Biobehavioral Changes Following Transition to Automated Insulin Delivery: A Large Real-life Database Analysis

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OBJECTIVE

To document glycemic and user-initiated bolus changes following transition from predictive low glucose suspend (PLGS) system to automated insulin delivery (AID) system during real-life use.

RESEARCH DESIGN AND METHODS

We conducted analysis of 2,329,166 days (6,381 patient-years) of continuous glucose monitoring (CGM) and insulin therapy data for 19,354 individuals with type 1 Diabetes, during 1-month PLGS use (Basal-IQ technology) followed by 3-month AID use (Control-IQ technology). Baseline characteristics are as follows: 55.4% female, age (median/quartiles/range) 39/19–58/1–92 years, mean ± SD glucose management indicator (GMI) 7.5 ± 0.8. Primary outcome was time in target range (TIR) (70–180 mg/dL). Secondary outcomes included CGM-based glycemic control metrics and frequency of user-initiated boluses.

RESULTS

Compared with PLGS, AID increased TIR on average from 58.4 to 70.5%. GMI and percent time above and below target range improved as well: from 7.5 to 7.1, 39.9 to 28.1%, and 1.66 to 1.46%, respectively; all *P* values <0.0001. Stratification of outcomes by age and baseline GMI revealed clinically significant differences. Glycemic improvements were most pronounced in those <18 years old (TIR improvement 14.0 percentage points) and those with baseline GMI >8.0 (TIR improvement 13.2 percentage points). User-initiated correction boluses decreased from 2.7 to 1.8 per day, while user-initiated meal boluses remained stable at 3.6 to 3.8 per day.

CONCLUSIONS

Observed in real life of >19,000 individuals with type 1 diabetes, transitions from PLGS to AID resulted in improvement of all glycemic parameters, equivalent to improvements observed in randomized clinical trials, and reduced user-initiated boluses. However, glycemic and behavioral changes with AID use may differ greatly across different demographic and clinical groups.

Over the past several years, numerous clinical trials have definitively demonstrated the safety, efficacy, and user acceptance of automated insulin delivery (AID) systems, transforming the landscape of diabetes self-management (1–4). These studies

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have shown positive glycemic outcomes across ages ranging from 1 year (5) to >65 years (6) and for individuals in a state of suboptimal as well as tight diabetes control (7). According to meta-analyses, across all patient groups tested, AID results in increased time in target range (TIR) (70–180 mg/dL) of ~10 percentage points, attributable to reductions in hyperglycemia without a clinically significant increase in hypoglycemia (1–4).

Today, after years of development and testing of system components and algorithms, AID is a clinical reality. Two AID systems, the Medtronic MiniMed 670G/770G (8) and Tandem Diabetes Care t:slim X2 pump with Control-IQ technology (9,10), have U.S. Food and Drug Administration (FDA) clearance for clinical use in the U.S. and CE (Conformité Européenne) marks for clinical use in Europe. Two other systems, Medtronic 780G (11), and CamAPS FX (12), have received CE mark for use in European countries, and Insulet's Omnipod 5 (13) was recently approved by the FDA in January 2022. These systems are at different stages of clinical use: while MiniMed 670G/770G and Control-IQ technology already have hundreds of thousands of users around the world, 780G, Omnipod 5, and CamAPS FX are making their first strides in real-life application. Several other systems are at various stages in their development, Diabeloop (14), Tidepool Loop (15), the bihormonal artificial pancreas (insulin plus glucagon) from Inreda Diabetic (16), and iLet, in two configurations, insulin only and insulin plus glucagon (17).

Consequently, the focus of research has shifted to real-world use. Early studies generally confirmed the glycemic benefits of AID in the real world (18–20), although there have been reports finding decreased use over time and even system use discontinuation (21–23). The retrospectively available data are usually limited to continuous glucose monitoring (CGM) readings for computation of glycemic outcomes along with percent time the AID system was connected to determine adequate usage. This restricts the ability to investigate questions that would contribute to a deeper understanding of the use of this technology, such as changes in daily diabetes self-management behaviors that might facilitate or act as barriers to achieving glycemic goals.

In 2019 and 2020, two articles in the *New England Journal of Medicine* reported randomized clinical trials of an AID system used in patients ages 14 year old and older (9) and 6–13 years old (10). Here, we attempt to answer the next logical question: the extent to which glycemic and behavioral outcomes reported in controlled trials are translated to real life when AID is the primary mode of daily diabetes self-management. We report findings from a unique real-world database for >19,000 individuals using the same previously reported (9,10) AID system (Tandem Care t:slim X2 pump with Control-IQ technology) who, in addition to CGM data, had insulin delivery data including user-initiated meal and correction boluses. The size of the sample allowed us to stratify the data by sex, five age-groups, and four groups based on baseline glucose management indicator (GMI) (24), used as a substitute for HbA_{1c} measurement.

