# Automated Insulin Delivery in Type 1 Diabetes

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# Disclosures

- Mannkind: Advisory Board
- Medtronic: Speaker and Consultant
- I will be discussing a non FDA approved device

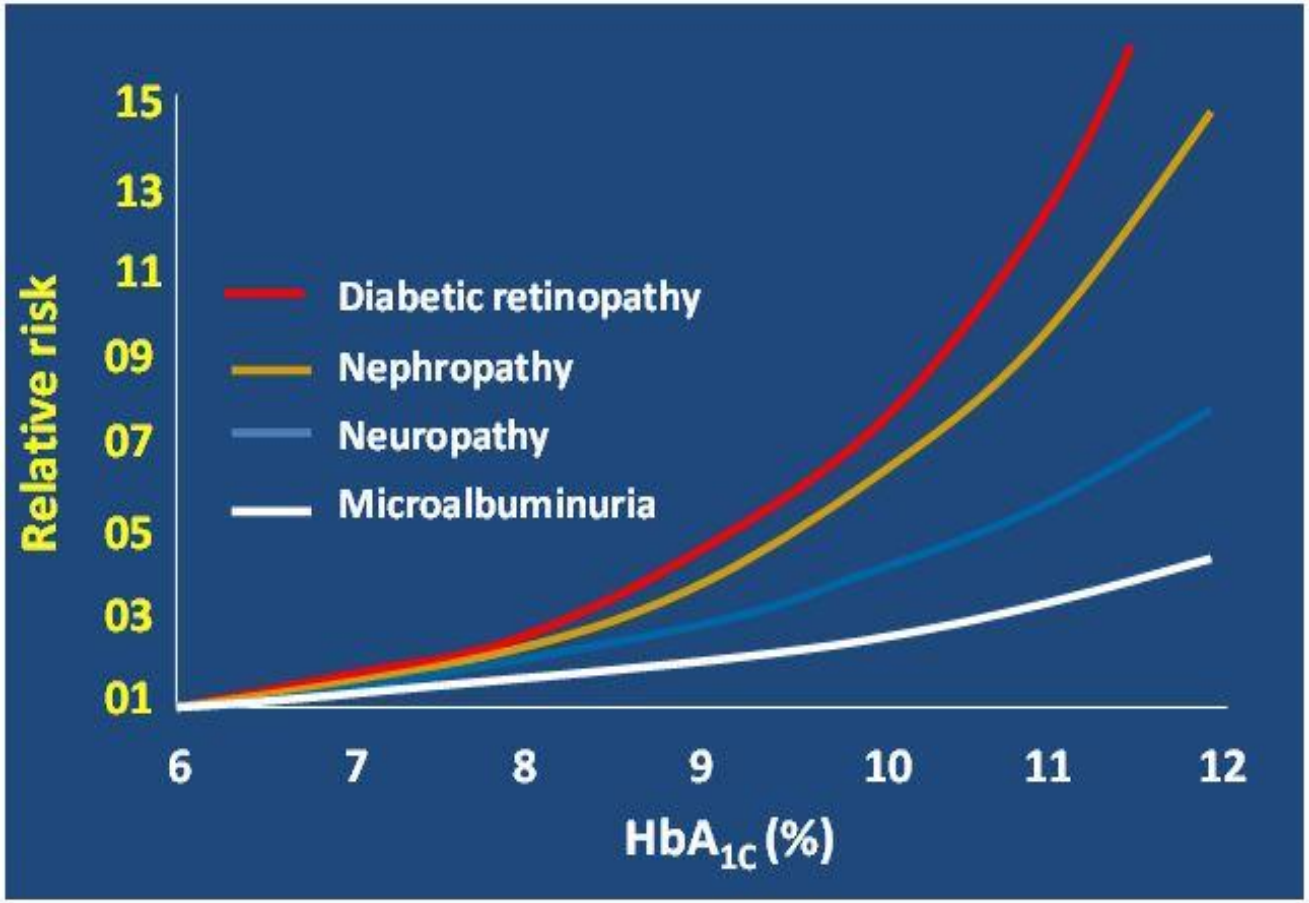
# Objectives

1)Explore the need for insulin automation

2)Discuss Time in Range and the results of Automated Insulin Delivery pivotal trials

3)Examine behavioral and clinical keys to success with Automated Insulin Delivery

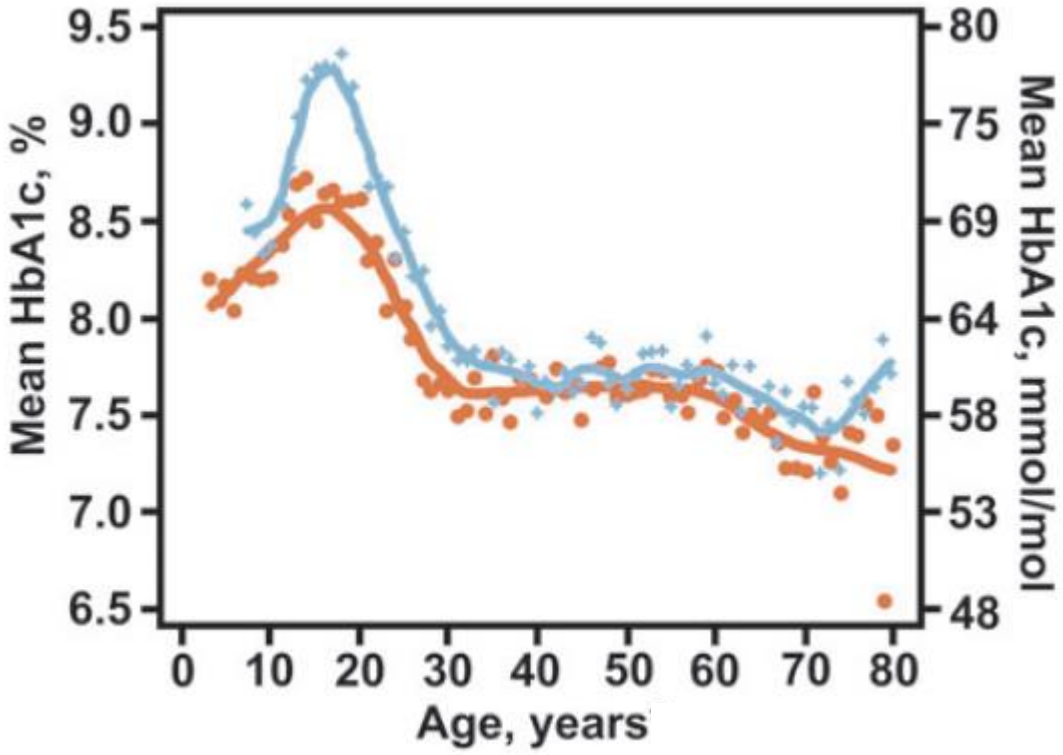
# WHAT ARE OUR GOALS IN TREATING DIABETES AND WHY?



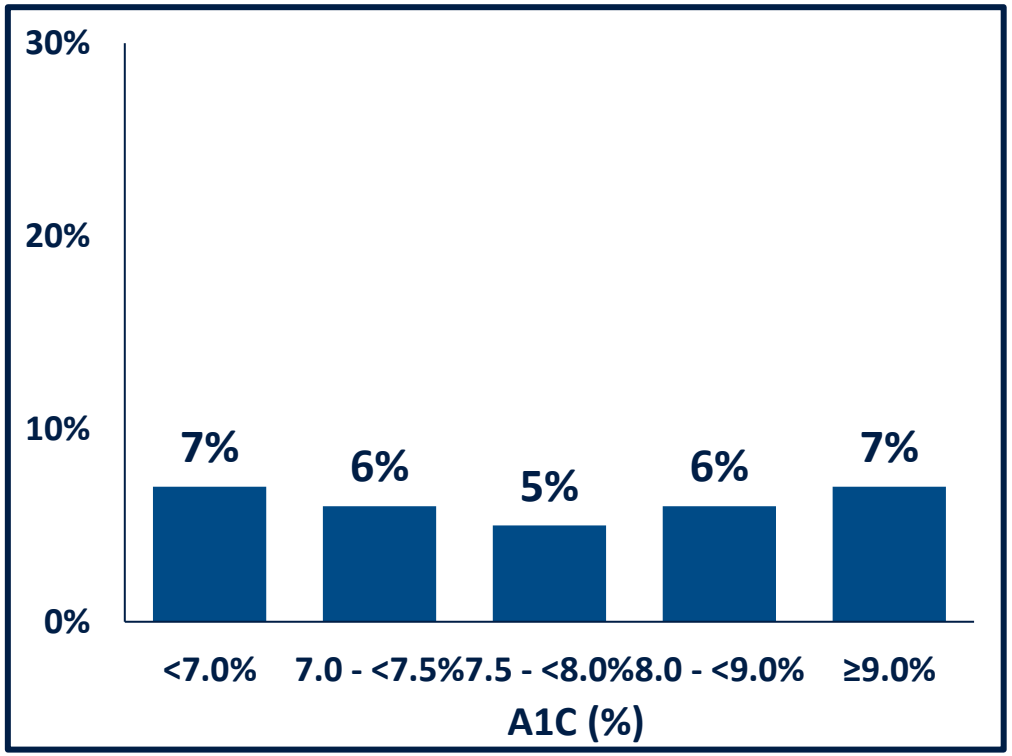
# WHAT IS THE CURRENT STATE OF GLYCEMIC CONTROL IN THE US?

## 67% OF TYPE 1 PATIENTS NOT AT TARGET DESPITE INTENSIVE MANAGEMENT[1]

### Average Current A1C by Age

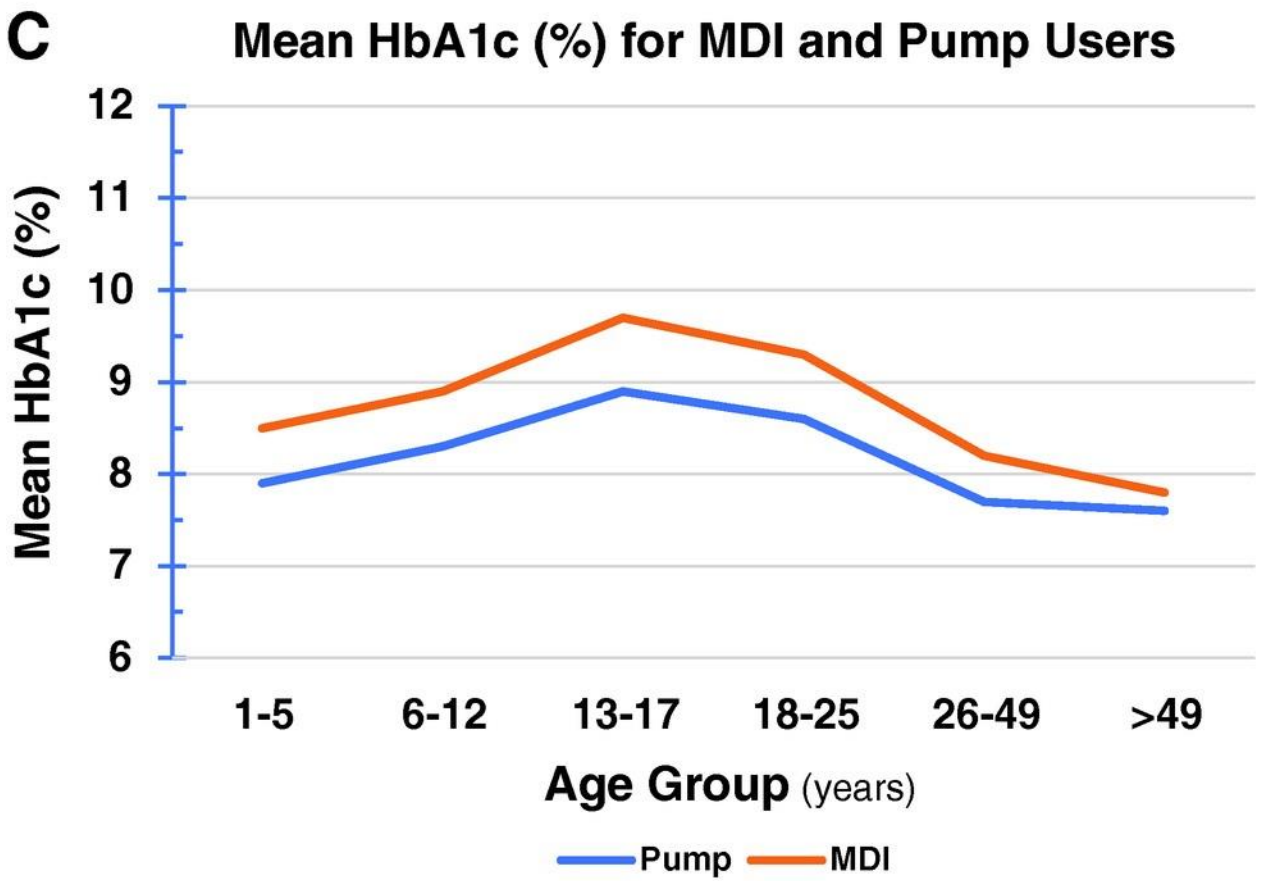



### 3-month Frequency of Severe Hypoglycemia by A1C




T1D Exchange data. Foster, NC, et al. *Diabetes Technol Ther.* 2019;21(2): 62-65.

