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Differences in Use of Glucose Rate of Change (ROC) Arrows to Adjust Insulin Therapy Among Individuals With Type 1 and Type 2 Diabetes Who Use Continuous Glucose Monitoring (CGM)

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Abstract

Objective: To understand differences between individuals with type 1 diabetes (T1D) and type 2 diabetes (T2D) in utilization of continuous glucose monitoring (CGM) data to adjust insulin therapy, either continuous subcutaneous insulin infusion (CSII) or multiple daily insulin injections (MDI).

Methods: We surveyed 300 individuals who regularly used real-time CGM, using 70 questions to obtain information about general CGM use and response to glucose rate of change (ROC) arrows.

Results: The survey was completed by 222 T1D and 78 T2D respondents treated with intensive insulin therapy. T1D respondents included CSII (n = 166) and MDI (n = 56) users. T2D respondents were more balanced: 34 (44%) versus 44 (56%), respectively. A larger percentage of T1D then T2D respondents reported a constant use of CGM (85% vs 61%, $P < .001$). T1D and T2D respondents reported similar substantial increases in correction dosages in response to rapidly increasing glucose (>3 mg/dL/min; 2 arrows up): +140% versus +136%, $P = .4534$. However, T1D respondents reported making smaller correction dosage reductions than T2D respondents in response to rapidly decreasing glucose (–42% vs –80%, $P < .001$). Differences between T1D and T2D respondents were also observed in mealtime dosage adjustments in response to rapidly increasing glucose compared to when glucose is stable (flat arrow) at 110 mg/dl: +81% versus +108%, respectively ($P = .003$). Although these adjustments are statistically different, both are large.

Conclusions: CGM users often rely on ROC information when determining insulin doses and tend to be more aggressive in their insulin adjustments despite differences in type of diabetes.

Keywords

continuous glucose monitoring, rate of change, type 1 diabetes, type 2 diabetes, insulin pump, multiple daily insulin injections

Numerous studies have demonstrated that utilization of real-time continuous glucose monitoring (CGM) improves glycemic control in individuals with type 1 diabetes (T1D),[1-7] and is becoming accepted as part of the standard of care in the treatment of patients within this population.[8,9] The benefits of real-time CGM data in individuals with insulin-treated type 2 diabetes (T2D) is also gaining recognition. In its recent consensus statement, the American Association of Clinical Endocrinologists and American College of Endocrinology recommended that CGM should be made available to T2D individuals treated with intensive insulin regimens and all patients who are at risk for hypoglycemia and/or have hypoglycemia unawareness.[10]

In 2013, we surveyed 300 individuals with T1D and insulin-treated T2D to assess how they are using real-time CGM and responding to their glucose information in real-world settings. Our subsequent report presented findings regarding CGM data utilization behaviors among the 222 T1D individuals who used real-time CGM and responded to the survey.[11] In a subsequent analysis, we reported differences in use of ROC arrows, comparing T1D respondents treated with continuous subcutaneous insulin infusion (CSII) versus multiple daily insulin injection (MDI) therapy.[12] For this

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report, we analyzed data from the full data set of survey respondents to determine and explore differences between T1D and T2D respondents in how they utilize real-time CGM data, specifically, rate of change (ROC) arrows to adjust their insulin therapy.

Methods

Design

In this national survey, we assessed insulin therapy adjustments and clinical outcomes among individuals with T1D and insulin-treated T2D individuals who were currently using real-time CGM as part of their diabetes management regimen. The on-line survey was available between May 28th to August 26th, 2013, using SurveyGizmo (Boulder CO, USA), and included 70 multiple-choice questions. An institutional review board waiver was obtained.

Subjects

Clinical endocrinologists and diabetes educators that actively prescribe real-time CGM from across the US were asked to recruit patients from their practices. Inclusion criteria were T1D or insulin-treated T2D and use regular use (average >6 days per week) of a Dexcom CGM system (Dexcom, Inc, San Diego, USA). Individuals who agreed to participate in the study were provided a web link to the survey.

