# Improved Glycemic Outcomes With Medtronic MiniMed Advanced Hybrid Closed-Loop Delivery: Results From a Randomized Crossover Trial Comparing Automated Insulin Delivery With Predictive Low Glucose Suspend in People With Type 1 Diabetes

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## OBJECTIVE

To study the MiniMed Advanced Hybrid Closed-Loop (AHCL) system, which includes an algorithm with individualized basal target set points, automated correction bolus function, and improved Auto Mode stability.

## RESEARCH DESIGN AND METHODS

This dual-center, randomized, open-label, two-sequence crossover study in automated-insulin-delivery–naive participants with type 1 diabetes (aged 7–80 years) compared AHCL to sensor-augmented pump therapy with predictive low glucose management (SAP + PLGM). Each study phase was 4 weeks, preceded by a 2- to 4-week run-in and separated by a 2-week washout.

## RESULTS

The study was completed by 59 of 60 people (mean age 23.3 ± 14.4 years). Time in target range (TIR) 3.9–10 mmol/L (70–180 mg/dL) favored AHCL over SAP + PLGM (70.4 ± 8.1% vs. 57.9 ± 11.7%) by 12.5 ± 8.5% ($P < 0.001$), with greater improvement overnight (18.8 ± 12.9%, $P < 0.001$). All age-groups (children [7–13 years], adolescents [14–21 years], and adults [>22 years]) demonstrated improvement, with adolescents showing the largest improvement (14.4 ± 8.4%). Mean sensor glucose (SG) at run-in was 9.3 ± 0.9 mmol/L (167 ± 16.2 mg/dL) and improved with AHCL (8.5 ± 0.7 mmol/L [153 ± 12.6 mg/dL], $P < 0.001$), but deteriorated during PLGM (9.5 ± 1.1 mmol/L [17 ± 19.8 mg/dL], $P < 0.001$). TIR was optimal when the algorithm set point was 5.6 mmol/L (100 mg/dL) compared with 6.7 mmol/L (120 mg/dL), 72.0 ± 7.9% vs. 64.6 ± 6.9%, respectively, with no additional hypoglycemia. Auto Mode was active 96.4 ± 4.0% of the time. The percentage of hypoglycemia at baseline (<3.9 mmol/L [70 mg/dL] and ≤3.0 mmol/L [54 mg/dL]) was 3.1 ± 2.1% and 0.5 ± 0.6%, respectively. During AHCL, the percentage time at <3.9 mmol/L (70 mg/dL) improved to 2.1 ± 1.4% ($P = 0.034$) and was statistically but not clinically reduced for ≤3.0 mmol/L (54 mg/dL) (0.5 ± 0.5%; $P = 0.025$). There was one episode of mild diabetic ketoacidosis attributed to an infusion set failure in combination with an intercurrent illness, which occurred during the SAP + PLGM arm.

## CONCLUSIONS

AHCL with automated correction bolus demonstrated significant improvement in glucose control compared with SAP + PLGM. A lower algorithm SG set point during AHCL resulted in greater TIR, with no increase in hypoglycemia.

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The importance of achieving healthy glycemic control to prevent long-term type 1 diabetes complications has been clearly established by previous landmark studies (1,2). However, achieving these recommended glycemic targets remains challenging. This is highlighted in the recently published T1D Exchange data that demonstrated only 21% of adults and 17% of youth achieve desired HbA$_{1c}$ targets (3). Hypoglycemia remains a major barrier to reaching glycemic targets. The overall burden of managing type 1 diabetes is another barrier; this appears to particularly impact adolescents and young adults, where the poorest glycemic outcomes are seen in available data sets (3–5).

In recent years, there has been an increase in the use of technology for diabetes care such as insulin pumps and continuous glucose monitoring (CGM) (5). While these technologies have independently demonstrated improvements in glycemic control (6), reduced hypoglycemia, and fear of hypoglycemia (7), the T1D Exchange data show there is still considerable opportunity to improve glycemic control and quality of life (by reducing burden) for people with type 1 diabetes.

