# Nuovi sistemi AHCL: presentazione di uno strumento

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La dott.ssa Marta Bassi dichiara di non aver ricevuto negli ultimi due anni compensi o finanziamenti
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# Control-IQ Software


Il sistema integrato AHCL è stato introdotto in Italia a partire **dall'autunno 2020**. La tecnologia Control-IQ permette di regolare automaticamente l'erogazione di insulina in base al dato glicemico fornito dal CGM, ridurre al minimo le difficoltà di gestione del diabete e garantendo un miglior controllo glicometabolico

## Adatta

l'erogazione di insulina basale in relazione al dato CGM

## Corregge

le iperglicemie con boli correttivi

## Sospende

l'erogazione di insulina in caso di ipoglicemia predetta

## Intensifica

l'erogazione di insulina basale Notturna

## Software aggiornabile

# TECNOLOGIA Control-IQ

- Pompa per insulina
- Algoritmo Control-IQ incorporato
- Sensore CGM

***senza calibrazioni****


La tecnologia Control-IQ rimane attiva anche in mancanza di letture CGM fino alle terza lettura mancante. A partire dalla quarta lettura (20 minuti) la tecnologia Control-IQ si disattiva e il sistema torna ad essere una SAP. Non appena la connettività CGM si ristabilisce la tecnologia Control-IQ si riattiva automaticamente.

## Componenti del sistema

# Funzionamento del sistema

La tecnologia Control-IQ utilizza:
- le **letture CGM** (valore corrente e previsione a 30 minuti)
- Il **Fattore di Sensibilità Insulinica** (**FSI**)
- L'**Insulina Attiva** (**IOB**)

per regolare la somministrazione di *Insulina Basale* e i *Boli Automatici di Correzione*

- Il **Rapporto Insulina Carboidrati (I:C)**

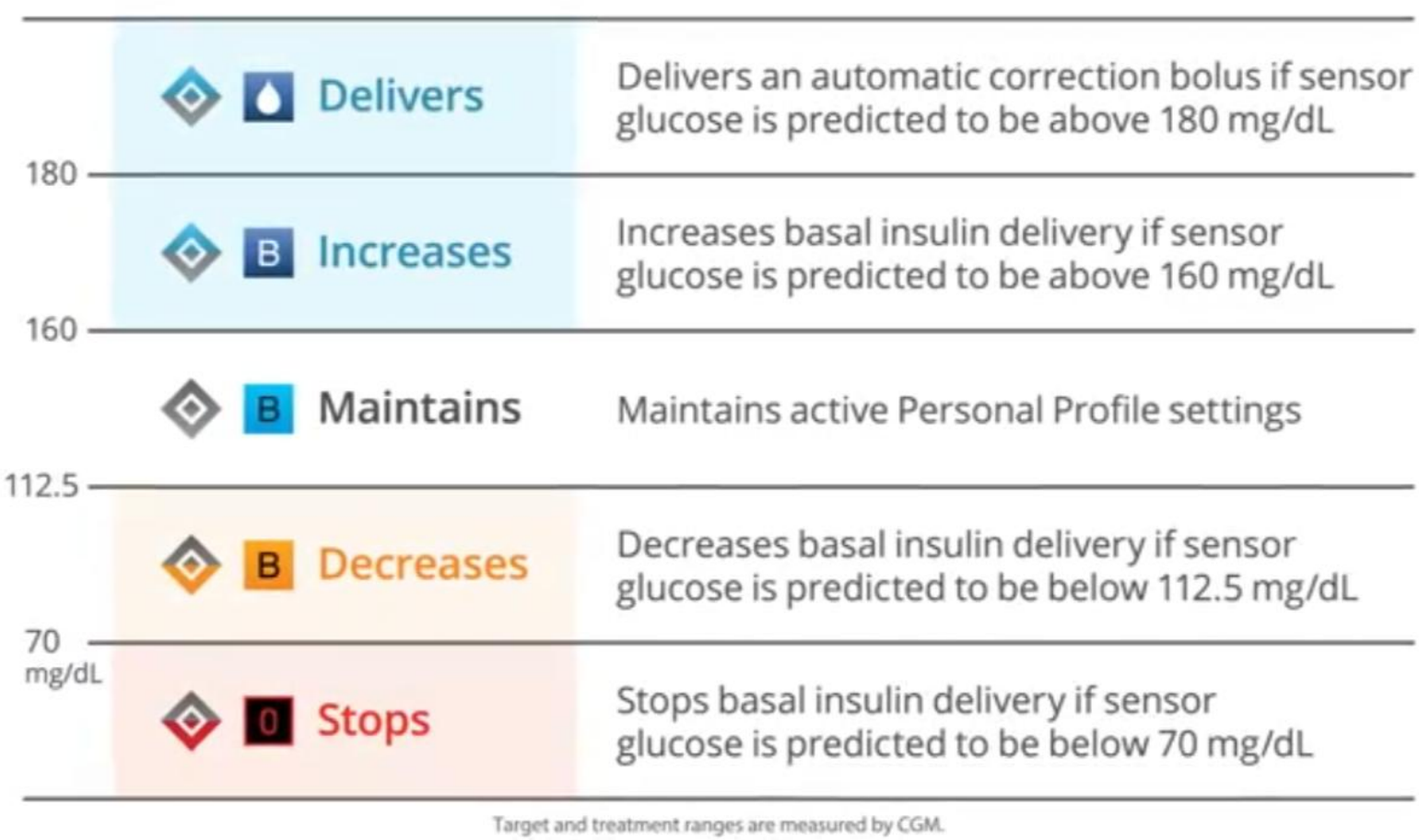
Per regolare la somministrazione dei *Boli di insulina pre-pasto*