RESEARCH DESIGN AND METHODS

We performed a retrospective analysis of users of Control-IQ technology (Tandem Diabetes Care) in the U.S. who had descriptive data available in the Tandem Diabetes Care Customer Relations Management database and had uploaded their glycemic data—either through the Tandem Diabetes Care t:connect Uploader or through the mobile app—to the t:connect Web application. The data extracted for analysis were de-identified. Participants consented to the use of their data for research purposes as part of their onboarding to Tandem Diabetes Care in initiating a t:connect account. Because de-identified health information is not PHI and is therefore not protected by the Privacy Rule (see https://privacyruleandresearch.nih.gov/pr_08.asp#8a), no institutional review board approval was sought for this retrospective analysis. We included 19,354 U.S.-based individuals with type 1 diabetes who were using a predictive low glucose suspend (PLGS) system (Basal-IQ technology) and then updated their insulin pumps to AID (Control-IQ technology). Each individual had to have at least 3 weeks of data with >75% CGM availability on PLGS within a month of updating to an AID system and at least 60 days of data in the following 3 months using the AID system. Insulin delivery data included the total number of insulin units delivered each day and the number of daily user-initiated meal boluses and hyperglycemia correction boluses.

Statistical Methods

The primary outcome, CGM-measured TIR (70–180 mg/dL), was compared between groups with use of a general linear model with four repeated measures, each reflecting 1 month of data as described above. Similar analyses were conducted for all other secondary CGM-based and insulin delivery–based outcomes, which included the metrics recommended by the International Consensus on Time in Range (25): time <54 and <70 mg/dL, time >180 and >250 mg/dL, coefficient of variation, total daily insulin, and the number of user-initiated correction and meal boluses. Due to the large sample size, stratification of the data by certain baseline variables was warranted, and was done by sex (male/female); age-group, defined as ages (0–12, 13–18, 19–25, 26–64, and ≥65 years); and baseline glycemic control, defined as GMI ≤6.9, 6.9 < GMI ≤ 7.4, 7.4 < GMI ≤ 8.0, and GMI >8.0. A difference was considered statistically significant if the *P* value was <0.001. All *P* values were two tailed, and all analyses were performed with IBM SPSS Statistics 28.

RESULTS

The database query yielded 2,329,166 days of CGM and insulin delivery data (6,381 patient-years) for 19,354 individuals with type 1 Diabetes, i.e., 120.3 days per person on average—1 month on Basal-IQ technology followed by 3 months on Control-IQ technology. The median number of days available within each time period was 31 (interquartile range 29–31) on PLGS, 30 (30–30) for AID months 1 and 2, and 30 (28–30) for AID month 3. The following patient characteristics were available at baseline: sex, *n* = 10,712 female (55.4%) and *n* = 8,637 male, and age median/quartiles/range 39 years/19–58 years/1–92 years old, respectively. Additional baseline CGM and insulin delivery parameters were computed with use of the first month of data during which the participants were using a PLGS system: mean (SD) GMI = 7.5 (0.8), total daily insulin 49.5 (26.2) units, number of user-initiated correction boluses per day

2.7 (2.3), and number of user-initiated meal boluses per day 3.6 (2.0). Note that the GMI is a unit-less linear function of average glucose, presented sometimes as a percentage because of its clinical analogy with HbA_{1c} (24). Outcome metrics were computed from each of the three consecutive 1-month data periods on AID. Thus, each person received four repeated measures for each CGM or insulin-delivery metric. The selection of individuals for analysis is presented in Supplementary Fig. 1.

Table 1 shows the primary outcome, TIR, increased on AID across the entire cohort, compared with PLGS, from 58.4 to 70.5% ($P < 0.001$). This increase occurred within the first week after switching from PLGS to AID and was sustained during the 3-month AID use. All secondary glycemic outcomes showed similar patterns of change—improvement in month 1 of AID, sustained thereafter (all P values <0.001). Table 1 also presents the glycemic outcome data stratified by the five age-groups. The age range was wide, 1–92 years old. The improved glycemic outcomes were most pronounced among those ages <18 years old with TIR increased by ≥ 13 percentage points. Overall, age-group was a significant factor for glycemic control improvement. The range of baseline control was wide as well, with GMI ranging from 5.2 to 12.3. Further, Table 1 shows the glycemic outcomes stratified by baseline glycemic control. Glycemic outcomes improved most in those with baseline GMI >8.0. These improvements were highly selective: individuals in an optimal state of glycemic control (baseline GMI ≤ 6.9) had TIR improved by ~ 4.0 percentage points and had rate of hypoglycemia on AID compared with PLGS reduced by 0.9 percentage points, while those with baseline GMI >8.0 had TIR improved by >20 percentage points, but time below range also increased slightly (Table 1). Finally, Table 1 shows that there were only subtle sex differences, statistically significant due to the large sample size, but with no clinical significance.

