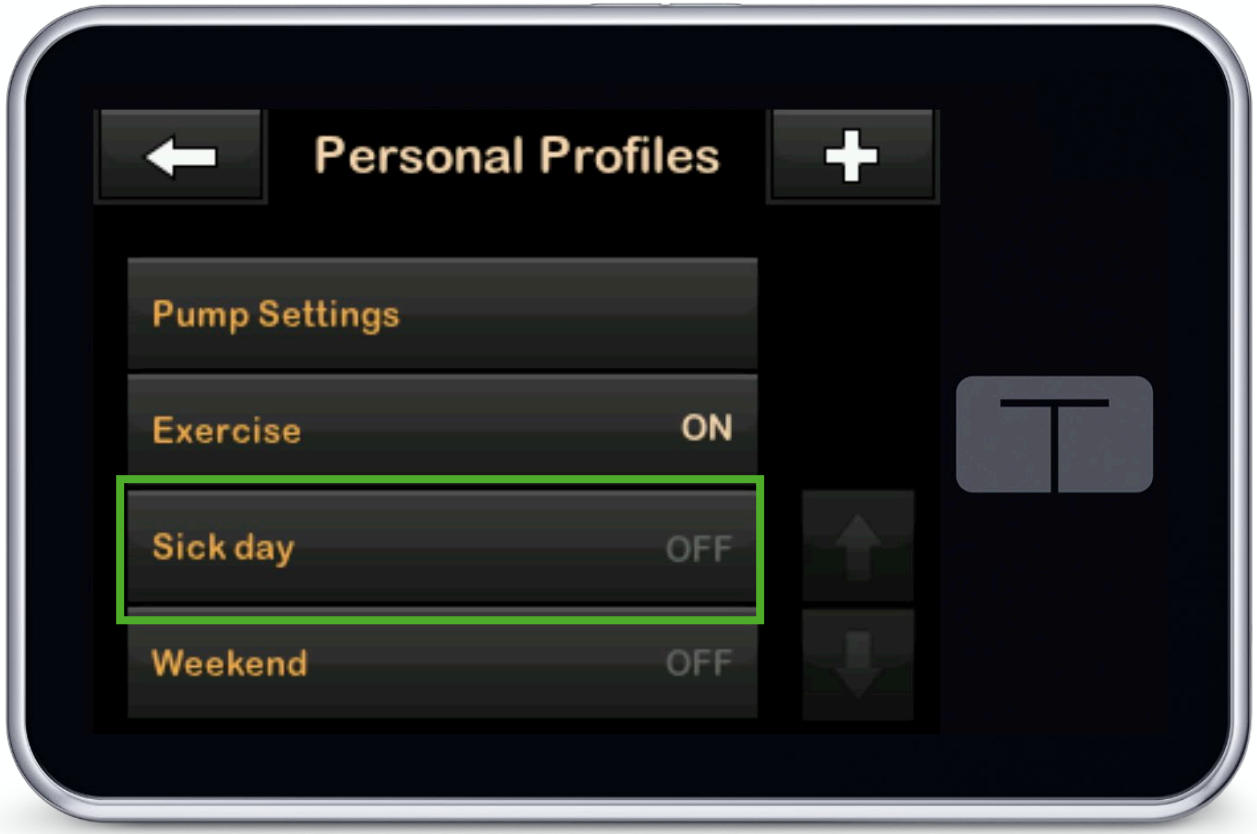
there were fewer adjustments for CLC than SAP (3.4 vs. 4.1/ participant). Adjustments involved BR (CLC 69%, SAP 80%), CR (CLC 68%, SAP 50%), CF (CLC 44%, SAP 41%), and overnight parameters (CLC 62%, SAP 75%). TIR before and after adjustments was 71.2% and 71.3% for CLC and 61.0% and 62.9% for SAP. The highest baseline HbA_{1c} CLC subgroup had the largest TIR improvement (51.2% vs. 57.7%). When a CR was made more aggressive in the CLC group, postprandial time >180 mg/dL was 43.1% before the change and 36.0% after the change. The median postprandial time <70 mg/dL before making CR less aggressive was 1.8%, and after the change was 0.7%.

Conclusions: No difference in TIR was detected with parameter changes overall, but they may have an effect in higher HbA_{1c} subgroups or following user-directed boluses, suggesting that changes may matter more in suboptimal control or during discrete periods of the day.

Clinical Trials Registration number: NCT03563313.

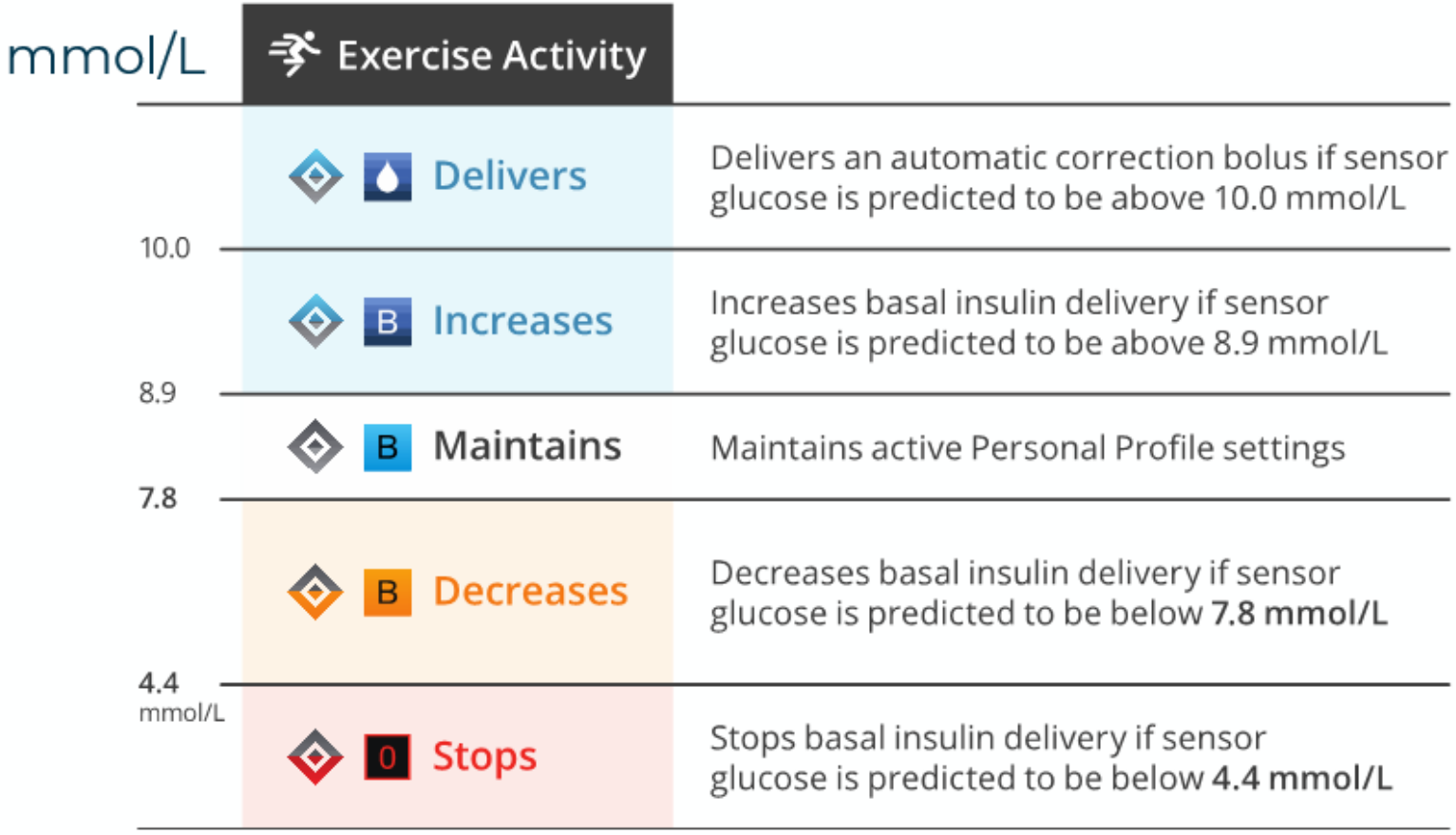
O'Malley G, Messer L, Levy CJ, Pinsker JE, Forlenza GP, Isganaitis E, Kudva YC, Ekhlaspour L, Raghinaru D, Lum J, Browns SA, for the iDCL Trial Research Group. **Clinical Management and Pump Parameter Adjustment of the Control-IQ Closed-loop Control System: Results from a 6-month Multicenter Randomized Clinical Trial.** *Diabetes Technol Ther.* 2021; 23(4):245-252.