# Algoritmo basato su Frecce di trend

| Dexcom G5 Trend Arrows | | | Change in Glucose |
|---|---|---|---|
| Receiver | App | Glucose Direction | |
| ⬆⬆ |  | Increasing | **Glucose is rapidly rising**<br>Increasing >3 mg/dL/min or >90 mg/dL in 30 minutes |
| ⬆ |  | Increasing | **Glucose is rising**<br>Increasing 2–3 mg/dL/min or 60–90 mg/dL in 30 minutes |
| ↗ |  | Increasing | **Glucose is slowly rising**<br>Increasing 1–2 mg/dL/min or 30–60 mg/dL in 30 minutes |
| ➡ |  | Increasing or Decreasing | **Glucose is steady**<br>Not increasing/decreasing >1 mg/dL/min |
| ↘ |  | Decreasing | **Glucose is slowly falling**<br>Decreasing 1–2 mg/dL/min or 30–60 mg/dL in 30 minutes |
| ⬇ |  | Decreasing | **Glucose is falling**<br>Decreasing 2–3 mg/dL/min or 60–90 mg/dL in 30 minutes |
| ⬇⬇ |  | Decreasing | **Glucose is rapidly falling**<br>Decreasing >3 mg/dL/min or >90 mg/dL in 30 minutes |
| No Arrow | N/A | System cannot calculate the velocity and direction of the glucose change | |

[16] *Lori M. Laffel, Grazia Aleppo, Bruce A. Buckingham et al. A Practical Approach to Using Trend Arrows on the Dexcom G5 CGM System to Manage Children and Adolescents With Diabetes. J Endocr. Society 2017 Nov 20;1(12):1461-1476*

# Attività normale: target 112.5-160 mg/dl



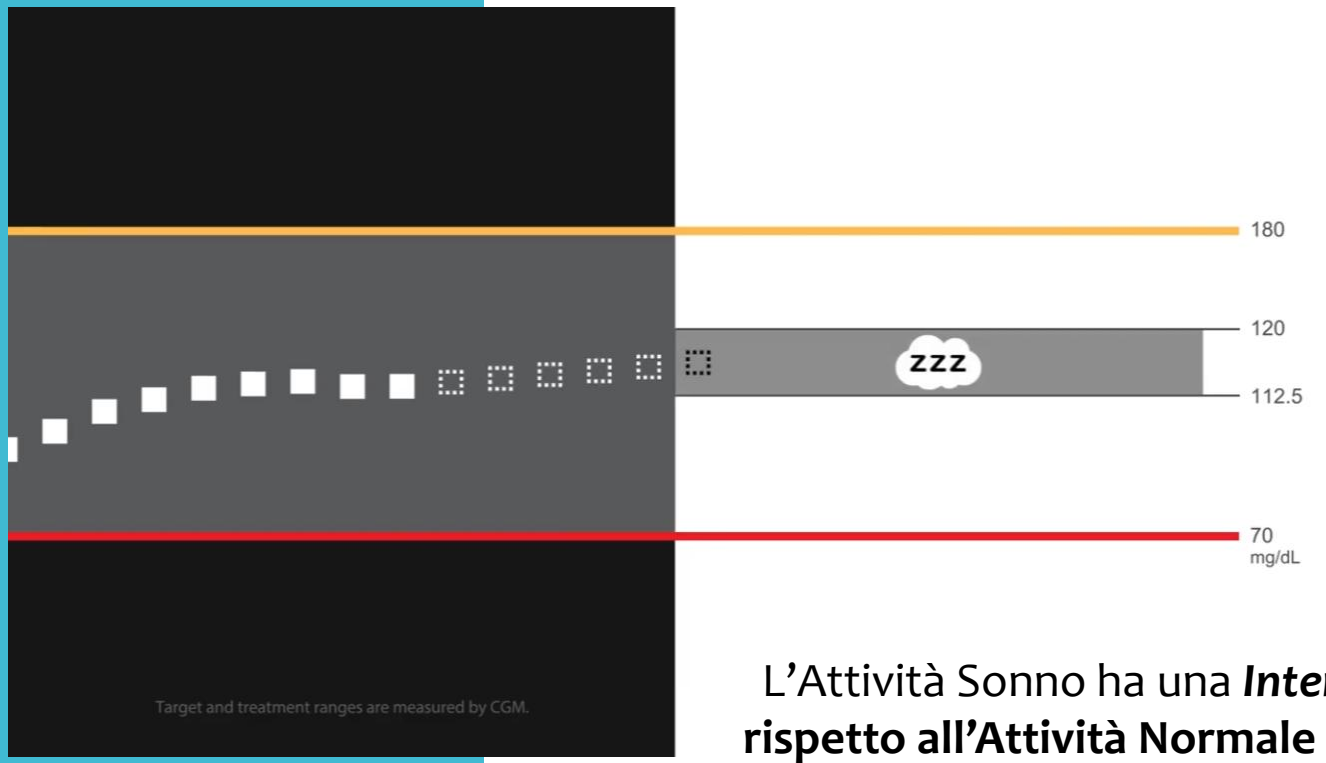

https://www.youtube.com/watch?v=ADUDwM1SxeE

# Funzionamento del sistema

## Il Bolo Automatico di Correzione

- utilizza un **Target di 110 mg/dL**
- viene erogato il **60% del Bolo di Correzione** previsto, calcolato in base a: FSI, lettura CGM e IOB
- l'**erogazione massima è di 6U**
- la distanza dal bolo precedente **è di minimo 60 minuti**
- **può essere cancellato manualmente**