The first commercially available hybrid closed-loop device, the MiniMed 670G system, combines a closed-loop algorithm controller with continuous subcutaneous insulin infusion and CGM to provide automated basal insulin delivery. The MiniMed 670G system has been available in the U.S. since 2016 and was subsequently made available in other countries. Real-world data from 3,141 people with type 1 diabetes living in the U.S. demonstrated improved time spent in target range (TIR) (from 66.0% to 73.3%) (8), and data from 4,959 people with type 1 diabetes living in 10 European countries demonstrated improved estimated HbA$_{1c}$ (from 7.2% to 6.9%) after MiniMed 670G automated insulin delivery initiation (9). However, there is impetus to further improve the user experience and glycemic outcomes, highlighted by significant discontinuation rates and glycemic outcomes that have not translated from clinical trials in the real world (10). Alternative automated insulin delivery systems have been commercially released, for example, the Control IQ by Tandem and the Cambridge system (CamAPS FX), which

have shown comparable outcomes in clinical trials (11,12).

As this was the first commercial system approved for clinical use, the design correctly prioritized safety, and therefore the automated features include conservative limitations. For example, in the MiniMed 670G system, automated bolus correction for hyperglycemia is not included, and maintaining Auto Mode is burdened by self-monitoring of blood glucose calibrations, which can result in Auto Mode exits (13). Therefore, with a goal of refining glycemic control further and reducing the burden of care, the automated basal insulin delivery system in the MiniMed 670G system has been enhanced with advanced hybrid closed-loop (AHCL) system. Intermediate iterations of the algorithm demonstrated feasibility and effectiveness (14).

The current study investigates the performance of the MiniMed AHCL system, which includes a target set point of 5.6 mmol/L (100 mg/dL) or 6.7 mmol/L (120 mg/dL) and an automated correction bolus feature up to every 5 min, in a randomized crossover trial to determine whether these features produce an increased TIR without increasing hypoglycemia compared with sensor-augmented pump therapy with predictive low-glucose monitoring (SAP + PLGM). Further, a range of secondary outcomes, including safety and user experience, were investigated. Here, we report the glycemic and safety outcomes.

## RESEARCH DESIGN AND METHODS
### Trial Design and Procedures
The study was a randomized, dual-center (Christchurch and Dunedin, New Zealand), open-label, two-sequence crossover study comparing AHCL to SAP + PLGM during free-living conditions. The study was conducted in compliance with the International Organization for Standardization (ISO) 14155:2011, the ethical principles that have their origin in the Declaration of Helsinki, and all applicable regulatory requirements. The study was approved by the Southern Health and Disability Ethics Committee and registered at ANZCTR (#12619000007134) and ClinicalTrials.gov (NCT04073576). The trial sponsor was the Christchurch Clinical Studies Trust.

The study consisted of two 4-week-long intervention periods separated by a 2-week washout period. This was

preceded by a 2- to 4-week run-in phase. During both the run-in and washout, participants used SAP therapy with low glucose suspend. The treatment intervention sequence was randomly assigned on a 1:1 basis at the enrollment visit and stratified by participants' age (7–13 years inclusive and 14–80 years inclusive) and study site.

Participants were enrolled between 20 May 2019 and 7 October 2019. The study visit schedule is shown in Supplementary Table 1. At enrollment, written consent was obtained from participants or parents, and baseline data were collected. Participants received training on the investigational AHCL system and CareLink Clinical therapy management software (Medtronic, Northridge, CA). Insulin-to-carbohydrate ratios were set per the participant's current device or per the investigators' discretion. Participants were advised to check their blood glucose four to six times per day and avoid use of acetaminophen. Participants had no restrictions on diet or activity. Participants continued their previously prescribed rapid-acting insulin (NovoRapid or Humalog). All participants were provided with a 24-h telephone helpline and were expected to upload their insulin pump data twice weekly. Participants then entered the 2- to 4-week run-in phase during which participants had an optional visit for support with their first pump (infusion set) site change.