Control-IQ Personalization



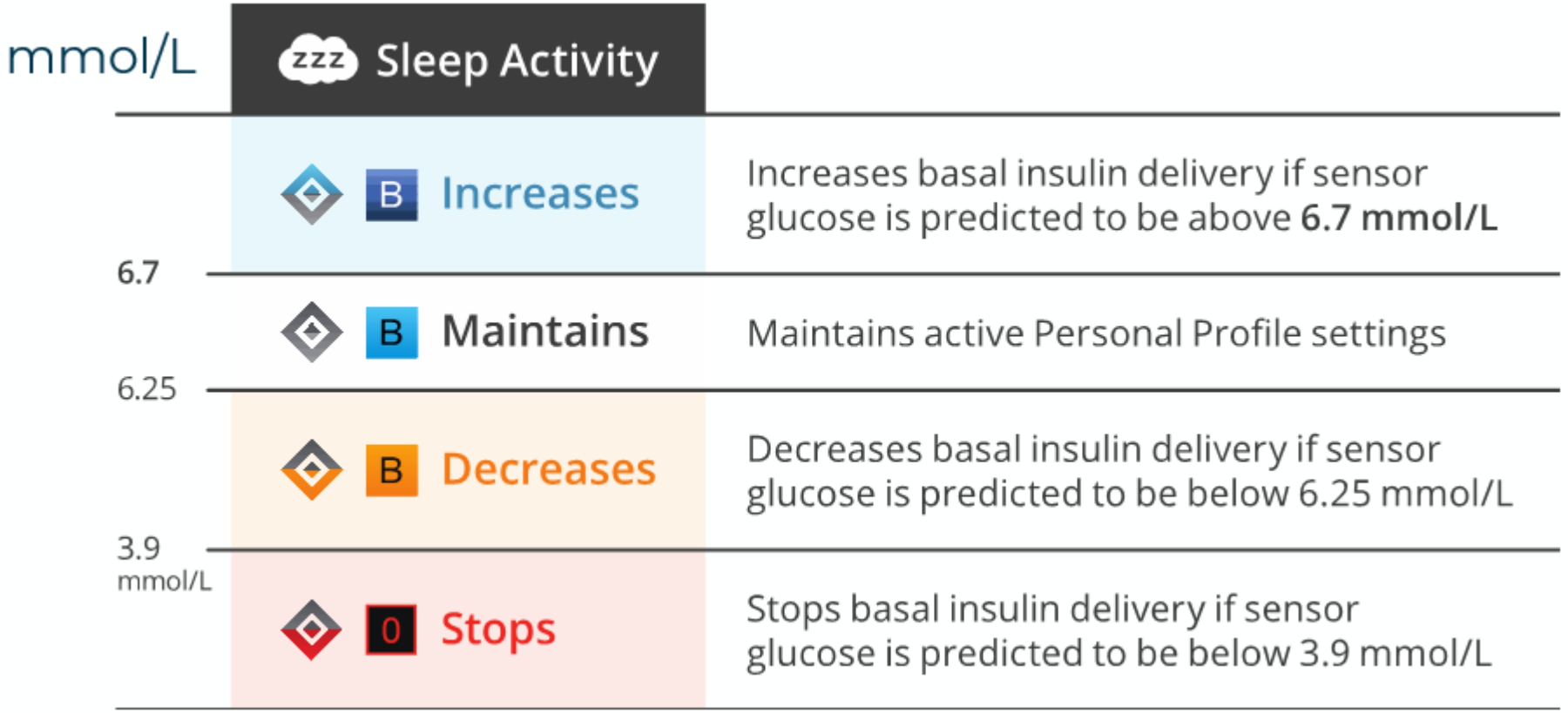
CONTROL-IQ TECHNOLOGY

How the Algorithm Works
Exercise Activity



CONTROL-IQ TECHNOLOGY

How the Algorithm Works
Sleep Activity



WHO

Who is a candidate for pump therapy in 2022?

Whose A1c improves?

Glycemic Outcomes in Baseline Hemoglobin A1C Subgroups in the International Diabetes Closed-Loop Trial

Laya Ekhlaspour, MD,[1,i] Marissa Town, RN,[1] Dan Raghinaru, MS,[2] John W. Lum, MS,[2] Sue A. Brown, MD,[3] and Bruce A. Buckingham, MD[1]; for the iDCL Trial Research Group

- All participants A1c < 6.5, 6.5 to <7, 7 to <8, 8 to <8.5, ≥ 8.5 showed improvements in outcomes.
- Those with HbA1c <6.5% improved mostly by reducing nocturnal hypoglycemia due to the automated basal insulin adjustments.
- Those with HbA1c ≥8.5% improved mostly by reducing daytime and nocturnal hyperglycemia due to both automated basal insulin adjustments and correction boluses during the day.

Ekhlaspour L, Town M, Raghinaru D, Lum JW, Brown SA, Buckingham BA. **Glycemic Outcomes in Baseline Hemoglobin A1C Subgroups in the International Diabetes Closed-Loop Trial.** *Diabetes Technol Ther.* 2022 Feb 8. doi: 10.1089/dia.2021.0524. Online ahead of print.

