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Comparison of MiniMed 780G system performance in users aged younger and older than 15 years: Evidence from 12 870 real-world users

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Abstract

Aim: To investigate real-world glycaemic outcomes and goals achieved by users of the MiniMed 780G advanced hybrid closed loop (AHCL) system aged younger and older than 15 years with type 1 diabetes (T1D).

Materials and Methods: Data uploaded by MiniMed 780G system users from 27 August 2020 to 22 July 2021 were aggregated and retrospectively analysed based on self-reported age (≤15 years and >15 years) for three cohorts: (a) post-AHCL initiation, (b) 6-month longitudinal post-AHCL initiation and (c) pre- versus post-AHCL initiation. Analyses included mean percentage of time spent in AHCL and at sensor glucose ranges, insulin delivered and the proportion of users achieving recommended glucose management indicator (GMI < 7.0%) and time in target range (TIR 70-180 mg/dl > 70%) goals.

Results: Users aged 15 years or younger (N = 3211) achieved a GMI of 6.8% ± 0.3% and TIR of 73.9% ± 8.7%, while spending 92.7% of time in AHCL. Users aged older than 15 years (N = 8874) achieved a GMI of 6.8% ± 0.4% and TIR of 76.5% ± 9.4% with 92.3% of time in AHCL. Time spent at less than 70 mg/dl was within the recommended target of less than 4% (3.2% and 2.3%, respectively). Similar outcomes were observed for each group (N = 790 and N = 1642, respectively) in the first month following AHCL initiation, and were sustained over the 6-month observation period.

Conclusions: This real-world analysis shows that more than 75% of users with T1D aged 15 years or younger using the MiniMed 780G system achieved international consensus-recommended glycaemic control, mirroring the achievements of the population aged older than 15 years.

KEYWORDS
adolescents, automated insulin delivery, closed-loop system, diabetes, glucose management indicator, hyperglycaemia, hypoglycaemia, paediatric, real-world evidence, time in range

1 | INTRODUCTION

Type 1 diabetes (T1D) during childhood presents a significant challenge worldwide.[1] Optimal glycaemic control at a paediatric age is paramount for normal growth, central nervous system structure, neurocognition and a reduction in long-term complications.[2-6] In addition, increased mortality in young people has been associated with higher HbA1c during childhood.[7]

Thus, the recently revised recommendation of a targeted HbA1c of less than 7% (<53 mmol/mol) for most children with T1D by the American Diabetes Association Standards of Medical Care in Diabetes, is opportune.[8] Recent position papers reporting continuous glucose monitoring (CGM) metrics such as time spent in target sensor glucose range (TIR) for adolescents and children further align with the glycaemic control goals for the adult population, and are testimony to the awareness of hyperglycaemia exposure and toxicity in youth living with T1D.[4,8,9]

However, achieving HbA1c goals seems to be elusive, as only 17% of youth aged younger than 18 years achieved the 2018 HbA1c goal of less than 7.5% (<58 mmol/mol) in the United States T1D Exchange[10] and only an estimated 10% to 15% of individuals diagnosed with T1D before 16 years of age had an HbA1c within target range by early adulthood.[11] Physiological and hormonal changes of puberty that affect insulin action and insulin requirements and multiple behavioural factors such as reduced engagement while transitioning to self-management, increased diabetes distress and fear of hypoglycaemia shared by both youth with T1D and their guardians/caretakers, are believed to contribute to these shortfalls.[12-14] While some registry-based analyses report a positive association with diabetes technology use and lower HbA1c, severe hypoglycaemia and diabetic ketoacidosis,[15-18] the low rates of target HbA1c can, in part, be attributed to barriers to diabetes technology access that allow a more effective means by which to achieve stringent glycaemic control safely.

The introduction of automated insulin delivery has shifted this paradigm. Clinical pivotal trials of the MiniMed 670G system,[19,20] followed by the MiniMed advanced hybrid closed-loop (AHCL) system,[21] showed that closed-loop control improved HbA1c, TIR and other glycaemic outcomes in youth and adults with T1D. Evidence from large populations of real-world MiniMed 670G[22] and MiniMed 780G system users[23] has also shown improved outcomes, which included a reduction in the glucose management indicator (GMI), a surrogate of HbA1c, and increased TIR, from baseline or before closed-loop initiation. Improvements also showed decreasing time spent in hypoglycaemia. Investigations of these closed-loop therapies in various trials[24-26] and in different paediatric studies of automated insulin delivery systems have shown similar findings of improved glycaemic control, while decreasing or not increasing hypoglycaemia.[27-29]

The aim of this study was to analyse the data from real-world users of the MiniMed 780G system aged 15 years or younger with T1D, from several different countries, in comparison with data from an older population of system users with T1D.

2 | MATERIALS AND METHODS

MiniMed 780G system data uploaded to CareLink personal software from 27 August 2020 to 22 July 2021 by individuals who provided consent for their data to be aggregated and who resided in countries (Belgium, Czech Republic, Denmark, Egypt, Finland, UK, Greece, Hungary, Iceland, Ireland, Israel, Italy, Luxemburg, The Netherlands, Poland, Portugal, Qatar, Romania, Slovakia, Slovenia, South Africa, Sweden, Switzerland and Turkey) where local data privacy regulation permitted data aggregation, were analysed. Outcomes were analysed for three cohorts of users (Figure S1). In cohort 1 (post-AHCL), the overall outcomes of users with at least 10 days of sensor glucose (SG) data after AHCL was initiated for the first time, were assessed. In cohort 2 (longitudinal), the sustainability of glycaemic outcomes reported for each month across 6 months post-AHCL initiation was evaluated. In cohort 3 (pre- vs. post-AHCL), glycaemic outcomes achieved before and after AHCL initiation were compared. To be included in the analyses, users needed to have a minimum of 10 days of SG data in each period evaluated: the post-AHCL initiation period (cohort 1); each month following AHCL initiation (cohort 2); and in both the pre- and post-AHCL initiation periods (cohort 3). This requirement of a minimum of 10 days of SG data was based on a previous publication validating a similar duration of CGM metrics to estimate or determine long-term glycaemic control.[30]