# THE USE OF TECHNOLOGY IN THE T1D EXCHANGE




David Rodbard.Diabetes Technology & Therapeutics.Feb 2019.62-65.http

# THE USE OF TECHNOLOGY IN THE T1D EXCHANGE

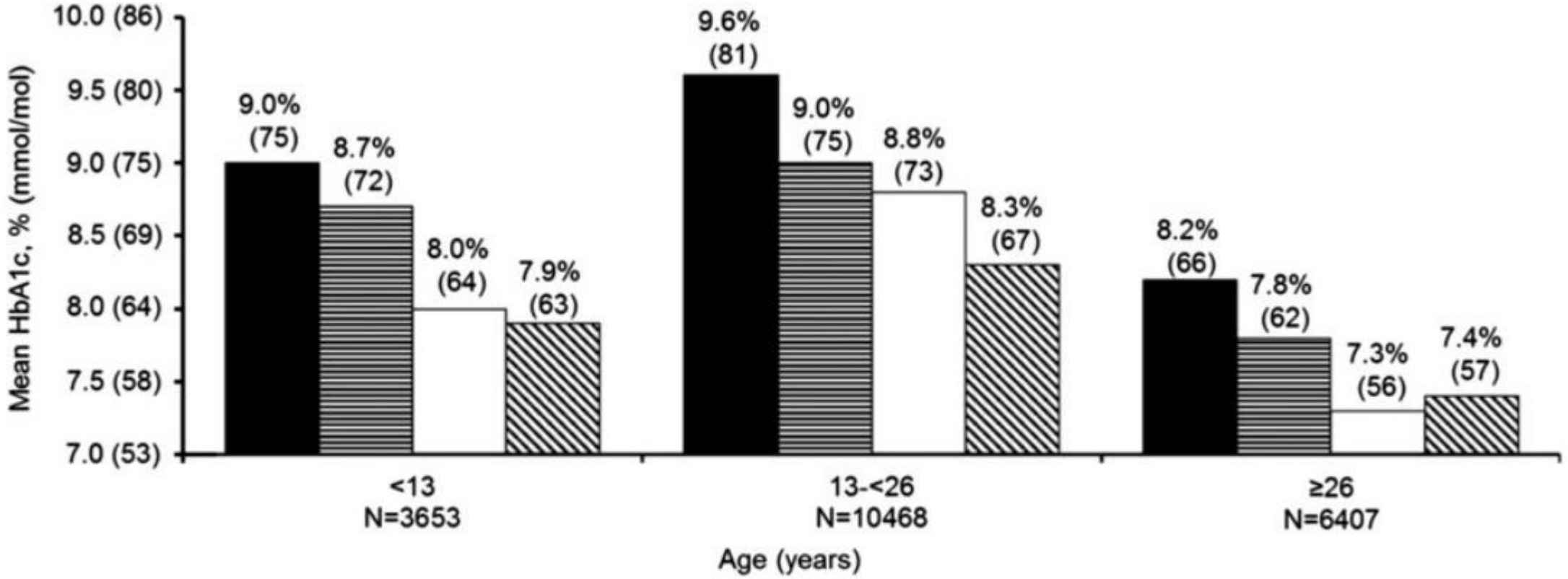
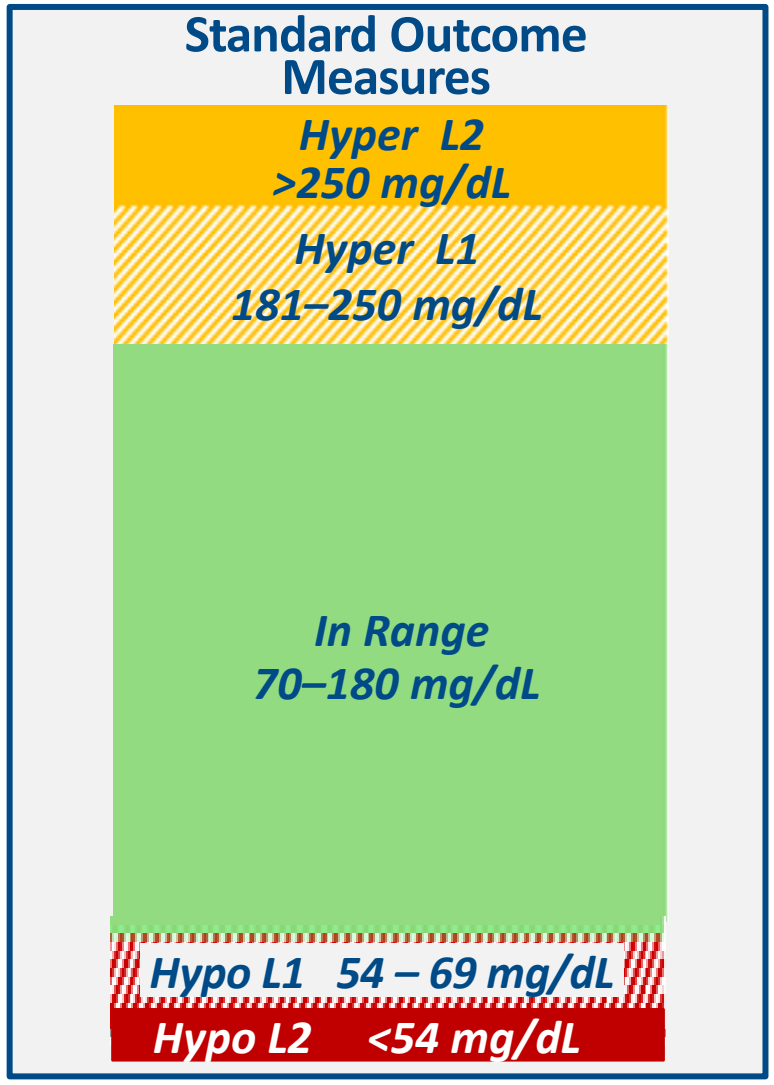



**FIG. 3.** Mean HbA1c by technology use in 2016–2018. Solid black represents injection only. Horizontal stripes represent pump only. Solid white represents injection+CGM. Diagonal stripes represent pump+CGM.

Foster NC, et al, Diabetes Technology & Therapeutics Vol 21 Published online 2019,
https://doi.org/10.1089/dia.2018.0384

# TIME IN RANGE
## CONSENSUS REPORT / DEFINES GLYCEMIC RANGES




***"Committee recommends use of defined clinically meaningful outcomes beyond A1C for research, development, and evaluation of type 1 diabetes therapies."***

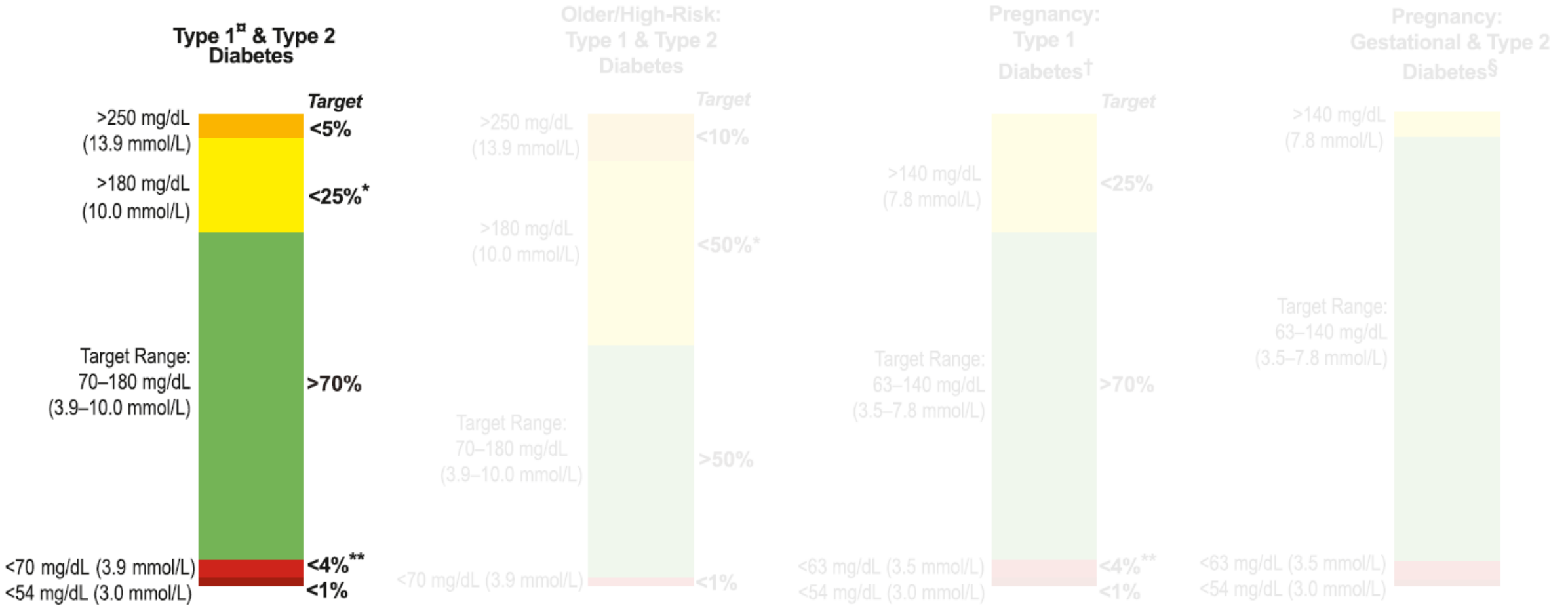
**Organizations:**

- **AACE:** American Association of Clinical Endocrinologists
- **AADE:** American Association of Diabetes Educators
- **ADA:** American Diabetes Association
- **Endocrine Society**
- **JDRF:** Juvenile Diabetes Research Foundation Int.
- **Leona M. and Harry B. Helmsley Charitable Trust**
- **PES:** Pediatric Endocrine Society
- **T1D Exchange**