After the run-in period, participants returned to their respective clinical research facility to start the first treatment period. Participants received further training on the use of AHCL or SAP + PLGM depending on the treatment sequence assigned. All device training was provided by a diabetes nurse educator and followed a standardized checklist of learning requirements. If randomized to AHCL, the initial AHCL algorithm glucose set point was determined by age, with subjects aged 7–13 years getting a glucose set point of 6.7 mmol/L (120 mg/dL) and subjects aged 14–80 years getting a set point of 5.6 mmol/L (100 mg/dL). A temporary set point of 8.3 mmol/L (150 mg/dL) could be used during exercise. For the 1st week of AHCL, participants were instructed to upload their insulin pumps daily. At 14 days after the start of the treatment period, participants in the AHCL arm received a phone call from a study investigator, and the set

point was adjusted based on time spent with sensor glucose (SG) in the <3.9 mmol/L (70 mg/dL) range. If the percentage of time spent with SG at <3.9 mmol/L (70 mg/dL) was <2% for subjects aged 7–13 years, the glucose set point was reduced to 5.6 mmol/L (100 mg/dL). If the percentage of time spent with glucose at <3.9 mmol/L (70 mg/dL) was >4% for subjects aged 14–80 years, the glucose set point was increased to 6.7 mmol/L (120 mg/dL). After the 4-week intervention, participants entered the 2-week washout period using SAP with low glucose suspend before entering the opposite intervention arm for a further 4 weeks. At each clinic visit, insulin pump settings, including insulin-to-carbohydrate ratios, active insulin time, and basal rates, were adjusted as per investigator discretion.

### Study Participants and Recruitment
Inclusion criteria were type 1 diabetes as per the American Diabetes Association classification (15) for at least 1 year, age between 7 and 80 years inclusive, insulin pump therapy for at least 6 months, minimum daily insulin requirement of ≥8 units, willingness and ability to adhere to the study protocol, and access to the internet and a computer system that met requirements for uploading the study pump data. Key exclusion criteria included mean HbA$_{1c}$ of >10.0% (86 mmol/mol), pregnancy, and use of a medication indicative of diabetes complications (ACE inhibitors and statins were permitted), systemic glucocorticoids, and sodium–glucose cotransporter 2 inhibitors or glucagon-like peptide 1 receptor agonists. Eligible study participants were identified from diabetes clinics based out of Christchurch and Dunedin (New Zealand) public hospitals. Recruitment was a convenience sample on a first-come, first-served basis.

### Study Objectives
The primary predefined objective was to evaluate a difference in the percentage of SG values in target range of 3.9–10.0 mmol/L (70–180 mg/dL) between AHCL and SAP + PLGM therapy. The secondary objective of this study was to confirm safety by comparing the percentage of SG values in the <3.9 mmol/L (70 mg/dL) range when using AHCL relative to SAP + PLGM therapy.

Additional exploratory analysis assessed the percentage of time spent in ≤3.0 mmol/L (54 mg/dL) and >10.0 mmol/L (180 mg/dL). The glycemic end points differentiated as 24 h, day (0600–2359 h), and night (0000–0559 h) were also assessed. Further, data on psychosocial factors, including fear of hypoglycemia, eating behavior, sleep quality, and device experience, were collected, with methodologies, results, and discussion reported elsewhere (pending).

### Closed-Loop System
Participants used the AHCL system that included the MiniMed 670G 4.0 insulin pump, the Guardian CGM components (Guardian Sensor [3] and Guardian Link [3] transmitter), and the Contour NEXT LINK 2.4 blood glucose meter (Ascensia Diabetes Care, Parsippany, NJ). The AHCL algorithm in the MiniMed 670G 4.0 insulin pump included a modified proportional-integral-derivative model with adaptive gains and insulin limits, insulin feedback, automated bolus function correcting to 6.7 mmol/L (120 mg/dL), and additional safety features. The algorithm used CGM data to provide a basal insulin delivery that was computed and adjusted every 5 min. Meals were announced and an insulin bolus delivered according to the patient's insulin-to-carbohydrate ratio. During Auto Mode, participants can bolus from the SG value. In contrast to previous iterations, this system can administer autocorrection boluses up to every 5 min based on SG, without user confirmation, to maintain a better glycemic control using the sensor values and all insulin delivery history, and has adjustable algorithm SG set points of 5.6 mmol/L (100 mg/dL) or 6.7 mmol/L (120 mg/dL) and accommodative parameters designed to keep the system in Auto Mode for longer while maintaining safety.