For each of the three cohorts described above, data were analysed per the two age groups (≤15 and >15 years). The information on age was self-reported by users within the CareLink Personal software, where they can select between five age groups (≤15, 16-28, 29-42, 43-55 and >56 years), or decide not to provide this information. All data available post-AHCL initiation were included, whether the system was in AHCL control or in open loop (i.e. following an AHCL exit triggered by either the system or the user). Data were assessed for individual countries that had at least 100 users in scope of the analysis. We performed a subanalysis based on system settings use, in which the percentage of time that the 100 mg/dl (5.6 mmol/L), 110 mg/d (6.1 mmol/L) or 120 mg/dl (6.7 mmol/L) was used as glucose target was calculated per individual, as well as the percentage of time where 2, 2-3, 3-4, or 4 or more hours was set as active insulin time (AIT). The outcomes were analysed for those who used one glucose target at least 95% of the time, one of the AIT ranges at least 95% of the time, and the combination of settings at least 90% of the time.

Glycaemic outcomes, including the mean percentage of time spent in 70-180 mg/dl (3.9-10.0 mmol/L) (TIR), at less than 54 mg/dl (<3.0 mmol/L) (TBR < 54), at less than 70 mg/dl (<3.9 mmol/L) (TBR < 70), at more than 180 mg/dl (>10.0 mmol/L) (TAR >180), and at more than 250 mg/dl (>13.9 mmol/L) (TAR > 250), were determined for the overall 24-hour day, daytime (06:01 AM to 11:59 PM) and night-time (12:00 AM to 06:00 AM) periods. The mean SG, its coefficient of variation (CV) and GMI were also assessed, as well as the sensor use, percentage of time spent in AHCL, number of self-monitored blood glucose measurements, insulin delivery patterns and system settings (i.e. glucose target and AIT).

	All users	Users ≤15 y	Users >15 y	P[a]
Users, n	12 870	3211	8874	-
Sensor use, %	90.5 ± 10.2	90.5 ± 10.0	90.5 ± 10.2	.271
Time in AHCL, %	92.3 ± 13.0	92.7 ± 12.3	92.3 ± 13.0	.260
SMBG measurements per day, n	3.4 ± 1.1	3.6 ± 1.1	3.4 ± 1.0	<.0001
AHCL exits per week, n				
Total	1.0 ± 1.1	1.1 ± 1.2	1.0 ± 1.0	<.0001
Initiated by the user	0.5 ± 1.0	0.6 ± 1.1	0.5 ± 0.9	.595
Initiated by the system	0.5 ± 0.6	0.6 ± 0.7	0.5 ± 0.6	<.0001
Glucose target, % *of time*				
100 mg/dl (5.6 mmol/L)	47.7 ± 43.9	45.1 ± 43.6	48.7 ± 43.9	.0008
110 mg/dl (6.1 mmol/L)	23.2 ± 36.0	25.7 ± 37.1	22.5 ± 35.7	<.0001
120 mg/dl (6.7 mmol/L)	22.3 ± 36.7	22.2 ± 36.1	22.1 ± 36.7	.883
150 mg/dl (8.3 mmol/L)	1.9 ± 4.5	2.2 ± 4.9	1.9 ± 4.4	.002
Open loop	4.8 ± 9.2	4.8 ± 8.7	4.8 ± 9.2	.961
Active insulin time, % *of time*				
2 h	37.6 ± 45.7	45.5 ± 47.2	35.5 ± 45	<.0001
>2 to 3 h	53.1 ± 46.5	48.7 ± 46.7	54.2 ± 46.4	<.0001
>3 to 4 h	8.9 ± 26.5	5.4 ± 20.7	10.0 ± 27.9	<.0001
>4 h	0.4 ± 5.3	0.3 ± 4.7	0.3 ± 5.1	.617

TABLE 1 MiniMed 780G system use and settings post-AHCL initiation (cohort 1)

Note. All values are shown as mean ± standard deviation.
Abbreviations: AHCL, advanced hybrid closed loop; SMBG, self-monitored blood glucose.
[a]Comparison between users aged ≤15 and >15 years.

2.1 | Statistics

The first two cohorts underwent descriptive analysis using mean and standard deviation (SD) for continuous variables and proportion (%) for categorical variable. In the post-AHCL cohort (cohort 1), the outcomes in individuals aged 15 years or younger were compared with those of individuals aged older than 15 years using a two-sample *t*-test in cases where the normality assumption was met, or a Wilcoxon rank sum test otherwise. For the longitudinal cohort (cohort 2), analyses of time spent in SG ranges and GMI were performed with a repeated measures model accounting for correlated data by using random intercepts. The pre- and post-AHCL initiation comparison of glycaemic outcomes in cohort 3 was performed using a paired *t* test in cases where the normality assumption was met, or a Wilcoxon signed-rank test otherwise. A McNemar's test was used to compare the change in the proportion of subjects meeting glycaemic targets in cohort 3. All statistical analyses were performed using SAS version 9.4 software (SAS Institute, Cary, NC) and *P* less than .05 was considered statistically significant.