Figure 1 presents TIR on PLGS and after initiation of AID for the five age-groups (Fig. 1*A*) and the four GMI groups (Fig. 1*B*), tracing over time the observed differences, stratified by age and glycemic status. It is evident that a rapid transition occurred when patients switched from PLGS to AID, and the glycemic benefits of AID were sustained thereafter.

Table 2 presents the insulin dose and user-initiated bolus data across all participants in the study. Total daily insulin increased on average by 2.9 units on AID versus PLGS, $P < 0.001$, which is consistent with the significantly lower average glucose; however, this intensified treatment did not result in increased hypoglycemia (Table 1). User-initiated correction boluses were reduced by one-third, from 2.7 to 1.8 per day on average, $P < 0.001$, while user-initiated meal boluses remained stable at 3.6–3.8 per day (Table 2). Further, Table 2 shows the insulin dose and user-initiated bolus data across the five age-groups. While total daily insulin dose increased in all age-groups, the number of additional units was higher in the younger age-groups (<19 years). The number of user-initiated correction boluses decreased across all age-groups, with a reduction of approximately one bolus in individuals <65 years old and less reduction in the older age-group. Table 2 also presents the insulin dose and bolusing behavior data for the four groups stratified by baseline GMI. The increase in insulin after AID initiation ranged from 1.4 units for the group in optimal control to almost 6.0 units for the group with GMI >8.0 ($P < 0.001$). The group with lowest GMI performed the most correction boluses at baseline, 3.1/day, which was reduced to 2.5/day on average across time. In contrast, the group with the highest GMI performed the least correction boluses at baseline, 2.4/day, with boluses further decreasing to 1.3/day after transitioning to AID—a nearly 50% reduction of manual corrections. The number of meal boluses remained stable for PLGS versus AID, with a clinically insignificant increase in the groups with baseline GMI <7.4 and a slight decrease with baseline GMI >8.0. Glycemic outcomes were correlated with the total number (meal plus correction) of user-initiated boluses—a positive partial correlation controlling for age-group was observed for TIR ($r = 0.36$, $P < 0.001$) and negative correlation was observed for GMI ($r = -0.36$, $P < 0.001$), indicating that people with lower GMI also fine-tuned their treatment with multiple user-initiated-boluses. Finally, Table 2 shows the sex-stratified insulin dose and bolus data, which did not yield clinically significant differences.

Figure 2 presents the user-initiated correction bolus data across the five age-groups (Fig. 2*A*) and the four GMI groups (Fig. 2*B*), again highlighting the differences in bolus-related behavior over time, with stratification by age and glycemic status. Supplementary Fig. 2 presents the user-initiated meal boluses across the five age-groups (Supplementary Fig. 2*A*) and the four GMI groups (Supplementary Fig. 2*B*). The number of meal boluses remained stable for PLGS versus AID, with a clinically insignificant increase in the groups with baseline GMI <7.4 and a slight decrease with baseline GMI >8.0. The spike in the number of meal boluses observed across all age-groups and GMI groups immediately after initiation of AID remains unexplained and is probably an artifact of closed-loop initiation. Supplementary Fig. 3 presents the total (meal plus correction) user-initiated boluses, while Supplementary Fig. 4 presents user-initiated correction (Supplementary Fig. 4*A*) and meal (Supplementary Fig. 4*B*) boluses stratified by sex.

CONCLUSIONS

Compared with data from two randomized controlled trials in patients ages ≥ 14 and 6–13 years, previously published in the *New England Journal of Medicine* (9,10), the outcomes from this real-life observation were remarkably similar. For example: with AID, TIR increased by 11 percentage points in the two clinical trials and by 12 percentage points in this observational study; time >180 mg/dL decreased by 11 percentage points in the two clinical trials and by 12 percentage points in this observational study; time <70 mg/dL decreased by 0.9, 0.4, and 0.2 percentage points, respectively; and HbA_{1c} decreased by 0.33%, 0.4%, and 0.4% (GMI used as a proxy to of HbA_{1c} in this study). Analyzed across sex, and a wide range of age (1–92 years) and baseline levels of glucose control, these results reaffirm that AID systems are beneficial acrossa broad spectrum of clinical and demographic groups when used in the real-world setting without the types of support, supervision, and incentives typically incorporated into clinical trials. Clinically, this should encourage diabetes health care workers to consider the use of AID systems with a wide range of patients.

