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Time in Tight Glucose Range in Type 1 Diabetes: Predictive Factors and Achievable Targets in Real-World Users of the MiniMed 780G System

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Time in Tight Range: Predictive Factors and Achievable Targets in Real-World Users of the MiniMed 780G System

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Some have proposed that the time spent in the **tight** glucose range of 70–140 mg/dL (time in **tight** range, or **TITR**) may better reflect the continuous glucose monitoring metric of euglycemia. This study demonstrated a high TITR in 13,812 real-world users of the MiniMed 780G system (>48%). Consistent use of optimal settings (i.e., glucose target of 100 mg/dL and active insulin time of 2 h) further improved TITR (>56%). A TITR target >50% is our suggested treatment goal.

	≤15 years			>15 years		
	Baseline	Post-AHCL		Baseline	Post-AHCL	
		Overall	Optimal settings		Overall	Optimal settings
Users, *n*	3,762	3,762	205	9,699	9,699	510
Time in AHCL, %		90.9 ± 15.9	96.0 ± 7.4		90.0 ± 16.0	93.5 ± 11.8
Mean SG, mg/dL	167.6 ± 26.4	151.0 ± 15.8	139.4 ± 12.3	164.2 ± 24.0	150.0 ± 16.5	139.2 ± 11.8
SD of SG, mg/dL	60.5 ± 13.1	55.9 ± 10.9	48.8 ± 9.4	55.7 ± 11.5	50.1 ± 9.8	45.2 ± 8.5
Mean GMI, %	7.3 ± 0.6	6.9 ± 0.4	6.6 ± 0.3	7.2 ± 0.6	6.9 ± 0.4	6.6 ± 0.3
Time in tight range (70–140 mg/dL), %	37.2 ± 14.3	48.9 ± 9.6	56.7 ± 9.4	37.2 ± 13.6	48.8 ± 10.9	57.0 ± 9.1
Time in range (70–180 mg/dL), %	59.9 ± 15.2	71.2 ± 9.4	78.3 ± 7.8	62.3 ± 14.7	73.9 ± 10.2	80.6 ± 7.5
Time in range, %	11.9 25.3 22.7 37.2 2.2 0.6	6.8 19.2 22.3 48.9 2.2 0.6	3.6 15.1 21.5 56.7 2.4 0.6	9.3 25.9 25.0 37.2 2.0 0.6	5.2 18.9 25.1 48.8 1.6 0.4	2.8 14.4 23.6 57.0 1.8 0.4

54 70 140 180 250 mg/dL
3.0 3.9 7.8 10.0 13.9 mmol/L

Glycemic control at baseline and post–advanced hybrid closed-loop (AHCL) initiation. Values are shown as mean or mean ± SD. The figure shows end points at baseline (before AHCL) and post-AHCL (overall cohort and optimal settings cohort). For the optimal settings cohort, individuals used a glucose target of 100 mg/dL and an active insulin time of 2 h for ≥95% of the time. GMI, glucose management indicator; SG, sensor glucose.

ARTICLE HIGHLIGHTS

- **Why did we undertake this study?**
  It has been suggested that time in tight range (TITR; 70–140 mg/dL) may better reflect the continuous glucose monitoring (CGM) metric of euglycemia.
- **What is the specific question(s) we wanted to answer?**
  We studied TITR in real-world users of the MiniMed 780G system (MM780G).
- **What did we find?**
  This study demonstrates high mean TITR in 13,461 real-world users of MM780G (48%). Consistent use of optimal settings (glucose target 100 mg/dL and active insulin time 2 h) further improved TITR (56%). A TITR target 50% is our suggested treatment goal based on associations with glucose management indicators.
- **What are the implications of our findings?**
  These findings are expected to be used in discussions regarding the international implementation of this new metric and the setting of TITR targets.

Time in Tight Glucose Range in Type 1 Diabetes: Predictive Factors and Achievable Targets in Real-World Users of the MiniMed 780G System

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ORIGINAL ARTICLE

OBJECTIVE

We studied time in tight range (TITR) (70–140 mg/dL) in real-world users of the MiniMed 780G system (MM780G).

RESEARCH DESIGN AND METHODS

CareLink Personal data were extracted (August 2020 to December 2022) to examine TITR and its relationship with time in range (TIR; 70–180 mg/dL), factors predicting higher TITR, and which TITR target is a reasonable treatment goal.

RESULTS

The 13,461 users (3,762 age ≤15 years and 9,699 age >15 years) showed an average TITR of 48.9% in those age ≤15 years and 48.8% in the older group (vs. TIR 71.2% and 73.9%, respectively). Consistent use of a glucose target (GT) of 100 mg/dL and active insulin time (AIT) of 2 h were the most relevant factors predicting higher TITR ($P < 0.0001$). In users consistently applying these optimal settings, TITR was 56.7% in those age ≤15 years and 57.0% in the older group, and the relative impact of these settings on TITR was 60% and 86% greater than that on TIR, respectively. TITRs of ∼45% (age ≤15 years 46.3% and older group 45.4%), ∼50% (50.7% and 50.7%) and ∼55% (56.4% and 58.0%) were best associated with glucose management indicators <7.0%, <6.8%, and <6.5%, respectively. TITRs of >45%, >50%, and >55% were achieved in 91%, 74%, and 55% of those age ≤15 years and 93%, 81%, and 57% of older group users, respectively, at optimal settings.