***"Time in range may be more likely than A1C to correlate with patient-reported outcomes, such as quality of life…"***

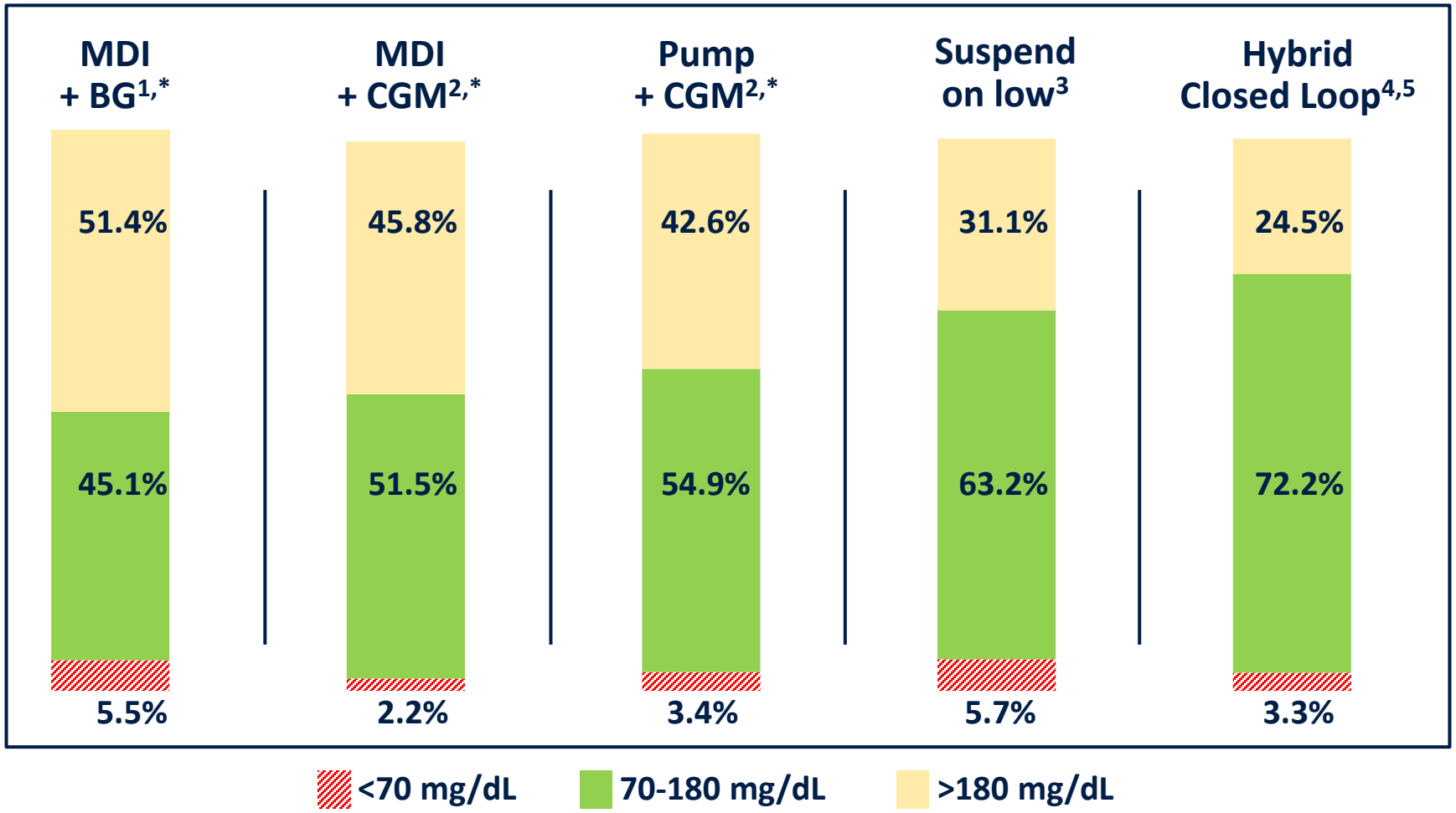
Agiostratidou G, et al. *Diabetes Care.* 2017;40:1622–1630.
Danne T, et al. *Diabetes*

# WHAT IS OUR GOAL?



# TIME IN RANGE BY THERAPY TYPE

## TIME SPENT >180 MG/DL, 70-180 MG/DL & <70 MG/DL




For every **10% drop** in TIR, risk of complications **increases**[6]:

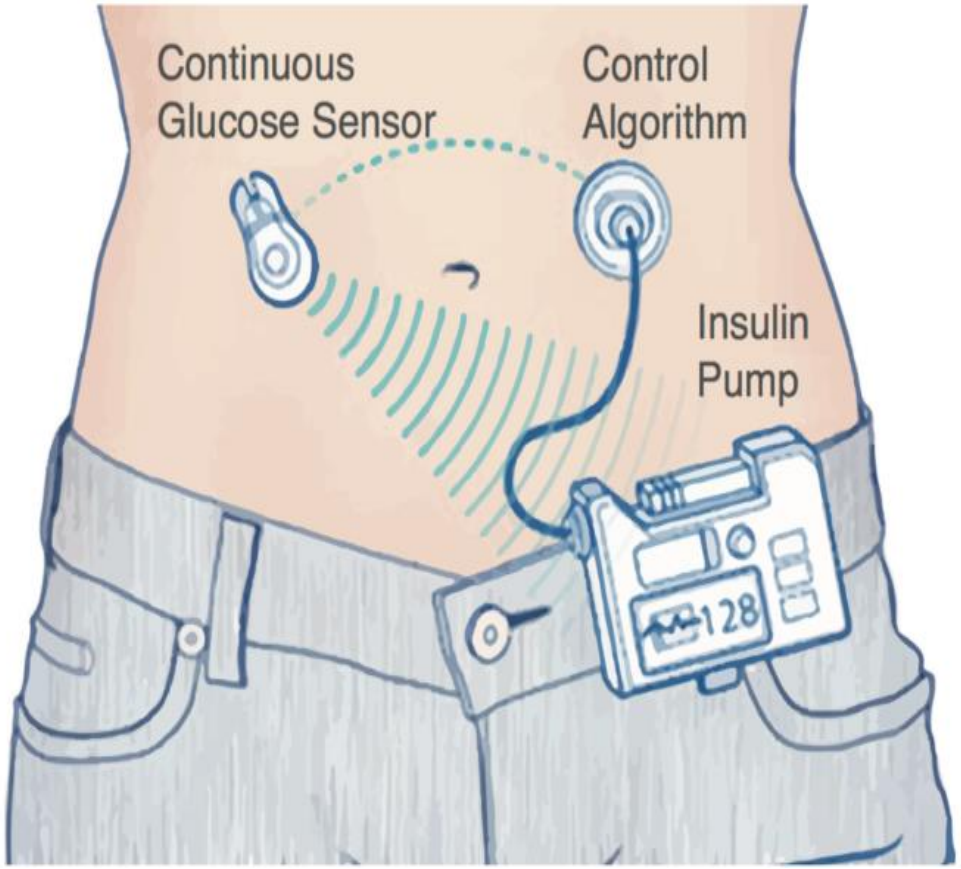
- Retinopathy by 64%
- Microalbuminuria by 40%

*Median time in range, may not equal 100%.

1. Beck R. *JAMA*. 2017;317( 4): 371-378. 2. Beck R, et al. *Lancet Diabetes Endocrinol.* 2017; 5:700-708. 3. Data on file.
4. Bergenstal RM, et al. *JAMA*. 2016;316(13):1407-1408. 5. Garg SK, et al. *Diabetes Technol Ther*. 2017;19(3):155-163. 6. Beck R, et.al. *Diabetes Care*. 2018. epub ahead of print online 10/23/2018

# THE NEED FOR IMPROVED GLYCEMIC CONTROL & INSULIN AUTOMATION

# Automated Insulin Delivery



# FUNDAMENTAL PREMISE OF AUTOMATED INSULIN DELIVERY

| | RESULT |
|---|---|
| **Normal Physiology**<br>Pancreas secretes insulin based on glucose. Varies day and night. | Euglycemia. |
| **MDI and Pump:**<br>Fixed basal insulin (injection, rate(s)). | Static insulin delivery and variable glycemia. |
| **Hybrid Closed Loop**<br>Auto Basal delivers every 5 minutes; adjusts based on sensor glucose. | Less glycemic variability and more time in target range.[1,2] |

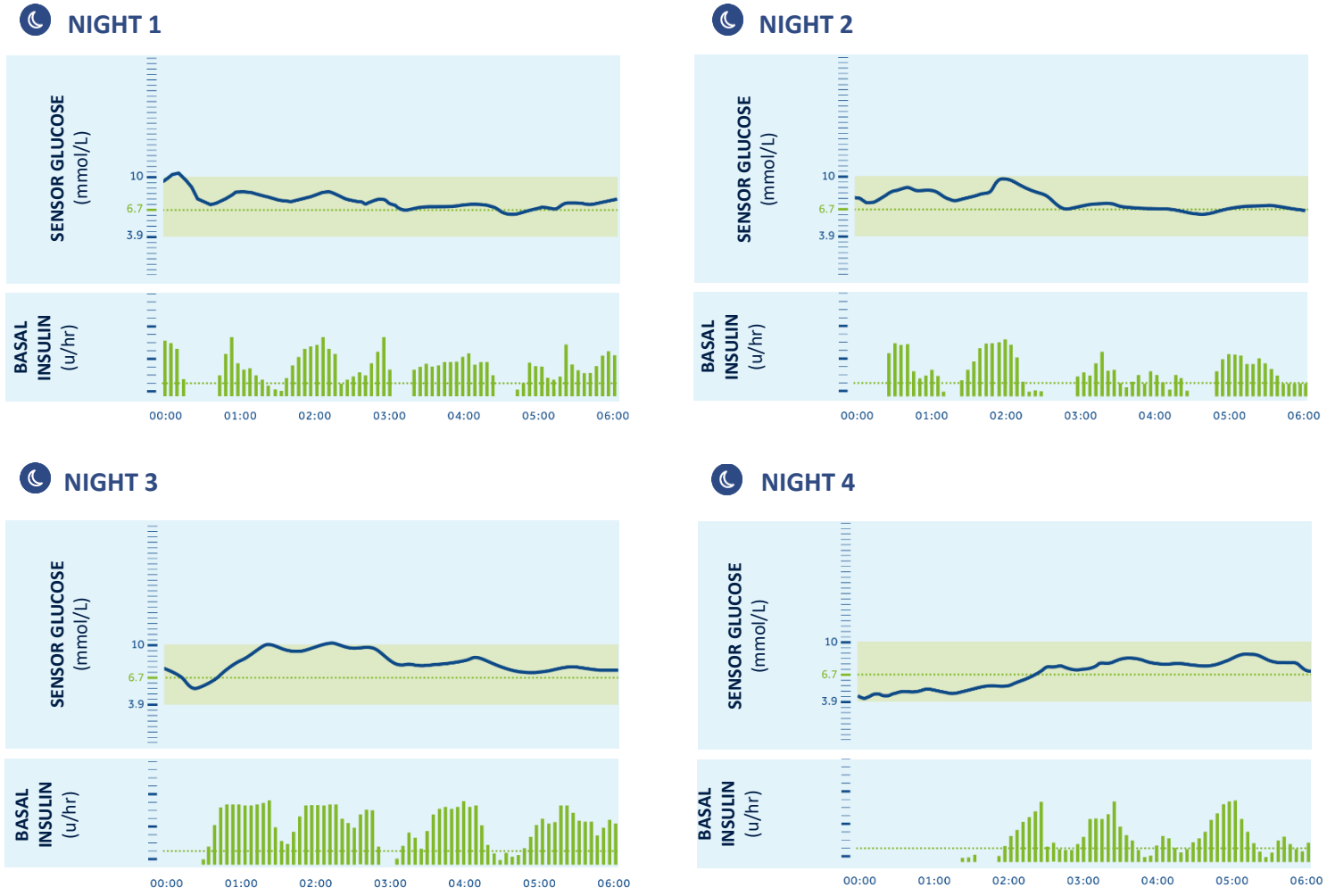
1. Bergenstal RM, et al. *JAMA*. 2016;316(13):1407-1408.
2. Garg SK, et al. *Diabetes Technol Ther*. 2017;19(3):155-163

# INSULIN DELIVERY GUIDED BY CGM: ESSENTIAL FOR CLOSING THE LOOP

## GLUCOSE LEVEL & INSULIN REQUIREMENT FOUR NIGHTS IN A SINGLE WEEK(12-6AM)

### Key Observations

- 120mg/dL glucose target achieved each morning despite varying 12am glucose
- Insulin requirements were not the same on any 2 nights
- Auto Basal adjusted based on glucose
- No overnight lows