Table 1—Primary and secondary glycemic outcomes, overall and stratified by age-group, baseline glycemic control, and sex

Glycemic outcomes	PLGS	AID month 1	AID month 2	AID month 3	AID-PLGS average difference	*P*
Primary and secondary glycemic outcomes*						
% TIR	58.4 ± 18.3	71.1 ± 12.9	70.4 ± 13.5	70.0 ± 13.8	12.06 ± 9.99	<0.001
GMI	7.47 ± 0.79	7.05 ± 0.51	7.08 ± 0.54	7.10 ± 0.56	−0.39 ± 0.44	<0.001
Glucose, mg/dL	174.0 ± 33.2	156.5 ± 21.2	157.7 ± 22.6	158.4 ± 23.3	−16.42 ± 18.43	<0.001
SD, mg/dL	52.2 ± 12.5	46.9 ± 11.4	47.4 ± 11.9	47.5 ± 12.0	−4.91 ± 6.3	<0.001
Coefficient of variation, %	30.2 ± 4.9	29.6 ± 4.8	29.7 ± 4.9	29.7 ± 4.9	−0.52 ± 3.31	<0.001
% time <54 mg/dL	0.32 ± 0.65	0.29 ± 0.49	0.29 ± 0.52	0.29 ± 0.52	−0.03 ± 0.42	<0.001
% time <70 mg/dL	1.66 ± 2.13	1.46 ± 1.64	1.47 ± 1.66	1.46 ± 1.67	−0.20 ± 1.31	<0.001
% time >180 mg/dL	39.9 ± 19.1	27.4 ± 13.3	28.1 ± 13.9	28.5 ± 14.3	−11.86 ± 10.34	<0.001
% time >250 mg/dL	14.2 ± 13.4	7.4 ± 7.5	7.9 ± 8.1	8.1 ± 8.4	−6.42 ± 8.23	<0.001
By age-group, years†						
% TIR						<0.001
0–12 (*N* = 1,877)	50.2 ± 17.3	65.4 ± 11.7	64.1 ± 12.6	63.5 ± 12.7		
13–18 (*N* = 2,759)	50.3 ± 18.4	65.0 ± 13.3	64.0 ± 13.8	63.3 ± 14.1		
19–25 (*N* = 1,670)	54.7 ± 18.6	68.3 ± 12.8	67.4 ± 13.6	67.4 ± 14.0		
26–64 (*N* = 9,335)	60.8 ± 17.7	72.9 ± 12.5	72.3 ± 12.9	71.9 ± 13.2		
≥65 (*N* = 3,250)	65.2 ± 15.8	76.0 ± 11.2	75.5 ± 11.6	75.3 ± 12.0		
% time <70 mg/dL						<0.001
0–12 (*N* = 1,877)	1.5 ± 1.8	1.7 ± 1.6	1.6 ± 1.5	1.5 ± 1.5		
13–18 (*N* = 2,759)	1.4 ± 1.8	1.2 ± 1.3	1.2 ± 1.4	1.2 ± 1.3		
19–25 (*N* = 1,670)	1.7 ± 2.1	1.5 ± 1.7	1.5 ± 1.7	1.4 ± 1.6		
26–64 (*N* = 9,335)	1.8 ± 2.4	1.6 ± 1.8	1.6 ± 1.8	1.6 ± 1.9		
≥65 (*N* = 3,250)	1.4 ± 1.9	1.3 ± 1.4	1.3 ± 1.5	1.3 ± 1.4		
% time >180 mg/dL						<0.001
0–12 (*N* = 1,877)	48.2 ± 18.0	32.9 ± 12.2	34.3 ± 13.1	34.9 ± 13.2		
13–18 (*N* = 2,759)	48.4 ± 19.1	33.8 ± 13.7	34.8 ± 14.2	35.5 ± 14.5		
19–25 (*N* = 1,670)	43.6 ± 19.4	30.3 ± 13.3	31.1 ± 14.1	31.2 ± 14.5		
26–64 (*N* = 9,335)	37.4 ± 18.5	25.5 ± 12.9	26.1 ± 13.4	26.5 ± 13.7		
≥65 (*N* = 3,250)	33.4 ± 16.3	22.7 ± 11.3	23.2 ± 11.8	23.5 ± 12.2		
By baseline GMI‡						
% TIR						<0.001
≤6.9 (*N* = 4,450)	80.6 ± 7.3	84.2 ± 6.8	83.8 ± 7.3	83.6 ± 7.6		
6.9–7.4 (*N* = 5,359)	65.9 ± 5.4	75.4 ± 7.0	74.8 ± 7.7	74.4 ± 8.1		
7.4–8.0 (*N* = 5,018)	51.8 ± 5.0	67.5 ± 7.8	66.6 ± 8.5	66.2 ± 8.9		
>8.0 (*N* = 4,064)	32.5 ± 9.5	55.7 ± 11.0	54.5 ± 11.5	54.1 ± 12.0		
% time <70 mg/dL						<0.001
≤6.9 (*N* = 4,450)	3.2 ± 3.2	2.3 ± 2.4	2.3 ± 2.4	2.4 ± 2.4		
6.9–7.4 (*N* = 5,359)	1.7 ± 1.6	1.5 ± 1.4	1.5 ± 1.4	1.5 ± 1.3		
7.4–8.0 (*N* = 5,018)	1.1 ± 1.2	1.2 ± 1.2	1.2 ± 1.2	1.1 ± 1.2		
>8.0 (*N* = 4,064)	0.6 ± 0.9	0.9 ± 1.0	0.9 ± 1.1	0.8 ± 1.0		
% time >180 mg/dL						<0.001
≤6.9 (*N* = 4,450)	16.2 ± 6.8	13.5 ± 6.5	13.8 ± 7.2	14.1 ± 7.6		
6.9–7.4 (*N* = 5,359)	32.4 ± 4.9	23.2 ± 6.8	23.8 ± 7.6	24.2 ± 8.0		
7.4–8.0 (*N* = 5,018)	47.1 ± 5.1	31.3 ± 7.9	32.2 ± 8.6	32.6 ± 9.0		
>8.0 (*N* = 4,064)	66.9 ± 9.8	43.5 ± 11.3	44.6 ± 11.8	45.0 ± 12.3		
By sex§						
% TIR						<0.001
Female (*N* = 10,495)	58.5 ± 18.2	71.8 ± 12.6	71.0 ± 13.3	70.6 ± 13.6		
Male (*N* = 8,392)	58.3 ± 18.4	70.3 ± 13.3	69.7 ± 13.8	69.3 ± 14.1		
% time <70 mg/dL						0.49
Female (*N* = 10,495)	1.6 ± 2.1	1.4 ± 1.6	1.4 ± 1.7	1.4 ± 1.7		
Male (*N* = 8,392)	1.7 ± 2.1	1.5 ± 1.7	1.5 ± 1.6	1.5 ± 1.6		
% time >180 mg/dL						<0.001
Female (*N* = 10,495)	39.9 ± 19.0	26.7 ± 13.0	27.6 ± 13.7	28.0 ± 14.1		
Male (*N* = 8,392)	40.0 ± 19.2	28.2 ± 13.6	28.8 ± 14.2	29.2 ± 14.5		