# Attività notturna: target 112.5-120 mg/dl
# NO boli automatici

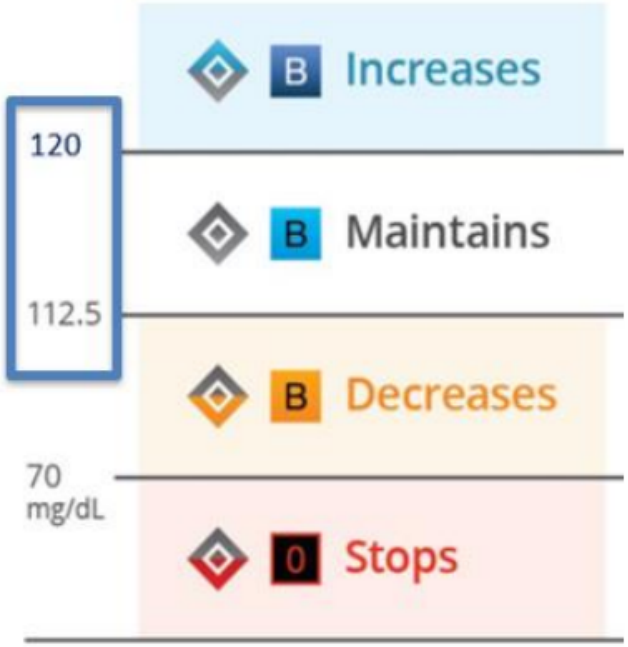



L'Attività Sonno ha una ***Intervallo Target ridotto*** **rispetto all'Attività Normale poiché vi sono meno variabili che influenzano la glicemia. Questo consente di arrivare al risveglio con valori glicemici ottimali.**

https://www.youtube.com/watch?v=eEJHFG3z8t4

## Attivazione MANUALE o AUTOMATICA

## Si possono impostare DUE PROGRAMMI SONNO




**Aumenta** l'erogazione della Basale se il valore glicemico del CGM prevede a 30 minuti di superare **120 mg/dL**

**Mantiene la Basale del Profilo Personale attivo**

**Riduce** l'erogazione della Basale se il valore glicemico del CGM prevede a 30 minuti di scendere al di sotto di **112,5 mg/dL**

**Sospende** l'erogazione della Basale se il valore glicemico del CGM prevede a 30 minuti di scendere al di sotto di **70 mg/dl**

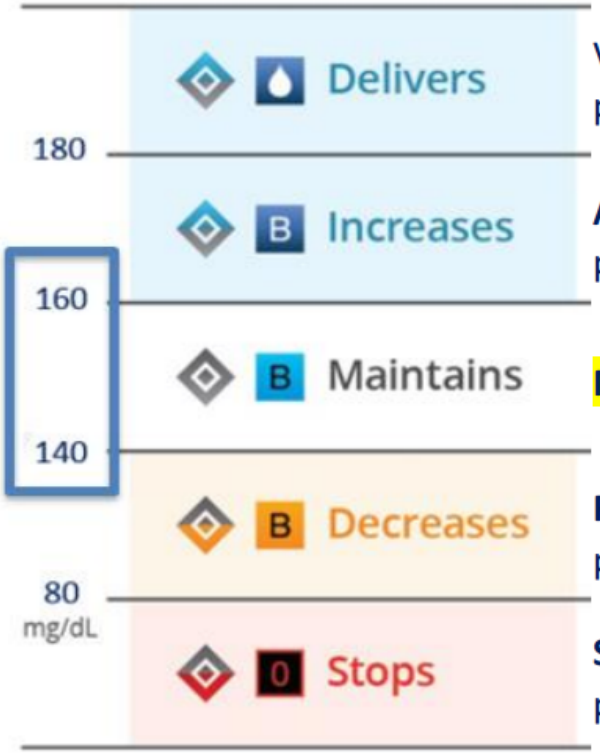
# Attività notturna

# Attività esercizio: target 140-160 mg/dl

## Boli automatici di correzione

L'Attività Esercizio ha una ***Intervallo Target più stringente e più elevato*** **rispetto all'Attività normale per adattarsi alla naturale riduzione dei livelli glicemici durante e dopo l'attività sportiva in modo da evitare il rischio di valori glicemici bassi**


https://www.youtube.com/watch?v=2wZ5v2NAits




Viene erogato un **Bolo Automatico di Correzione** se il valore glicemico del CGM prevede a 30 minuti di superare **180 mg/dL**

**Aumenta** l'erogazione della Basale se il valore glicemico del CGM prevede a 30 minuti di superare **160 mg/dL**

**Mantiene la Basale del Profilo Personale attivo**

**Riduce** l'erogazione della Basale se il valore glicemico del CGM prevede a 30 minuti di scendere al di sotto di **140 mg/dL**

**Sospende** l'erogazione della Basale se il valore glicemico del CGM prevede a 30 minuti di scendere al di sotto di **80 mg/dL**

# Attività esercizio

| | | Control-IQ | Sleep Activity | Exercise Activity |
|---|---|---|---|---|
| Delivers | Delivers an automatic correction bolus if sensor glucose is predicted to be above ____ mg/dL | 180 | -- | 180 |
| Increases | Increases basal insulin delivery if sensor glucose is predicted to be above ____ mg/dL | 160 | 120 | 160 |
| Maintains | Maintains active Personal Profile settings when sensor glucose is between ____ - ____ mg/dL | 112.5 - 160 | 112.5 - 120 | 140 - 160 |
| Decreases | Decreases basal insulin delivery if sensor glucose is predicted to be below ____ mg/dL | 112.5 | 112.5 | 140 |
| Stops | Stops basal insulin delivery if sensor glucose is predicted to be below ____ mg/dL | 70 | 70 | 80 |

# Control IQ – Modalità di attività

| | Basal-IQ | Control-IQ |
|---|---|---|
| Basale Massima | 15 U/h | 15 U/h |
| Basale Minima | 0.01 U/h | 0.01 U/h |
| **Bolo Massimo** | **25 U + 25 U di Boli aggiuntivi** | **25 U, no Boli aggiuntivi** |
| Rapporto Insulina Carboidrati (I:C) | 1:1 – 1:300 gr | 1:1 – 1:300 gr |
| Fattore di Sensibilità (FSI) | 1:1 – 1:600 mg/dL | 1:1 – 1:600 mg/dL |
| **Durata Bolo Esteso** | **15 minuti – 8 ore** | **15 minuti – 2 ore** |
| **Basale Temporanea** | **15 minuti – 72 ore** | **Non disponibile** |
| **Durata Insulina Attiva (IOB)** | **2 – 8 ore** | **5 ore** |

**A differenza del Basal -IQ: durante la sospensione automatica dell'erogazione Basale è possibile effettuare un Bolo manuale e la somministrazione del bolo esteso prosegue.**