CONCLUSIONS

This study demonstrates that *1*) mean TIR is high with a high mean TITR in MM780G users (>48%), *2*) consistent use of optimal GT/AIT improves TITR (>56%), *3*) the impact of these settings on TITR is larger than on TIR, and *4*) a TITR target >50% is our suggested treatment goal.

Continuous glucose monitoring (CGM) is currently the most advanced method for monitoring glucose levels in the treatment of type 1 diabetes (T1D) (1) and is now also used to monitor individuals with type 2 diabetes (T2D) receiving insulin therapy (2). CGM data sets have allowed for the introduction of new glycemic metrics

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See accompanying article, p. 782.

and reassessment of the limitations of previous measures of glycemia. The concept of time spent in specific glucose ranges, as derived from CGM measurements, has emerged as a measure that benefits both individuals living with diabetes and health care professionals (3). In contrast to the conventional measure of HbA_{1c}, time in range (TIR) provides a measure of dispersion; monitoring of TIR enables differentiation between individuals with high and low variability in glucose levels even if their HbA_{1c} values are similar (4). Although it remains uncertain whether TIR measures can replace HbA_{1c} in the long term (HbA_{1c} is the standard for assessing long-term diabetes-related complications risk), they are already predominant in the management of T1D, with growing use in T2D.

Current glucose ranges and treatment goals were determined by consensus efforts to align with the definitions used before the introduction of CGM. These goals were mainly not based on clinical or participant-related outcomes. As a result, the therapeutic goal of an HbA_{1c} of 7% was equated to spending 70% of time within the sensor glucose (SG) range of 70–180 mg/dL (i.e., TIR). Since the 2019 consensus report (5), discussions have taken place regarding the need for adjustments to these ranges and goals based on new observations. Studies in children and adults (excluding pregnancy), for instance, have shown that individuals without diabetes spend 96% of their time between 70 and 140 mg/dL (6). They rarely reach glucose levels between 140 and 180 mg/dL, and if they do, it is only for a short time interval after meals (7). Therefore, some have proposed that time spent in the tight glucose range of 70–140 mg/dL (i.e., time in tight range [TITR]) may better reflect the CGM metric of euglycemia (6).

Progress in automated insulin delivery technology has improved glucose level management substantially compared with earlier methods, such as multiple daily injections and nonconnected CGM. For instance, randomized controlled studies (8,9) and real-world evidence (10,11) have demonstrated that users of the MiniMed 780G (MM780G) advanced hybrid closed-loop (AHCL) system can achieve an average TIR >80% without increased risk of hypoglycemia, when users consistently use optimal system settings. Other systems have also reported good TIR (12,13). Here, we report on a comprehensive study of TITR in real-world users of the MM780G system with T1D. The threefold aim of this study was to *1*) calculate TITR and explore its relationship with TIR, *2*) identify factors that predict a higher TITR, and *3*) explore TITR targets that can serve as treatment goals for individuals living with T1D.

RESEARCH DESIGN AND METHODS

Design

This was a retrospective observational analysis using real-world anonymized data obtained from voluntary uploads from individuals living with T1D in Europe, the Middle East, and Africa (EMEA). Data were collected through the CareLink Personal platform for individuals using the MM780G system. The analyses consisted of three parts. Firstly, we calculated TITR and explored its relationship with TIR; secondly, we used predictive modeling to assess factors predicting a high TITR; and thirdly, we explored TITR targets that can be reasonably achieved and serve as goals in the treatment of individuals living with T1D. This study followed Strengthening the Reporting of Observational Studies in Epidemiology guidelines.

Data Source and Data

CareLink Personal is a software program that collects information directly from MiniMed systems and can be used to generate reports and monitor disease progress. In terms of data representativeness, CareLink Personal contains data from all users who have created an account. In EMEA, individuals living with T1D who start using the MM780G system undergo device training by certified diabetes educators (or Medtronic personnel), and creating an account is part of the training. The conservative estimate is that at least 90% of the EMEA MM780G system users have an account. Most users (~92%) consented for their data to be used for research. In terms of data quality, device data are collected through periodic data uploads. Users can upload either automatically (every night), manually, or at download stations in clinics. Because the MM780G system has a 3-month data storage capacity, upload gaps shorter than 3 months do not lead to missing data. Apart from device data, CareLink Personal also contains self-reported data on sex, age group (≤15, 16–28, 29–42, 43–55, or ≥56 years), and diabetes type.

To be eligible, individuals living with T1D were required to have a registered CareLink Personal account in EMEA and provide consent for data use. Users also had to have ≥10 days of SG data in the period after the AHCL system was enabled for the first time (post-AHCL) (5) as well as in the period before (baseline).