3 | RESULTS

A total of 16 672 users from 24 countries uploaded data into CareLink personal software and provided consent for their data to be aggregated (Table S1). There were 12 870 users with at least 10 days of SG data post-AHCL initiation who were included in the analysis. The mean ± SD and median (IQR) of the observation period for this group was 112 ± 69 and 102 (54-160) days, respectively. There were 3211 (27%) users who reported to be aged 15 years or younger, and for whom the observation period was a mean ± SD of 120 ± 71 days and median (IQR) of 113 (61-170) days. There were 8874 users who reported to be aged older than 15 years, and for whom the mean ± SD and median (IQR) of the observation period was 110 ± 68 and 110 (52-156) days, respectively. There were 785 users who did not report their age. A summary of all users and their stratification across cohorts 1, 2 and 3 are shown in Table S1.

3.1 | MiniMed 780G system performance (cohort 1)

System usage and settings (i.e. glucose target and AIT) of all users, those aged 15 years or younger and those aged older than 15 years, are shown in Table 1. The mean SG, CV of SG, GMI and time spent in glucose ranges after AHCL initiation for all users and those within each age group are shown in Figure 1. The TIR was 75.8% for all users, 73.9% for those aged 15 years or younger and 76.5% for those aged older than 15 years, after AHCL initiation (Figure 1). For the younger group, TIR increased to 76.5% and 78.9% at the 110 mg/dl + 2 hours AIT and 100 mg/dl + 2 hours AIT settings, respectively. For both groups and at the lowest target of 100 mg/dl, the average
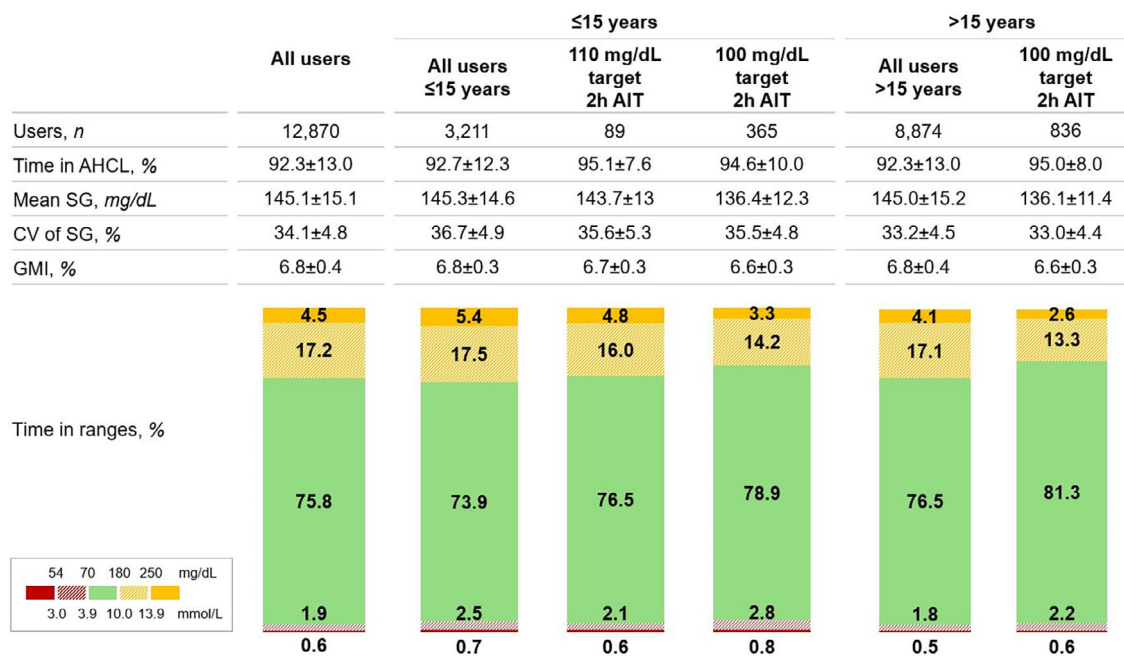
| | All users | ≤15 years | | | >15 years | |
		All users ≤15 years	110 mg/dL target 2h AIT	100 mg/dL target 2h AIT	All users >15 years	100 mg/dL target 2h AIT
Users, n	12,870	3,211	89	365	8,874	836
Time in AHCL, %	92.3±13.0	92.7±12.3	95.1±7.6	94.6±10.0	92.3±13.0	95.0±8.0
Mean SG, mg/dL	145.1±15.1	145.3±14.6	143.7±13	136.4±12.3	145.0±15.2	136.1±11.4
CV of SG, %	34.1±4.8	36.7±4.9	35.6±5.3	35.5±4.8	33.2±4.5	33.0±4.4
GMI, %	6.8±0.4	6.8±0.3	6.7±0.3	6.6±0.3	6.8±0.4	6.6±0.3

FIGURE 1 MiniMed 780G system performance post-AHCL initiation (cohort 1). Values are shown as mean or mean ± standard deviation. For the specified glucose target and AIT settings, individuals used both for ≥90% of the time. AHCL, advanced hybrid closed-loop; AIT, active insulin time; CV, coefficient of variation; GMI, glucose management indicator; SG, sensor glucose

TABLE 2 Percentage of time spent in glucose ranges during daytime and night-time, post-AHCL initiation (cohort 1)