Data are means ± SD. **P* values refer to baseline PLGS vs. 3 months of AID treatment. †*P* values refer to age-group–by–treatment (PLGS vs. AID) contrast. ‡*P* values refer to baseline GMI–by–treatment (PLGS vs. AID) contrast. §*P* values refer to sex-by-treatment (PLGS vs. AID) contrast.

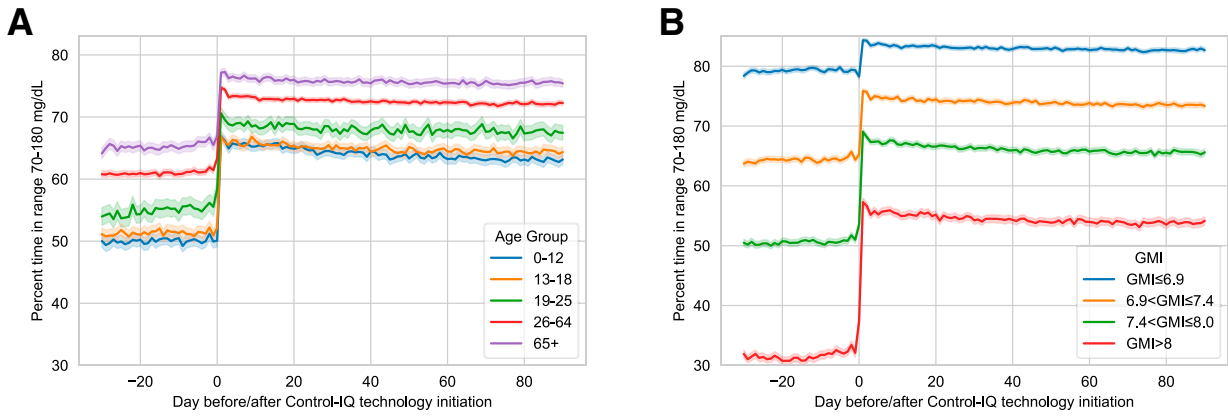

Figure 1—Traces (mean, 95% CI) of TIR on PLGS (1 month) and AID (3 months), stratified by five age groups, i.e., 0 to 12 years old; 13 to 18 years old; 19 to 25 years old; 26 to 64 years old; and 65 or older (*A*), and by four GMI groups, i.e., GMI ≤ 6.9; 6.9 < GMI ≤ 7.4; 7.4 < GMI ≤ 8.0; and 8.0 < GMI (*B*). A rapid transition occurs when patients switch from PLGS to AID, and the glycemic benefits of AID are sustained thereafter.

When stratified by sex, there were no clinically significant differences in glycemic outcomes and bolusing behavior. However, across age-groups, younger individuals showed the greatest percent increase in TIR but also achieved a lower overall percentage of glucose readings between 70 and 180 mg/dL than older users. This reflects the unique challenges of optimal diabetes management in these age-groups, including unpredictable and erratic patterns in physical activity and food consumption for the very young, hormonal changes as part of normal growth and development in adolescence along with tendencies to omit meal boluses in this age-group, and other life transitions that impact self-care during young adulthood.