# MINMED 670G PIVOTAL TRIAL

## TIME IN RANGE: LOWS & HIGHS, 14-75 YEARS

## Auto Mode Use: Adults 88.0%, Adolescents 75.8%

### Day and Night (p<0.001)

| Sensor Glucose | Run-in % Time in Range | Study % Time in Range |
|---|---|---|
| > 300 mg/dL | 2.3 | 1.7 |
| > 180 mg/dL | 27.4 | 24.5 |
| 71 – 180 mg/dL | 66.7 | 72.2 |
| ≤ 70 mg/dL | 5.9 | 3.3 |
| ≤ 50 mg/dL | 1.0 | 0.6 |
| Within-day SD | 2.8 | 2.6 |

### Night Time Only*

| Sensor Glucose | Run-in % Time in Range | Study % Time in Range |
|---|---|---|
| > 300 mg/dL* | 2.1 | 1.4 |
| > 180 mg/dL | 26.8 | 21.6 |
| 71 – 180 mg/dL | 66.8 | 75.3 |
| ≤ 70 mg/dL | 6.4 | 3.1 |
| ≤ 50 mg/dL* | 1.1 | 0.6 |
| | | |

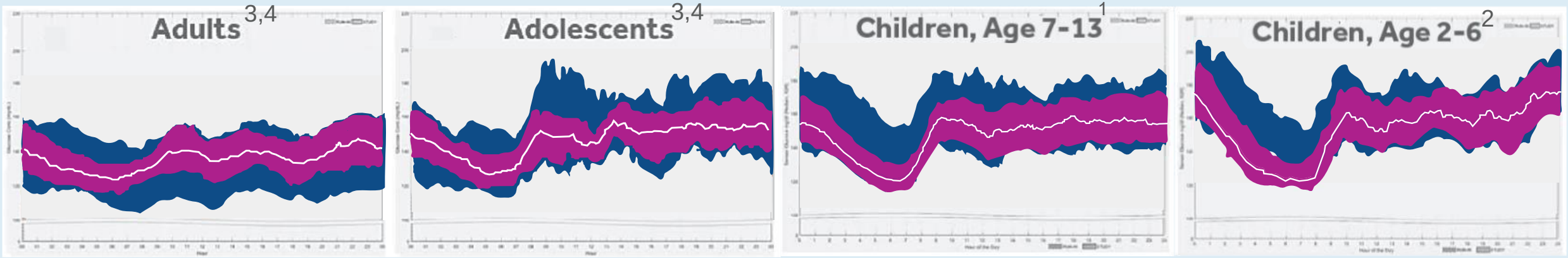
Due to inherent study limitations, caution is advised when attempting to extrapolate these results to new patients. There could be significant differences.

Bergenstal RM, et al. *JAMA*. 2016;316(13):1407-1408.
Garg SK, et al. *Diabetes Technol Ther*. 2017;19(3

# PIVOTAL HCL TRIAL

## Median and Interquartile SG Values, Day & Night

**Run-In Phase** **Study Phase**




**In over 28,000 patient days of exposure:**

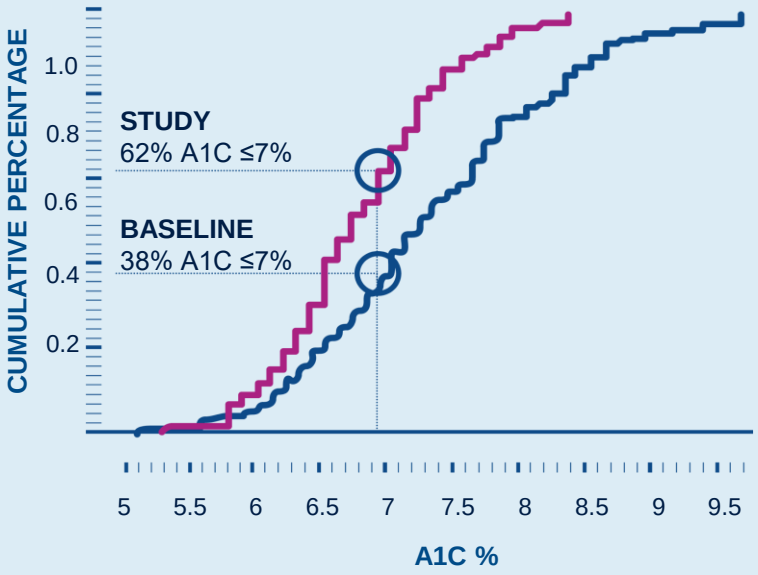
- **ZERO** Severe Hypoglycemia
- **ZERO** DKA

Since the pivotal study did not include a control group, no effectiveness claims can be made. The study does support that the system is relatively safe. However, the study had limitations, including a relatively small number of patients, no comparative control group, and a study period that lasted only three months. In addition, the amount of time the system was used in the Manual Mode was shorter than the time in Auto Mode. Due to these study limitations, caution is advised when attempting to extrapolate these results to individual patient results. There could be significant differences.

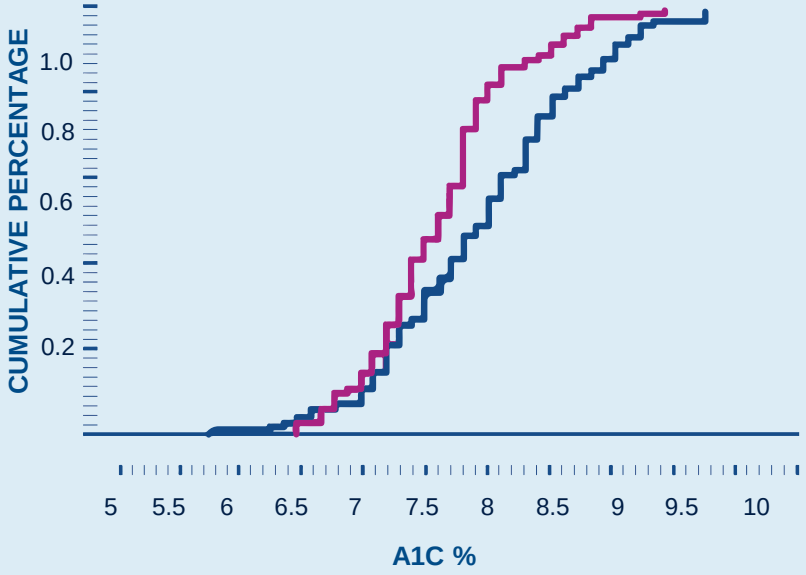
[1]Forlenza GP, et al. *Diabetes Technol Ther.* 2019; https://doi.org/10.1089/dia.2018.0264. [2]Data on file from CEP302: Pivotal Trial (Age 2-6). N=46. 2019; 10 US sites and 1 EMEA site. [3]Bergenstal RM, et al. *JAMA*. 2016;316(13):1407-1408. [4]Garg SK, et al. *Diabetes Technol Ther*. 2017;19(3):155-163.

# MINIMED™ 770G SYSTEM PIVOTAL STUDIES
## A1C DISTRIBUTION

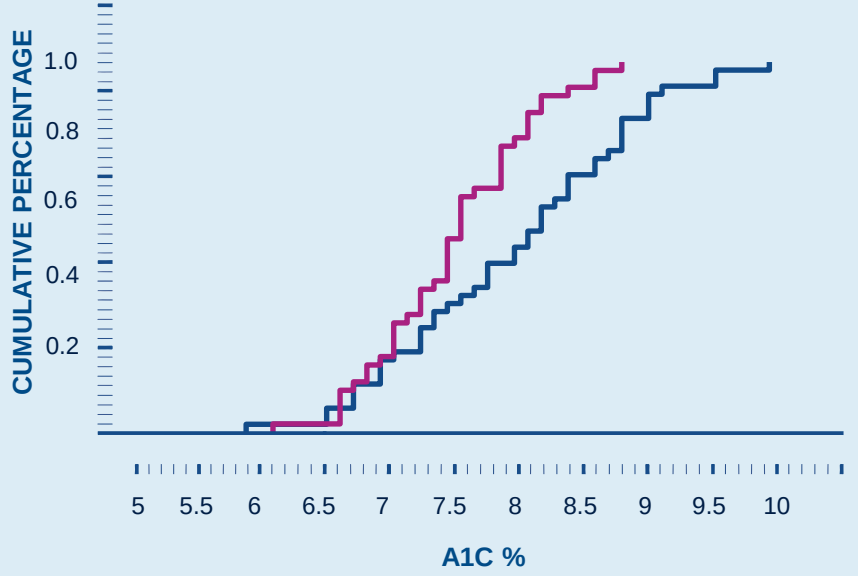
### Adults + Adolescents[1,2]
(14-75 yrs)




### Pediatrics[3]
(7-13 yrs)




### Pediatrics[4]
(2-6 yrs)




Since the pivotal study did not include a control group, no effectiveness claims can be made. The study does support that the system is relatively safe. However, the study had limitations, including a relatively small number of patients, no comparative control group, and a study period that lasted only three months. In addition, the amount of time the system was used in the Manual Mode was shorter than the time in Auto Mode. Due to these study limitations, caution is advised when attempting to extrapolate these results to individual patient results. There could be significant differences.

| BASELINE A1C | STUDY END A1C | BASELINE A1C | STUDY END A1C | BASELINE A1C | STUDY END A1C |
|---|---|---|---|---|---|
| 7.4% | 6.9% | 7.9% | 7.5% | 8.0% | 7.5% |

[1]Bergenstal RM, et al. *JAMA*. 2016;316(13):1407-1408. [2]Garg SK, et al. *Diabetes Technol Ther*. 2017;19(3):155-163. [3]Forlenza GP, et al. *Diabetes Technol Ther*. 2019; https://doi.org/10.1089/dia.2018.0264. [4]Data on file from CEP302: Pivotal Trial (Age 2-6). N=46. 2019; 10 US sites and 1 EMEA site.

# Six-Month Randomized, Multicenter Trial of Closed-Loop Control in Type 1 Diabetes

•Sue A. Brown, M.D.,Boris P. Kovatchev, Ph.D., Dan Raghinaru, M.S., John W. Lum, M.S., Bruce A. Buckingham, M.D., Yogish C. Kudva, M.D., Lori M. Laffel, M.D., M.P.H., Carol J. Levy, M.D. Jordan E. Pinsker, M.D., R. Paul Wadwa, M.D., Eyal Dassau, Ph.D., Francis J. Doyle, III, Ph.D., for the iDCL Trial Research Group* October 31, 2019 N Engl J Med 2019; 381:1707-1717

**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 |
| 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 |

**71 % TIR**

* Plus–minus values are means ±SD. To convert the values for glucose to millimoles per liter, multiply by 0.05551.

