Original Article

Evaluating Glucose Control With a Novel Composite Continuous Glucose Monitoring Index

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Abstract

Objective: The objective was to describe a novel composite continuous glucose monitoring index (COGI) and to evaluate its utility, in adults with type 1 diabetes, during hybrid closed-loop (HCL) therapy and multiple daily injections (MDI) therapy combined with real-time continuous glucose monitoring (CGM).

Methods: COGI consists of three key components of glucose control as assessed by CGM: Time in range (TIR), time below range (TBR), and glucose variability (GV) (weighted by 50%, 35% and 15%). COGI ranges from 0 to 100, where 1% increase of time <3.9 mmol/L (<70 mg/dl) is equivalent to 4.7% reduction of TIR between 3.9-10 mmol/L (70-180 mg/dl), and 0.5 mmol/L (9 mg/dl) increase in standard deviation is equivalent to 3% reduction in TIR.

Results: Continuous subcutaneous insulin infusion (CSII) users with HbA1c >7.5-10%, had significantly higher COGI during 12 weeks of HCL compared to sensor-augmented pump therapy, mean (SD), 60.3 (8.6) versus 69.5 (6.9), $P < .001$. Similarly, in CSII users with HbA1c <7.5%, HCL improved COGI from 59.9 (11.2) to 74.8 (6.6), $P < .001$. In MDI users with HbA1c >7.5% to 9.9%, use of real-time CGM led to improved COGI, 49.8 (14.2) versus 58.2 (9.1), $P < .0001$. In MDI users with impaired awareness of hypoglycemia, use of real-time CGM led to improved COGI, 53.4 (12.2) versus 66.7 (11.1), $P < .001$.

Conclusions: COGI summarizes three key aspects of CGM data into a concise metric that could be utilized to evaluate the quality of glucose control and to demonstrate the incremental benefit of a wide range of treatment modalities.

Keywords

continuous glucose monitoring, type 1 diabetes, closed-loop insulin delivery

Real-time continuous glucose monitoring (CGM) and intermittently viewed continuous glucose monitoring has transformed the management of type 1 diabetes[1] and paved the way to novel therapeutic interventions such as automated insulin delivery.[2] Usage of real-time CGM by multiple daily injection (MDI) users has been shown to improve HbA1c[3] and reduce the burden of hypoglycemia.[4] There is increasing recognition of the limitations of HbA1c as the sole measure of glycemic control, as it provides little or no information on clinically relevant outcomes such as hypoglycemia or glucose variability.[5,6] In contrast, continuous glucose monitoring (CGM) data provide detailed information about multiple aspects of glucose control such as time spent in the target glucose range (TIR), time spent in hypoglycemia and hyperglycemia, as well as glucose variability (GV). An international panel of experts has recently agreed on reporting of various CGM based metrics under research and clinical care setting.[7]

Given the limitation of HbA1c and the greater appreciation of CGM-derived glycemic outcomes, there is a growing interest to develop composite CGM indices.[8] Such composite indices may provide adjuvant information related to dysglycemia in people living with type 1 diabetes and may provide a tool to assess the therapeutic response to novel interventions such as automated insulin delivery or other therapies incorporating CGM.[9] Composite indices are widely

Table 1. Composition of the Continuous Glucose Monitoring Index (COGI).

Glucose control components	CGM metric	Scoring of the component	Overall weight
Time in range (TIR)	Percentage time sensor glucose between 3.9 and 10 mmol/L (70 to 180 mg/dl)	• 0% TIR is assigned 0 points • 100% TIR is assigned 100 points • Linear scoring between 0% and 100% TIR, ie, 67% TIR is assigned 66.7 points	50%
Time below range (TBR)	Percentage time sensor glucose below 3.9 mmol/L (70 mg/dl)	• 0% TBR is assigned 100 points • TBR 15% and above is assigned 0 points • Linear scoring between 0% and 15% TBR, ie, 5% TBR is assigned 66.7 points	35%
Glucose variability (GV)	Standard deviation	• SD 1 mmol/L (18 mg/dl) and below is assigned 100 points • SD 6 mmol/L (108 mg/dl) and above is assigned 0 points • Linear scoring between 1 and 6 mmol/L (18 and 108 mg/dl), ie, 2.7 mmol/L (48 mg/dl) is assigned 67 points	15%