	All users	Users ≤15 y	Users >15 y	P[a]
Users, n	12 870	3211	8874	-
Daytime in ranges, %				
<54 mg/dl (3.0 mmol/L)	0.6 ± 0.8	0.8 ± 0.8	0.5 ± 0.8	<.0001
<70 mg/dl (3.9 mmol/L)	2.7 ± 2.3	3.5 ± 2.5	2.5 ± 2.2	<.0001
70-180 mg/dl (3.9-10.0 mmol/L)	73.7 ± 10.1	71.1 ± 9.5	74.6 ± 10.2	<.0001
>180 mg/dl (10.0 mmol/L)	23.6 ± 10.6	25.4 ± 10.0	22.9 ± 10.7	<.0001
>250 mg/dl (13.9 mmol/L)	5.0 ± 4.8	6.2 ± 5.0	4.6 ± 4.6	<.0001
Night-time in ranges, %				
<54 mg/dl (3.0 mmol/L)	0.4 ± 0.8	0.5 ± 0.8	0.4 ± 0.7	<.0001
<70 mg/dl (3.9 mmol/L)	1.9 ± 2.2	2.4 ± 2.5	1.7 ± 2.1	<.0001
70-180 mg/dl (3.9-10.0 mmol/L)	81.9 ± 11.2	82.2 ± 10.3	82.1 ± 11.4	.297
>180 mg/dl (10.0 mmol/L)	16.2 ± 11.3	15.4 ± 10.3	16.2 ± 11.5	.055
>250 mg/dl (13.9 mmol/L)	2.8 ± 3.8	3.0 ± 3.6	2.7 ± 3.8	<.0001

Note. All values are shown as mean ± standard deviation.
Daytime was 06:01 AM to 11:59 PM and night-time was 12:00 AM to 06:00 AM.
Abbreviation: AHCL, advanced hybrid closed loop.
[a]Comparison between users aged ≤15 and >15 years.

time spent at TBR less than 70 and TBR less than 54 was low (for ≤15 years, <2.8% and <0.8%, respectively, and for >15 years, 2.2% and 0.6%, respectively). The mean CV of SG trended lower for the older group (33.0% vs. 35.5%). The median (IQR) values of all aforementioned data are presented in Table S2. Time spent at SG ranges for the daytime, including TIR (≤15 years: 71.1% vs. >15 years: 74.6%), differed between the age groups (P < .001) (Table 2). By contrast, TIR during the night-time was 82.2% versus 82.1%, respectively, and did not differ between the groups.

For cohort 1, there were 75.3% of users aged 15 years or younger who achieved a GMI of less than 7.0%, 69.6% who achieved a TIR of more than 70%, and 71.7% who achieved a TBR of less than 70 of less than 4.0% (Figure 2A). There were 67.5% who achieved the first two goals combined and 47.0% who achieved all three goals. Similar achievements were observed in the older group, although a greater proportion achieved the two- (74.2%) and three-metric (61.3%) treatment goals (Figure 2B). A further evaluation of system settings (i.e. glucose target and AIT) showed that more individuals in the

(A) Users ≤15 years
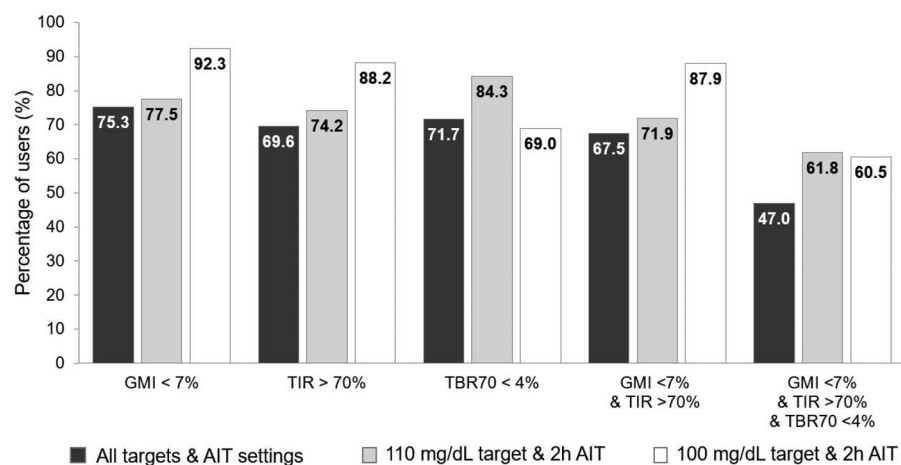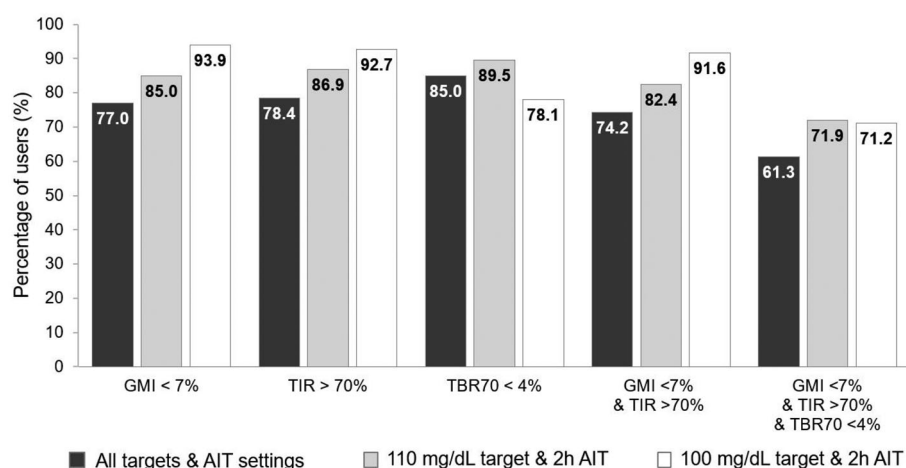