# Basal IQ vs Control IQ

# Allarmi e avvisi

- ***Avviso glicemia bassa:*** *glicemia predetta a 15 minuti < 70 mg/dl (< 80 mg/dl se modalità esercizio)*
- ***Avviso glicemia alta:*** *glicemia > 350 mg/dl senza previsione di riduzione nonostante aumento basale* ***(!! SET)***
- *Limite basale*
- *Livello massimo insulina*
- *Avviso Fuori Range*
- *Errore segnale*

**iDCL Trial**
International Diabetes Closed Loop Trial

# Objective

Assessing the efficacy and safety of a closed-loop system as compared with a sensor augmented pump

**Primary outcome**:
Percentage of Time in Range (70-180 mg/dl)

**Secondary outcomes:**

- Percentage of time > 180 mg/dl
- Mean glucose concentration
- HbA1c 26 weeks
- Percentage of time < 70 mg/dl and < 54 mg/dl

**Safety outcomes:** severe hypoglicemia, ketoacidosis, other AEs

*Brown SA, Kovatchev BP, Raghinaru D, Lum JW, Buckingham BA, Kudva YC, Laffel LM, Levy CJ, Pinsker JE, Wadwa RP, Dassau E, Doyle FJ 3rd, Anderson SM, Church MM, Dadlani V, Ekhlaspour L, Forlenza GP, Isganaitis E, Lam DW, Kollman C, Beck RW; iDCL Trial Research Group. Six-Month Randomized, Multicenter Trial of Closed-Loop Control in Type 1 Diabetes. N Engl J Med. 2019 Oct 31;381(18):1707-1717. doi: 10.1056/NEJMoa1907863. Epub 2019 Oct 16. PMID: 31618560; PMCID: PMC7076915.*

# Study population and design

(7 University Centers in the USA)