For TBR and GV components higher score indicates lower time below range and lower variability.

used in other clinical specialties to complement decision making, for example in intensive care medicine (APACHE score), neonatology (APGAR score), and stroke medicine (Glasgow Coma Scale). Previous attempts at summarizing CGM data include "Glucose Pentagon Model"[8] and "Q score."[10]

Here we describe a novel and easy to understand, composite continuous glucose monitoring index (COGI) encompassing three vital elements of CGM-derived glucose control. We then use data from four recently published randomized controlled trials (RCTs) to demonstrate the utility of COGI index. We hypothesized that COGI might reveal important glycemic benefits of novel treatment modalities such automated insulin delivery with hybrid closed-loop and addition of real-time CGM to those using MDI therapy, beyond merely reporting changes in HbA1c.

Methods

We constructed the COGI from three key elements of CGM representing euglycemia, hypoglycemia, and GV: time in range (TIR) between 3.9 and 10 mM (70 to 180 mg/dl) and time below range (TBR) <3.9 mmol/L (70 mg/dl) were used as measures for euglycemia and hypoglycemia, respectively (Table 1). Standard deviation (SD) of overall glucose was used as a measure of GV. The relative contributions from these components where TIR, TBR, and GV contributed 50%, 35%, and 15% to the total COGI were pragmatically based on investigator consensus.

We allocated 0 points to 0% TIR and 100 points where TIR between 3.9 and 10 mM (70 to 180 mg/dl) is 100%. For TBR, 100 points were allocated if the TBR <3.9 mmol/L (<70 mg/dl) was 0% and 0 points if TBR 15% and above. GV as measured by SD was scaled from 1 to 6 mmol/L (18 to 108 mg/dl) where SD of 1 mmol/L (18 mg/dl) and below is given 100 points, and SD of 6 mmol/L (108 mg/dl) and above is given 0 points. For each of these elements, points were linearly interpolated between their boundaries.

The total index ranges from 0 to 100. The above allocation of scoring means, 1% increase in time <3.9 mmol/L (<70 mg/dl) is equivalent to 4.7% decrease in time in range (TIR) (penalty for time below range), and 0.5 mmol/L (9 mg/dl) increase in SD of glucose is equivalent to 3% decrease in TIR (penalty of higher variability). It also means

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Table 2. Details of Studies Used for the COGI Calculation.

Study name	Population	Intervention and duration	Primary outcome
AP@Home04 (Cross-over design) (11)	Adults with T1D on CSII HbA1c 7.5-10% mean age 40 (9) years mean baseline HbA1c 8.5% (0.7%)	Hybrid closed-loop vs sensor-augmented pump therapy 12 weeks (n = 32)	Time in range improved by 11 percentage points with closed-loop
AP@Home04 Extension (Cross-over design) (12)	Adults with T1D on CSII HbA1c <7.5% mean age 41 (13) years mean baseline HbA1c 6.9% (0.5)	Hybrid closed-loop vs CSII 4 weeks (n = 28)	Time in range improved by 10.5 percentage points with closed-loop
DIAMOND (Parallel design) (3)	Adults with T1D on MDI HbA1c 7.5-9.9% mean age 48 (13) years mean baseline HbA1c 8.6% (0.6%)	Real-time CGM using Dexcom G4 (n = 115) vs self-monitoring of blood glucose (n = 53) 24 weeks	HbA1c improved in real-time CGM group—adjusted treatment difference −0.6%
HypoDE (Parallel design) (4)	Adults with T1D on MDI History of impaired awareness of hypoglycemia or severe hypoglycemia, HbA1c ≤9.0% mean age 46 (11) years mean baseline HbA1c 7.5% (1.0%)	Real-time CGM using Dexcom G5 (n = 75) vs self-monitoring of blood glucose (n = 74) 26 weeks	Incidence of hypoglycemia events reduced by 72% in the real-time CGM group