(B) Users >15 years

FIGURE 2 Percentage of users achieving treatment goals with the MiniMed 780G system and optimized settings (cohort 1). The percentage of real-world users aged A, 15 years or younger, and B, Older than 15 years achieving each treatment goal (GMI of <7%, TIR of >70% and TBR70 of <4%) and a combination of the treatment goals are shown when the 100 mg/dl (5.6 mmol/L) or 110 mg/dl (6.1 mmol/L) glucose target was used with the 2 hours AIT setting. Analyses are based on individuals who used the specified glucose target and AIT setting 90% or more of the time. AIT, active insulin time; GMI, glucose management indicator; TBR70, time below range (<70 mg/dl [<3.9 mmol/L]); TIR, time in range (70-80 mg/dl [3.9-18 mmol/L])

TABLE 3 MiniMed 780G system insulin delivered post-AHCL initiation (cohort 1)

	All users	Users ≤15 y	Users >15 y	P^a
Total daily dose of insulin, U	45.1 ± 22.8	39.0 ± 21.2	47.4 ± 23.0	<.0001
System-initiated insulin, U (% of TDD)	25.5 ± 14.9 (56.1 ± 11.0)	21.0 ± 12.7 (53.3 ± 9.6)	27.1 ± 15.2 (57.0 ± 11.3)	<.0001
Basal, U (% of TDD)	19.1 ± 10.8 (42.2 ± 8.2)	15.1 ± 8.8 (38.3 ± 6.1)	20.5 ± 11.0 (43.5 ± 8.3)	<.0001
Auto correction, U (% of TDD)	6.4 ± 5.0 (13.9 ± 6.0)	6.0 ± 4.4 (15.0 ± 5.7)	6.6 ± 5.1 (13.5 ± 6.1)	<.0001
User-initiated bolus insulin, U (% of TDD)	19.5 ± 10.6 (43.9 ± 11.0)	18.0 ± 10.2 (46.7 ± 9.6)	20.2 ± 10.7 (43.0 ± 11.3)	<.0001
User-initiated boluses per day, n	5.3 ± 2.0	6.0 ± 2.0	5.1 ± 1.9	<.0001

Note. All values are shown as mean ± standard deviation.
Abbreviations: AHCL, advanced hybrid closed loop; TDD, total daily dose.
[a]Comparison between users aged ≤15 and >15 years.

younger group achieved the treatment goals when using either the lower 100 or 110 mg/dl glucose target with the 2 hours AIT (Figure 2A). The older users also experienced better outcomes with the aforementioned settings (Figure 2B). The number of users (i.e. all those aged ≤15 years and those aged >15 years) who used each glucose target and at each AIT setting, in addition to the resulting GMI, TIR and TBR less than 70 achieved, are shown in Table S3.

The mean total daily dose (TDD) of users aged 15 years or younger was 39.0 ± 21.2 units, of which 15.1 ± 8.8 units (38% of TDD) were automated basal and 6.0 ± 4.4 units (15% of TDD and 25% of total boluses) were auto corrections (Table 3). These users self-administered a total of 18.0 ± 10.2 units of insulin per day. Compared with younger users, the older group had a higher proportion of basal insulin (43.5% ± 8.3% vs. 38.3% ± 6.1%, P < .0001) and a lower
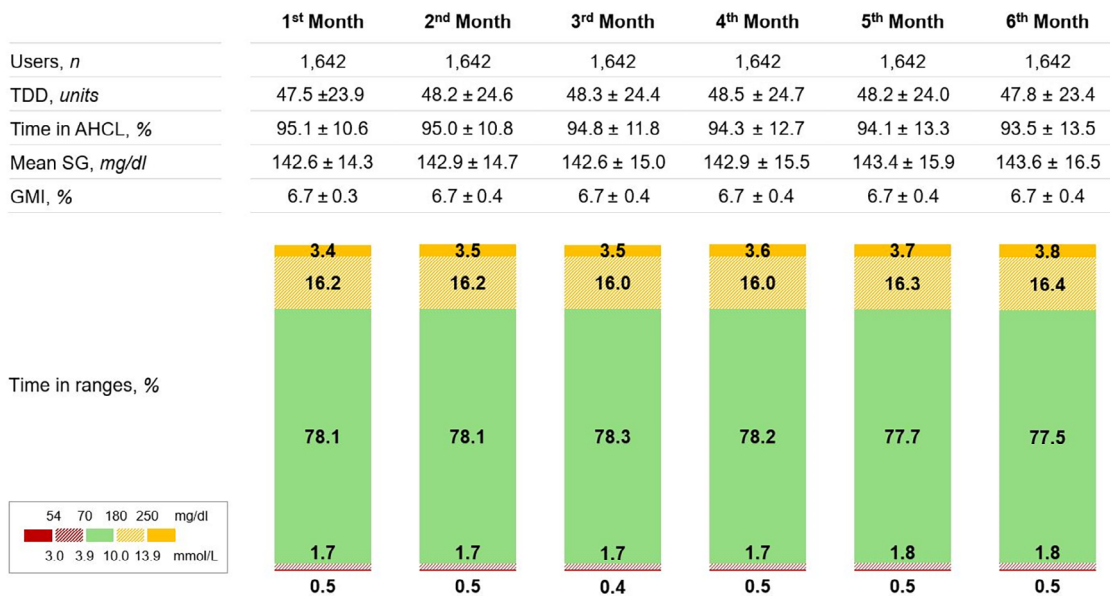
(A) Users ≤15 years