Survey Instrument

The survey comprised 6 sections: (1) patient characteristics, (2) general CGM use, (3) hypoglycemia prevention and management, (4) hyperglycemia prevention and management, (5) insulin dosing adjustments (both for incidental hyperglycemia not at meals and at mealtimes), and (6) real-time use versus retrospective analysis. To contextualize the information, many of the survey questions were framed as clinical scenarios that would be commonly experienced by patients either on multiple daily injections or using an insulin pump. For correction insulin adjustments, respondents were provided a scenario in which it had been 4 hours since taking any insulin or eating and their CGM device showed a glucose value of 220 mg/dL (confirmed by self-monitored blood glucose (SMBG) with a horizontal ROC arrow (less than 1 mg/dl per min change), 1 or 2 up ROC arrows and 1 or 2 down ROC arrows (Figure 1A). For mealtime insulin adjustments, respondents were provided a scenario in which their CGM showed a glucose value of 110 mg/dL and they were planning to eat 50g of carbohydrates. They were asked how much insulin they would take for that meal when the trend arrow showed 2 up ROC arrows and 2 down ROC arrows (Figure 1B). The questions were beta-tested in 20 experienced CGM users and refined repeatedly to assure the questions were well understood, clear and unambiguous. Based on beta testing, it was estimated to take 20-30 minutes to complete the survey. Respondents chose from 1 of 3 different surveys in which the questions were identical but the order of the sections varied. The survey instrument has published previously.[11] Respondents received a $30 gift card for completing the survey.

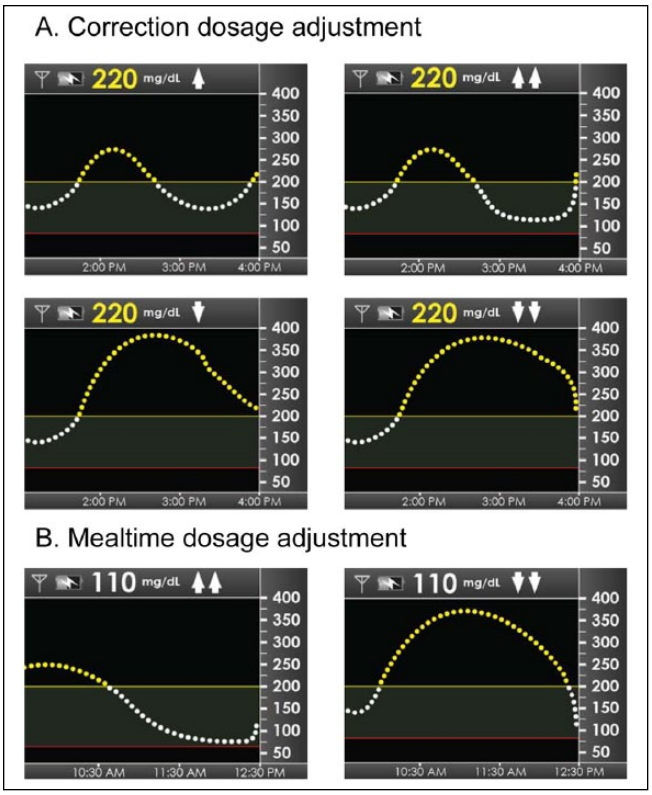

Figure 1. (A) Scenarios for correction to 120 mg/dL in which respondents showed current glucose at 220 mg/dL but changing (1 arrow up/1 arrow down) or rapidly changing (2 arrows up/2 arrows down). (B) Scenarios in which respondents' CGM showed a glucose value of 110 mg/dL and they were planning to eat 50 g of carbohydrates (2 arrows up/2 arrows down).

CGM System

The Dexcom CGM system includes a 7-day transcutaneous sensor, a transmitter, and a receiver for 7-day wearing periods. The system measures interstitial glucose every 5 minutes and displays the numerical value and glucose trend line in the hand-held receiver. Users can set audible alerts for current or impending hypoglycemia and hyperglycemia. ROC arrows indicate the direction and velocity of changing glucose levels. In this analysis, the focus was on 1 arrow (up or down) and 2 arrows (up or down) compared with typical dosages when glucose is static (flat arrow) (Figure 2).