REAL WORLD RESULTS

One-year Glycemic Outcomes

TABLE 1. BASELINE ATTRIBUTES OF SYSTEM USERS WITH AT LEAST 12 MONTHS OF CONSECUTIVE CONTROL-IQ TECHNOLOGY SOFTWARE DATA AVAILABLE

N	9451
Age	41.9 ± 20.8, minimum 6 years; maximum 91 years
Gender	Female: 52% (*n* = 4905) Male: 48% (*n* = 4540)
eA1c	7.3%
Diabetes type	Type 1 diabetes: 83% (*n* = 7813) Type 2 diabetes: 4% (*n* = 378) Not self-reported: 13% (*n* = 1260)
Diabetes duration	Type 1 diabetes: 21.84 ± 20.6 Type 2 diabetes: 20.76 ± 10.3
Prior insulin pump software	Tandem t:slim X2 pump with Dexcom G5 Mobile CGM: 1.26% (*n* = 119) Tandem t:slim X2 pump with Basal-IQ technology: 98.74% (*n* = 9332)

Data presented as mean ± SD or % (*n*)
CGM, continuous glucose monitoring; eA1c, estimated hemoglobin A1C.

§ Control-IQ technology is not indicated for use in people with type 2 diabetes.

Breton MD, Kovatchev BP. **One Year Real-World Use of the Control-IQ Advanced Hybrid Closed-Loop Technology.** *Diabetes Technol Ther.* 2021;23(9):601-608.

REAL WORLD RESULTS

One-year Glycemic Outcomes

+ Glycemic control improved rapidly (within two weeks of initiating Control-IQ technology) and was maintained for the entirety of the study period

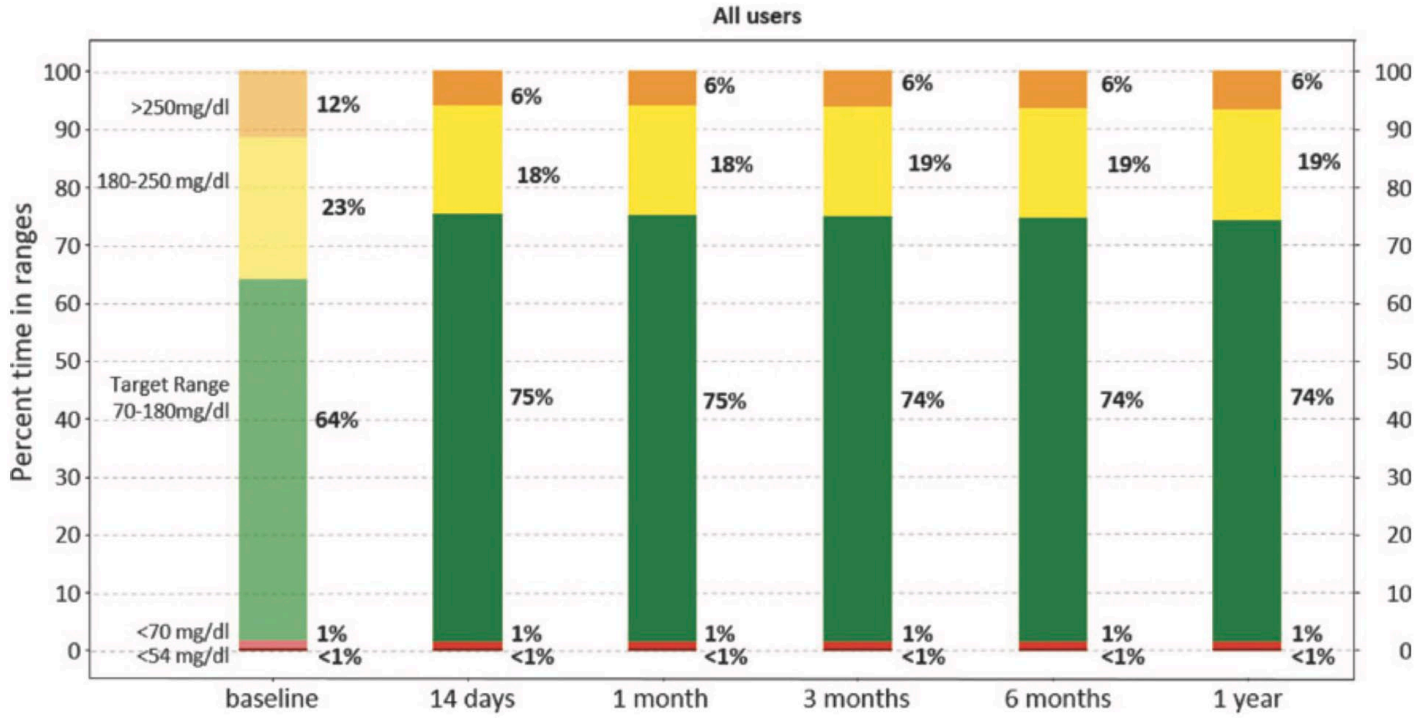
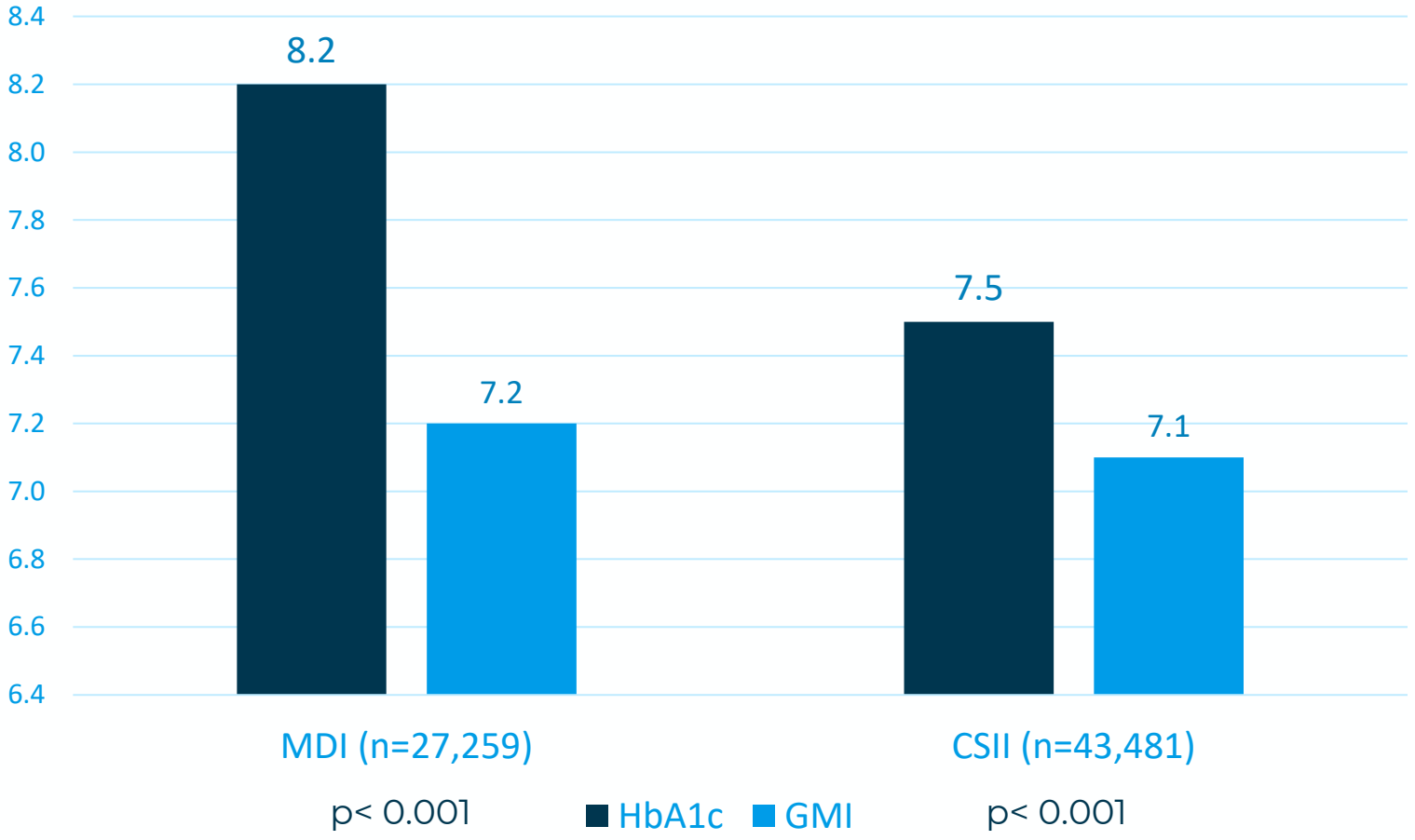