With stratification by baseline GMI as a proxy measure for glycosylated hemoglobin, TIR and other glycemic metrics improved across all GMI groups, but there were also profound differences. In the group with the lowest GMI at baseline, TIR increased to >83%, reflecting a 3–4 percentage point improvement, while their percent time <70 mg/dL decreased by 0.9 percentage points. While a 4% increase in TIR may not be clinically significant by itself, it becomes a sign of further optimized glycemic control when accompanied by a nearly one-third reduction in the frequency of hypoglycemia, since increased hypoglycemia is a major risk factor with stringent avoidance of hyperglycemia.

The group with the highest GMI, >8.0, showed the greatest percent improvement in TIR with a 22–23 percentage point change, and they achieved this change with no clinically significant increase in time spent in a state of hypoglycemia. Percent time >250 mg/dL was reduced by nearly one-half along with a reduction in time >180 mg/dL of 22–23 percentage points. This finding, with a large group of >4,000 individuals with suboptimal control at baseline, is particularly important and confirms a previous recommendation that AID systems be considered for those with poorly managed diabetes (26).

However, the TIR achieved with AID in this group was 54.1%, significantly lower than in the other groups. This is likely related in part to behavioral factors; e.g., this group decreased their number of manual (meal plus correction) boluses by 1.4/day (Fig. 2*B* and Supplementary Fig. 2*B*). Concurrently, the AID system delivered 6 more insulin units daily, which suggests the possibility of under-insulinization at baseline and decreased engagement with bolusing after switching to AID, leaving the controller to "do the job." A critical question for future research is whether individuals in this group might be able to increase their TIR with interventions, ranging from providing more training support and patient education aimed at establishing realistic expectations regarding the need for ongoing correction boluses to reevaluating the insulin dosing parameters programmed into the device. Because glycemic improvements occur quickly after AID initiation, and do not further change with time, these interventions can be triggered rapidly when initial outcomes are suboptimal.

User-initiated correction boluses changed in a linear fashion across the four GMI groups. The lowest GMI group performed the most daily user-initiated boluses at baseline (mean 6.9), which remained relatively stable after transition to AID, with only a 0.4 decrease in boluses across time. The GMI group differences highlight the need to stratify data by clinically relevant dimensions when evaluating AID outcomes and that not doing so may obscure important differences in individual glycemic responses to this technology.

Similar to findings of previous studies, current findings also demonstrate that improvements in glycemic metrics occur rapidly after transition to AID. After the initial significant progress, however, continued use of AID seems to only maintain these glycemic improvements without further substantial changes. It is important to understand the factors that contribute to this pattern of early rapid improvement that quickly plateaus characteristic of AID use and whether there is indeed a ceiling effect for TIR for people with type 1 diabetes, as seen in these data and with other AID systems (20,27). Research in this area will be essential to the development of interventions to support users in achieving their own optimal glycemic outcomes. At present, there are many questions that will require longitudinal studies to examine individuals' interactions with AID systems and changes in patterns of use over time, as well as the sociodemographic, psychosocial, and environmental factors that affect these patterns.

An evident limitation of this study is that the conclusions are derived from a retrospective real-world database, which is not equivalent to a gold standard randomized controlled trial. Because of the data sample used, information was

Table 2—Insulin dose and user-initiated bolus data, overall, and stratified by age-group, baseline glycemic control, and sex