Measures

We assessed real-time CGM utilization behaviors, comparing individuals with T1D versus T1D. Study measures included

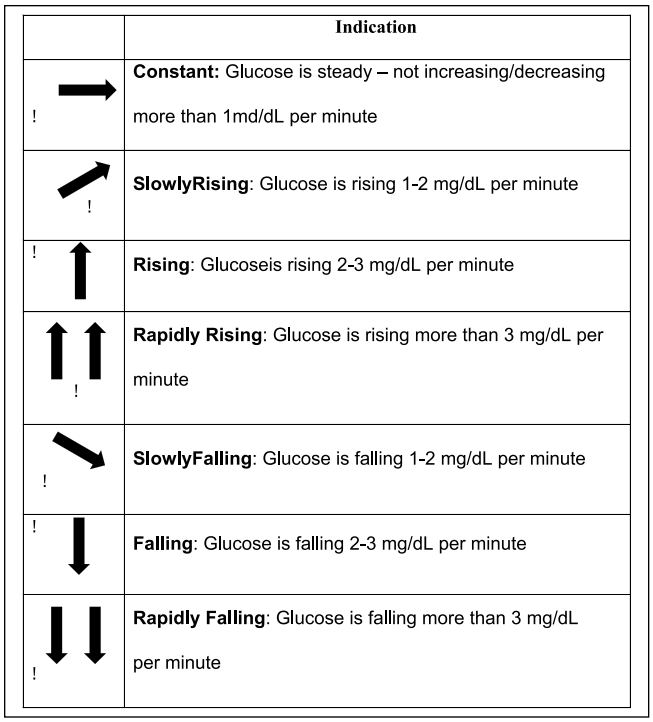

Figure 2. Rate of change (ROC) arrows indicate the direction and velocity of changing glucose.

use of ROC arrows to adjust insulin therapy, use of alarms/alerts, general CGM use, and overall response to CGM.

Statistical Methods

The survey is descriptive; no hypothesis testing was performed and no comparative analyses are made. Categorical variables are summarized using counts and percentages. Summary statistics for continuous variables are summarized using mean and standard deviation. Histogram and other graphical display are used to illustrate the distribution of the survey responses. SAS version 9.3 or later was used to conduct data conversion and analysis.

Results

Patient Characteristics

A total of 300 individuals with T1D (n = 222) and T2D (n = 78) from 22 states across the US responded to the survey. Among the T1D respondents, the mean age was 46 ± 14 years with the duration of diabetes 22 ± 14 years, 52% were male, self-reported HbA1c was 6.9 ± 0.8%, 166 (75%) used CSII, and 56 (25%) used MDI. Among the T2D respondents, the mean age was 47 ± 10 years with the duration of diabetes 14 ± 10 years, 45% were male, and the self-reported A1C was 7.4 ± 1.0%. Use of CSII and MDI among T2D respondents was more balanced: 34 (44%) versus 44 (56%), respectively.

There was no significant age difference between T1D and T2D respondents, and education levels were similar: 96% of T1D respondents and 95% of T2D respondents reported having education after high school. T1D respondents reported a longer duration of diabetes ($P < .001$) and lower HbA1c levels ($P < .0001$), and were more likely to use an insulin pump than T2D respondents ($P < .001$).

General Real-Time CGM Use

A larger percentage of T1D then T2D respondents reported a constant use of the CGM: 85% versus 61%, respectively ($P < .001$). Respondents could choose from the following answers: "mainly when I see my control is slipping," "mainly just before I see my clinician," "most of the time," "all of the time," or "other." Among T1D respondents, 66% reported wearing their CGM all the time and 19% reported wearing their CGM most of the time. Among T2D respondents, 28% reported wearing their CGM all the time and 33% reported wearing their CGM most of the time. Most T1D and T2D respondents reported using their CGM device for >1 year: 75% versus 85%, respectively ($P = .12$).