1% increase in time <3.9 mmol/L (<70 mg/dl) will decrease COGI by 2.3 points, whereas an increase of TIR by 1 percentage point will increase the COGI by 0.5 points. A healthy individual without diabetes who spent 2% time below 3.9 mmol/L (70 mg/dl) will have a COGI of 90.6, while if the time spent below 3.9 mmol/L is zero will have maximum COGI of 100. (based on reference 16)

The total and individual components of COGI were calculated in adults with type 1 diabetes treated with multiple daily injection therapy (MDI) or continuous subcutaneous insulin infusion (CSII) from 4 previously published RCTs.[3,4,11,12] Study design and methods of these studies have been published and described in detail elsewhere. Summaries of these studies are shown in Table 2.

Briefly, AP@home04 phase 1 study[11] evaluated the safety and effectiveness of hybrid closed-loop in comparison to sensor-augmented pump therapy in adults with type 1 diabetes and HbA1c between 7.5% to 10% (58 to 86 mmol/mol) for 12 weeks, while AP@home04 phase 2 study[12] evaluated the safety and effectiveness of hybrid closed-loop in comparison to insulin pump therapy with or without real-time CGM in adults with type 1 diabetes and HbA1c <7.5% (<58 mmol/mol) for 4 weeks.

DIAMOND study[3] evaluated the effectiveness of real-time CGM in adults with type 1 diabetes and HbA1c levels between 7.5% (58 mmol/mol) to 9.9% (85 mmol/mol) treated with MDI where participants were allocated 2:1 to either real-time CGM (Dexcom G4 Platinum system, Dexcom Inc, San Diego, CA, USA) or usual care group for 24 weeks. HypoDE study[4] evaluated the effectiveness of real-time CGM (Dexcom G5, Dexcom Inc, San Diego, CA, USA) in avoidance of hypoglycemia in adults with type 1 diabetes treated with MDI and history of impaired awareness of hypoglycemia or severe hypoglycemia and HbA1c ≤9.0% (75 mmol/mol).

Data and Statistical Analysis

We calculated TIR between 70 to 180 mg/dl, TBR <70 mg/dl and GV as measured by the SD for each study participant. We then calculated the individual and total components of the COGI score using Microsoft Excel. SD are reported for means and interquartile ranges (IQRs) for medians where applicable. We used SPSS (v.22) or SAS (version 9.3) for statistical analysis. Either paired samples t-tests or analysis of covariance (ANOVA) were performed for comparison of treatment groups. For the DIAMOND and Hypo-DE parallel design studies, when calculating paired differences, we adjusted each analysis for the baseline value of the respective parameter. For example when calculating paired difference of total COGI score, we included baseline COGI as a covariate in the analysis of covariance models. Each analysis was tested at a two-sided significance levels of 0.05.

Results

Twelve-weeks of hybrid closed-loop by type 1 diabetes adults with HbA1c >7.5%[11] led to a significant improvement in COGI index (Table 3). Although all three components of COGI improved, the highest contribution came from TIR. HbA1c and COGI improvement by hybrid closed-loop use in the whole cohort was −0.3% (0.6) ($P = .002$) and +9.2 ($P < .005$, 95% confidence interval [CI] 7 to 11%) respectively. Subgroup analysis in those without HbA1c improvement (n = 15, HbA1c improvement <0.3%) showed that total and individual COGI components improved with hybrid closed-loop use (Table 3).

Table 3. Comparison of COGI During Hybrid Closed-Loop Insulin Delivery Compared With Sensor Augmented or Standard CSII.