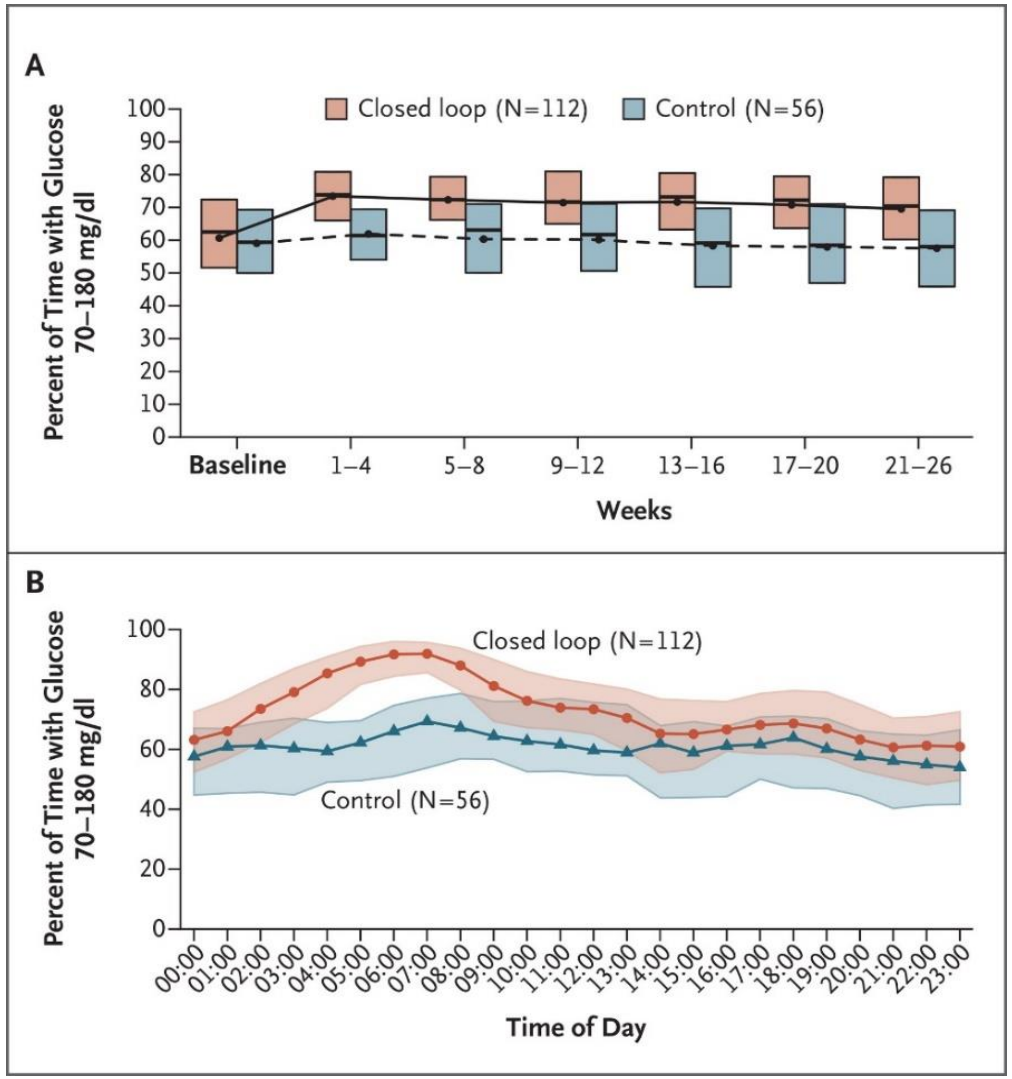
† Data are means or medians over the 26 weeks of the trial period with the exception of the glycated hemoglobin level, for which data are the mean at the 26-week follow-up visit.

‡ The differences were adjusted for the baseline value of the dependent variable plus age, previous use of a continuous glucose monitor, previous use of an insulin pump, and clinical center (random effects). To control the type I error, a hierarchical approach was used in which hypothesis testing was performed sequentially in the order listed in the table. If the result for an outcome metric had not reached significance (i.e., P>0.05), statistical testing would not have been conducted for the subsequent outcomes in the hierarchy. In this trial, the results for all six outcomes were significant, and therefore testing was not stopped. Differences in outcomes that were measured as percentages are given in percentage points.

§ These results were additionally adjusted for the 13-week values and the same-visit local values. One participant in the control group and one participant in the closed-loop group completed the 26-week visit outside the prespecified window, and these 26-week values were excluded from the analyses.

¶ The percentage of time that the glucose level was below 70 mg per deciliter (3.9 mmol per liter) had a skewed distribution; however, the residuals from the regression model were approximately normally distributed. The medians at baseline were 2.69% (IQR, 1.02 to 5.42) in the closed-loop group and 2.10% (IQR, 1.04 to 4.02) in the control group, and the medians after randomization were 1.40% (IQR, 0.67 to 2.29) in the closed-loop group and 1.93% (IQR, 1.15 to 3.06) in the control group.

‖ The percentage of time that the glucose level was below 54 mg per deciliter (3.0 mmol per liter) had a skewed distribution; however, the residuals from the regression model were approximately normally distributed. The medians at baseline were 0.32% (IQR, 0.05 to 1.23) in the closed-loop group and 0.31% (IQR, 0.07 to 0.54) in the control group, and the medians after randomization were 0.21% (IQR, 0.07 to 0.42) in the closed-loop group and 0.24% (IQR, 0.11 to 0.49) in the control group.



# A Randomized Trial of Closed-Loop Control in Children with Type 1 Diabetes

L

•Marc D. Breton, Ph.D., Lauren G. Kanapka, M.Sc., Roy W. Beck, M.D., Ph.D., Laya Ekhlaspour, M.D., Gregory P. Forlenza, M.D., Eda Cengiz, M.D., Melissa Schoelwer, M.D., Katrina J. Ruedy, M.S.P.H., Emily Jost, M.P.H., R.D., C.D.E., Lori Carria, M.S.,Emma Emory, R.N., Liana J. Hsu, B.S., for the iDCL Trial Research Group* August 27, 2020 N Engl J Med 2020; 383:836-845

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

| Outcome | Baseline† | | 16-Wk Trial Period‡ | | | |
|---|---|---|---|---|---|---|
| | Closed Loop (N=77) | Control (N=23) | Closed Loop (N=78) | Control (N=22) | Risk-Adjusted Difference (95% CI)§ | P Value |
| Hours of sensor data | 306±33 | 311±23 | 2637±134 | 2609±128 | | |
| Primary outcome: glucose level in range of 70 to 180 mg/dl — % of time | 53±17 | 51±16 | 67±10 | 55±13 | 11 (7 to 14) | <0.001 |
| Secondary hierarchical outcomes in prespecified order¶ | | | | | | |
| Glucose level >180 mg/dl — % of time | 45±18 | 47±17 | 31±10 | 43±14 | −10 (−14 to −6) | <0.001 |
| Glucose level — mg/dl | 183±34 | 189±34 | 162±18 | 179±26 | −13 (−20 to −7) | <0.001 |
| Glycated hemoglobin level — %‖ | 7.6±1.0 | 7.9±0.9 | 7.0±0.8 | 7.6±0.9 | −0.4 (−0.9 to 0.1) | 0.08 |
| Glucose level <70 mg/dl — median % of time (IQR)** | 1.2 (0.5 to 2.4) | 1.0 (0.2 to 2.1) | 1.6 (0.8 to 2.4) | 1.8 (1.1 to 3.0) | −0.40 (−0.83 to −0.02) | NA |
| Glucose level <54 mg/dl — median % of time (IQR)** | 0.1 (0.0 to 0.4) | 0.1 (0.0 to 0.3) | 0.2 (0.1 to 0.4) | 0.3 (0.1 to 0.6) | −0.07 (−0.19 to 0.02) | NA |
| Glucose level >250 mg/dl — median % of time (IQR)** | 17.2 (8.6 to 27.6) | 20.7 (12.4 to 32.6) | 7.8 (5.1 to 14.3) | 18.4 (9.4 to 24.6) | −5.8 (−8.7 to −3.0) | NA |
| Coefficient of variation in the sensor glucose measurement — % | 38±5 | 38±4 | 38±4 | 39±4 | −1.6 (−2.8 to −0.4) | NA |

**67% TIR**

* Plus–minus values are means ±SD. One patient in the closed-loop group was missing baseline continuous glucose-monitoring data, and 1 patient in the control group was missing follow-up data. All the patients were included in the model on an intention-to-treat basis. Missing data were handled by means of direct likelihood analyses. In the control group, 15 of 23 patients used the t:slim X2 pump with a predictive low-glucose suspend feature (Tandem Diabetes Care), 3 used an OmniPod pump (Insulet), and 5 used a Medtronic pump. To convert the values for glucose to millimoles per liter, multiply by 0.05551. IQR denotes interquartile range, and NA not applicable.

† Baseline outcomes measured by the continuous glucose monitor were calculated with the data obtained in the 14 days before randomization. These data were obtained with the use of a personal Dexcom continuous glucose monitor for the 50 patients in the closed-loop group and the 17 patients in the control group who were allowed to skip the run-in phase. The baseline glycated hemoglobin level was measured at the randomization visit.

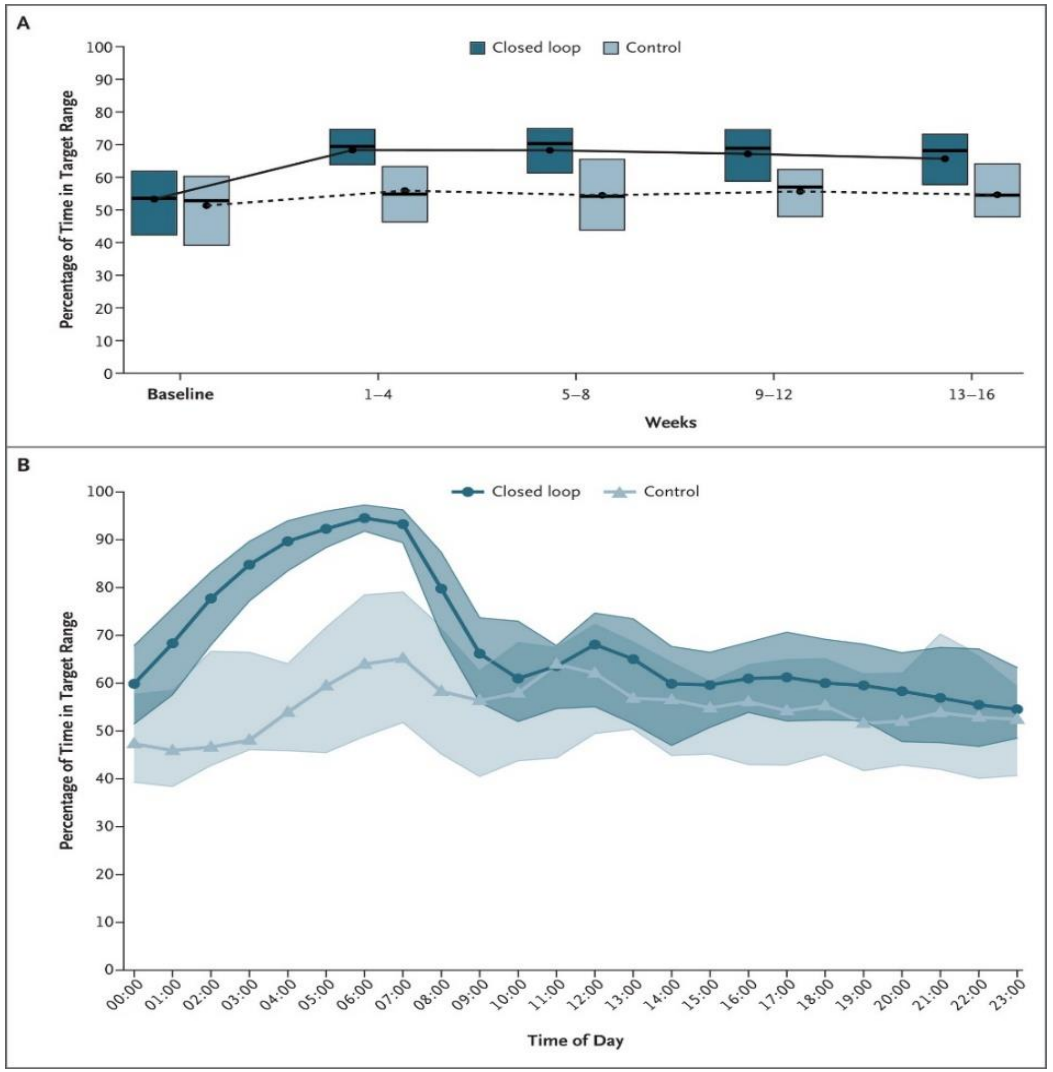
‡ Data are means or medians over the 16-week trial period with the exception of glycated hemoglobin level, for which data are the mean at the 16-week trial visit.

§ Differences were calculated as percentage points (the value in the closed-loop group minus the value in the control group) and were model-adjusted for the baseline value of the metric, age, previous continuous glucose monitor and pump use, and clinical center (random effect).

¶ To control the type 1 error, a hierarchical approach was used in which hypothesis testing was performed sequentially in the order listed in the table. When a P value of 0.05 or higher was observed, the outcomes below that finding on the list were not formally tested.