FIG. 2. Consensus CGM outcomes for baseline and Control-IQ use over time. CGM, continuous glucose monitoring.

Breton MD, Kovatchev BP. **One Year Real-World Use of the Control-IQ Advanced Hybrid Closed-Loop Technology.** *Diabetes Technol Ther.* 2021;23(9):601-608.

REAL-WORLD DATA / N=71,686

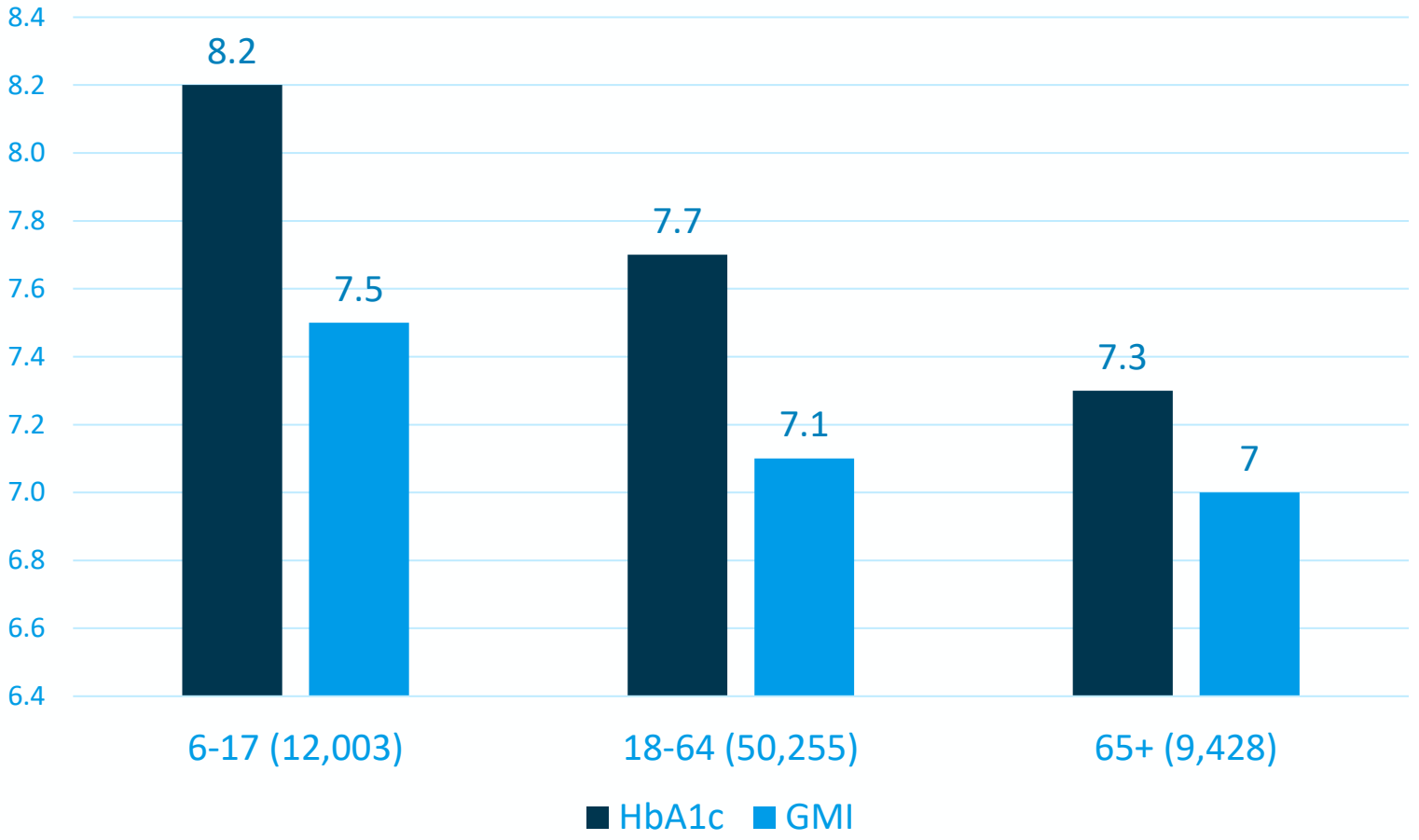
Glycemic improvement by prior therapy



Harsimran Singh PhD, Lars Mueller PhD, Gabriel Alencar, Steph Habif EdD, Jordan Pinsker MD
Real-World Evidence for Long-Term Improvements in Glycemic Control Using Control-IQ Technology in a Large Cohort with Type 1 Diabetes from the United States. ePoster, Australian Diabetes Conference Aug. 2022.

REAL-WORLD DATA / N=71,686

Glycemic improvement by age



p< 0.001

Harsimran Singh PhD, Lars Mueller PhD, Gabriel Alencar, Steph Habif EdD, Jordan Pinsker MD
Real-World Evidence for Long-Term Improvements in Glycemic Control Using Control-IQ Technology in a Large Cohort with Type 1 Diabetes from the United States. ePoster, Australian Diabetes Conference Aug. 2022.