	Hybrid closed-loop	SAP or CSII	Paired difference**	*P* value
	AP@Home04 study (phase 01) (n = 32)			
Total COGI	69.5 (6.9)	60.3 (8.6)	9.2 (7.0, 11.4)	<.001*
TIR component (out of 50)	33.8 (5.3)	28.3 (7.2)	5.4 (4.0, 6.9)	<.001*
TBR component (out of 35)	28.2 (24.5, 31.7)	28 (20.1, 30.5)	0.9 (−0.7, 4.5)	.023˜
GV component (out of 15)	7.9 (2.0)	7.1 (2.0)	0.7 (0.4, 1.1)	<.001*
	AP@Home04 study (phase 01, without HbA1c improvement (n = 15)			
Total COGI	70.8 (6.4)	60.4 (10.5)	10.3 (6.0, 14.8)	<.001
TIR component (out of 50)	36.4 (5.0)	33.4 (6.1)	3.1 (1.2, 4.9)	.003
TBR component (out of 35)	25.0 (24.1, 28.6)	20.7 (13.4, 27.3)	4.5 (1.5, 10.8)	.002˜
GV component (out of 15)	8.6 (2.1)	8.1 (2.0)	0.6 (0.1, 1.1)	.029
	AP@Home04 study (phase 02) (n = 28)			
Total COGI	74.8 (6.6)	59.9 (11.2)	14.8 (11.2, 18.5)	<.001*
TIR component (out of 50)	38.0 (3.3)	32.8 (4.1)	5.2 (3.7, 6.6)	<.001*
TBR component (out of 35)	28.2 (25.8, 30.0)	22.7 (11.7, 26.8)	5.0 (3.2, 12.4)	<.001˜
GV component (out of 15)	9.6 (1.1)	8.0 (1.5)	1.5(1.0, 2.2)	<.001*

Mean (SD) or median (IQR). *Paired samples *t*-test. ˜Wilcoxon Signed rank test. **Paired difference mean (95% CI) except for TBR where median (IQR) is shown. For TBR and GV components higher score indicates lower time below range and lower variability.

Table 4. DIAMOND Study: Comparison of COGI at 6 Months Between Treatment Groups.

	Baseline phase (n = 158)		Month 6 phase (n = 146)			
	CGM (n = 105)	SMBG (n = 53)	CGM (n = 93)	SMBG (n = 53)	Adjusted group difference (95% CI)	*P* value*
Total COGI	50.8 (10.6)	48.8 (11.3)	58.2 (9.1)	49.8 (14.2)	7.1 (4.2,10.1)	<.0001
TIR component (out of 50)	23.1 (6.2)	22.6 (5.9)	25.2 (7.1)	22.3 (7.2)	2.6 (0.7,4.5)	.01
TBR component (out of 35)	22.6 (8.6)	21.1 (10.2)	28.5 (24.6, 30.9)	25.7 (16.0, 30.9)	3.1 (0.8,5.3)	.01
GV component (out of 15)	5.1 (2.1)	5.1 (2.1)	6.3 (2.1)	4.7 (2.7)	1.6 (0.9,2.2)	<.0001

*ANOVA, adjusting for baseline levels. For TBR and GV components, higher score indicates lower time below range and lower variability.

Table 5. HypoDE Study: Comparison of COGI at 6 Months Between Treatment Groups.

	Baseline phase (n = 141)		Month 6 phase (n = 141)			
	CGM (n = 75)	SMBG (n = 66)	CGM (n = 75)	SMBG (n = 66)	Adjusted group difference (95% CI)	*P* value*
Total COGI	57.4 (13.3)	55 (13.1)	66.7 (11.1)	53.4 (12.2)	11.7 (9, 14.4)	<.001
TIR component (out of 50)	28.9 (7.7)	29.5 (6.6)	29.2 (8.9)	28.2 (6.1)	1.5 (−0.02, 3.1)	.054
TBR component (out of 35)	24 (14.7, 29.1)	19.7 (7.4, 27)	31 (26.8, 33.2)	21.1 (8.1, 27)	9.4 (7.1, 11.5)	<.001
GV component (out of 15)	7.4 (2.5)	7.4 (2.3)	8.2 (2.4)	7.0 (2.4)	1.3 (0.87, 1.7)	<.001

*ANOVA, adjusting for baseline levels.
For TBR and GV components, higher score indicates lower time below range and lower variability.