When the investigational system was operating in SAP + PLGM mode, the "suspend before low" function suspended basal insulin infusion when the SG fell within 3.9 mmol/L (70 mg/dL) above the set low limit and SG was predicted to be 1.1 mmol/L (18 mg/dL) above the set low limit in 30 min. The low limit was set at 3.2 mmol/L (58 mg/dL) in this study. If the "alert before low" function is selected, the subject receives an alert when insulin delivery is suspended. In the absence of any participant interaction, the insulin infusion resumed once autoresumption requirements are met or after a maximum suspend period of 2 h. The infusion could be resumed earlier if the patient intervened during the suspend time.

### Statistical Methods
A total of 50 subjects would be required to provide >90% power to detect a simple superiority of AHCL compared with SAP + PLGM, with the assumption being a mean difference in time spent in range (3.9–10.0 mmol/L) (70–180 mg/dL) between AHCL and SAP + PLGM of 8%, with an SD of change in percentage of time in target range of 15%. In consideration of potential subject attrition, a sample size of 60 subjects was set. To ensure balance, it was planned that 20 adults and 10 pediatric subjects with type 1 diabetes were to be recruited at each study site.

The analyses and summaries were conducted with the intention-to-treat population. For the primary end point, the overall mean difference in percentage TIR (3.9–10.0 mmol/L [70–180 mg/dL]) between AHCL and SAP + PLGM treatment periods was estimated and compared by paired $t$ test and a significance level of 0.025 (one-sided). The goal was to show superiority of the AHCL compared with the SAP + PLGM. Once the primary efficacy measure was successful, subsequent secondary measures were evaluated to show a statistically significant ($P$ values with no adjustment for multiple comparisons) advantage to the AHCL intervention to support further use or research for this intervention. All analyses of efficacy incorporated the between-subject treatment randomization sequence as a factor in the models to test that the sequence of treatments did not affect the relative efficacy of the treatments. All available data from the two 28-day-long treatment periods (day 1–day 28 and day 43–day 70) were used to estimate the percentage glycemic data for all analyses. Analyses were performed using SAS 6.4, SPSS 25.0, and MATLAB_R2019b software.

### RESULTS
A total of 59 participants (35 females), mean age 23.5 years (range 7–65; 19 subjects aged 7–13 years, and 40 subjects aged 14–80 years), completed the study. One participant withdrew during the

run-in phase. Baseline demographics (Table 1) show a mean HbA$_{1c}$ of 7.6 ± 0.9%, length of diagnosis of 13.2 ± 10.2 years, and mean time on insulin pump therapy of 6.3 ± 4.2 years. With respect to previous technology use, 14 participants (23%) were using real-time CGM, 20 participants (33%) were using intermittently scanned CGM (Abbott FreeStyle Libre) >70% of the time, and 25 participants (44%) were using capillary blood glucose testing alone. No participants had any previous automated insulin delivery experience.

AHCL improved TIR 3.9–10.0 mmol/L (70–180 mg/dL) compared with SAP + PLGM by 12.5 ± 8.5% (70.4 ± 8.1% vs. 57.9 ± 11.7%, respectively; P < 0.001) (Table 2). This improvement was greatest overnight (18.8 ± 12.9%). When these data were stratified into clinically meaningful age-groups, comprising children aged 7–13 years (n = 19), adolescents aged 14–21 years (n = 14), and adults aged >22 years (n = 26), the total TIR during AHCL in these cohorts was 66.8 ± 6.5%, 68.6 ± 7.6%, and 73.9 ± 8.2%, respectively, during AHCL. The adolescent cohort demonstrated the largest improvement (14.4 ± 8.4%) in TIR. The proportion of participants attaining TIR >70% improved from 12% (7 of 59) at baseline to 51% (30 of 59) during AHCL. During PLGM, 15% (9 of 59) achieved TIR >70%.