	1st Month	2nd Month	3rd Month	4th Month	5th Month	6th Month
Users, n	790	790	790	790	790	790
TDD, units	36.2 ± 20.7	37.0 ± 20.7	37.4 ± 20.4	38.1 ± 20.7	38.1 ± 20.2	38.4 ± 20.2
Time in AHCL, %	94.8 ± 11.2	94.9 ± 11.6	95.7 ± 10.1	95.3 ± 10.1	94.8 ± 11.3	94.9 ± 10.5
Mean SG, mg/dl	142.8 ± 13.6	144.2 ± 14.5	143.9 ± 14.5	144.7 ± 14.4	144.9 ± 14.7	145.9 ± 15.1
GMI, %	6.7 ± 0.3	6.8 ± 0.3	6.8 ± 0.3	6.8 ± 0.3	6.8 ± 0.4	6.8 ± 0.4

Time in ranges, %

	1st Month	2nd Month	3rd Month	4th Month	5th Month	6th Month
>250	4.7	4.9	4.9	5.1	5.2	5.4
180–250	16.8	17.3	17.1	17.4	17.3	17.8
70–180	75.3	74.8	75.0	74.5	74.3	73.9
54–70	2.5	2.3	2.4	2.4	2.4	2.3
<54	0.7	0.6	0.6	0.6	0.7	0.6

Legend: 54 70 180 250 mg/dl — 3.0 3.9 10.0 13.9 mmol/L

(B) Users >15 years

	1st Month	2nd Month	3rd Month	4th Month	5th Month	6th Month
Users, n	1,642	1,642	1,642	1,642	1,642	1,642
TDD, units	47.5 ±23.9	48.2 ± 24.6	48.3 ± 24.4	48.5 ± 24.7	48.2 ± 24.0	47.8 ± 23.4
Time in AHCL, %	95.1 ± 10.6	95.0 ± 10.8	94.8 ± 11.8	94.3 ± 12.7	94.1 ± 13.3	93.5 ± 13.5
Mean SG, mg/dl	142.6 ± 14.3	142.9 ± 14.7	142.6 ± 15.0	142.9 ± 15.5	143.4 ± 15.9	143.6 ± 16.5
GMI, %	6.7 ± 0.3	6.7 ± 0.4	6.7 ± 0.4	6.7 ± 0.4	6.7 ± 0.4	6.7 ± 0.4

Time in ranges, %

	1st Month	2nd Month	3rd Month	4th Month	5th Month	6th Month
>250	3.4	3.5	3.5	3.6	3.7	3.8
180–250	16.2	16.2	16.0	16.0	16.3	16.4
70–180	78.1	78.1	78.3	78.2	77.7	77.5
54–70	1.7	1.7	1.7	1.7	1.8	1.8
<54	0.5	0.5	0.4	0.5	0.5	0.5

Legend: 54 70 180 250 mg/dl — 3.0 3.9 10.0 13.9 mmol/L

FIGURE 3 Performance of the MiniMed 780G system over 6 months (cohort 2). The total daily dose of insulin, percentage of time in AHCL and glycaemic outcomes are shown for users aged A, 15 years or younger, and B, Older than 15 years who had 10 or more days of SG data in each of the 6 months following AHCL initiation. AHCL, advanced hybrid closed loop; GMI, glucose management indicator; SG, sensor glucose; TDD, total daily dose

proportion of self-administered insulin (43.0% ± 11.3% vs. 46.7% ± 9.6%, P < .0001), with a lower number of daily insulin boluses (5.1 ± 1.9 vs. 6.0 ± 2.0, P < .0001); auto correction boluses represented 13.5% of TDD and 24.6% of total bolus insulin.

To visualize system performance across real-world users from the different countries, a similar analysis of glycaemic outcomes and the proportion achieving a GMI of less than 7% and TIR of more than 70% treatment goals was performed per country (Figure S2). Among the nine countries having at least 100 users aged 15 years or younger,

the mean GMI ranged from 6.5% to 7.0%, TIR ranged from 68.9% to 82.0%, and TBR less than 70 ranged from 2.6% to 4.9% (Figure S2A). There were 12 countries with at least 100 users aged older than 15 years for whom GMI ranged from 6.6% to 7.0%, TIR ranged from 71.4% to 79.8%, and TBR less than 70 ranged from 1.4% to 2.8% (Figure S2B). For the 16 countries that comprised all users, GMI ranged from 6.6% to 7.0%, TIR from 70.1% to 81.2%, and TBR less than 70 from 1.3% to 2.6% (Figure S2C). The overall percentage achieving a GMI of less than 7% and TIR of more than 70% was
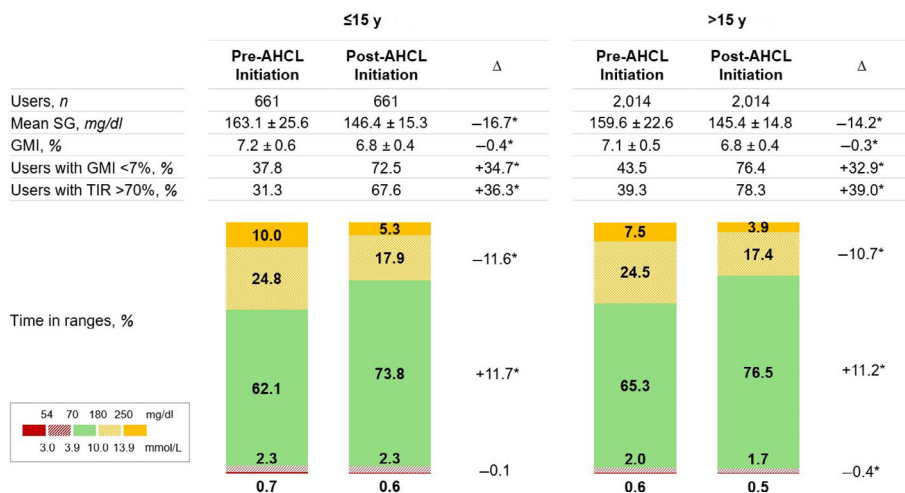
	≤15 y			>15 y		
	Pre-AHCL Initiation	Post-AHCL Initiation	Δ	Pre-AHCL Initiation	Post-AHCL Initiation	Δ
Users, *n*	661	661		2,014	2,014	
Mean SG, *mg/dl*	163.1 ± 25.6	146.4 ± 15.3	−16.7*	159.6 ± 22.6	145.4 ± 14.8	−14.2*
GMI, %	7.2 ± 0.6	6.8 ± 0.4	−0.4*	7.1 ± 0.5	6.8 ± 0.4	−0.3*
Users with GMI <7%, %	37.8	72.5	+34.7*	43.5	76.4	+32.9*
Users with TIR >70%, %	31.3	67.6	+36.3*	39.3	78.3	+39.0*