Overall Response to CGM

Respondents could choose from the following answers: "increased a lot," "increased a little," "neither increased nor decreased," "decreased a little," or "decreased a lot." Most T1D (78%) than T2D (62%) respondents reported a decrease in the frequency and severity of hypoglycemia since starting CGM; however a higher percentage of T1D than T2D respondents reported hypoglycemia severity and frequency decreased "a lot" subsequent to CGM use: 37% versus 17%, respectively ($P = .007$). A smaller percentage of T1D than T2D respondents reported clinically significant reductions in HbA1c subsequent to starting CGM: 34% of T1D respondents reported HbA1c reductions of 0.5%-1.0%, and 25% reported reductions of >1.0%, whereas 46% of T2D respondents reported HbA1c reductions of 0.5%-1.0% and 33% reported reductions of >1.0% ($P = .03$).

Changes in Injection/Bolus Frequency

Most T1D (65%) and T2D (52%) respondents reported that the number of daily injections or boluses had increased since starting CGM. A larger percentage of T2D than T1D respondents reported that they were taking fewer daily injections or boluses: 49% versus 15%, respectively ($P < .001$). The remaining respondents reported no change.

Use of Alerts and Alarms

Among T1D respondents, most reported using a low threshold alert (99%) and high threshold alert (98%). All T2D respondents reported using a low threshold alert and most