TIR as the primary outcome was also analyzed according to adjustable parameters (apart from individualized insulin-to-carbohydrate ratios). TIR was greater when AHCL operated at the lower 5.6 mmol/L (100 mg/dL) set point

(72.0 ± 7.9%) compared with 64.6 ± 6.9% when the set point was 6.7 mmol/L (120 mg/dL). The improved TIR with the lower set point occurred without an increase in hypoglycemia, with time spent <3.9 mmol/L (70 mg/dL) being 2.2 ± 1.6% and 2.3 ± 1.6% at set point 5.6 mmol/L (100 mg/dL) and 6.7 mmol/L (120 mg/dL), respectively.

The secondary glycemic end points of percentage of time in various SG ranges are shown in Table 2, all favoring AHCL, in all age-bands. For example, time spent <3.9 mmol/L improved by 0.4% (P = 0.032) and >10 mmol/L by 12.1% (P < 0.001). The mean SG values favored AHCL (8.5 ± 0.7 mmol/L [153 ± 13 mg/dL]) over SAP + PLGM (9.5 ± 1.1 mmol/L [171 ± 19 mg/dL], P < 0.001). This mean SG during AHCL equates to a glucose management indicator (16) of 6.8% (51.3 mmol/mol) compared with the observed baseline HbA$_{1c}$ of 7.6 ± 0.9%. The 24-h ambulatory glucose profile for the entire group and by age-group is shown in Fig. 1. The median and interquartile range for the AHCL group was lower compared with the SAP + PLGM group. The lower interquartile range suggests that there is reduced glycemic variability using AHCL. Total insulin use was 0.76 ± 0.28 units/kg/day for both arms of the study. The percentage of the autocorrection based on the total bolus amount delivered was 21.5 ± 9.6%. Glycemic variability as measured by SD and coefficient of variation was 3.5 mmol/L and 37.6% at baseline. Comparatively, this was 3.1 mmol/L and 36.6% for AHCL with a 100 mg/dL set point and 3.5 mmol/L and 36.8% for PLGM.

Sensor adherence was high during both study arms, with valid sensor values for >90% of the time. This was sustained in all age-groups, with no clinically significant difference noted in the adolescent group (sensor use 90.2%). As expected, due to high sensor use and AHCL design features, participants were in Auto Mode for a high proportion of time (96.4 ± 4.0%). The frequency of Auto Mode interruption was 1.2 events per week, with one-third of exits initiated by the user.

There was one episode of mild diabetic ketoacidosis in the study, which occurred in the SAP + PLGM treatment period due to possible infusion set occlusion and a concurrent viral infection. There were no episodes of severe hypoglycemia in the study. The total number of adverse events was similar between AHCL and SAP + PLGM (19 vs. 18). Five adverse effects were deemed to be possibly or probably related to the device, and the rest were deemed unrelated. All of the adverse events were skin reactions, and one was an infusion site infection that required oral antibiotics. All participants fully recovered.

## CONCLUSIONS

This is the first randomized controlled trial investigating the MiniMed AHCL system performance in free-living children, adolescents, and adults with type 1 diabetes. The AHCL algorithm is now commercially available in the MiniMed 780G system. The study demonstrated a significant improvement in TIR, with no increase in hypoglycemia for AHCL compared with SAP + PLGM. Few studies in the literature have compared automated insulin delivery to SAP + PLGM, and those that have been conducted were brief (17) or not studied as a randomized controlled trial (18). Head-to-head studies of available automated insulin delivery technology (e.g., Control IQ, or CamAPS FX) and the algorithm used in this study are not available. Comparing different clinical trials that have different trial environments (e.g., study participants and design) would be unscientific. Nevertheless, our findings demonstrating improved TIR using AHCL are consistent with a systematic review of automated insulin delivery studies in demonstrating improved glycemic control and safety (19). The greatest improvements were seen overnight, as is