Insulin dose and user-initiated bolus data	PLGS	AID month 1	AID month 2	AID month 3	AID-PLGS average difference	*P*
Total daily insulin (units)*	49.5 ± 26.1	52.2 ± 27.5	52.3 ± 27.6	52.4 ± 27.8	2.89 ± 8.55	<0.001
No. of user-initiated correction boluses*	2.7 ± 2.3	1.8 ± 2.0	1.8 ± 2.0	1.8 ± 2.0	0.9 ± 1.35	<0.001
No. of user-initiated meal boluses*	3.6 ± 2.0	3.8 ± 1.9	3.7 ± 2.0	3.6 ± 2.0	0.1 ± 1.13	<0.001
By age-group, years†						
Total daily insulin (units)						<0.001
0–12 (*N* = 1,877)	28.0 ± 14.9	30.5 ± 16.4	31.0 ± 16.6	31.7 ± 17.0		
13–18 (*N* = 2,759)	56.7 ± 23.1	60.7 ± 24.8	61.0 ± 25.0	61.6 ± 25.3		
19–25 (*N* = 1,670)	58.9 ± 23.9	62.0 ± 25.3	61.7 ± 25.3	61.3 ± 25.8		
26–64 (*N* = 9,335)	52.0 ± 27.2	54.7 ± 28.4	54.7 ± 28.6	54.7 ± 28.9		
≥65 (*N* = 3,250)	43.5 ± 23.7	45.5 ± 24.9	45.6 ± 25.2	45.5 ± 25.1		
No. of user-initiated correction boluses						<0.001
0–12 (*N* = 1,877)	2.2 ± 1.7	1.2 ± 1.3	1.2 ± 1.4	1.2 ± 1.4		
13–18 (*N* = 2,759)	2.3 ± 2.1	1.3 ± 1.5	1.3 ± 1.6	1.3 ± 1.6		
19–25 (*N* = 1,670)	2.6 ± 2.3	1.7 ± 1.9	1.7 ± 2.1	1.6 ± 1.9		
26–64 (*N* = 9,335)	3.1 ± 2.5	2.1 ± 2.2	2.1 ± 2.2	2.1 ± 2.2		
≥65 (*N* = 3,250)	2.6 ± 2.2	1.9 ± 1.9	1.9 ± 2.0	1.9 ± 2.0		
No. of user-initiated meal boluses						<0.001
0–12 (*N* = 1,877)	4.8 ± 1.8	4.8 ± 1.7	4.8 ± 1.8	3.9 ± 2.1		
13–18 (*N* = 2,759)	4.1 ± 2.0	4.1 ± 2.0	4.0 ± 2.1	3.2 ± 2.1		
19–25 (*N* = 1,670)	3.5 ± 2.1	3.5 ± 2.0	3.3 ± 2.1	3.4 ± 2.0		
26–64 (*N* = 9,335)	3.2 ± 2.0	3.6 ± 2.0	3.5 ± 2.1	3.6 ± 1.8		
≥65 (*N* = 3,250)	3.4 ± 1.8	3.7 ± 1.7	3.6 ± 1.8	3.6 ± 2.0		
By baseline GMI‡						
Total daily insulin (units)						<0.001
≤6.9 (*N* = 4,450)	43.9 ± 23.1	44.4 ± 22.7	45.2 ± 23.4	45.3 ± 23.7		
6.9–7.4 (*N* = 5,359)	48.4 ± 24.7	50.1 ± 24.9	50.3 ± 25.4	50.4 ± 25.4		
7.4–8.0 (*N* = 5,018)	51.4 ± 26.8	54.5 ± 27.8	54.4 ± 28.0	54.4 ± 28.1		
>8.0 (*N* = 4,064)	54.5 ± 28.8	60.7 ± 31.9	60.2 ± 31.7	60.3 ± 32.1		
No. of user-initiated correction boluses						<0.001
≤6.9 (*N* = 4,450)	3.1 ± 2.8	2.5 ± 2.5	2.5 ± 2.5	2.5 ± 2.5		
6.9–7.4 (*N* = 5,359)	2.8 ± 2.3	1.9 ± 2.0	1.9 ± 2.0	1.9 ± 2.0		
7.4–8.0 (*N* = 5,018)	2.6 ± 2.1	1.6 ± 1.6	1.6 ± 1.7	1.6 ± 1.7		
>8.0 (*N* = 4,064)	2.4 ± 1.9	1.3 ± 1.4	1.3 ± 1.5	1.3 ± 1.5		
No. of user-initiated meal boluses						<0.001
≤6.9 (*N* = 4,450)	3.8 ± 2.3	4.2 ± 2.1	4.1 ± 2.2	4.1 ± 2.2		
6.9–7.4 (*N* = 5,359)	3.7 ± 2.0	4.0 ± 1.8	3.9 ± 2.0	3.8 ± 1.9		
7.4–8.0 (*N* = 5,018)	3.6 ± 1.9	3.8 ± 1.9	3.7 ± 1.9	3.6 ± 1.9		
>8.0 (*N* = 4,064)	3.2 ± 1.9	3.2 ± 1.8	2.9 ± 1.9	2.9 ± 1.9		
By sex§						
Total daily insulin (units)						<0.001
Female (*N* = 10,496)	45.7 ± 24.0	48.2 ± 25.5	48.4 ± 25.8	48.5 ± 26.0		
Male (*N* = 8,392)	54.2 ± 27.8	57.2 ± 29.0	57.2 ± 29.0	57.3 ± 29.2		
No. of user-initiated correction boluses						0.008
Female (*N* = 10,495)	2.6 ± 2.1	1.8 ± 1.8	1.7 ± 1.8	1.7 ± 1.8		
Male (*N* = 8,391)	2.9 ± 2.6	1.9 ± 2.2	1.9 ± 2.3	1.9 ± 2.2		
No. of user-initiated meal boluses						0.381
Female (*N* = 10,495)	3.6 ± 1.9	3.8 ± 1.9	3.7 ± 2.0	3.7 ± 2.0		
Male (*N* = 8,391)	3.5 ± 2.1	3.8 ± 2.0	3.6 ± 2.1	3.6 ± 2.1		

Data are means ± SD. **P* values refer to baseline PLGS vs. 3 months of AID treatment. †*P* values refer to age-group–by–treatment (PLGS vs. AID) contrast. ‡*P* values refer to baseline GMI–by–treatment (PLGS vs. AID) contrast. §*P* values refer to sex-by-treatment (PLGS vs. AID) contrast.