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DOI: 10.1089/dia.2021.0217

COMMENTARY

Candidate Selection for Hybrid Closed Loop Systems

Gregory P. Forlenza, MD,[1,i] Marc D. Breton, PhD,[2,ii] and Boris P. Kovatchev, PhD[2,iii]

TABLE 1. COMPARISON OF GLYCEMIC OUTCOMES AT BASELINE VERSUS 12-MONTH USE OF CONTROL-IQ, FOR USERS WHO HAD HIGH BASELINE GLUCOSE MANAGEMENT INDICATOR

	Baseline (basal-IQ)	*12-month CIQ use*	*CIQ-baseline difference*	P
Baseline GMI ≥9 ($N=242$)				
GMI	9.5 (0.5)	8.1 (0.5)	−1.4	<0.001
TIR 70–180 mg/dL [%]	19.6 (7.6)	46.7 (10.7)	+27.1%	<0.001
Time below range <70 mg/dL [%]	0.26 (0.4)	0.49 (0.46)	+0.23%	<0.001
Time above 180 mg/dL [%]	80.1 (7.8)	52.7 (10.9)	−27.4%	<0.001
TIR 181–250 mg/dL [%]	27.0 (7.4)	27.6 (5.2)	+0.6%	n.s.
Time above 250 mg/dL [%]	53.1 (10.1)	25.1 (10.4)	−28.0%	<0.001
Mean sensor glucose [mg/dL]	258.2 (21.0)	200.9 (22.2)	−57.2 mg/dL	<0.001
Baseline GMI ≥10 ($N=36$)				
GMI	10.5 (0.4)	8.6 (0.6)	−1.9	<0.001
TIR 70–180 mg/dL [%]	10.5 (5.4)	38.6 (11.1)	+28.1%	<0.001
Time below range <70 mg/dL [%]	0.10 (0.2)	0.28 (0.33)	+0.18%	<0.001
Time above 180 mg/dL [%]	89.4 (5.5)	61.1 (11.3)	−28.3%	<0.001
TIR 181–250 mg/dL [%]	17.4 (5.4)	27.9 (4.1)	+10.5%	<0.001
Time above 250 mg/dL [%]	72.0 (8.5)	33.2 (11.6)	−38.8%	<0.001
Mean sensor glucose [mg/dL]	300.2 (18.3)	219.6 (25.4)	−80.6 mg/dL	<0.001

Data are expressed as mean (SD).
CIQ, Control-IQ; GMI, glucose management index; n.s., not statistically significant; SD, standard deviation; TIR, time in range.

Forlenza GP, Breton MD, Kovatchev BP. **Candidate Selection for Hybrid Closed Loop Systems.** *Diabetes Technol Ther.* 2021;23(11):760-762.

REAL WORLD RESULTS

Efficacy and Safety of Control-IQ technology without User-Initiated Boluses in Adults with Uncontrolled Type 1 Diabetes

+ A1c decreased by 1.6% and TIR increased by 19.3% in the autoboluses > 90% group.
+ No difference in TDI/kg between groups.

NO BOLUSES	Baseline	1 Year	change
A1c	9.7%	8.2%	-1.5% (p<0.05)
TIR	39%	54%	+3.6 hrs/day

+ Adding bolusing further improves A1c and TIR

50-90% BOLUSES	Baseline	1 Year	change
A1c	9.4%	7.4%	-2.0% (p<0.05)
TIR	40%	70%	+7.2 hrs/day

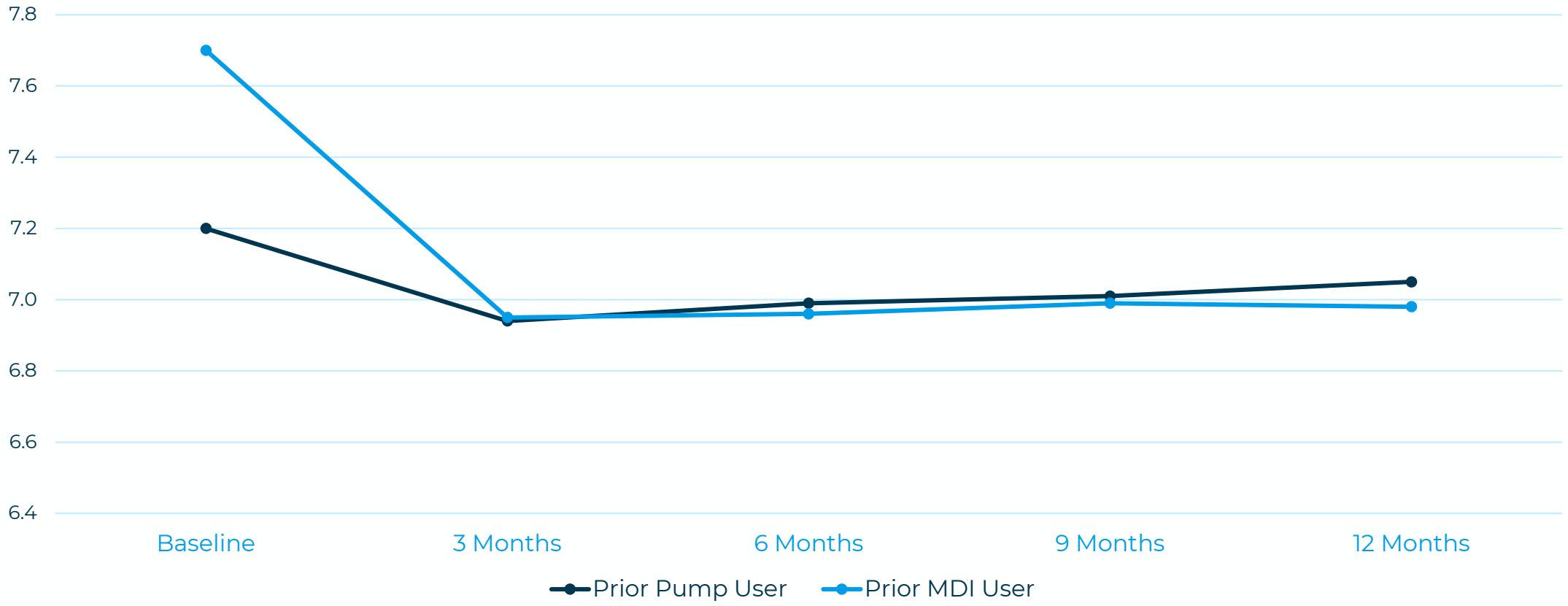
Akturk H, Shah V, Snell-Bergeon J. **Efficacy and Safety of Tandem Control IQ without User-Initiated Boluses in Adults with Uncontrolled Type 1 Diabetes.** *Diabetes Technol Ther.* 2022. DOI: 10.1089/dia.2022.0162

WHEN

When should MDI patients transition to Control-IQ technology?

Results: Outcomes by prior therapy modality

Comparison of Baseline HbA1c and GMI at 3, 6, 9 and 12 Months based on Prior Therapy Modality for Adults in the CLIO Study



Graham R, Singh H, Alencar G, Mueller L, Manning ML, White KN, Wheatcroft A, Carmelo K, Aronoff-Spencer ES, Habif S, Pinsker JE. **Long-Term Glycemic Control in Adult Participants Using Control-IQ Technology: Real-World Evidence.** American Diabetes Association, June 2022 [Diabetes. 2022; 71(Supplement_1):761-P]

When to start ‘closed loop?’

+ Do patients coming from MDI need pump practice before starting closed loop?