> 14 years
T1DM
Insulin therapy > 1 yr

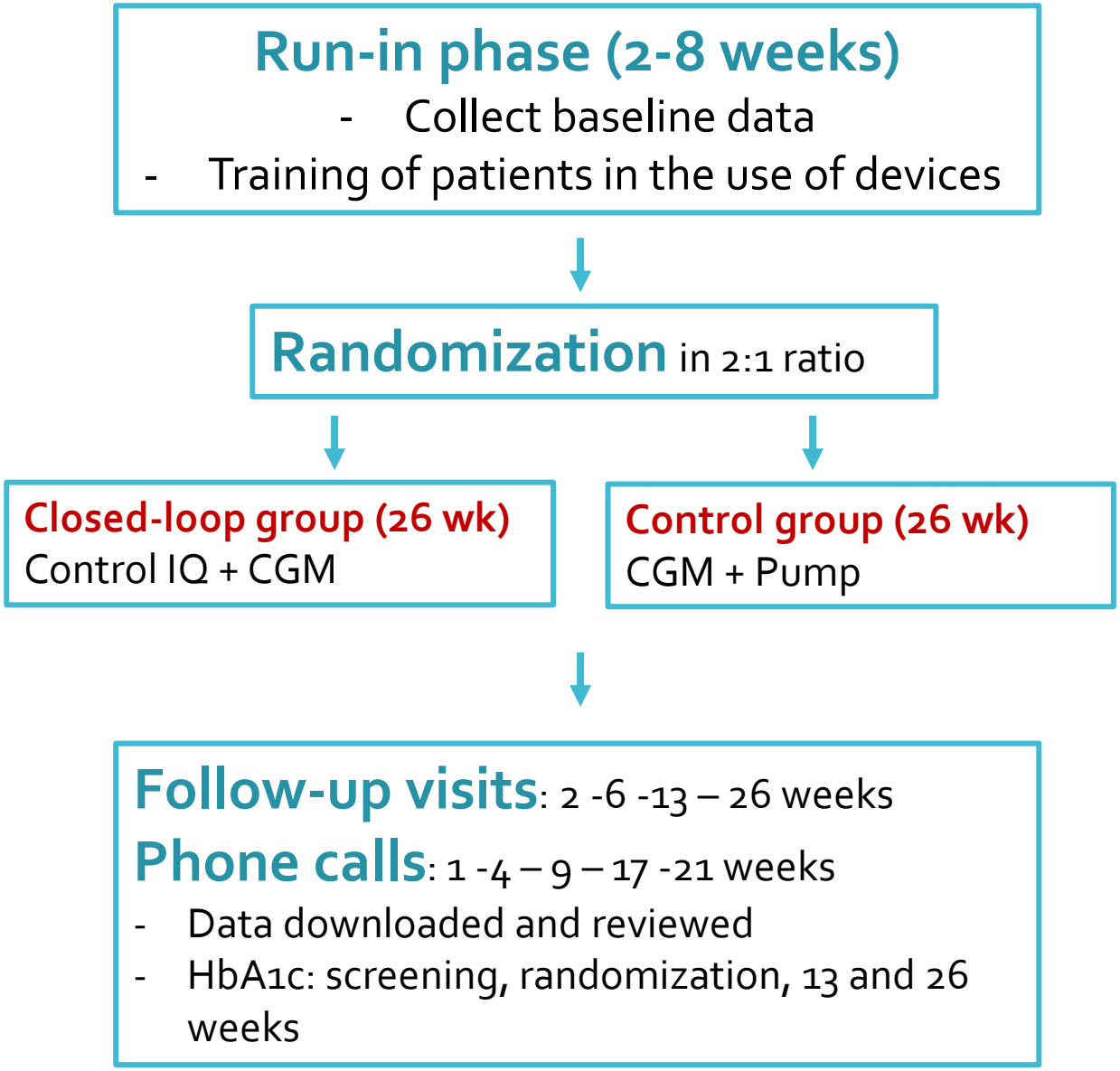


**Table 1. Characteristics of the Patients.***

168

| Characteristic | Closed Loop (N=112) | Control (N=56) |
|---|---|---|
| Age — yr (14-71) | 33±16 | 33±17 |
| Age group — no. (%) | | |
| ≥18 Yr | 81 (72) | 39 (70) |
| <18 Yr | 31 (28) | 17 (30) |
| Median duration of diabetes (IQR) — yr (1-62) | 17 (8–28) | 15 (7–23) |
| Means of insulin administration — no. (%) | | |
| Insulin pump | 90 (80) | 43 (77)† |
| Multiple daily injections | 22 (20) | 13 (23) |
| Use of continuous glucose monitor at enrollment — no. (%) | 78 (70) | 40 (71) |
| Median body-mass index (IQR)‡ | 25 (23–29) | 25 (22–28) |
| Female sex — no. (%) | 54 (48) | 30 (54) |
| White race — no./total no. (%)§ | 94/109 (86) | 53/56 (95) |
| Hispanic or Latino ethnic group — no. (%)§ | 13 (12) | 5 (9) |
| Annual household income — no./total no. (%) | | |
| <$50,000 | 10/89 (11) | 2/50 (4) |
| $50,000 to <$100,000 | 24/89 (27) | 18/50 (36) |
| ≥$100,000 | 55/89 (62) | 30/50 (60) |
| Highest education level — no./total no. (%)¶ | | |
| Less than bachelor's degree | 16/111 (14) | 13/56 (23) |
| Bachelor's degree | 51/111 (46) | 21/56 (38) |
| Advanced degree | 44/111 (40) | 22/56 (39) |

# The baseline characteristics were similar in the two groups

| | | |
|---|---|---|
| Private medical insurance — no./total no. (%) | 102/109 (94) | 50/55 (91) |
| Glycated hemoglobin level — % | | |
| Screening | 7.6±1.1 | 7.6±1.0 |
| Baseline | 7.4±1.0 | 7.4±0.8 |
| Glycated hemoglobin level at baseline — no. (%) | | |
| <7.0% | 38 (34) | 19 (34) |
| 7.0 to <7.5% | 23 (21) | 10 (18) |
| 7.5 to <8.0% | 22 (20) | 12 (21) |
| 8.0 to <9.0% | 23 (21) | 14 (25) |
| ≥9.0% | 6 (5) | 1 (2) |
| Median blood glucose meter tests per day (IQR) — no. | 3 (2–5) | 3 (2–4) |
| Diabetic ketoacidosis in past 12 mo — no. (%) | 4 (4) | 1 (2) |
| Severe hypoglycemia in past 12 mo — no. (%) | 6 (5) | 1 (2) |

5.4-10.6

* Plus–minus values are means ±SD. IQR denotes interquartile range.
† Among the 43 patients in the control group who were using a personal pump, the companies supplying the pumps were Medtronic (17 patients), Tandem (16), Insulet (6), and Animas (4).
‡ Body-mass index is the weight in kilograms divided by the square of the height in meters.
§ Race and ethnic group were reported by the patients.
¶ Data are for the highest level of education completed by patient or, if patient was younger than 18 years of age, by the primary caregiver.

**All 168 patients completed the trial**

# Primary outcome

# Results

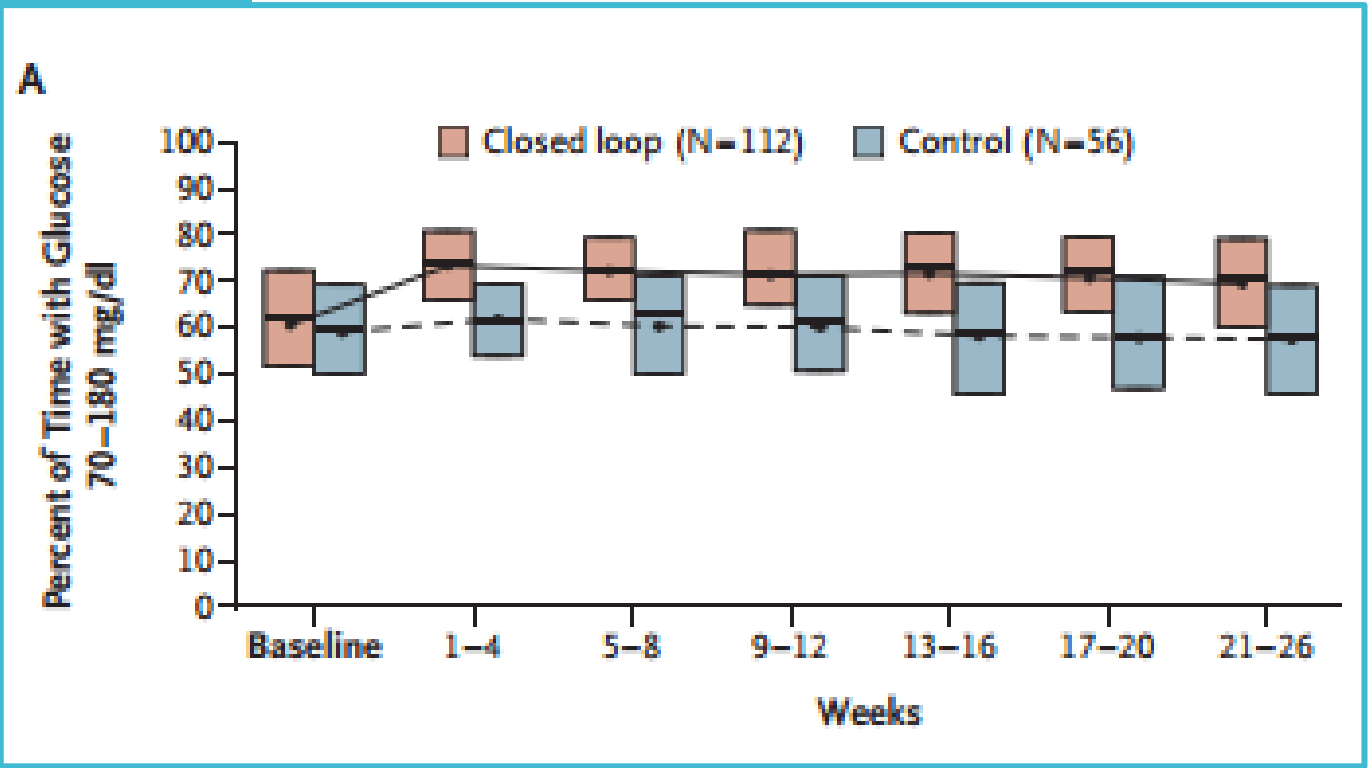
**Table 2. Primary and Secondary Hierarchical Efficacy Outcomes.***