CGM data uploaded between August 2020 and December 2022 were extracted from CareLink Personal. All available CGM data from all eligible users were used, regardless of whether the system was in AHCL or open loop. The primary end point was the mean percentage of time with SG levels between 70 and 140 mg/dL (3.9–7.8 mmol/L; TITR). Other end points were metrics of glycemic control, system characteristics, and metrics of insulin use. The full list of end points is included in Supplementary Table 1.

Part 1: Calculating TITR and Exploring Its Relationship With TIR

In this part of the study, we calculated TITR and explored its relationship with TIR. CGM end points, including TITR and TIR, were calculated for baseline and the post-AHCL period and statistically compared using the Student paired *t* test (when normality assumption was met) or Wilcoxon signed rank test (otherwise). Furthermore, a correlation analysis was performed between TITR and TIR, and the Pearson correlation coefficient was calculated. Finally, to characterize improvements in TITR and time below range post-AHCL, users were categorized into quartiles based on the average baseline TITR, and a figure was composed showing these outcomes in each quartile post-AHCL.

Part 2: Identifying Predictors of High TITR

In this part, we identified factors predicting a high TITR post-AHCL using univariate linear regression analyses, followed by multivariable linear regression analyses. TITR post-AHCL was used as a continuous dependent variable, whereas other factors were used as independent variables. Included factors are listed in Supplementary Table 1. To assess the effect of glucose target (GT) and active insulin time (AIT) settings, those using a specific GT or AIT ≥95% of the time were grouped into that setting. Those not using any particular setting ≥95% of the time were grouped into the mix category.

Factors with $P < 0.2$ in the univariate analysis were retained for additional analyses, and correlations between these factors were assessed. To avoid multicollinearity, in cases of high correlation, some factors were not included in the multivariable model. Users' weights were not available, so insulin dose units per kilogram could not be calculated. To account for this, the percentages of basal, bolus, and autocorrective bolus insulin doses (of the total daily insulin dose) were given priority at the stage of selecting among correlated factors. The multivariable model was selected by backward selection, where the most insignificant factors were eliminated one at a time until a parsimonious model with significant factors (two-sided $P < 0.05$) was identified. The multivariable model was adjusted for baseline TITR, because baseline glycemic control is an important contributor to post-AHCL glycemic control in the MM780G system (11). When compared with lasso regression, this model was robust against variable selection based on statistical significance.

Some of the predictive factors in the final model were modifiable, and a subcohort was formed with users who had been applying these predictive modifiable factors consistently (optimal settings cohort including users spending ≥95% of the time with optimal GT and ≥95% of the time with optimal AIT). Another subcohort was formed with users not applying these optimal settings (nonoptimal settings cohort). TITR and TIR were calculated for both cohorts, as was the relative contribution of optimal settings to the improved TITR and TIR post-AHCL.

Part 3: Exploring Achievable TITR Targets

In this part, we explored TITR targets that could serve as treatment goals for individuals living with T1D. Firstly, we used receiver operating characteristic curves to determine the most appropriate TITR target (cutoff point) distinguishing individuals meeting or not meeting GMI targets of <7%, <6.8%, and <6.5%. The cutoff point was identified by selecting the point on the receiver operating characteristic curve closest to the top-left corner, thereby maximizing sensitivity and specificity. To avoid overfitting, a training set (random sample of 70% of the observations) and test set (remaining 30%) were used. Secondly, we applied these three TITR targets in cumulative distribution plots to illustrate the percentage of MM780G system users meeting targets.

Statistics

Means and SDs were used for continuous variables and number of users, and proportions were used for categorical variables. For statistical testing, two-sided P values <0.05 were considered significant. In the examination of predetermined comparisons, no adjustments were made for multiple testing. Analyses were conducted in SAS (version 9.4). All analyses were performed separately for two groups: users age ≤15 years (pediatric group) and those age >15 years (older group).

Data and Resource Availability

The data sets generated during and/or analyzed in the current study are available from the corresponding author upon reasonable request.

RESULTS

A total of 13,461 users (Europe 94%, Middle East 5%, and Africa 1%) from 33 EMEA countries were included, of whom 51.0%, 48.8%, and 0.2% self-reported as male, female, and undisclosed in the age ≤15 years group and 42.8%, 57.0%, and 0.2% in the older group, respectively. In terms of age, 3,762 self-reported as ≤15 years and 9,699 as older (16–28 years 26.4%, 29–42 years 29.8%, 43–55 years 26.1%, and >56 years 17.7%). The median duration of system use (post-AHCL) was 240 (25th percentile 107 and 75th percentile 414) days for those age ≤15 years and 229 (100 and 425) days for the older group.