Four-week hybrid closed-loop use by type 1 diabetes adults with HbA1c <7.5%[12] also showed significant improvements in total and all three components of the COGI index (Table 3).

In the 6-month study of real-time CGM use among MDI users with suboptimal control (DIAMOND study),[3] a significant improvement of all three components of COGI was shown (Table 4). During the HypoDE study, which included individuals with impaired awareness of hypoglycemia, as expected the most noticeable improvements were noted in the hypoglycemia component (Table 5). The between-group HbA1c difference in the study involving type 1 diabetes individuals with impaired awareness of hypoglycemia (HypoDE study) was nonsignificant at 0.03% ($P = .66$),[4] however a significant improvement in the total COGI index was observed notably within the hypoglycemia component, highlighting the utility of COGI beyond HbA1c (Table 5).

Discussion

The multiple glucometric data provided by CGM present an excellent opportunity to define a composite index which can be utilized in clinical and research settings. Here we present such a novel composite CGM index, encompassing three key aspects of CGM-based assessment of glucose control: time spent in normal glucose, hypoglycemia, and GV. These are aspects of glucose control which are arguably most important for people living with type 1 diabetes. We show that by using COGI, the incremental benefits of hybrid closed-loop use on glucose control can be demonstrated even in those individuals with very good HbA1c. Furthermore, COGI demonstrates the additional benefit of real-time CGM use even without apparent HbA1c improvements.

Pernick and Rodbard previously developed and implemented a scoring system for SMBG glucose data in 1986 that included measures of mean glucose, % hyperglycemia, % hypoglycemia, variability, and adequacy of the data.[13] The original Glucose Pentagon Model described by Thomas et al in 2009[8] included five metrics: mean glucose, SD of the mean glucose, amount of time per day in which hyperglycemic values (>160 mg/dl) were recorded, the area below the curve of hyperglycemic values (>160 mg/dl), and HbA1c. Each parameter formed a single axis of a five-sided figure. By taking the area within the glucose pentagon of a given individual with diabetes and normalizing it to the standard area of a healthy individual without diabetes, a Glycaemic Risk Parameter (GRP) was defined. Subsequently, authors reanalyzed a subset of data from the JDRF real-time CGM study showing a more substantial percentage improvement of GRP than HbA1c improvement with real-time CGM.[9]

Hypoglycemia is one of the most significant barriers to achieving near-normal glucose control for people living with diabetes and their caregivers.[14] One of the limitations of the original glucose pentagon may be the noninclusion of a measure of hypoglycemia. In 2018 (2017), Vigersky et al presented the comprehensive glucose pentagon (CGP) which included several changes to the original pentagon model.[15] In the CGP, the HbA1c axis was eliminated, and glycemic variability was measured with CV rather than SD. New aspects included the time outside range and intensity of hypoglycemia and hyperglycemia reflecting a composite of frequency, severity and duration.

Q score is another novel concept in analyzing CGM profiles presented by Augstein et al in 2015.[10] The authors identified four key factors using 1562 historic CGM profiles in people with type 1 and type 2 diabetes. These four factors were central tendency and hyperglycemia, hypoglycemia, intraday variability, and interday variability. They choose mean glucose, time spent above the target range, the range of glucose, time spent below target range and mean of daily difference (MODD) in calculating the Q score. They used Q score to categorize the quality of glucose control ranging from poor to very good. One potential limitation of glucose pentagon models and Q score may be the difficulty in interpreting values obtained with these methods under day-to-day clinical practice conditions. On the other hand, a single index expressed as a score from 100 (where 100 reaches the glucose profile of people without diabetes) might be expected to be easier to understand and interpret. A previous real-time CGM study looking at the characterization of interstitial glucose levels in individuals without diabetes have shown that virtually all glucose levels were <140 mg/dl (<7.8 mM) and that 0.6 to 2.9% of real-time CGM glucose levels could be below 70 mg/dl (<3.9 mM).[16] In that study, GV measured with SD was below 18 mg/dl (<1 mmol/L) in all age groups.