| Outcome | 2-Wk Baseline Period | | 26-Wk Trial Period† | | | |
|---|---|---|---|---|---|---|
| | Closed Loop (N=112) | Control (N=56) | Closed Loop (N=112) | Control (N=56) | Risk-Adjusted Difference, Closed Loop Minus Control (95% CI)‡ | P Value‡ |
| Median hours of sensor data (IQR) | 307 (285–327) | 306 (283–320) | 4267 (4133–4348) | 4141 (3922–4280) | | |
| Primary outcome: percentage of time with glucose level in target range of 70 to 180 mg/dl | 61±17 | 59±14 | 71±12 | 59±14 | 11 (9 to 14) | <0.001 |

**= + 2.6 hours/day TIR in closed-loop group**

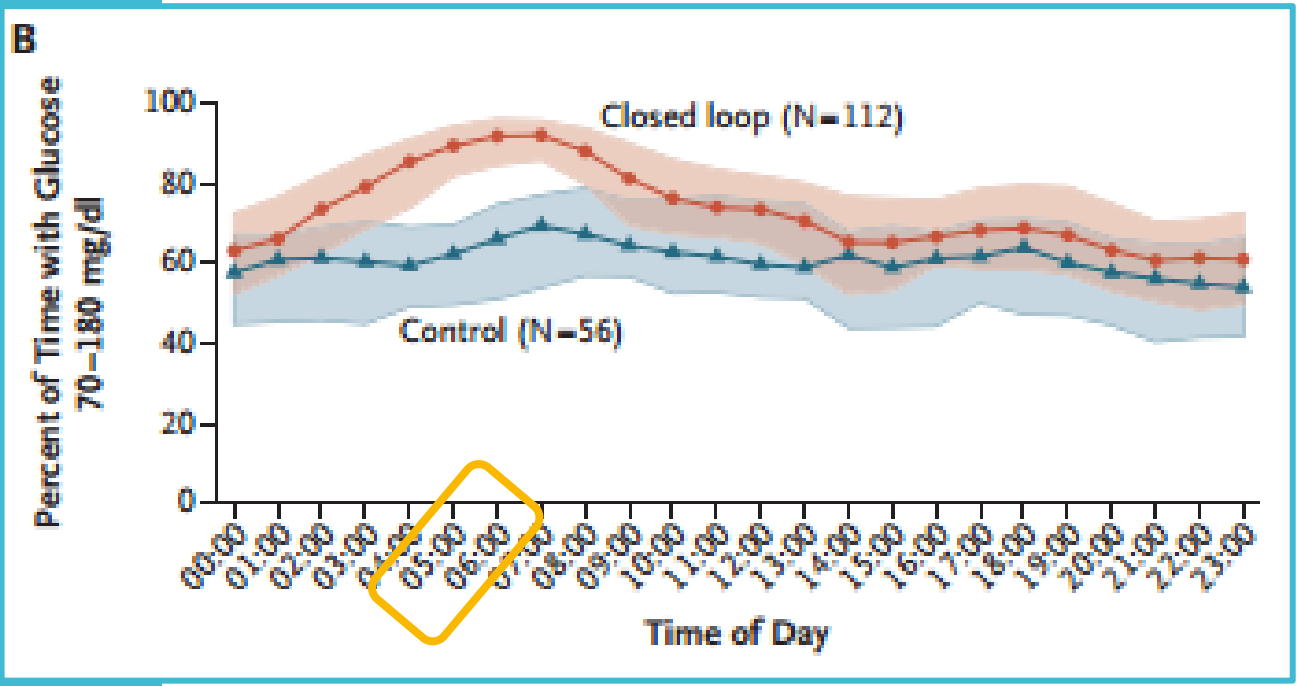
# Primary outcome

**= + 2.6 hours/day TIR in closed-loop group**




Panel A shows a box plot of the percentage of time that the glucose level was within the range of 70 to 180 mg per deciliter (3.9 to 10.0 mmol per liter), as measured by continuous glucose monitoring, during 4-week periods over 6 months among patients who were assigned to receive treatment with either a closed-loop system (closed loop) or a sensor-augmented pump (control).

# Primary outcome




75th percentiles, respectively. Panel B shows an envelope plot of the same outcome according to the time of day. Symbols denote the hourly median values, and the shaded regions are defined by the 25th and 75th percentiles.