Part 1: Calculating TITR and Exploring Its Relationship With TIR

Figure 1 shows glycemic control at baseline and post-AHCL. Compared with baseline, the mean TITR increased significantly in both the age ≤15 years and older groups, with an absolute TITR increase of 11.7% ± SD 10.8% (37.2% ± 14.3% to 48.9% ± 9.6%; $P < 0.0001$) and 11.6% ± 10.2% (37.2% ± 13.6% to 48.8% ± 10.9%; $P < 0.0001$), respectively. The increase in TIR was of roughly the same magnitude, with an absolute TIR increase of 11.3% ± 11.3% (59.9% ± 15.2% to 71.2% ± 9.4%; $P < 0.0001$) in those age ≤15 years and 11.7% ± 10.5% (62.3% ± 14.7% to 73.9% ± 10.2%; $P < 0.0001$) in the older group. Interestingly, the percent time in the 140–180 mg/dL range was maintained post-AHCL in both groups (∼22% to ∼25%). Additionally, the mean GMI decreased by 0.4% ± 0.5% (7.3% ± 0.6% to 6.9% ± 0.4%; $P < 0.0001$) in those age ≤15 years and 0.3% ± 0.4% (7.2% ± 0.6% to 6.9% ± 0.4%; $P < 0.0001$) in the older group. TITR post-AHCL and TIR post-AHCL showed a high but nonlinear correlation ($r = 0.94$).

Figure 2*A* and *B* shows the average TITR, time below 70 mg/dL (TB70), and time below 54 mg/dL (TB54) at baseline and post-AHCL, grouped by quartile of baseline TITR. The three quartiles representing the lowest baseline TITR visually showed substantial improvements in TITR post-AHCL in both age groups. For the quartile that was best controlled at baseline, TITR remained high. In terms of safety, TB70 and TB54 decreased for most quartiles and fell well within the international hypoglycemia targets in both age groups. Additionally, the figure shows that the large variability in baseline TITR decreased post-AHCL, as did the variability in TB70 and TB54.

Part 2: Identifying Predictors of High TITR

Supplementary Table 1 summarizes the univariate and multivariable analyses. Baseline TITR, percentage of time in AHCL, use of GT of 100 mg/dL, use of AIT of 2 h, use of two to three daily distinct insulin-to-carbohydrate ratios, and daily number of self-monitoring of blood glucose measurements were positively associated with TITR post-AHCL in the multivariable analyses for both age groups. In the older group, daily number of user-initiated boluses was also positively associated. Larger values of these factors predicted a larger mean TITR post-AHCL. Factors inversely associated with TITR post-AHCL in both age groups included percentage of daily basal dose (of the total daily insulin dose), daily autocorrective doses, number of daily AHCL exits triggered by the system, and number of daily alarms. In the older group, an additional inversely associated factor was number of daily AHCL exits triggered by the user. Larger values predicted a lower mean TITR post-AHCL.

Modifiable factors that predicted the largest mean TITR post-AHCL were GT of 100 mg/dL and AIT of 2 h. In the older group, GT of 100 mg/dL led to an absolute increase in TITR of 2.89 percentage points

	≤15 years			>15 years		
	Baseline	Post-AHCL		Baseline	Post-AHCL	
		Overall	Optimal Settings		Overall	Optimal Settings
Users, n	3,762	3,762	205	9,699	9,699	510
Time in AHCL, %		90.9 ± 15.9	96.0 ± 7.4		90.0 ± 16.0	93.5 ± 11.8
Mean SG, mg/dL	167.6 ± 26.4	151.0 ± 15.8	139.4 ± 12.3	164.2 ± 24.0	150.0 ± 16.5	139.2 ± 11.8
Standard Deviation of SG, mg/dL	60.5 ± 13.1	55.9 ± 10.9	48.8 ± 9.4	55.7 ± 11.5	50.1 ± 9.8	45.2 ± 8.5
Mean GMI, %	7.3 ± 0.6	6.9 ± 0.4	6.6 ± 0.3	7.2 ± 0.6	6.9 ± 0.4	6.6 ± 0.3
Time in tight range (70-140 mg/dL), %	37.2 ± 14.3	48.9 ± 9.6	56.7 ± 9.4	37.2 ± 13.6	48.8 ± 10.9	57.0 ± 9.1
Time in range (70-180 mg/dL), %	59.9 ± 15.2	71.2 ± 9.4	78.3 ± 7.8	62.3 ± 14.7	73.9 ± 10.2	80.6 ± 7.5
Time in ranges, %	11.9 25.3 22.7 37.2 2.2 0.6	6.8 19.2 22.3 48.9 2.2 0.6	3.6 15.1 21.5 56.7 2.4 0.6	9.3 25.9 25.0 37.2 2.0 0.6	5.2 18.9 25.1 48.8 1.6 0.4	2.8 14.4 23.6 57.0 1.8 0.4

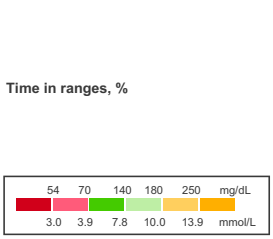

Figure 1—Glycemic control at baseline and post-AHCL initiation. Values are shown as mean or mean ± SD. The figure shows end points at baseline and post-AHCL (overall cohort and optimal settings cohort). For the optimal settings cohort, individuals used both GT of 100 mg/dL and AIT of 2 h for ≥95% of the time.