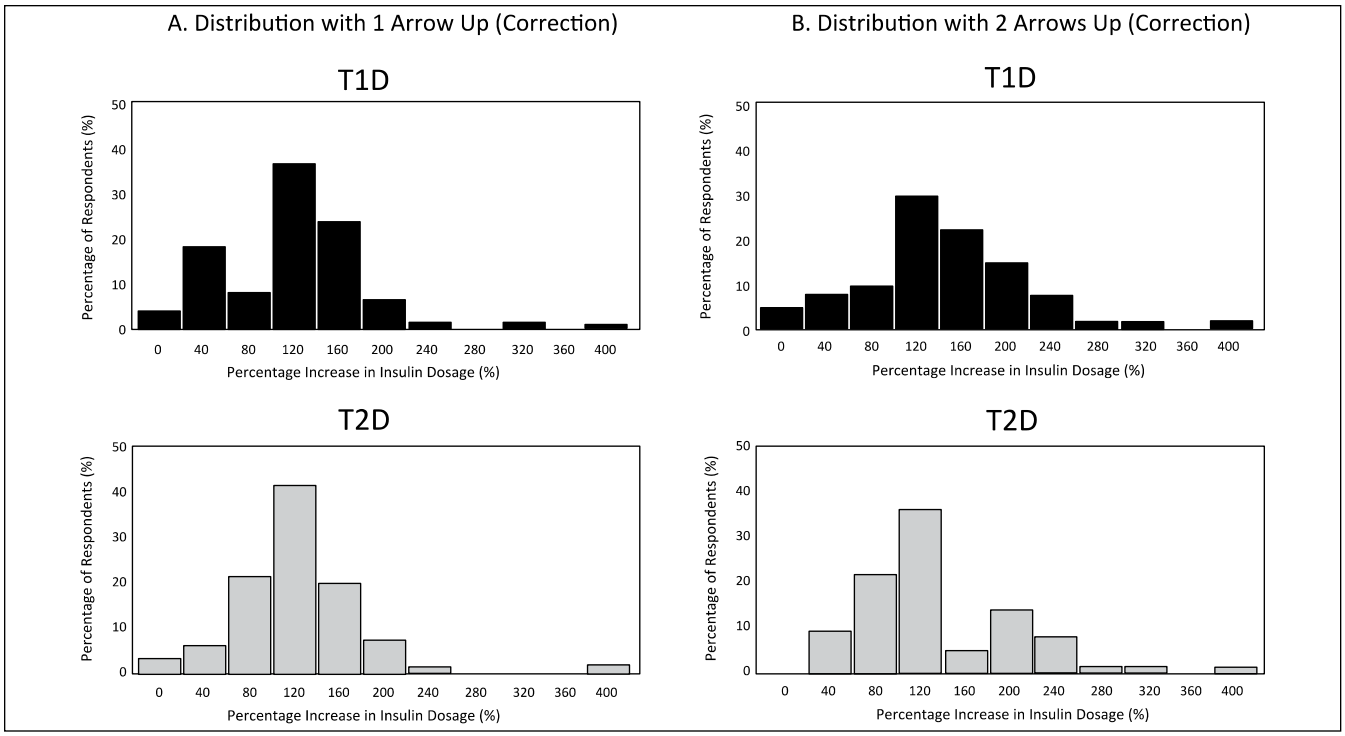

Figure 3. Distribution of insulin dosing adjustments based on the direction and rate of glucose change (1 arrow up [**A**] and 2 arrows up [**B**]) for a correctional insulin dose at hyperglycemia (220 mg/dL) between T1D and T2D respondents.

(98%) reported using a high threshold alert. Fewer T1D than T2D respondents felt they were alerted to hypoglycemia prior to symptoms being present: 33% versus 72%, P = .0002, whereas more T1D than T2D respondents reported waking up at night at least once per week in response to their low glucose alert: 70% versus 52%, P = .0105. Fewer T1D than T2D respondents reported that their CGM device alerted somebody around them to respond to their hypoglycemia alarm when they themselves were unable to respond at least 1 time in the last 6 months: 42% versus 64%, P = .0003. Similar percentages of T1D and T2D respondents stated that they woke up at least once per week at night in response to their hyperglycemia alert (66% vs 59%, P = .1663) and that they would respond by taking an extra insulin injection/bolus on the majority of occasions (79% vs 73%, P = .3898).

Use of ROC Arrows to Adjust Insulin Therapy

Determining Insulin Adjustments. A larger percentage of T1D (61%) than T2D (24%) respondents reported determining their insulin adjustments based on the CGM data by estimating from their previous experiences (P < .001), and a larger percentage of T2D (40%) than T1D (14%) respondents reported taking an extra fixed dose of insulin in response to increasing glucose (P < .001).

Use of Arrows: Correction Dosages. T1D and T2D respondents reported similar substantial increases in correction dosages in response to increasing glucose (one arrow up) compared with their typical dosage when glucose is stable (flat arrow) at 220 mg/dL to correct to 120 mg/dL: +110% and +120%, respectively (P = .4534) (Figure 3A). T1D and T2D respondents also reported similar substantial increases in correction dosages in response to rapidly increasing (2 arrows up): +140% versus +136%, respectively (P = .26) (Figure 3B).

T1D respondents reported making smaller correction dosage reductions than T2D respondents in response to decreasing glucose (one arrow down) compared to their typical correction dose when glucose is stable (flat arrow): –40% versus –72%, respectively (P < .0001) (Figure 4A). T1D respondents also reported making smaller correction dosage reductions than T2D respondents in response to rapidly decreasing glucose (2 arrows down): –42% versus –80%, respectively (P < .001) (Figure 4B).

Use of Arrows: Mealtime Dosages. T2D respondents reported making larger increases in their mealtime dosage than T1D respondents in response to rapidly increasing glucose (2 arrows up) compared to their typical mealtime dose when glucose is stable (flat arrow) at 110 mg/dl: +108 versus +81%, respectively (P = .003) (Figure 5A). T2D respondents also reported making larger reductions in their typical mealtime dosage than T1D respondents in response to rapidly decreasing glucose (2 arrows down) when glucose is stable (flat arrow) at 110 mg/dl: –78% versus –46%, respectively (P < .001) (Figure 3B).