**Daytime (h 6-24)**

**Closed-loop group: TIR 70%**

**Control group: TIR 59%**

**Night time (h 24-6)**

**Closed-loop group: TIR 76%**

**Control group: TIR 59%**

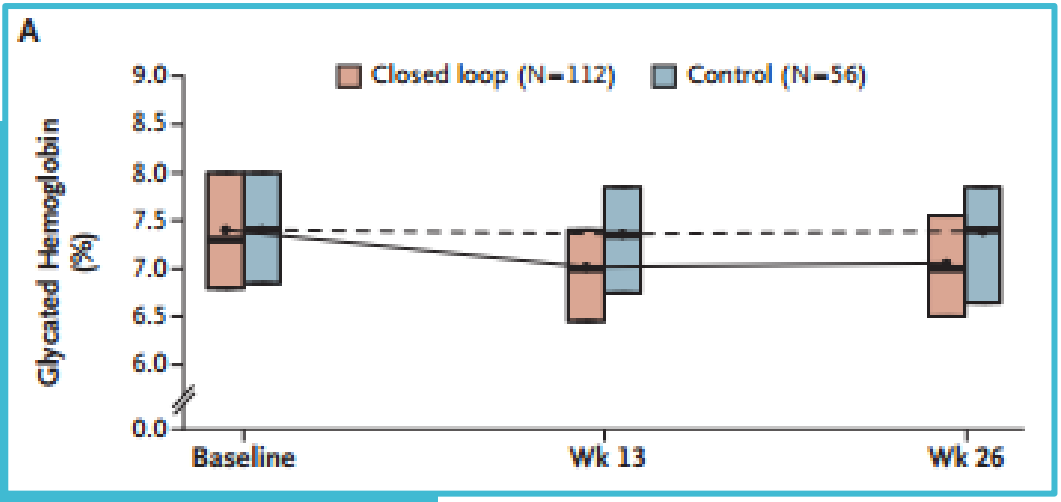
# Secondary outcomes

| Outcome | 2-Wk Baseline Period | | 26-Wk Trial Period† | | | |
|---|---|---|---|---|---|---|
| | Closed Loop (N=112) | Control (N=56) | Closed Loop (N=112) | Control (N=56) | Risk-Adjusted Difference, Closed Loop Minus Control (95% CI)‡ | P Value‡ |
| Median hours of sensor data (IQR) | 307 (285–327) | 306 (283–320) | 4267 (4133–4348) | 4141 (3922–4280) | | |
| Primary outcome: percentage of time with glucose level in target range of 70 to 180 mg/dl | 61±17 | 59±14 | 71±12 | 59±14 | 11 (9 to 14) | <0.001 |
| Secondary hierarchical outcomes | | | | | | |
| Percentage of time with glucose level >180 mg/dl | 36±19 | 38±15 | 27±12 | 38±15 | −10 (−13 to −8) | <0.001 |
| Glucose level — mg/dl | 166±32 | 169±25 | 156±19 | 170±25 | −13 (−17 to −8) | <0.001 |
| Glycated hemoglobin — %§ | 7.40±0.96 | 7.40±0.76 | 7.06±0.79 | 7.39±0.92 | −0.33 (−0.53 to −0.13) | 0.001 |
| Percentage of time with glucose level <70 mg/dl¶ | 3.58±3.39 | 2.84±2.54 | 1.58±1.15 | 2.25±1.46 | −0.88 (−1.19 to −0.57) | <0.001 |
| Percentage of time with glucose level <54 mg/dl‖ | 0.90±1.36 | 0.56±0.79 | 0.29±0.29 | 0.35±0.32 | −0.10 (−0.19 to −0.02) | 0.02 |

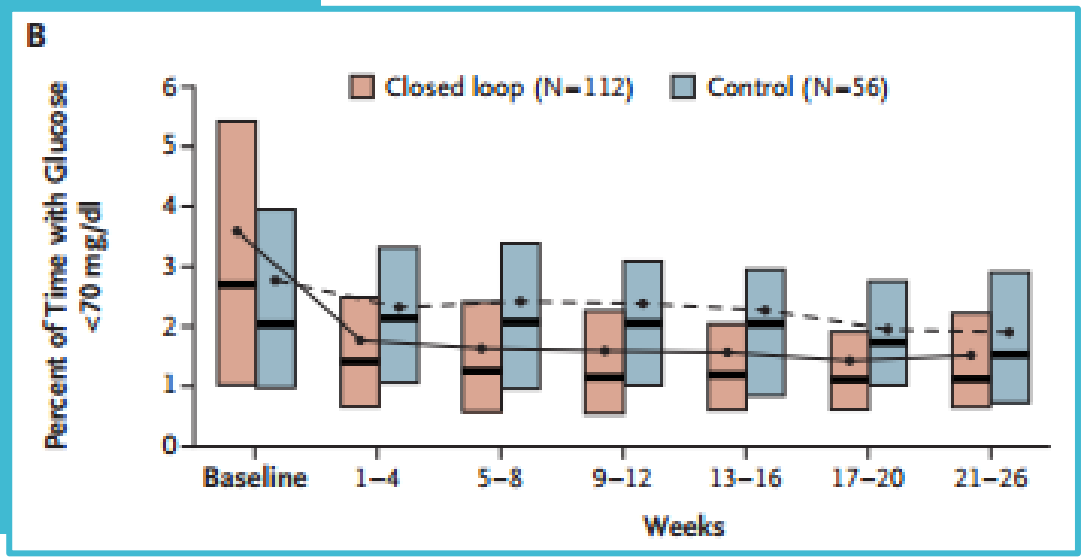
All five secondary outcomes met the prespecified criterion for significance in favor of the closed-loop system.

= - 2.4 hours/day > 180 mg/dl

= - 13 min/day < 70 mg/dl




Panel A shows a box plot of the glycated hemoglobin level at baseline, week 13, and week 26 among patients who were assigned to receive treatment with either a closed-loop system (closed loop) or a sensor-augmented pump (control). One patient in the control group and one patient in the




shows a box plot of the percentage of time that the glucose level was less than 70 mg per deciliter, as measured by continuous glucose monitoring.

# Results

There was **no significant difference** between the groups in:

- **Blood glucose measurements per day**
- **Daily insulin amount**
- **Weight change**

**Use of CGM** over the 6 months of the trial:

- Closed-loop group: **97%** (closed-loop mode 90%, open-loop mode because of a software error)
- Control group: 96%