FIGURE 4 MiniMed 780G system performance pre- and post-AHCL initiation (cohort 3). The glycaemic outcomes and proportion of users achieving treatment goals (GMI of <7.0% and TIR of >70%) are shown for those aged 15 years or younger and older than 15 years who had at least 10 days of SG data pre- and post-AHCL initiation. The asterisk (*) indicates *P* < .001 for the comparison between pre-AHCL initiation and post-AHCL. AHCL, advanced hybrid closed loop; GMI, glucose management indicator; SG, sensor glucose; TIR, time in range

75.3% and 69.6%, respectively, for the younger group; 77.0% and 78.4%, respectively, for the older group; and 76.4% and 76.0%, respectively, for all users.

3.2 | MiniMed 780G system performance over 6 months (cohort 2)

The sustainability of MiniMed 780G performance across 6 months post-AHCL initiation showed that users aged 15 years or younger (N = 790) had a GMI of 6.7% ± 0.3% within the first month that was 6.8% ± 0.4% by the sixth month (Figure 3A). Their averaged TIR was 75.3% 1 month after initiation, which remained 73.9% or higher over the 6 months. Users aged older than 15 years (N = 1642) had a GMI of 6.7% ± 0.3% 1 month after initiation, which remained unchanged over the 6 months (Figure 3B). Their TIR in the first month was 78.1% and remained 77.5% or higher over the 6 months. The glycaemic outcomes of all real-world users over the 6-month period of system use are shown in Figure S3.

3.3 | Impact of AHCL initiation comparison (cohort 3)

There were 2977 users within cohort 3 who had at least 10 days of SG data both pre- and post-AHCL initiation (Figure 4). The mean SG of the group aged 15 years or younger significantly decreased by 16.7 ± 18.5 mg/dl (*P* < .0001) after AHCL initiation. Statistically significant improvement was also observed in their mean GMI, TIR and TAR more than 180 (*P* < .0001 for all, compared with pre-AHCL initiation). There was no change in TBR less than 70 or TBR less than 54. There were 2014 users aged older than 15 years for whom the comparison pre- and post-AHCL initiation resulted in similarly improved outcomes. However, their TBR less than 70 significantly decreased from 2.6% ± 2.7% to 2.2% ± 1.9% (*P* < .0001).

Figure 4 also shows that the proportion of users aged 15 years or younger who achieved the glycaemic treatment goal of GMI less than

7.0% and TIR of more than 70% was 1.9 and 2.2 times greater, respectively, after initiating AHCL (*P* < .001 for both). Similar improvements were observed in the older users, where those achieving GMI and TIR goals were 1.8 and 2.0 times greater, respectively, after AHCL initiation (*P* < .0001 for both). The cumulative distributions of users achieving GMI and TIR goals before and after AHCL initiation, for each age group and all users, are shown in Figure S4.

The insulin delivered before and after AHCL initiation is shown in Table S4. The mean TDD of younger users increased significantly by 13.4% (from 30.5 ± 18.5 units to 34.6 ± 19.8 units, *P* < .0001). This increase appeared primarily driven by auto corrections that averaged 5.4 ± 4.0 units (15.0% of TDD and 25.5% of total boluses) of insulin per day. The user-initiated boluses decreased in both number and amount of insulin administered (Table S4). Insulin delivery patterns post-AHCL initiation were similar in adult users.

4 | DISCUSSION

The expanding clinical use of the MiniMed 780G system enables outcomes analysis of a greater number of users in real-world settings. In this report we analysed the data from 3211 users who reported their age as 15 years or younger and compared their achievements with those of 8874 users who reported to be aged older than 15 years. After initiating AHCL for the first time, younger users achieved a TIR of 73.9% and a GMI of 6.8%, while spending 92.7% of time in AHCL, which mirrored the outcomes of the older users with a 76.5% TIR, 6.8% GMI and 92.3% of time spent in AHCL. In addition, the improvement observed from open-loop use by the younger group (+11.7% TIR) was similar to that observed in older users (+11.2% TIR). Also, the majority of users aged 15 years or younger achieved the target of GMI less than 7.0% and TIR less than 70% (75.3% and 69.6%, respectively), as did the older users (77.0% and 78.4%, respectively). Differences in glycaemic control between both age groups were apparent during the daytime, where the TIR was 71.1% and 74.6% for the younger and older users, respectively (*P* < .0001), while night-time TIR was equivalent. The daytime versus night-time results may be related

to differences in eating and activity between the age groups. Previous research reports that hypoglycaemia and its association with glucose variability appears to be age-dependent,[31] and we observed this in the younger group with higher CV (36.7% vs. 33.2%) and greater TBR less than 70 (3.2% vs. 2.3%), when compared with the older group.