## Table 1—Baseline demographics

|  | Values (N = 60) |
| --- | --- |
| Age, years (mean [range]) | 23.5 [7.0–65] |
| Female sex | 35 (58) |
| Race/ethnicity | |
| New Zealand European | 41 (68) |
| Maori | 11 (18) |
| Other ethnicity | 8 (13) |
| Freestyle Libre | 20 (33) |
| Real-time CGM | 14 (23) |
| Capillary glucose testing | 26 (44) |
| BMI, kg/m$^2$ | 24.1 ± 5.8 |
| Years since diagnosis | 13.2 ± 10.2 |
| Years on insulin pump | 6.3 ± 4.2 |
| Baseline HbA$_{1c}$, % | 7.6 ± 0.9 |

Data are presented as n (%), mean ± SD, or as indicated otherwise.

**Table 2—Glycemic outcomes**

| Category* | Total | | | | | | Children aged 7–13 years | | Adolescents aged 14–21 years | | Adults aged 22–80 years | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Run-in | PLGM | AHCL 5.6 mmol/L | AHCL total | % change AHCL vs. PLGM | P value§ | % change AHCL vs. PLGM | P value§ | % change AHCL vs. PLGM | P value§ | % change AHCL vs. PLGM | P value§ |
| Subjects, n | 59 | 59 | 52 | 59 | | | 19 | | 14 | | 26 | |
| Average SG mmol/L overall | 9.3 ± 0.9 (9.2) | 9.5 ± 1.1 (9.4) | 8.3 ± 0.7 (8.1) | 8.5 ± 0.7 (8.4) | −0.6 ± 0.4 (−0.6)† | <0.001 | −0.5 ± 0.4 (−0.6)† | <0.001 | −0.7 ± 0.4 (−0.7)† | <0.001 | −0.5 ± 0.5 (−0.5)† | <0.001 |
| % CGM 3.9–10 mmol/L overall | 59.0 ± 10.4 (60.8) | 57.9 ± 11.7 (58.4) | 72.0 ± 7.9 (71.9) | 70.4 ± 8.1 (70.8) | 12.5 ± 8.5 (11.2)‡ | <0.001 | 11.8 ± 7.4 (11.8)‡ | <0.001 | 14.4 ± 8.4 (12.3)‡ | <0.001 | 11.9 ± 9.5 (10.6)‡ | <0.001 |
| % CGM 3.9–10 mmol/L day | 58.2 ± 11.0 (57.9) | 56.5 ± 12.2 (56.4) | 68.7 ± 10.0 (69.5) | 66.8 ± 9.9 (65.7) | 10.4 ± 8.7 (9.0)‡ | <0.001 | 7.9 ± 7.1 (8.3)‡ | <0.001 | 14.1 ± 8.4 (13.6)‡ | <0.001 | 10.1 ± 9.4 (8.5)‡ | <0.001 |
| % CGM 3.9–10 mmol/L night | 61.2 ± 14.7 (63.5) | 62.0 ± 15.0 (64.9) | 81.9 ± 10.6 (82.3) | 80.8 ± 10.4 (81.5) | 18.8 ± 12.9 (19.3)‡ | <0.001 | 23.6 ± 11.3 (22.6)‡ | <0.001 | 15.1 ± 11.5 (11.6)‡ | <0.001 | 17.2 ± 14.0 (13.7)‡ | <0.001 |
| % CGM >10 mmol/L overall | 37.9 ± 10.6 (37.7) | 39.6 ± 12.1 (39.2) | 25.8 ± 8.2 (24.4) | 27.5 ± 8.1 (27.7) | −12.1 ± 9.0 (−12.1)‡ | <0.001 | −11.2 ± 8.0 (−12.6)‡ | <0.001 | −14.0 ± 8.5 (−12.5)‡ | <0.001 | −11.8 ± 10.0 (−9.5)‡ | <0.001 |
| % CGM ≤3.0 mmol/L overall | 0.5 ± 0.6 (0.3) | 0.5 ± 0.5 (0.3) | 0.4 ± 0.4 (0.3) | 0.5 ± 0.5 (0.4) | −0.1 ± 0.4 (−0.1)‡ | 0.025 | −0.2 ± 0.5 (−0.1)‡ | 0.0676 | −0.1 ± 0.3 (−0.0)‡ | 0.2441 | −0.0 ± 0.2 (−0.1)‡ | 0.5462 |
| % CGM <3.9 mmol/L overall | 3.1 ± 2.1 (2.7) | 2.5 ± 1.6 (2.2) | 2.2 ± 1.6 (1.9) | 2.1 ± 1.4 (1.9) | −0.4 ± 1.3 (−0.4)‡ | 0.0318 | −0.7 ± 1.8 (−0.6)‡ | 0.1216 | −0.4 ± 1.1 (−0.4)‡ | 0.1804 | −0.1 ± 0.9 (−0.2)‡ | 0.5184 |