‖ Data on glycated hemoglobin level at baseline were available for 78 patients in the closed-loop group and 23 patients in the control group, and data on glycated hemoglobin level at the 16-week trial visit were available for 77 patients and 22 patients, respectively.

** Distributions were skewed for the percentages of time with the glucose level below 70 mg per deciliter, below 54 mg per deciliter, and above 250 mg per deciliter and were thus modeled with the use of rank-based transformation.



# Minimed 670G and 770G

- Minimed 670/770G automate basal insulin delivery every 5 minutes
- HCL Target = 120mg/dL
- System corrects to 150mg/dL
- HCL requires 8 unit minimum dose
- PLGS or suspend before low included

**Clinician settings for HCL:**

- I:C ratios (strengthen)
- Active insulin time (3 hours)

- Temporary target: 150 mg/dL helpful for exercise

# Control IQ

- Control-IQ automates basal insulin by modulating programmed basal rates
- Automated correction dose (max 1/hour)- delivers 60% of calculated dose,
- HCL target range = 112.5-160 mg/dl
- 10 unit and 55 pound minimum

**Clinician settings for HCL:**

- I:C ratios
- ISF
- Basal rates


- Active insulin **set** at 5 hours (not modifiable)

**Exercise/sleep modes:**

- Exercise mode (target range 140-160 mg/dl)
- Sleep mode (target range 112.5-120 mg/dl)

# Minimed 780G

- Not FDA approved
- Received CE mark June, 2020
- Minimed 780G automates basal insulin delivery every 5 minutes
- HCL Target = 100mg/dL or 120mg/dL
- Automated correction dose every 5 minutes
- System corrects to 120mg/dL

# CLINICAL PEARLS

## BOLUSING TIMING

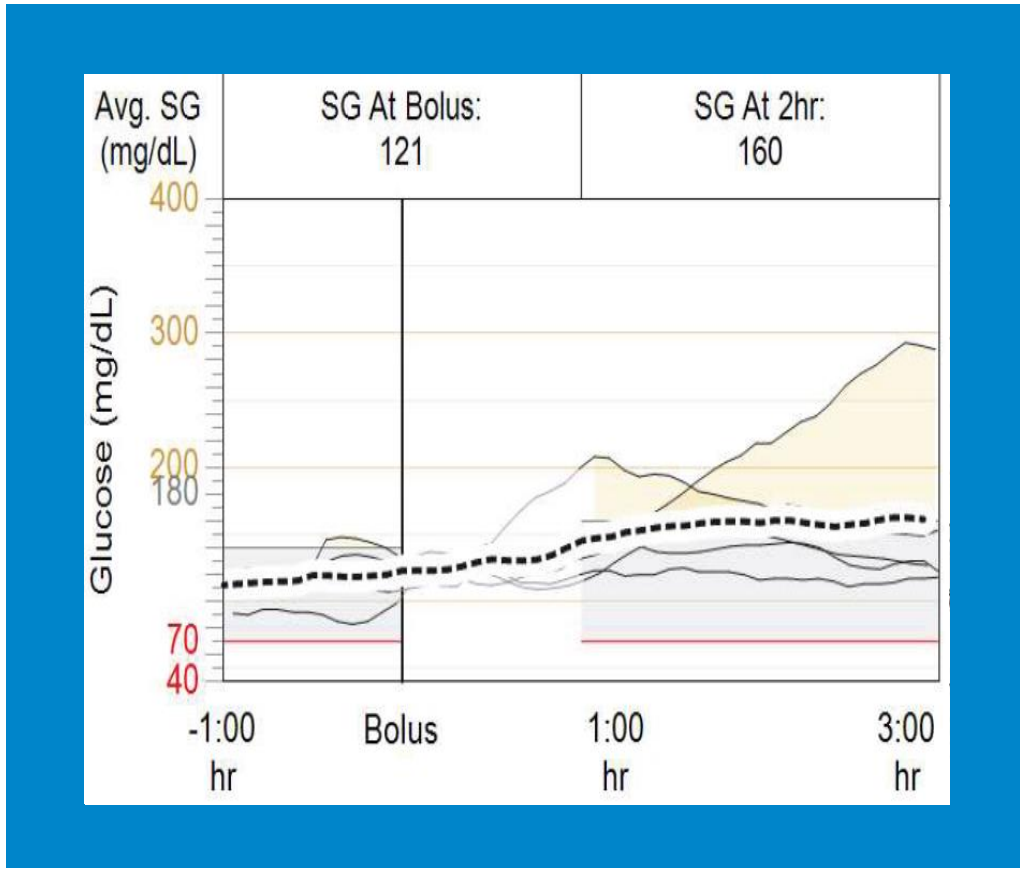
### LATE BOLUS: POST-MEAL HIGHS FOLLOWED BY SHARP DECLINE IN GLUCOSE

- When boluses are delivered after meals, glucose from food enters the bloodstream before insulin.  This causes glucose to rise rapidly and Auto Basal to increase substantially. The increase in Auto Basal, coupled with the meal bolus, can result in too much insulin and post-meal lows.

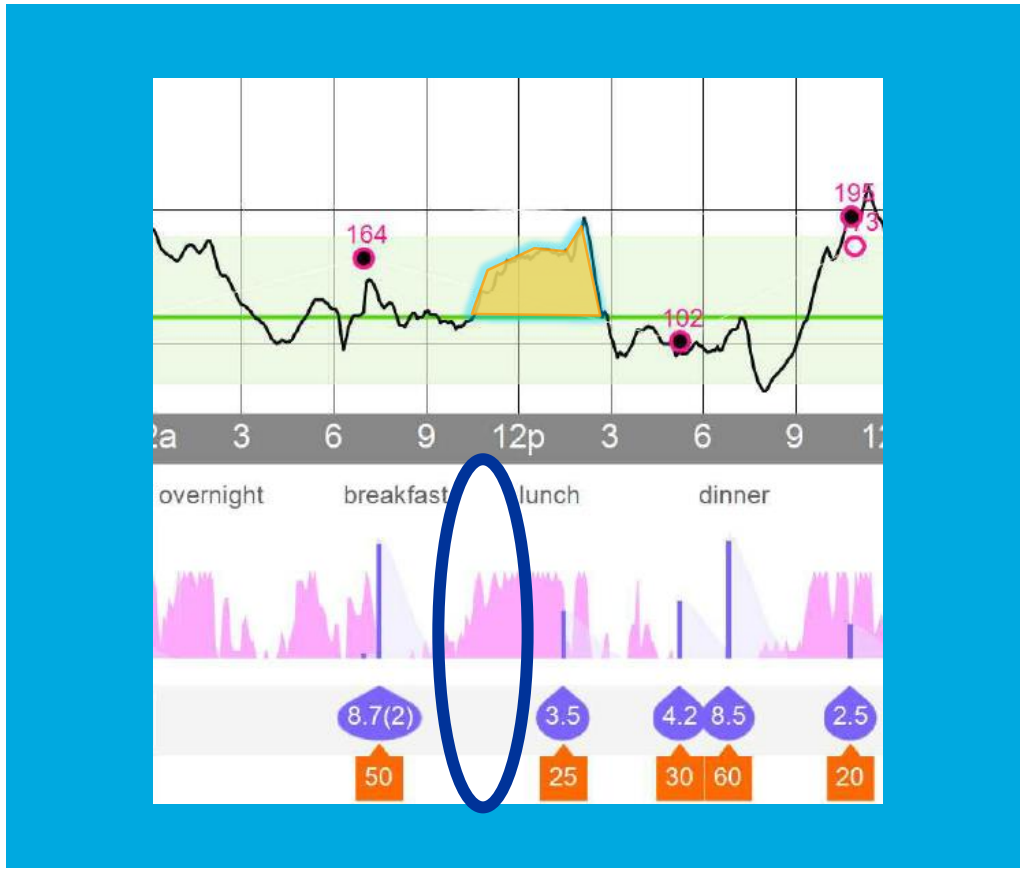
- Encourage patients to bolus before eating to help mitigate this post-meal issue.

# BEHAVIORS
## ENCOURAGE THE RIGHT BEHAVIORS

Bolus 5-15 minutes before eating

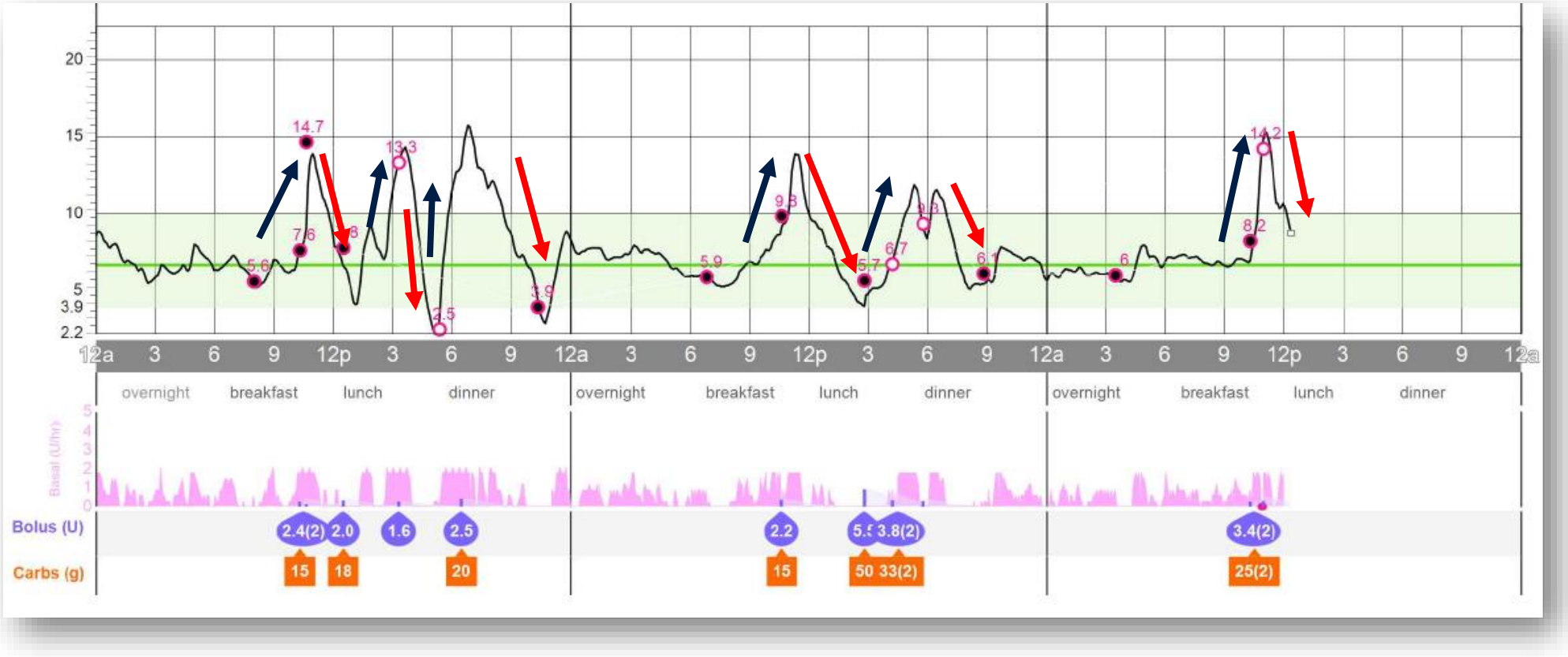



Missed bolus



# BOLUSING AFTER EATING

## ISSUE: POST-MEAL HIGHS FOLLOWED BY SHARP DECLINE IN GLUCOSE




**Eats before bolusing**

- Result:  1) Sharp rise in SG,  2) Auto Basal increase, 3) SG may go low to near-low (“yo-yo”)

# TREATING HYPOGLYCEMIA WITH AUTOMATED INSULIN DELIVERY

- Fewer carbs may be needed to treat mild lows (i.e. 5 to 10 g)
- Starburst or glucose tabs = 4 grams each