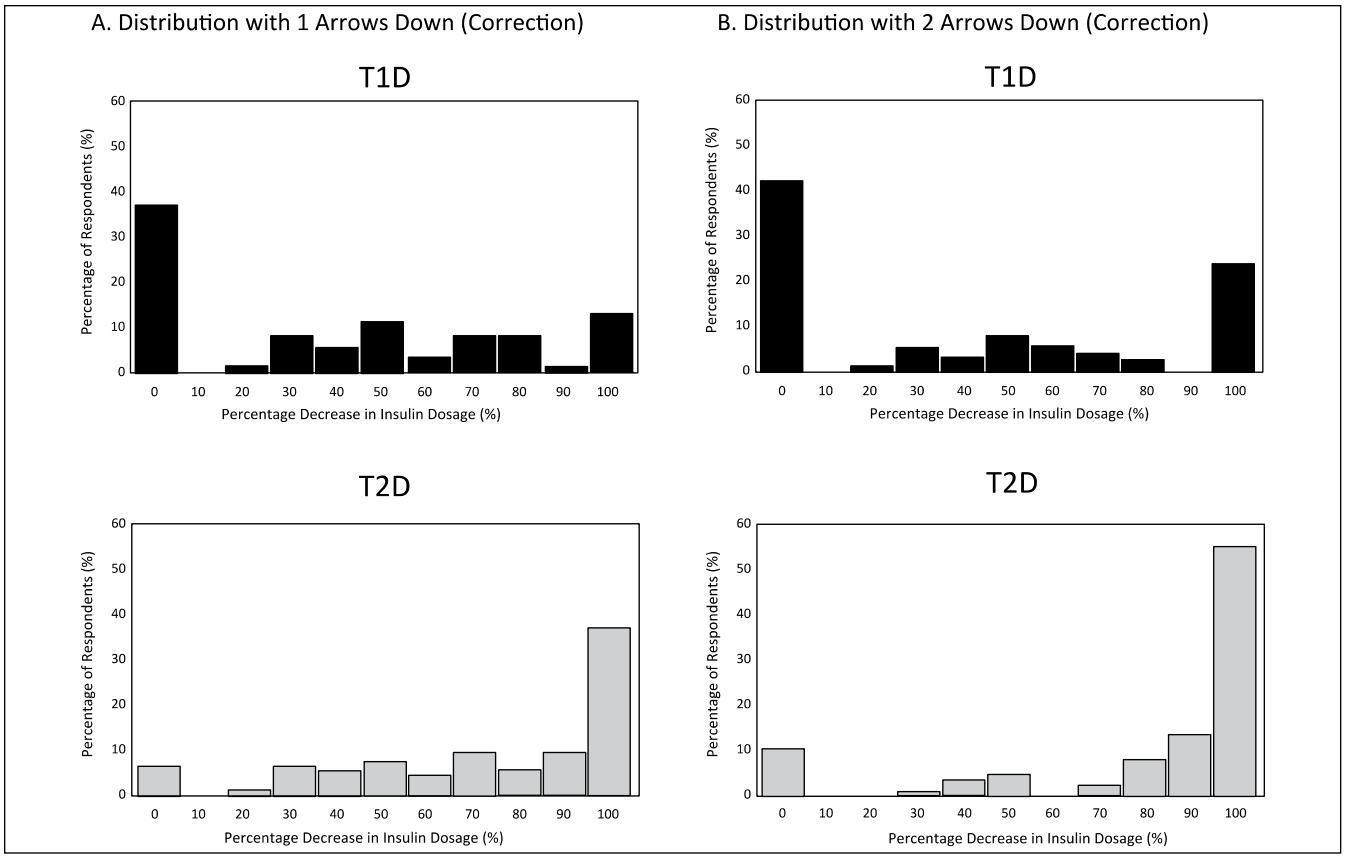

Figure 4. Distribution of insulin dosing adjustments based on the direction and rate of glucose change (1 arrow down [**A**] and 2 arrows down [**B**]) for a correctional insulin dose at hyperglycemia (220 mg/dL) between T1D and T2D respondents.

Timing of Meal Insulin Dose. Most T1D (59%) and T2D (67%) reported adjusting the timing of their mealtime insulin dose relative to the meal based on the ROC; meals were delayed following mealtime insulin administration when arrows indicated increasing glucose.