Time of Initiation of Advanced Hybrid Closed-Loop Therapy and Related Glycemic Outcomes in People with Type 1 Diabetes Transitioning from Multiple Daily Injections

Lars Mueller PhD, Harsimran Singh PhD, Steph Habif EdD,
Molly McElwee Malloy RN CDCES, J. Wesley Morberg BA, Jordan Pinsker MD

Results

Overall, the sample included 17,540 participants – mean age (SD) of 34 years (20) and 52% female – categorized into three groups for analysis:

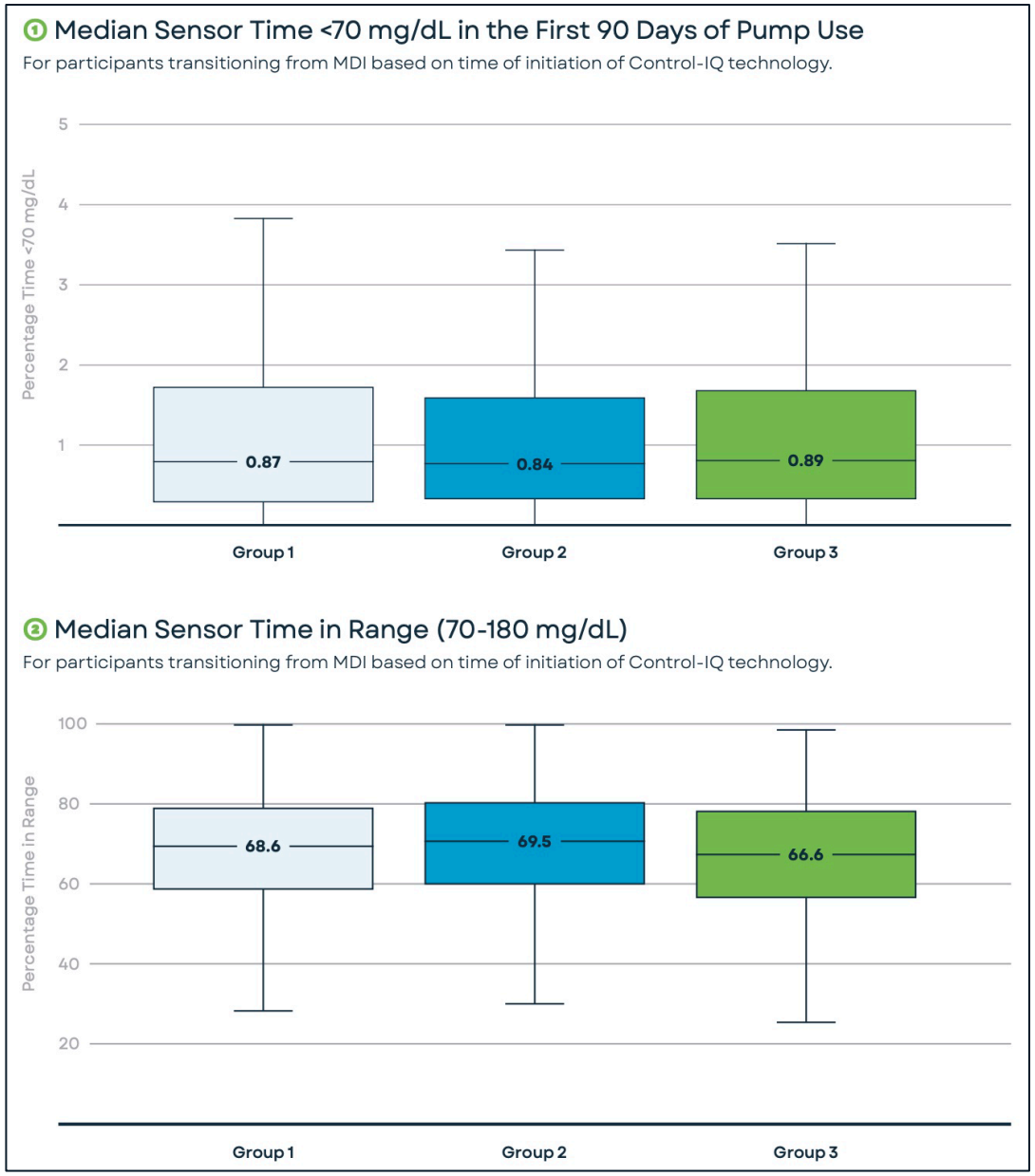
- ✔ **Group 1** (n=14,222) with mean age of 37.2 years (19.8), initiated Control-IQ technology within two days of pump start
- ✔ **Group 2** (n=2,448) with mean age of 31.2 years (19.7), initiated between 2-14 days of pump start
- ✔ **Group 3** (n=870) with mean age of 34.6 years (20.8), initiated within 15-90 days of pump start

Mueller L, Singh H, Habif S, et al. **Time of Initiation of Advanced Hybrid-Closed Loop Therapy and Related Glycemic Outcomes in People with Type 1 Diabetes Transitioning from Multiple Daily Injections.** *Diabetes Technol Ther*. 2022;24(S1):EP07.

When to start ‘closed loop?’

Conclusions

While all three groups experienced success with Control-IQ technology, Group 3 (i.e., participants initiating Control-IQ technology within 15-90 days of pump start) showed lower TIR with delayed initiation.



Mueller L, Singh H, Habif S, et al. **Time of Initiation of Advanced Hybrid-Closed Loop Therapy and Related Glycemic Outcomes in People with Type 1 Diabetes Transitioning from Multiple Daily Injections.** *Diabetes Technol Ther*. 2022;24(S1):EP07.