- Total Carbohydrate = 24g

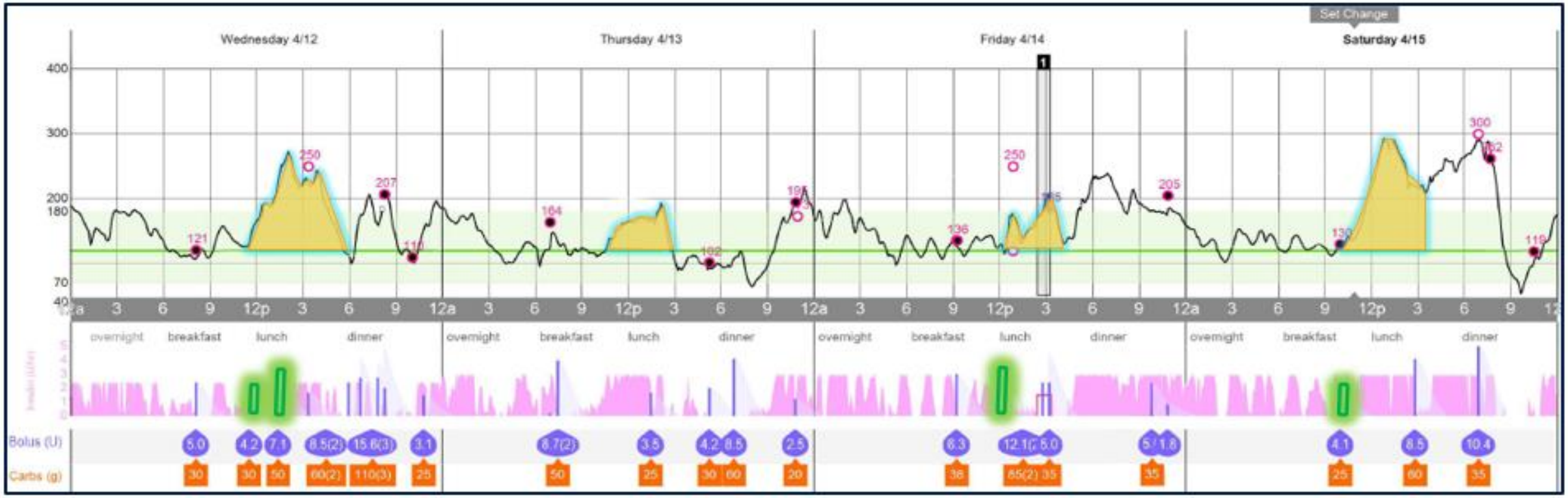
# EXERCISE TIPS

- Exercise with little or no active insulin
- Use temporary target or exercise mode:
  - Start 1-2 hours before and continue 1-2 hours after
  - May need to run overnight (12 hours)
- Have carbs available during activity
- Replenish carbs for long periods of activity
- Suspend if having lows during spontaneous activity

If eating carbs without insulin before activity:

- Ensure food is eaten within 20-30 min prior to exercise
- If glucose rises excessively, Auto Basal will begin to increase

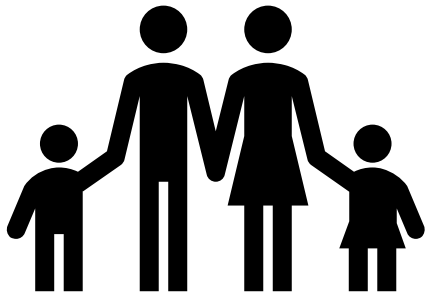
# OPTIMIZE CARB RATIOS



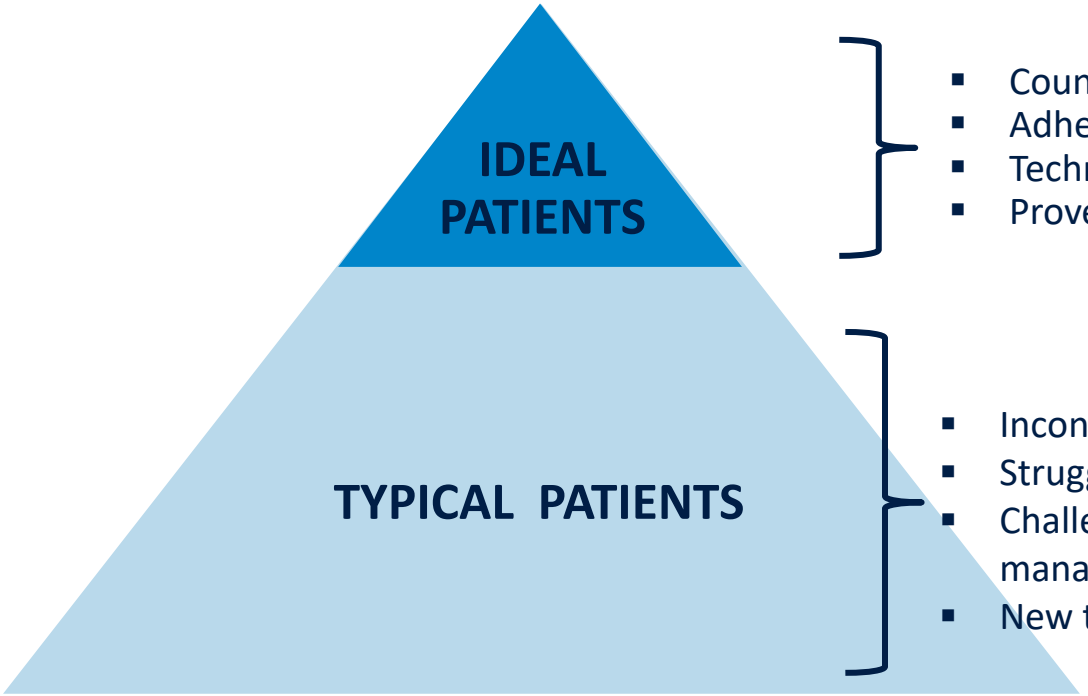

If lows / highs occurring post-meal, adjust carb ratio by 10-20%

# PATIENT SELECTION
## CLINICAL INDICATIONS

The same clinical indications for pump technology apply to Automated Insulin Delivery Systems.



# “IDEAL” VERSUS “TYPICAL” PATIENTS




- Count carbs well
- Adherent to diabetes management tasks
- Technically capable
- Prove they are ready to HCPs

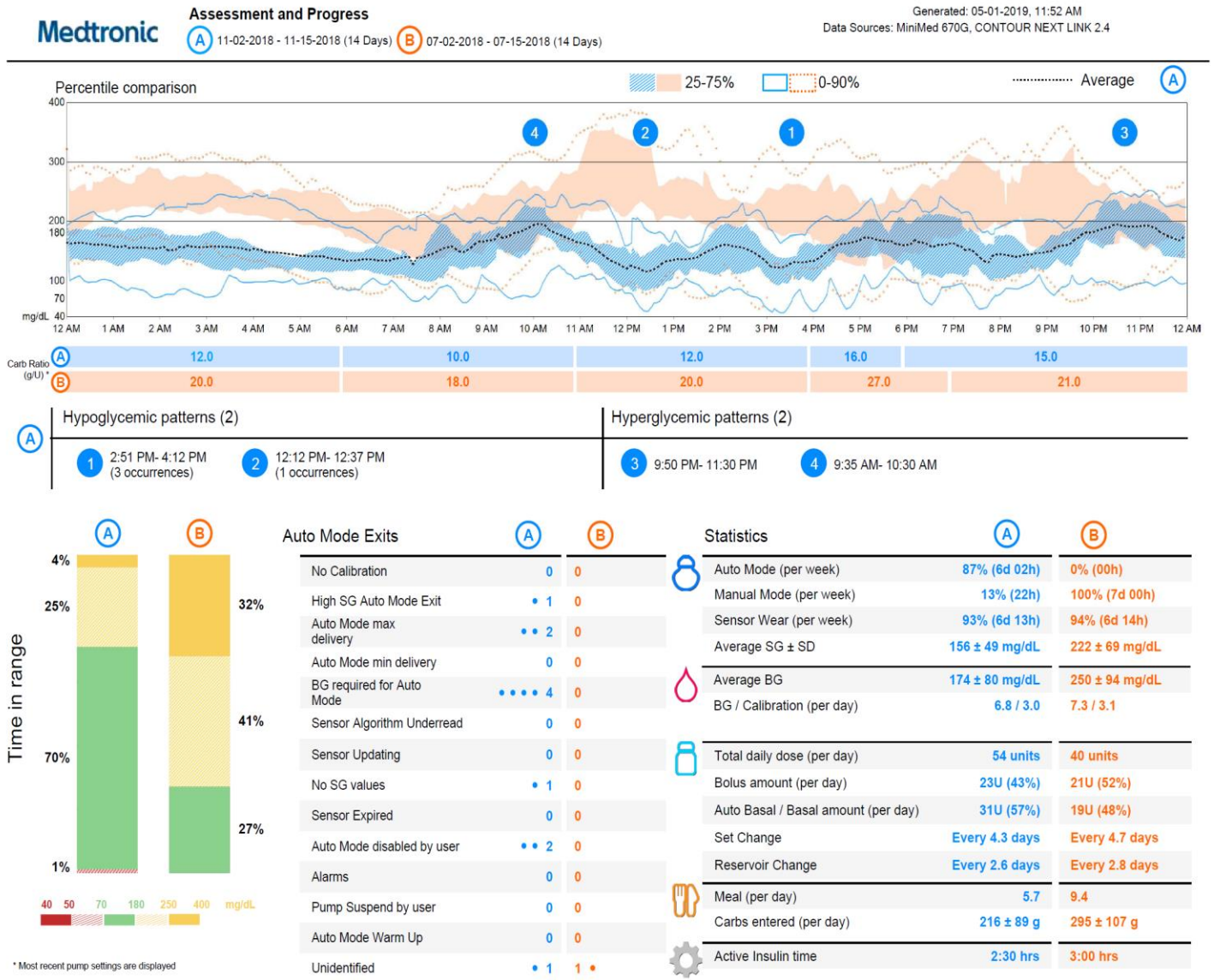
- Inconsistent or do not count carbs
- Struggle with technology
- Challenged in executing diabetes management tasks
- New to insulin therapy

Automated Insulin delivery can help a **broad spectrum of patients** improve outcomes and reduce burden

# PATIENT SUCCESS

12 year old boy diagnosed at 6 years of age

- 9/2017 : On pump + CGM and had two hypoglyc seizures
- 1/2018: Transitioned to AID
- HbA1c at time of transition 9.3%
- TIR at time of transition 27%