Discussion

Our survey showed that most respondents persistently used their CGM devices at frequencies associated with significant glycemic improvements in large clinical trials.[3,6,13-17] After 1 year of CGM use, most respondents reported reductions in frequency and severity of hypoglycemia, improvements in HbA1c levels, increased number of daily injections/boluses and aggressive correction and mealtime insulin dosage adjustments based on ROC arrows.

T1D respondents reported greater reductions in the frequency and severity of hypoglycemia. However, this may be related to more T1D than T2D respondents having problematic hypoglycemia prior to CGM use, their absolute need for exogenous insulin and counterregulatory hormone deficiencies.

The notable HbA1c improvements reported by T2D respondents were likely due to the lower average HbA1c reported by T1D respondents at baseline. However, it also suggests that the glycemic benefits reported by T2D respondents may be related to changes in health behaviors prompted by CGM data.

Most respondents reported an increase in the number of daily insulin injections/boluses. However, significant differences between T1D and T2D respondents were seen. For example, a larger percentage of T2D respondents reported taking fewer daily injections/boluses compared with T1D respondents, 75% of whom a treated with CSII. This suggests that use of CSII makes it easier to give extra boluses and provides the ability to fine tune insulin dose adjustments and decrease or suspend basal infusion may explain these increase; 75% of T1D respondents

It is also notable that a significantly larger percentage of T2D than T1D respondents reported taking an extra fixed dose of insulin in response to increasing glucose rather than considering past responses and adjusting based on experience or calculating a more exact dosage. This may be due to lack of confidence among T2D users regarding their dosage calculation accuracy or inconvenience of making these calculations; only 44% of T2D respondents were using CSII, which likely included an automated bolus calculator feature. However, it is also possible that they felt confident that their