WHY

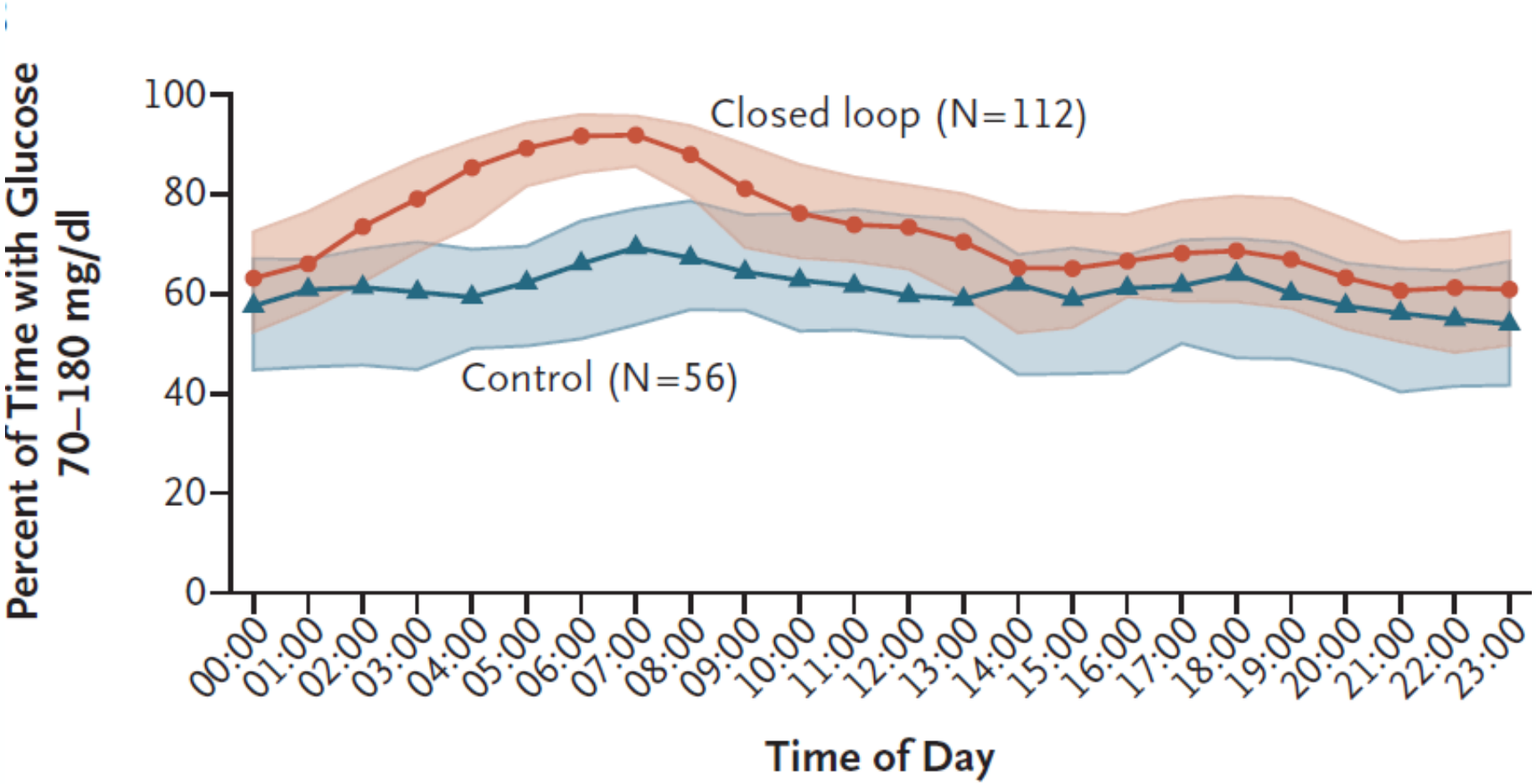
Example: Overnight 12-hour trend line

Why does overnight control matter?

Does it improve sleep?

Pivotal Trial Results

Time in Range 3.9-10.0mmol/L *: Day vs Night



**As measured by CGM*

Brown SA, Kovatchev BP et.al. **Six-Month Randomized, Multicenter Trial of Closed-Loop Control in Type 1 Diabetes**, NEJM Oct 2019, DOI: 10.1056/NEJMoa1907863.

DCLP5 Sleep Data

- Pittsburgh Sleep Quality Index (PSQI) scores were assessed at baseline to identify parents as "poor" sleepers (PSQI >5)
- Glycemic and psycho-behavioral outcomes before and after Control-IQ technology use were analyzed in poor sleepers (n=49) and their children
- All survey scores improved
- Of poor sleepers, 27 became good sleepers (PSQI score <5)

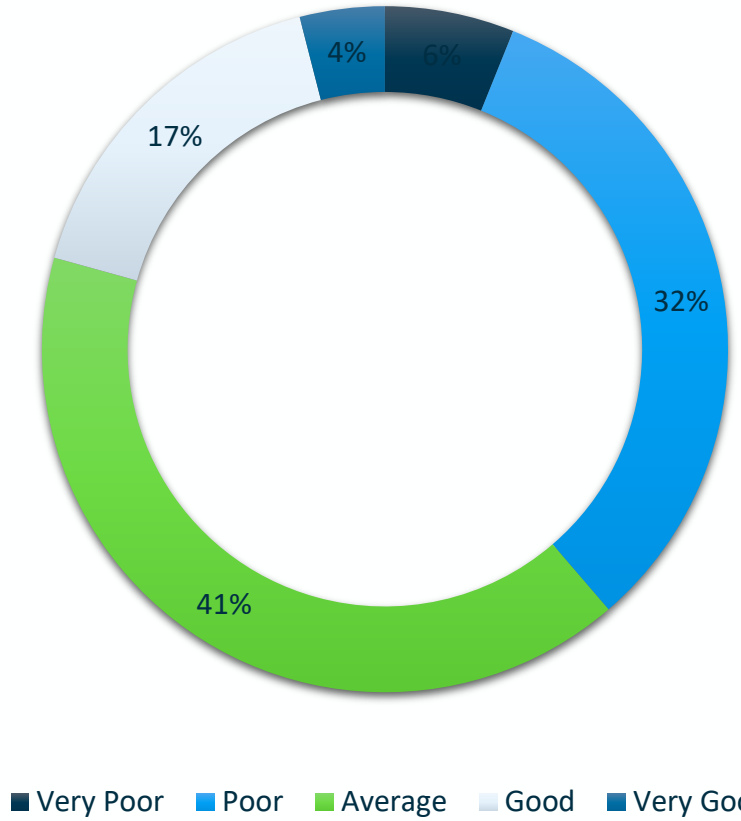
Table 1—Pre- and postintervention analysis for parents with PSQI score >5 (poor sleepers) at baseline (n = 49)

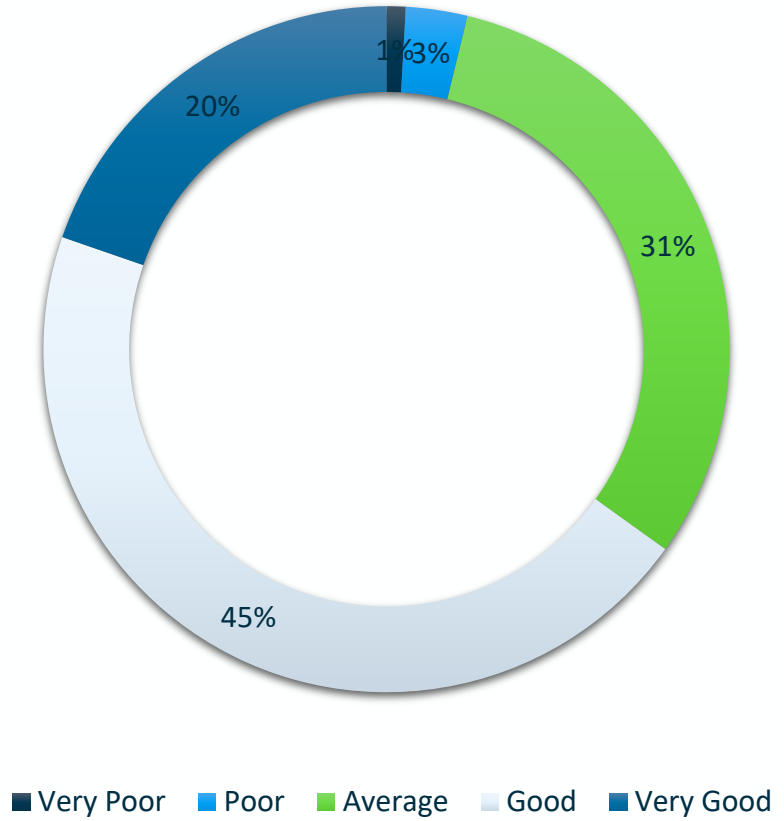
	Preintervention	Postintervention	P
Child PROs			
HFS-C total score	57 (51–67)	55 (48–67)	**0.025**
HFS-C behavior subscale score	30 (26–33)	30 (24–32)	0.144
HFS-C worry subscale score	27 (23–34)	27 (21–33)	0.096
PAID score	23 (17–32)	21 (17–31)	0.153
Parent PROs			
PSQI score	7 (6–10)	5 (3–8)	**<0.001**
HFS-P total score	73 (63–81)	65 (54–74)	**<0.001**
HFS-P behavior subscale score	33 (29–37)	29 (24–33)	**<0.001**
HFS-P worry subscale score	37 (34–47)	33 (29–40)	**0.011**
PAID score	44 (36–56)	35 (26–43)	**<0.001**
Nocturnal CGM (12:00 A.M.–6:00 A.M.)			
Mean glucose, mg/dL	182.16 ± 38.94	148.80 ± 19.11	**<0.001**
Glucose SD, mg/dL	64.00 ± 16.66	51.16 ± 14.51	**<0.001**
% time with glucose <54 mg/dL	0.00 (0.00–0.20)	0.10 (0.00–0.40)	**0.040**
% time with glucose <70 mg/dL	0.50 (0.00–2.70)	0.80 (0.40–1.60)	0.703
% TIR (70–180 mg/dL)	54.43 ± 20.85	78.53 ± 11.09	**<0.001**
% time with glucose >180 mg/dL	43.92 ± 21.08	20.35 ± 11.17	**<0.001**
HbA_{1c}, %, mmol/L	7.55 (6.9–8.3), 59 (52–67)	7.05 (6.6–7.6), 54 (49–60)	**<0.001**