available only on age and sex, with no access to other variables that would have enhanced the study, such as sociodemographic features, duration of diabetes, or carbohydrates consumed at meals. Another important consideration is the participant population in the study. These individuals were early adopters of diabetes technology, already using PLGS before transitioning to AID when it became available for home use. Consequently, these results may not be generalizable to other more diverse patient groups, such as individuals using multiple daily injections or those who have not adopted CGM. Four months is a relatively short observation period, compared with lifelong use, but appears adequate to establish the PLGS-AID transition effects we were aiming to evaluate and is of clinical value because it provides a window of opportunity for

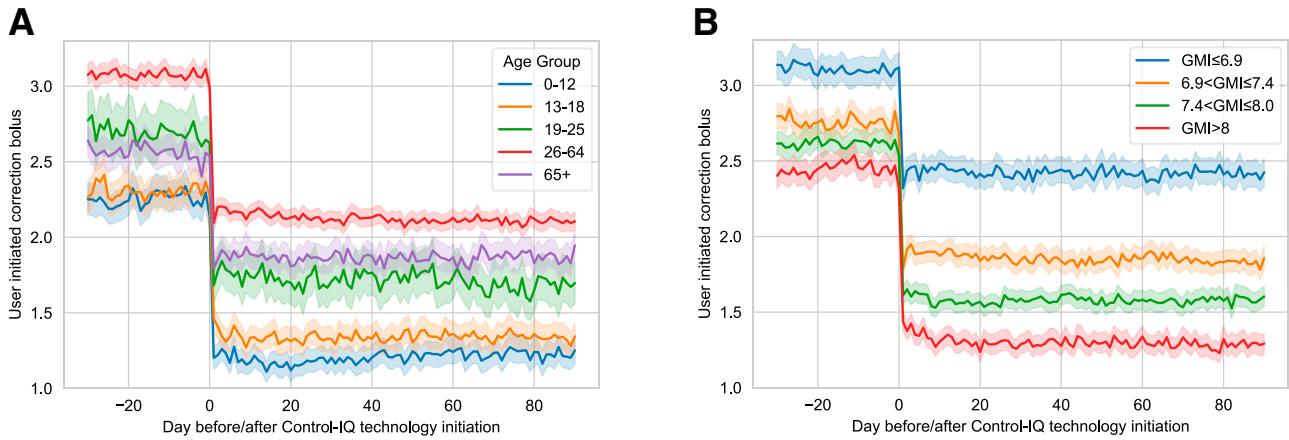

Figure 2—Traces (mean, 95% CI) of the number of user-initiated correction boluses on PLGS (1 month) and AID (3 months), stratified by five age groups, i.e., 0 to 12 years old; 13 to 18 years old; 19 to 25 years old; 26 to 64 years old; and 65 or older (*A*), and by four GMI groups, i.e., GMI $\leq$ 6.9; 6.9 $<$ GMI $\leq$ 7.4; 7.4 $<$ GMI $\leq$ 8.0; and 8.0 GMI (*B*). A rapid transition occurs when patients switch from PLGS to AID, and the reduced correction bolusing patterns on AID are sustained thereafter.

health care providers to intervene and modify patient behavior to support optimal use of therapy. The sample is representative of early adopters of home use of AID, which is the current stage of development and dissemination of the artificial pancreas. In spite of any limitations, all of the findings of this study are consistent with results previously reported from randomized trials with the same AID system (9,10). This alone is a finding worth noting because too frequently treatments that perform well in controlled clinical trial settings perform suboptimally in real life for a variety of reasons, including human factors (23).

In conclusion, in addition to presentation of the largest real-life AID cohort to date, this is the first study with assessment of changes in user-initiated bolusing behavior after transition from PLGS to AID use. Additionally, the study demonstrates that AID use results in clinically significant improvements in glycemic outcomes, even in individuals who are using sophisticated PLGS systems. For individuals who already have near-optimal maintenance of in-range glucose levels, AID provides further improvement while providing increased protection against hypoglycemic glucose excursions. Numerically, and clinically, these results are remarkably consistent between randomized clinical trials and real-life observation. Clinical implications are as follows: *1*) monitor and support early months of AID use, especially for individuals who continue to struggle to meet recommended glycemic goals after transitioning, since further improvements over time may not occur; *2*) individuals unable to meet glycemic targets on other therapies achieve clinically significant improvements with AID; and *3*) the barriers impacting optimal use of AID systems to achieve uniformly positive outcomes across diverse groups of patients are likely behavioral and in part related to user-initiated bolusing patterns.

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Author Contributions. B.P.K. performed statistical analyses and wrote and edited the manuscript. H.S. and L.M. provided the raw data for analysis and edited the manuscript. L.A.G.-F. wrote and edited the manuscript. B.P.K. 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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