**Device problems**: 137 (> **connectivity problems**)

**Adverse events**:

- Closed-loop group: 17
- Control group: 2

**Table 3. Adverse Events.***

| Event | Closed Loop (N=112) | Control (N=56) | P Value† |
|---|---|---|---|
| Any adverse event | | | |
| No. of events | 17 | 2 | |
| No. of patients (%) | 16 (14) | 2 (4) | 0.05 |
| No. of events per 100 person-yr | 30.2 | 7.1 | |
| Specific events — no. of patients (%) [no. of events] | | | |
| Severe hypoglycemia | 0 | 0 | |
| Diabetic ketoacidosis | 1 (1) [1]‡ | 0 | |
| Serious adverse events related to trial device | 1 (1) [1]‡ | 0 | |
| Other serious adverse events | 3 (3) [3]§ | 0 | |
| Hyperglycemia or ketosis without diabetic ketoacidosis | 12 (11) [13] | 2 (4) [2] | |
| Glycated hemoglobin level worsening by >0.5% — no. of patients (%)¶ | 8 (7) | 5 (9) | 0.60 |
| Median hypoglycemic events per wk (IQR)‖ | 0.4 (0.1–0.9) | 0.5 (0.2–0.9) | 0.06 |
| Median hyperglycemic events per wk (IQR)** | 1.2 (0.4–2.6) | 2.7 (1.1–4.6) | <0.001 |
| Days with at least one blood glucose measurement <54 mg/dl — no./total person-days of follow-up (%) | 129/20,571 (0.63) | 72/10,285 (0.70) | |
| Days with at least one blood glucose measurement >350 mg/dl — no./total person-days of follow-up (%) | 243/20,571 (1.18) | 181/10,285 (1.76) | |
| Days with ≥1 ketone measurement >1.0 mmol/liter — no./total person-days of follow-up (%) | 14/20,571 (0.07) | 15/10,285 (0.15) | |

**Pump infusion set failure**

# Conclusions

**The use of Control-IQ improved glycemic control in patients with T1DM**

- The percentage of **TIR in in closed-loop group was 10 points higher** than in control group
- **HbA1c improved among patients who used closed-loop system** and remained unchanged among those in control
- Beneficial glycemic effects in the control group were seeing during both daytime and night time and were **particularly prominent in the second half of the night**
- **More AE were reported in the closed-loop group** than in the control group (**pump infusion set failure!**)
- **No severe hypoglycemic events** occured in either group

*Brown SA, Kovatchev BP, Raghinaru D, Lum JW, Buckingham BA, Kudva YC, Laffel LM, Levy CJ, Pinsker JE, Wadwa RP, Dassau E, Doyle FJ 3rd, Anderson SM, Church MM, Dadlani V, Ekhlaspour L, Forlenza GP, Isganaitis E, Lam DW, Kollman C, Beck RW; iDCL Trial Research Group. Six-Month Randomized, Multicenter Trial of Closed-Loop Control in Type 1 Diabetes. N Engl J Med. 2019 Oct 31;381(18):1707-1717. doi: 10.1056/NEJMoa1907863. Epub 2019 Oct 16. PMID: 31618560; PMCID: PMC7076915.*

Randomized Controlled Trial > Diabetes Technol Ther. 2019 Apr;21(4):159-169.
doi: 10.1089/dia.2019.0011. Epub 2019 Mar 19.

# Successful At-Home Use of the Control-IQ Artificial Pancreas System in Young Children During a Randomized Controlled Trial

Gregory P Forlenza [1], Laya Ekhlaspour [2], Marc Breton [3], David M Maahs [2], R Paul Wadwa [1],

> Diabetes Technol Ther. 2021 Sep;23(9):601-608. doi: 10.1089/dia.2021.0097. Epub 2021 Apr 21.

# One Year Real-World Use of the Control-IQ Advanced Hybrid Closed-Loop Technology

Marc D Breton [1], Boris P Kovatchev [1]

> Diabetes Technol Ther. 2021 Jun 21. doi: 10.1089/dia.2021.0165. Online ahead of print.

# Real-World Use of a New Hybrid Closed Loop Improves Glycemic Control in Youth with Type 1 Diabetes

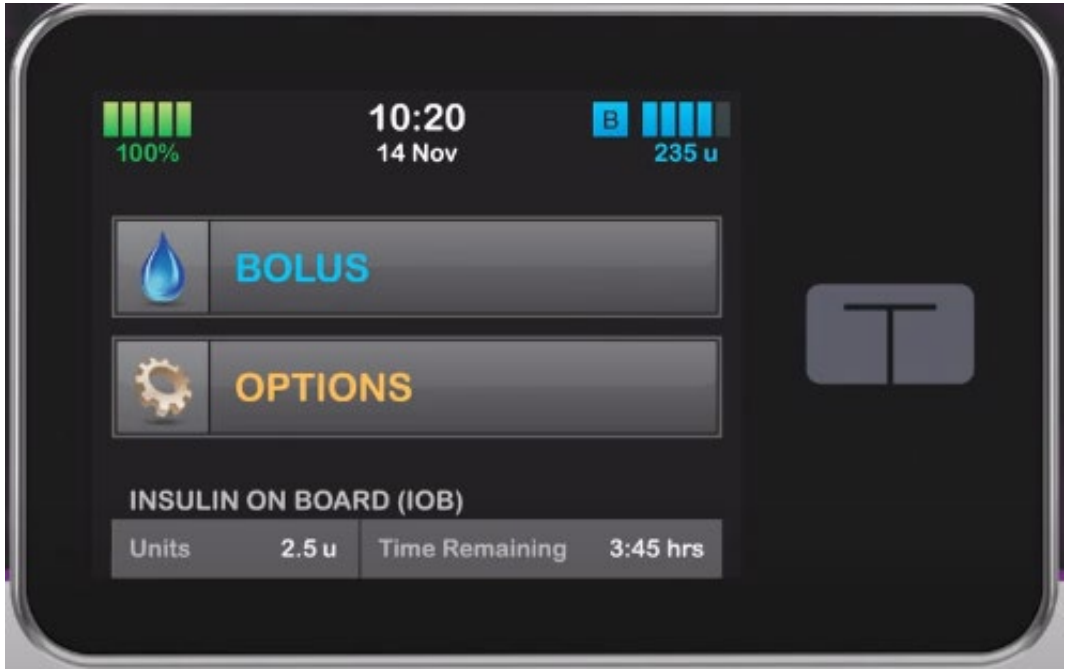
Laurel H Messer [1], Cari Berget [1], Laura Pyle [1], Timothy Vigers [1], Erin Cobry [1], Kimberly A Driscoll [2], Gregory P Forlenza [1]

# Control IQ

# Utilizzo base
# Boli pasto

## Aspetti pratici

https://www.youtube.com/watch?v=tqnjNOqxk4M




**EROGAZIONE BOLI**

https://www.youtube.com/watch?v=9Gu6h4OiR5E

# GRAZIE PER L'ATTENZIONE