($P < 0.0001$) when compared with GT of 110 mg/dL and an increase of 6.76 percentage points ($P < 0.0001$) when compared with GT of 120–150 mg/dL. AIT of 2 h resulted in an absolute TITR increase of 2.77 percentage points ($P < 0.0001$) when compared with AIT of 2–3 h and an increase of 5.20 percentage points ($P < 0.0001$) when compared with AIT of 3–4.5 h. Similar patterns were seen in those age ≤15 years. An overview of all modifiable factors (among quartiles of baseline TITR) is presented in Supplementary Table 2.

Figure 1 shows glycemic control for the optimal settings cohort. The eligibility criteria for this cohort were based on outcomes from the multivariable analyses and were defined as users spending ≥95% of the time at a GT of 100 mg/dL and ≥95% of the time in an AIT of 2 h. TITR post-AHCL for this cohort was 56.7% ± 9.4% in those age ≤15 years and 57.0% ± 9.1% in the older group and was substantially higher when compared with the overall cohort. TIR post-AHCL was 78.3% ± 7.8% in those age ≤15 years and 80.6% ± 7.5% in the older group in the optimal settings cohort. For the nonoptimal settings cohort (not part of the figure), TITR post-AHCL was 48.5% ± 9.4% in those age ≤15 years and 48.3% ± 10.8% in the older group, and TIRs post-AHCL were 70.8% ± 9.4% and 73.5% ± 10.2%, respectively. TITR post-AHCL and TIR post-AHCL in the optimal settings cohort were larger than those in the nonoptimal settings cohort (all $P < 0.0001$). The relative impact of optimal settings on TITR post-AHCL was 60% (age ≤15 years) and 86% (older group) larger than the relative impact of optimal settings on TIR post-AHCL.

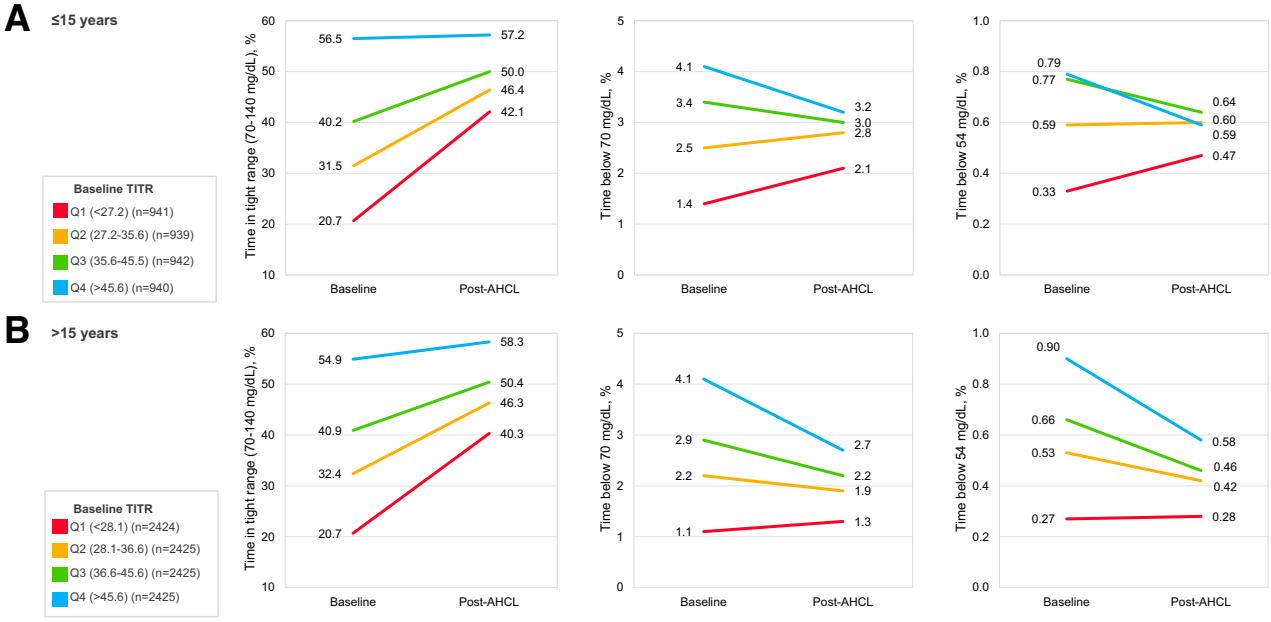

Figure 2—Glycemic control at baseline and post-AHCL initiation grouped by quartile (Q) of baseline TITR for those age ≤15 years (*A*) and the older group (*B*). The figure shows the mean percentage of TITR (70–140 mg/dL), TB70, and TB54 at baseline and post-AHCL initiation, grouped by quartile of the baseline TITR.