Data are mean ± SD or median (interquartile range). Bold values indicate significance ($P < 0.05$).

Cobry EC, Bisio A, Wadwa RP, Breton MD. **Improvements in Parental Sleep, Fear of Hypoglycemia, and Diabetes Distress With Use of an Advanced Hybrid Closed-Loop System.** *Diabetes Care*. 2022;45(5):1292-1295. doi:10.2337/dc21-1778

Patient-Reported Quality of Sleep*



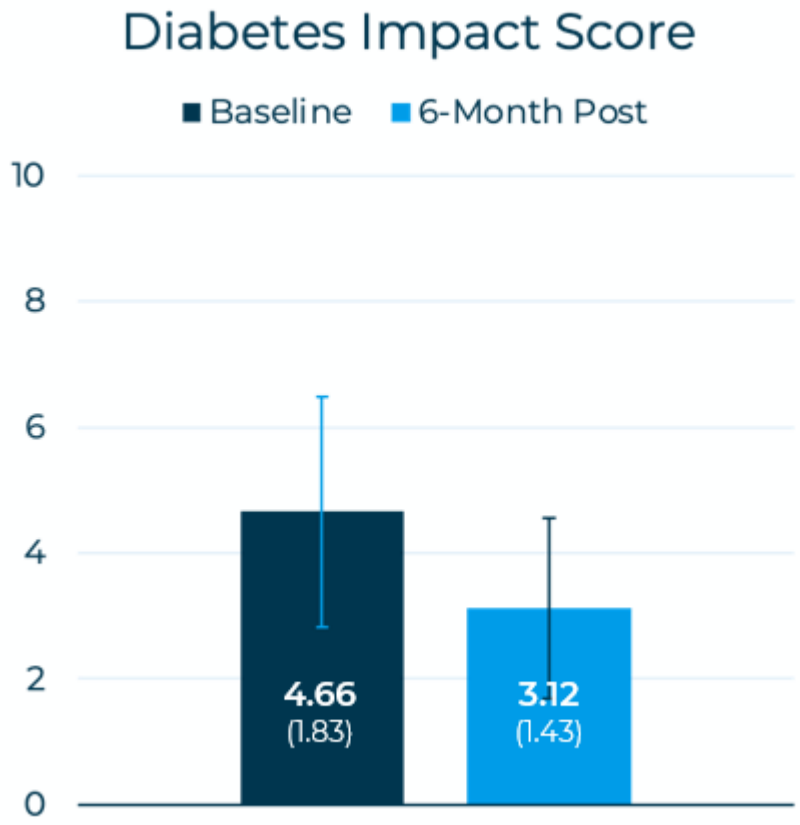


*96% of study participants reported improved sleep quality at post assessment.
Habif S, et al. Quality of life outcomes and glycemic control from the t:slim X2 pump with Control-IQ technology – Real world observations from the CLIO Study. *Diabetes Technol Ther.. 2021;23(S2):A-66.*

RESULTS: DIABETES IMPACT & DEVICE SATISFACTION SCALE

Diabetes Impact (DI)

Impact	Baseline Mean (SD)	6-Month Post Mean (SD)
Bad Night's Sleep due to Diabetes*	5.05 (2.46)	3.26 (1.91)
Wake up at Night to Treat a Low BG*	4.94 (2.36)	3.37 (1.87)
Miss Work, School, etc. due to Diabetes*	3.06 (2.35)	2.00 (1.63)
Worry About Going Low*	5.54 (2.70)	3.83 (2.29)
DI Overall Score*	**4.66** (1.83)	**3.12** (1.43)



Singh H, Alencar G, Manning M, White K, Mueller L, Pinsker J, Habif S. **Long-term improvements in patient-reported outcomes irrespective of baseline glycemic control and previous insulin delivery method with the t:slim x2 pump with Control-IQ technology.** *Diabetes Technol Ther*. 2022; 24(S1): OP094.

Control-IQ technology does not prevent all highs and lows. Users must still bolus for meals and actively manage their diabetes. Visit tandemdiabetes.com/safetyinfo for additional important safety information.

Important Safety Information: RX ONLY. The t:slim X2 pump and Control-IQ technology are intended for single patient use. The t:slim X2 pump and Control-IQ technology are indicated for use with NovoLog or Humalog U-100 insulin. t:slim X2 insulin pump: The t:slim X2 insulin pump with interoperable technology is an alternate controller enabled (ACE) pump that is intended for the subcutaneous delivery of insulin, at set and variable rates, for the management of diabetes mellitus in people requiring insulin. The pump is able to reliably and securely communicate with compatible, digitally connected devices, including automated insulin dosing software, to receive, execute, and confirm commands from these devices. The t:slim X2 pump is indicated for use in individuals six years of age and greater. Control-IQ technology: Control-IQ technology is intended for use with a compatible integrated continuous glucose monitor (iCGM, sold separately) and ACE pump to automatically increase, decrease, and suspend delivery of basal insulin based on iCGM readings and predicted glucose values. It can also deliver correction boluses when the glucose value is predicted to exceed a predefined threshold. Control-IQ technology is intended for the management of Type 1 diabetes mellitus in persons six years of age and greater.

WARNING: Control-IQ technology should not be used by anyone under the age of six years old. It should also not be used in patients who require less than 10 units of insulin per day or who weigh less than 25 kilograms.

Control-IQ technology is not indicated for use in pregnant women, people on dialysis, or critically ill patients. Do not use Control-IQ technology if using hydroxyurea. Users of the t:slim X2 pump and Control-IQ technology must: use the insulin pump, CGM, and all other system components in accordance with their respective instructions for use; test blood glucose levels as recommended by their healthcare provider; demonstrate adequate carb-counting skills; maintain sufficient diabetes self-care skills; see healthcare provider(s) regularly; and have adequate vision and/or hearing to recognize all functions of the pump, including alerts, alarms, and reminders. The t:slim X2 pump, and the CGM transmitter and sensor must be removed before MRI, CT, or diathermy treatment. Visit tandemdiabetes.com/safetyinfo for additional important safety information.