*Results presented as mean ± SD (median). †SG % change is expressed as relative % reduction (% − %)/%) comparing overall value in AHCL. ‡TIR differences are expressed as absolute difference (% − %). §Analyses using paired t test.
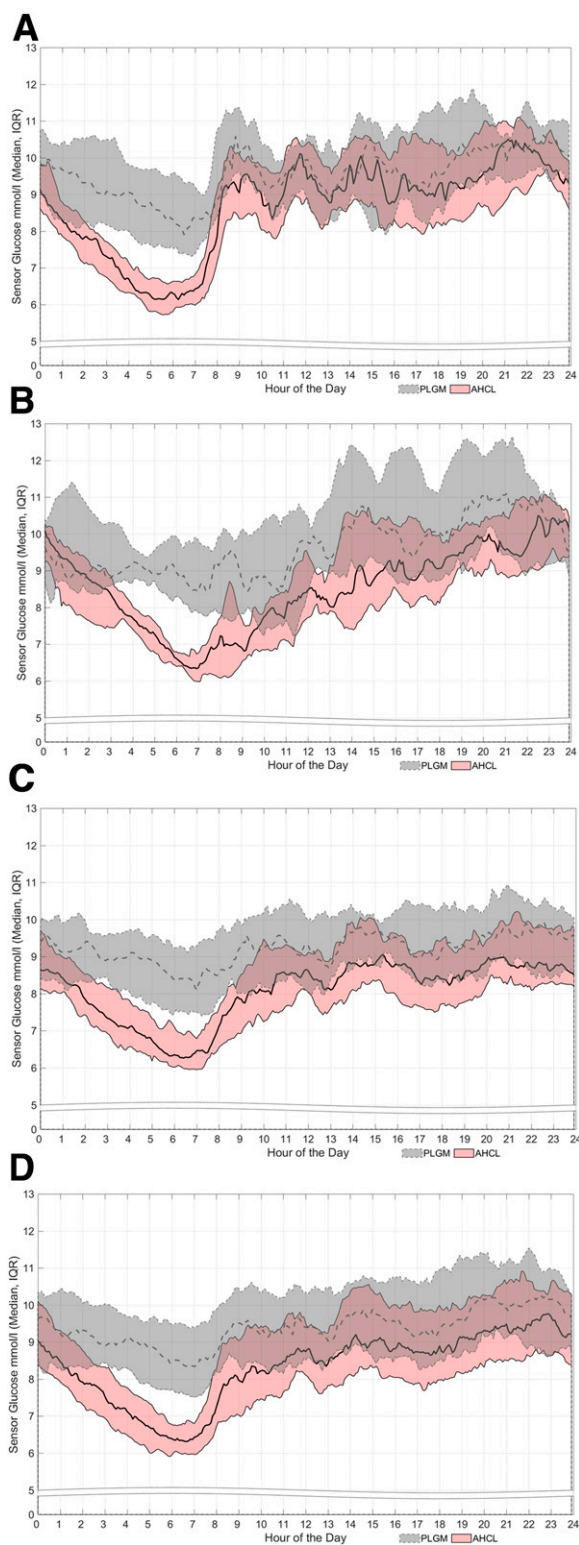
**Figure 1**—Ambulatory SG profiles illustrating mean SG and interquartile range (IQR) in participants 7–13 years old (*A*), 14–21 years old (*B*), >21 years old (*C*), and all participants (*D*).

typical in automated insulin delivery studies.