Users aged 15 years or younger in the present study who used an AIT of 2 hours and a glucose target of 100 mg/dl (5.6 mmol/L) achieved the highest glycaemic control: a GMI of 6.6% and a TIR of 78.9%. Nevertheless, these settings were associated with a TBR of less than 70 of 3.6% and, although below the recommended goal of 4%, the glucose target of 110 mg/dl (6.1 mmol/L) provided similar achievements (GMI of 6.7% and a TIR of 76.5%) with a TBR of less than 70 of only 2.7%. Therefore, users aged 15 years or younger may benefit from initiating AHCL with an AIT of 2 hours and a glucose target of 110 mg/dl (6.1 mmol/L) and, afterwards, reducing it to 100 mg/dl (5.6 mmol/L) if there are no concerns regarding hypoglycaemia.

The present study's longitudinal analysis of younger users showed a substantial amount of time in AHCL and sensor use was associated with improved glycaemic control within the first month after AHCL initiation. GMI and time spent in range were maintained for the 6-month observation period, which has previously been reported for other age groups using automated insulin delivery systems.[23,27,32]

Partitioned insulin administration between system-initiated and user-initiated insulin delivery sheds some light on why younger MiniMed 780G system users successfully achieved the aforementioned therapeutic goals. Table S4 presents the well-known practice of lower basal rate settings in youth (40.1% of TDD), in comparison with older individuals (48.3% of TDD), during open-loop use (pre-AHCL). This practice has long since been attributed to the aim of lowering hypoglycaemia risk in paediatric T1D and compensating with more frequent meal and correction boluses. By contrast, adults have been traditionally dosed with a 1:1 ratio[33] between basal and meal bolus insulin. Following AHCL initiation, both cohorts were closer to a 1:1 ratio, with system-initiated insulin delivery in the younger group mirroring that in adults (53.5% and 57.6% driven by the algorithm, in youth and adults, respectively). Both age groups had approximately the same amount of auto correction bolus as a percentage of all boluses (25.0% and 24.6%, respectively). These results are similar to those reported for the system in Collyns et al. (25.1%)[26] and Carlson et al. (22.0%),[21] yet substantially less than that observed in the FLAIR trial (36%),[25] although a direct comparison between these studies is limited because of differences in participants' ages. The amount of automated bolus, as a percentage of total daily insulin dose, or all boluses administered per day, provide an important and sensitive view for the healthcare provider in that it may highlight behavioural issues that prevent the best glycaemic outcomes. These issues may include failure to bolus before meals or omitting meal boluses entirely. Alternatively, if meal bolus delivery is mostly on time, this metric may suggest the need to intensify the insulin-to-carbohydrate ratio. Ideally, the percentage of automated correction boluses should be in the low-to-mid 20% range.

A recent study of real-world paediatric (mean ± SD of 11 ± 1.9 years) use of another automated insulin delivery therapy showed a median of 67% (IQR = 60%-74%) TIR, 0.06% (IQR = 0.06%-2.1%) TBR less than 70 and 31% (IQR = 24%-39%) TAR more than 180.[34] In our analysis, real-world paediatric users of the MiniMed 780G system achieved a higher median TIR of 74.3% (IQR = 68.7%-79.6%) with a lower TAR of more than 180 of 22.3% (IQR = 16.7%-28.4%), while median TBR of less than 70 was higher at 2.7% (IQR = 1.5%-4.3%) (Table S2). The improvements in paediatric TIR, TBR and TAR afforded by automated insulin delivery therapies are important, as HbA1c has been shown to increase in adolescence,[10] which spans the age ranges of the two cohorts in the present study. However, data privacy regulations precluded a more granular understanding of the effects of adolescence on glycaemic control in this real-world study.

The strengths of our analysis include the large number of users from numerous countries and the single selection criterion of having at least 10 days of sensor data in each period analysed. This provides a fair representation of the expectations people may have when using the MiniMed 780G system. The limitations of the analysis include the lack of demographic data, medical history (including HbA1c) and users' duration of diabetes, which are not available in the CareLink software platform. While there is a clinically important difference between HbA1c and the GMI,[35] the latter provides a validated correlation between CGM metrics and managed glycaemia over time.[36] As GMI has become a CGM-derived standard for glycaemic control, it was used as a surrogate for HbA1c for determining treatment goal achievement.

It is important to add that there are no true baseline data pertaining to the users' previous therapy, which prevents proper assessment of the full clinical benefits of AHCL technology. Our analysis is also based on the age voluntarily reported by users (which could not be verified) and is limited to a large range because of privacy regulations. Nevertheless, a sensitivity analysis showed that the two groups defined by the reported ages indeed differ in their TDD, providing support that they represent distinct age groups. Additionally, 90% of system users who uploaded data to the CareLink platform provided their consent for data aggregation and analysis, eliminating bias of voluntary agreement on data sharing. The MiniMed 780G system also performs daily automatic downloads that do not require user action, which further minimizes selection bias.

In conclusion, youth aged 15 years or younger with T1D using the MiniMed 780G system in real-world conditions achieved international consensus-recommended glycaemic control, mirroring the achievements of the older population (aged ≥15 years) using the system. Thus, it is apparent that more stringent glycaemic control is obtainable for a broad age range of individuals with T1D, with time spent below range remaining within the recommended safe threshold.

AUTHOR CONTRIBUTIONS

data; critically reviewed, drafted or edited the manuscript; and approved the final work for submission. AA and JDS contributed equally to the development of the manuscript.

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DATA AVAILABILITY STATEMENT

The data supporting the findings of this study are available in the manuscript and supplemental materials of this article.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.