Part 3: Exploring Achievable TITR Targets

Table 1 shows the optimal TITR cutoff points. For those age ≤15 years, a TITR target of 46.3% best distinguished if a user met the GMI of <7.0%. For more stringent GMI targets of <6.8% and <6.5%, the TITR cutoff points were 50.7% and 56.4%, respectively. In the older group, the cutoff points were 45.4% (GMI <7.0%), 50.7% (GMI <6.8%), and 58.0% (GMI <6.5%).

Figure 3*A* and *B* shows the cumulative distribution plots and percentage of users meeting candidate TITR targets. Candidate targets were TITR >45%, >50%, and >55%, based on rounding of the above calculated cutoff points. In those age ≤15 years, the percentage of users achieving TITR >45% was 68%; TITR >50%, 45%; and TITR >55%, 24%. In the older group, these percentages were 65%, 46%, and 27%, respectively. However, focusing on the optimal settings cohort only, the percentage of users achieving these TITR targets increased substantially. In the age ≤15 years group, 91% achieved TITR >45%; 74%, TITR >50%; and 55%, TITR >55%. In the older group, these percentages were 93%, 81%, and 57%, respectively.

Table 1—Optimal TITR targets associated with GMI targets of <7%, <6.8%, and <6.5%

	Age ≤15 years		Age >15 years	
Metric	Value	95% CI	Value	95% CI
GMI <7%				
Optimal TITR target, %*	>46.3	46.2–46.8	>45.4	45.2–45.8
Sensitivity	0.93	0.9–0.94	0.93	0.92–0.94
Specificity	0.92	0.89–0.94	0.92	0.91–0.94
Accuracy	0.92	0.91–0.94	0.93	0.92–0.94
AUC	0.98		0.98	
GMI <6.8%				
Optimal TITR target, %*	>50.7	50.1–51.2	>50.7	50.2–50.7
Sensitivity	0.9	0.87–0.93	0.94	0.92–0.95
Specificity	0.9	0.88–0.92	0.93	0.92–0.94
Accuracy	0.9	0.88–0.92	0.93	0.93–0.94
AUC	0.98		0.99	
GMI <6.5%				
Optimal TITR target, %*	>56.4	56.1–58	>58.0	57.3–59
Sensitivity	0.94	0.88–0.97	0.94	0.91–0.96
Specificity	0.9	0.88–0.92	0.93	0.92–0.94
Accuracy	0.91	0.89–0.92	0.93	0.92–0.94
AUC	0.98		0.99	

Optimal TITR target and area under the curve (AUC) calculated from the training set. Sensitivity, specificity, and accuracy calculated from the test set. *70–140 mg/dL.

CONCLUSIONS

This study evaluated TITR (70–140 mg/dL) in 13,461 real-world users of the MM780G system who self-reported as having T1D. Key findings were an average TITR of 48.9% in those age ≤15 years and 48.8% in the older group. Several factors were found to increase TITR, with GT and AIT being the most relevant. When applying the optimal (modifiable) settings, defined as a GT of 100 mg/dL for ≥95% of the time and an AIT of 2 h for ≥95% of the time, TITR improved even further to 56.7% in those age ≤15 years and 57.0% in the older group. Lastly, potential TITR treatment targets were explored, and targets of ∼45%, ∼50%, and ∼55% best distinguished users meeting GMI targets of <7.0%, <6.8%, and <6.5%, respectively. TITRs of >45%, >50%, and >55% were achieved in 91%, 74%, and 55% of those age ≤15 years at optimal settings and 93%, 81%, and 57% of older users, respectively.

The initiation of AHCL therapy resulted in a large increase in the average TITR. In comparison with baseline, the mean TITR post-AHCL showed a significant increase in both age groups, with an absolute increase of 11.7% in those age ≤15 years and 11.6% in the older group. This is equivalent to spending >2.5 h per day more within tight range. The increase in TIR was of the same magnitude, with values of 11.3% and 11.6% in those age ≤15 years and the older group, respectively. Notably, the time spent between 140 and 180 mg/dL remained constant when comparing baseline with post-AHCL, with values of 22.7% and 22.3% for those age ≤15 years and 25.0% and 25.1% for the older group, respectively. This led us to speculate that the increase in TIR was primarily due to the increase in TITR. Additionally, other measures of glycemic control (e.g., GMI) showed significant improvement post-AHCL, consistent with previously published real-world evidence (10,11) and clinical studies (14–16) in T1D. Importantly, the improvements in glycemic control were achieved safely, indicated by TB70 (2.8% for those age ≤15 years and 2.0% for the older group) and TB54 (0.6% and 0.4%), which fell well within the internationally recommended targets for hypoglycemia in T1D (5).

The initiation of AHCL therapy was found to be beneficial for all groups of users, irrespective of baseline glycemic control; however, those with the poorest baseline control demonstrated the greatest TITR improvement. The study population was divided into four quartiles based on baseline TITR, and the group with the lowest baseline TITR exhibited the steepest improvement in both the age ≤15 years and older groups. Importantly, the quartile with the highest baseline TITR experienced the greatest reduction in TB70 and TB54 post-AHCL. Overall, the initiation of AHCL therapy resulted in a reduction in the variability of average TITR, TB70, and TB54.