The AHCL system has two major differences compared with the commercially available automated insulin delivery

system (the MiniMed 670G system): a modifiable algorithm set point (5.6 mmol/L [100 mg/dL] or 6.7 mmol/L [120 mg/dL]) and the delivery of autocorrection boluses every 5 min when

certain parameters are met. This evolution adds both further automation and individualization, which people with type 1 diabetes have desired. Our data show that autocorrection appears to contribute to the improved TIR. It provided 21.5% of the total bolus insulin, which likely reflects more physiological insulin delivery distribution. Furthermore, the lower set point achieves a greater TIR without an increase in an already acceptable proportion of time spent at <3.9 mmol/L (70 mg/dL). The design features that keep the AHCL system safely in Auto Mode have been improved compared with the 670G system. The demonstration of >90% of time spent in Auto Mode suggests that improvements in glycemia will be sustained. The Auto Mode interruption frequency using AHCL of 1.2 episodes per week is much lower than the previously reported 6.3 exits per week using the MiniMed 670G (13).

The TIR of 72.6% using AHCL at the more aggressive set point demonstrated in this study should be interpreted in relation to the population demographics and study design. The study population in the current trial included a wide range of ages (7–65 years). Further, the mean age of study participants was 23.5 years (and >50% of the cohort was <21 years of age) and encompasses a large proportion of people with type 1 diabetes who have been most resistant to improvements conferred by AHCL in other studies (20). The data also provide confidence in the system's performance in the 7–14 age-group, which reached a TIR of 89.2 ± 6.7% at night when the set point was 5.6 mmol/L (100 mg/dL), while maintaining a low time below range. Further, the greatest improvement in TIR observed in the adolescent group is encouraging because it suggests that the increased automation of the AHCL design is highly effective in improving glycemic control in this challenging study population. Finally, we observed a daily insulin requirement during AHCL of 0.76 units/kg/day, comparably higher than a recent study demonstrating similar TIR (11). This is important because other studies have shown that higher total daily doses of insulin have correlated with worse TIR, likely reflecting larger carbohydrate meals and/or less insulin sensitivity (20). Our results show a robust TIR without decreasing the daily insulin often seen in

automated insulin delivery studies, which we attribute to AHCL effectively delivering extra insulin to overcome glycemic excursions due to inaccurate carbohydrate announcement. However, we acknowledge the short duration of the study limits interpretation of this result.

As previously stated, the AHCL system in the current study used two set point options (5.6 or 6.7 mmol/L [100 mg/dL or 120 mg/dL]), which allowed for more flexibility for the physician and the person with diabetes. Our results and experience using the lower set points suggest that in the clinical setting a default option of 5.6 mmol/L (100 mg/dL) would be safe and effective for all age-groups. The higher set point may be a satisfactory transitional setting in those people with significant fear of hypoglycemia. The high use of the sensor and AHCL mode seen across all age-groups, including adolescents, suggests a promising level of acceptance of AHCL in real-world settings.

This study is limited by its relatively short duration. A longer study would confirm whether the results are sustained and allow for optimization of AHCL (insulin-to-carbohydrate ratios and active insulin time settings), possibly translating into an additionally increased TIR. While the mean age reflects a more challenging demographic, they still reflected a relatively well-controlled group who are likely to be more adherent than in the generalized population. Offsetting these limitations is the strength in study design (randomized crossover), a contemporary comparator (SAP + PLGM), and studying an automated-insulin-delivery–naive population.

We conclude that AHCL, with automated corrections, is an innovation that effectively targets postprandial hyperglycemia by mitigating factors such as carbohydrate underestimation or late/missed boluses. Additionally, with flexible set points, AHCL allows different options to deliver individualized effective therapy to improve glycemic control, especially with the lower set point delivering the better TIR without increased hypoglycemia. A much-reduced Auto Mode exit frequency, combined with the reported high sensor use, indicates an improved user experience over previous systems.

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