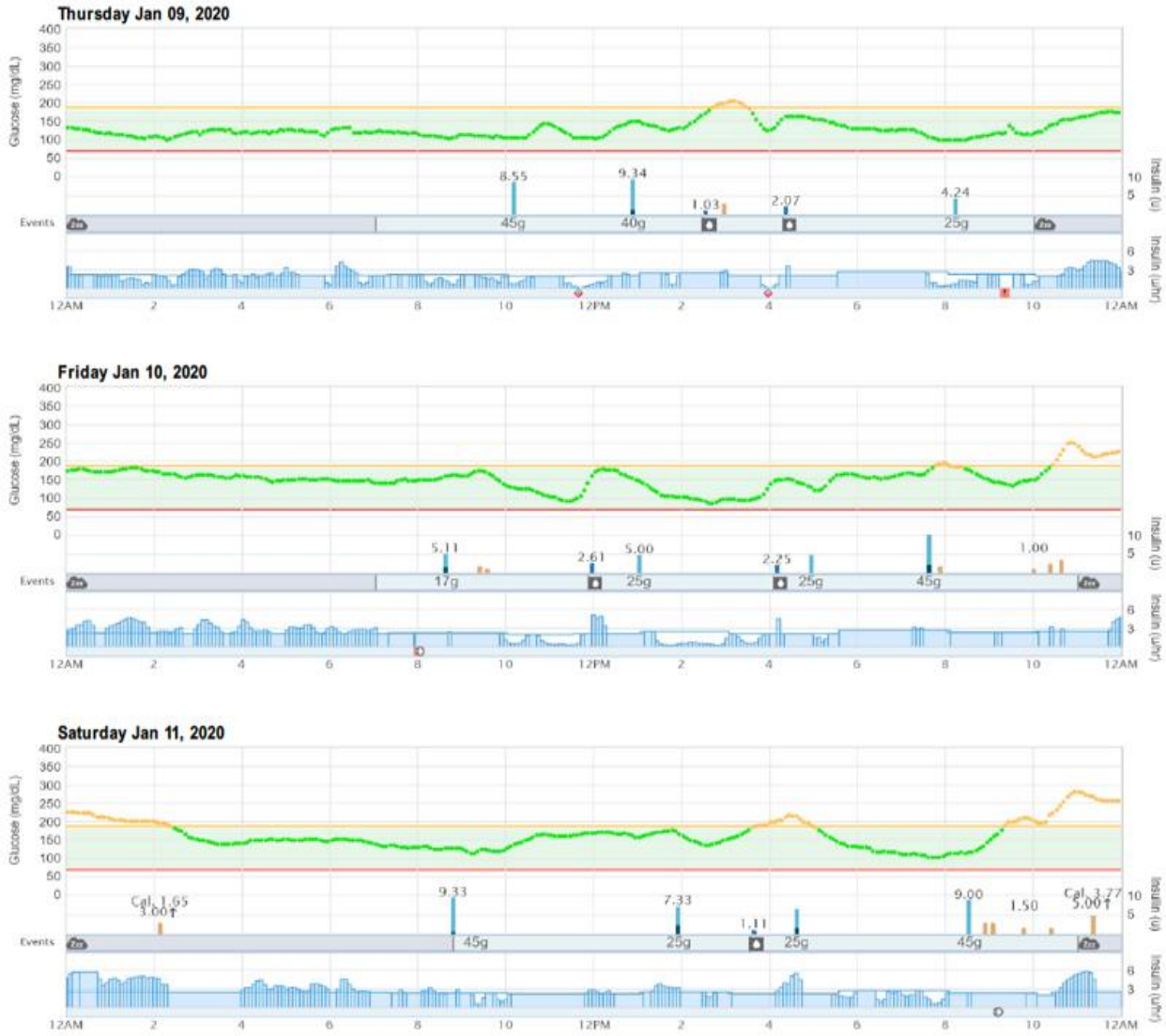
# PATIENT SUCCESS

14 year old girl diagnosed with T1D at age 8 years

- Started AID 1/2020
- HbA1c 8.1% LOWEST EVER!!

Lab Results:

| | | |
|---|---|---|
| A1C | 8.1 | 12/08/2020 |
| A1C | 8.3 | 10/13/2020 |
| A1C | 9.7 | 08/04/2020 |
| A1C | 10.5 | 03/10/2020 |
| A1C | 11.4 | 01/28/2020 |

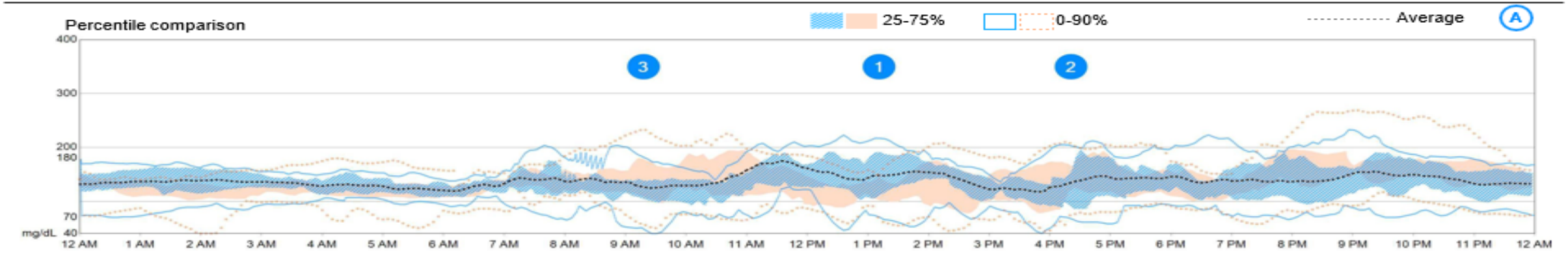


Medtronic

# Assessment and Progress

A 01-12-2019 - 01-25-2019 (14 Days)  B 12-29-2018 - 01-11-2019 (14 Days)

## Percentile comparison




| Carb Ratio (g/U) | | | | |
|---|---|---|---|---|
| A | 5.2 | 7.8 | 7.0 |
| B | 5.2 | 7.8 | 7.0 |

## Hypoglycemic patterns (3)

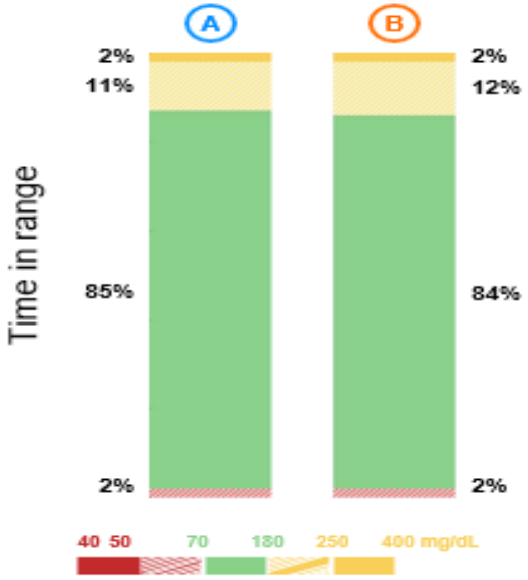
1 12:26 PM- 1:55 PM (2 occurrences)

2 3:36 PM- 5:07 PM (2 occurrences)

3 8:50 AM- 9:45 AM (1 occurrences)

## Hyperglycemic patterns (0)

None



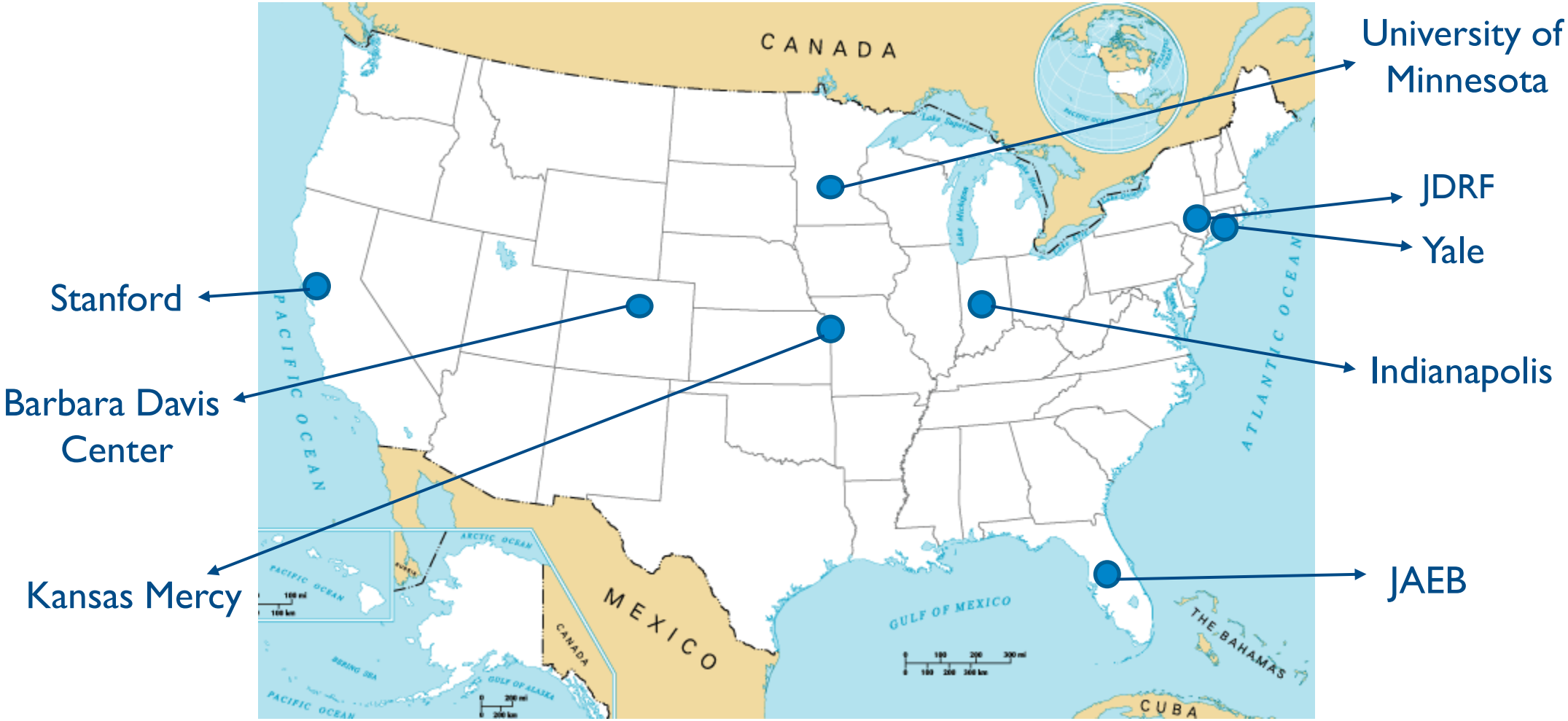

## Auto Mode Exits

| | A | B |
|---|---|---|
| No Calibration | 0 | 0 |
| High SG Auto Mode Exit | 0 | 0 |
| Auto Mode max delivery | • 1 | 1 • |
| Auto Mode min delivery | • • • 3 | 1 • |
| BG required for Auto Mode | 0 | 2 • • |
| Sensor Algorithm Underread | • • 2 | 0 |
| Sensor Updating | 0 | 0 |
| No SG values | 0 | 0 |
| Sensor Expired | 0 | 0 |
| Auto Mode disabled by user | • • 2 | 1 • |
| Alarms | 0 | 0 |
| Pump Suspend by user | 0 | 0 |
| Auto Mode Warm Up | 0 | 0 |

## Statistics

| | A | B |
|---|---|---|
| Auto Mode (per week) | 94% (6d 14h) | 91% (6d 09h) |
| Manual Mode (per week) | 6% (10h) | 9% (15h) |
| Sensor Wear (per week) | 97% (6d 19h) | 97% (6d 19h) |
| Average SG ± SD | 138 ± 42 mg/dL | 138 ± 44 mg/dL |
| Average BG | 176 ± 69 mg/dL | 175 ± 76 mg/dL |
| BG / Calibration (per day) | 6.2 / 3.5 | 7.7 / 3.7 |
| Total daily dose (per day) | 31 units | 32 units |
| Bolus amount (per day) | 18U (58%) | 19U (59%) |
| Auto Basal / Basal amount (per day) | 13U (42%) | 13U (41%) |
| Set Change | Every 5.5 days | Every 4.7 days |
| Reservoir Change | Every 5.5 days | Every 4.7 days |
| Meal (per day) | 5.2 | 6.4 |
| Carbs entered (per day) | 115 ± 25 g | 120 ± 22 g |
| Active Insulin time | 2:30 hrs | 2:30 hrs |

# CLVER HYBRID CLOSED LOOP THERAPY AND VERAPAMIL
## FOR BETA CELL PRESERVATION IN NEW ONSET TYPE 1 DIABETES



# HYBRID CLOSED LOOP THERAPY AND VERAPAMIL FOR BETA CELL PRESERVATION IN NEW ONSET TYPE 1 DIABETES
(CLINICALTRIALS.GOV IDENTIFIER: NCT04233034)

- Does tight glycemic control with HCL plus intensive diabetes management and/or Verapamil help preserve β-cell function?
- Randomized trial: ages 7-17 years with new dx T1D (n = 131)
- Primary Outcome: 12m C-peptide AUC after 2-hour MMTT
- Key Secondary Outcomes:  C-peptide AUC at 6 months; CGM parameters, HbA1c mechanistic studies
- Key Safety Outcomes: Severe hypoglycemia and DKA


# GRACIAS!