TITR in this study exceeded the values reported in most previous studies. TITR is a relatively new metric and has been investigated in only a few trials. Reported TITR ranges in individuals living with T1D who used automated insulin delivery systems other than the MM780G system varied from 27% to 49% (17,18). However, when specifically considering the MM780G system, Seget et al. (19) found a TITR of 61.7% in children and adolescents with well-controlled disease. The underlying reason for the results from the current study as well as that by Seget et al. is potentially related to the AHCL technology; besides controlling basal insulin delivery, the MM780G system delivers autocorrective boluses. The system autocorrects to a target glucose of 120 mg/dL, and an autocorrective bolus is delivered automatically up to every 5 min if the algorithm realizes SG is

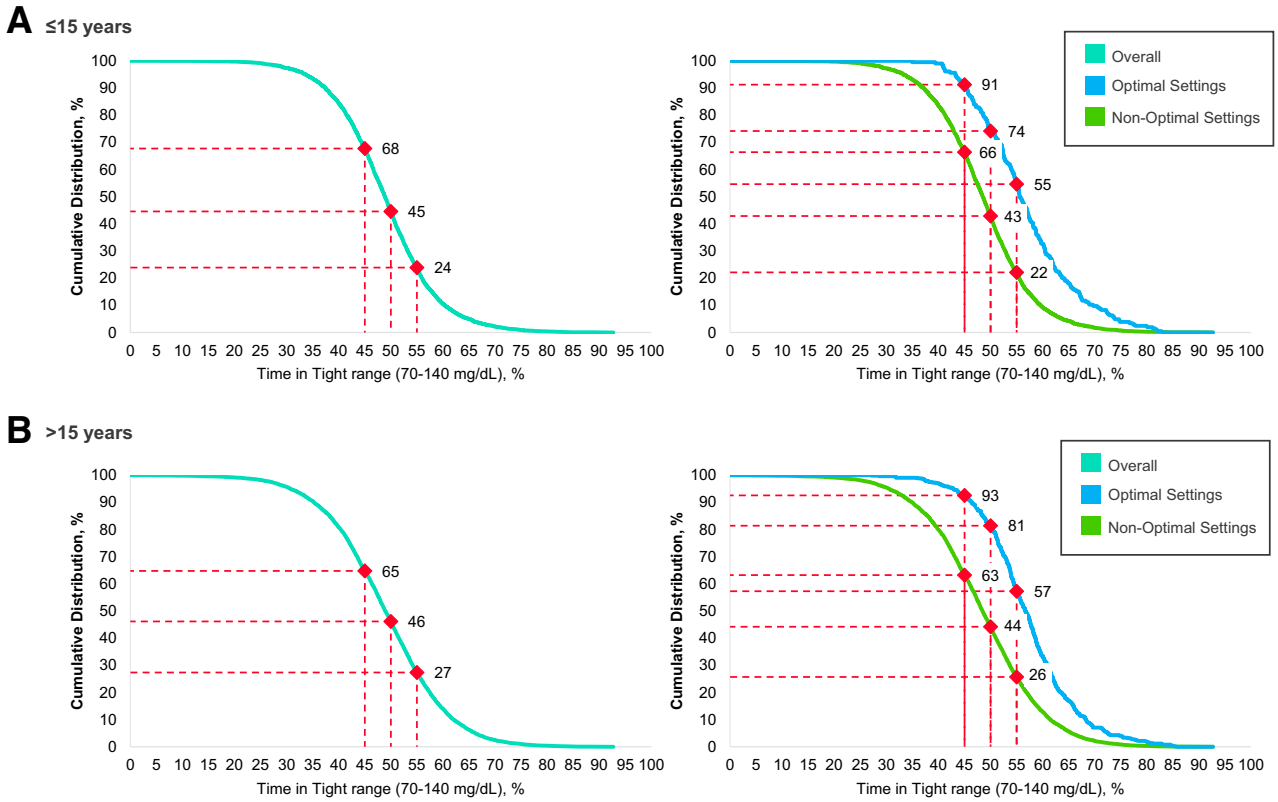

Figure 3—Cumulative distribution plots showing the percentage of users meeting the candidate TITR targets for those age ≤15 years (*A*) and the older group (*B*). The figure shows the percentages of users meeting candidate TITR targets (i.e., >45%, >50%, and >55%). Percentages are shown for the overall cohort (left) as well as the optimal and nonoptimal settings cohorts (right). For the optimal settings cohort, individuals used both GT of 100 mg/dL and AIT of 2 h for ≥95% of the time.

>120 mg/dL despite maximum basal insulin delivery (20).

Several factors were identified as predictors of TITR post-AHCL. Briefly, factors positively associated included baseline TITR, percentage of time in AHCL, use of GT of 100 mg/dL, use of AIT of 2 h, use of two to three daily distinct insulin-to-carbohydrate ratios, and daily number of self-monitoring of blood glucose measurements in both age groups. Additionally, for the older group, daily number of user-initiated bolus doses was positively associated. Conversely, factors inversely associated with high TITR post-AHCL included percentage of daily basal insulin dose of the total daily insulin dose, daily autocorrective doses, number of AHCL exits triggered by the system, and number of daily alarms in both age groups. For the older group, number of AHCL exits triggered by the user was also inversely associated. These findings align with previous research investigating predictors of high TIR in real-world users of the MM780G system (11).