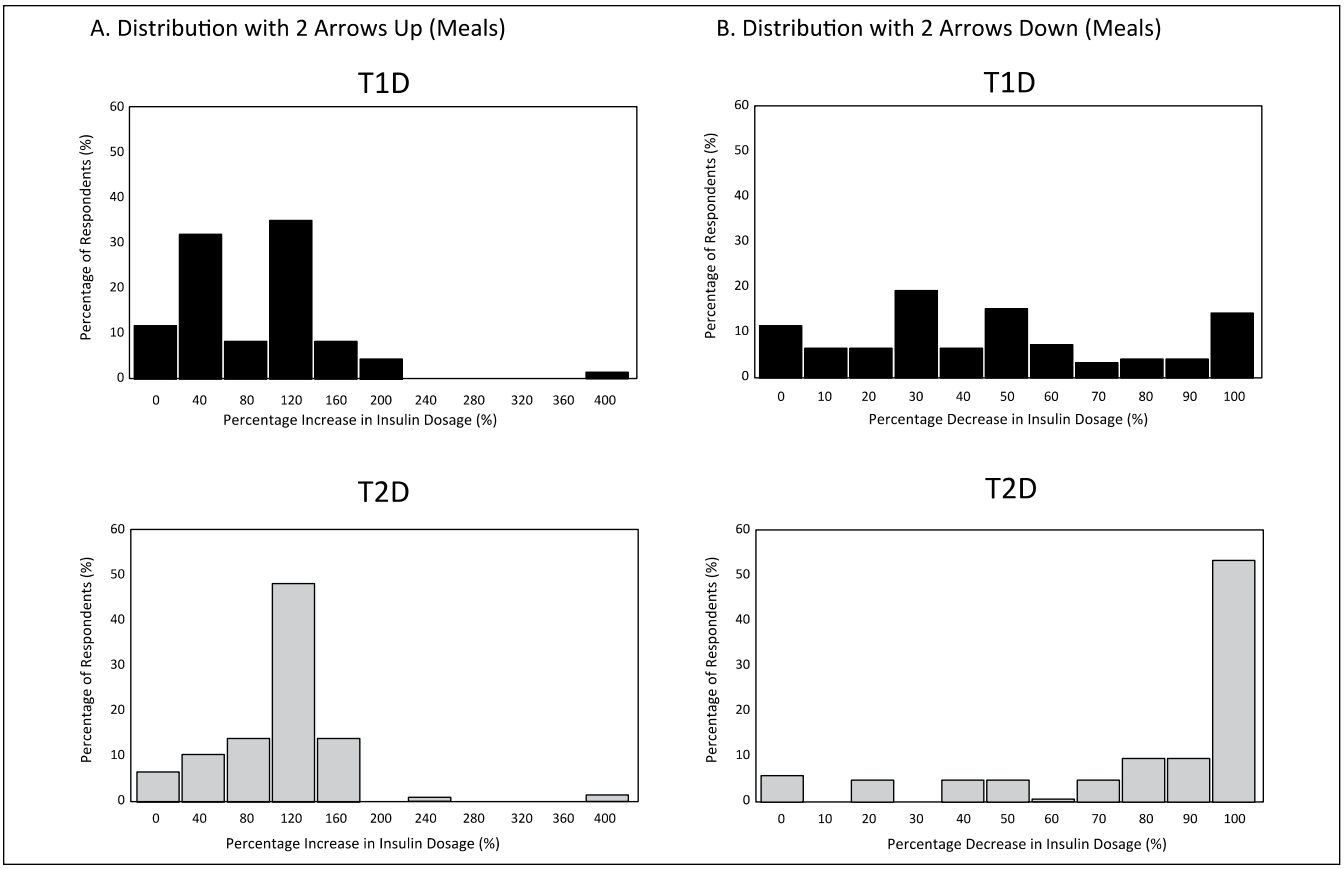

Figure 5. Distribution of insulin dosing adjustments based on the direction and rate of glucose change (2 arrows up [A] and 2 arrows down [B]) for a mealtime insulin dose at euglycemia (110 mg/dL) between T1D and T2D respondents.

CGM device would alert them to impending hyperglycemia or hypoglycemia if their fixed dose was inaccurate.

Predominant use of ROC arrows and subsequent aggressive correction and mealtime dosage adjustments among all respondents regardless of type of diabetes was a key finding of our survey. Most respondents reported using ROC arrows to make multiple and more significant changes in their insulin dosages than the 10% to 20% adjustments commonly recommended.[1,18,19]

A key issue is that although the ROC arrows were the driving factor in insulin dose adjustment, confidence in the accuracy of the glucose value was crucial. This suggests that respondents may have felt confident in the accuracy and reliability of their CGM device and their ability to closely monitor the effects of the dosage and take corrective action if needed.

A limitation of our survey was the use of self-reported data, which may not accurately reflect participants' actual frequency of CGM use or specific behaviors and/or dosage adjustments. Our findings are further limited by a lack of objective measurements of clinical outcomes (eg, change in HbA1c, hypoglycemia frequency and severity). Use of a single CGM device also limits the generalizability of our findings to other CGM systems. As demonstrated in an earlier study by Chamberlain and colleagues,[20] performance differences between CGM systems can impact users' perceptions of and trust in the accuracy and reliability of their CGM data. Our findings strongly suggest that user trust played a significant role in respondents' use of ROC arrows.

Conclusions

Findings from our survey demonstrated that many CGM users rely heavily on ROC arrows and alerts/alarms to make adjustments in their insulin dosages, regardless of their type of diabetes or insulin therapy. These findings are supported in previous studies, which demonstrated similar use of ROC arrows among individuals with T1D regardless of insulin delivery method.[11,12] Going forward, our role as providers, educators and researchers is to further clarify and quantify use of ROC arrows in adjusting insulin therapy to help individuals with diabetes navigate CGM technology, rather than having each patient "figure it out" on their own. More research is needed to differentiate between the various CGM systems currently available and, more importantly, to help establish guidelines for insulin dose adjustments based on ROC in users with T1D and T2D.

Abbreviations

CGM, continuous glucose monitoring; CSII, continuous subcutaneous insulin infusion; HbA1c, glycated hemoglobin; MDI, multiple

daily insulin injection; ROC, rate of change; T1D, type 1 diabetes; T2D, type 2 diabetes.

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Declaration of Conflicting Interests

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