Factors that can be modified by the user are of particular importance, and the most significant modifiable contributors to high TITR were maintaining a GT of 100 mg/dL and an AIT of 2 h. Consistently adhering to optimal GT resulted in an average increase of 2.3 percentage points in TITR for those age ≤15 years and 2.9 percentage points for the older group, compared with a GT of 110 mg/dL. Furthermore, compared with consistently using even higher GTs (120–150 mg/dL), the TITR gain exceeded 6 percentage points. Similarly, consistent use of a 2-h AIT yielded superior TITR compared with other durations. These findings led us to speculate that most users can achieve the best outcomes by using these optimal settings, assuming there are no contraindications. When the optimal GT and AIT were indeed applied consistently, TITR reached 56.7% in those age ≤15 years and 57.0% in the older group, representing a substantial 7.8 and 8.2 percentage points more than in the overall cohorts, while safety remained. Although less pronounced than GT and AIT, other modifiable factors, such as number of daily manual boluses and number of distinct insulin-to-carbohydrate ratios, were also associated with higher TITR; five to six manual boluses and one to three distinct insulin-to-carbohydrate ratios per day were found to be optimal. Other factors probably associated with TITR, such as timing of boluses, were not part of the data set.

The impact of optimal settings on the increase in TITR was larger compared with the impact of optimal settings on the increase in TIR. The AHCL algorithm is designed to be most effective (while maintaining safety) when using a GT of 100 mg/dL and an AIT of 2 h (20). Interestingly, the impact of these optimal settings on TITR post-AHCL was 60% (age ≤15 years) to 86% (older group) greater than their impact on TIR post-AHCL. Previous evidence has already indicated the importance of using optimal settings in achieving high TIR (10,11), but here we show that it is even more

crucial to consistently adhere to the optimal settings if the objective is to achieve high TITR.

A TITR target of >50% is a reasonable treatment goal in individuals living with T1D. It is widely accepted that high TITR is desirable; however, a specific TITR treatment goal for those living with T1D has not yet been established. Table 1 provides evidence that a TITR greater than ∼45% has the greatest potential to accurately determine whether users achieve a GMI <7%. Additionally, TITR greater than ∼50% is optimal for classifying GMI <6.8%, and TITR greater than ∼55% is optimal for GMI <6.5%. When these candidate TITRs are applied to distribution plots, >90% of the MM780G system users using optimal settings achieve a TITR target of >45%, which seems considerably high. Many users can benefit from a more elevated goal, such as TITR >50%, which is reasonably attainable because >70% of users would still reach that target if optimal settings were used. The target TITR of >50% is supported by a previous study by Peterson et al., which revealed that a TITR of 50% corresponds to an HbA_{1c} level of 6.5% (21). Further research on TITR, conducted in different settings among diverse populations (including T2D) and using various treatment modalities, is needed to facilitate a comprehensive discussion aimed at establishing a consensus target.

One limitation of this study pertains to the constraints of the data collected in CareLink Personal. Certain (sociodemographic) variables, such as sex, age, and diabetes type, are self-reported because of privacy regulations. Furthermore, age information is grouped. Secondly, despite extensive precautions for bias mitigation (refer to section on data source and data, including large data set, high rate of users with a Carelink Personal account, high consent rates, and seamless nightly data uploads), the potential impact of missing data on outcomes remains uncertain. A third limitation is that HbA_{1c} could not be used as an end point in this study, necessitating the selection of an achievable TITR target based on GMI. The study also possesses several strengths. It benefits from a large real-world study population sourced from a well-documented data repository, which helps mitigate selection bias and enhances the generalizability of the findings.

In conclusion, this extensive real-world study demonstrates TITR exceeding 48% in individuals living with T1D both younger and older than age 15 years using the MiniMed 780G system. Significant contributors to achieving higher TITR were consistent adherence to GT of 100 mg/dL and AIT of 2 h. The impact of these optimal settings on the increase in TITR was larger compared with the impact on the increase in TIR. With consistent use of AHCL and optimal settings, TITR even surpassed 56% in both age groups. Finally, we suggest that a TITR target of >50% can be considered a reasonable and safe target for treatment goals in individuals living with T1D, but a target of >55% can be reasonably achieved in MiniMed 780G users applying optimal settings.

Duality of Interest. J.C., A.A., T.H., and O.C. are employees of Medtronic Europe. T.B. has served as a speaker for Medtronic events. No other potential conflicts of interest relevant to this article were reported.

Author Contributions. J.C. and A.A. performed the statistical analyses. J.C., T.v.d.H., and O.C. wrote the manuscript. All authors were involved in the design and conduct of the study and the interpretation of the results and edited, reviewed, and approved the final version of the manuscript. O.C. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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