There has been other notable proposed approaches which provides quantification and/or visualization of glycemic control quality. The weighted average of glucose values (M_R) provides a measure of glycemia stability in comparison with an arbitrary assigned "ideal" glucose value labelled as "R", ranging from 4.4 to 7.8 mmol/l[17] The Glycemic Risk Assessment in Diabetes Equation (GRADE) formula converts glucose values to a risk score, calculates the median, and provides the risk attributable to hypoglycemia and hyperglycemia[18] The use of graphical displays to facilitate interpretation of glucose data by clinicians and researchers have been proposed by Rodbard, for example utilizing a 2-dimensional triangular graph which simultaneous display of %High (above a specified threshold for hyperglycemia), %Low (below a specified threshold for hypoglycemia), and percentage in target range that facilitate rapid analysis of hypo- and hypoglycemia risks.[19] Furthermore, Rodbard also discussed frequency of hypoglycemia versus A1C and frequency of hypoglycemia versus mean glucose, and %hypoglycemia versus %target range in this article.[19] There has also been other graphical approachers delineating the relationship between CGM data and glycemic control quality in recent clinical studies utilizing CGM, for example combining mean glucose and visual markers of hypoglycemia frequency before and after study intervention.[11,20]

COGI summarizes CGM data using a single index ranging from 0 to 100. It is easy to interpret, that is, those with COGI close to 100 have a glucose profile similar to someone without diabetes while COGI of 50 indicates that quality of glucose control is 50% of that in a healthy individual without diabetes. COGI can be calculated using three widely available CGM metrics. As shown by variety of recently published studies, COGI could be easily applied in a wide number of study design and settings using CGM to assess study outcomes. Due to its cumulative effects, it may generate higher statistical power over individual components of CGM or HbA1c but this remains to be proven in future studies and further data analysis. To further highlight the effectiveness of the combined index, we have looked at the *t* values and *F* values in statistical testing for some of the comparisons presented in Tables 3 and 5. In Table 3, AP@home04 study (phase 01, n = 32), the *t* value of the paired samples test for the total COGI index was 8.4 while

individual component *t* values for TIR, TBR, and GV were 7.4, 5.4, and 5.5. Similarly, Table 5, HypoDE study, *F* value for ANCOVA testing for total COGI was 75.2, while individual component *F* values for TIR, TBR, and GV were 3.7, 68.7, and 35.3. Serial COGI scores could also be used as a relatively convenient and understandable method by people living with type 1 diabetes and caregivers to assess the progress of treatment during routine care.

Future iterations of COGI may include replacing components of COGI with alternative metrics. There is currently no consensus on the optimal metric for assessing GV. Previous work has demonstrated strong correlation between SD and mean glucose [21] However, there is currently no consensus on the optimal metric for assessing GV.7 SD was used to measure GV in our analysis. As COGI does not include mean glucose, use of SD is justifiable and potentially advantageous. It is however possible to replace SD with the coefficient of variation with the appropriate scale as the metric choice of variability. Similarly, time spent below 54 mg/dl could be used instead of 70 mg/dl. Reporting on COGI outcomes could potentially be incorporated into many clinical software programs currently available such as Medtronic Carelink, Dexcom Clarity, Glooko, Diasend, Freestyle Libreview, and many others, as part of type 1 diabetes management.

Previous work has also shown high degree of correlation among various CGM metrics. In a review article, Rodbard cross-validated several metrics for quality of glycemic control, hypoglycemia, and hyperglycemia.[22] There were consistently high correlations between %Time in range (%TIR) and previously described risk indices such as M100, Blood Glucose Risk Index, Glycemic Risk Assessment Diabetes Equation, Index of Glycemic Control, and J-Index. There were also high correlations among %Hypoglycemia, Low Blood Glucose Index (LBGI), percentage of GRADE attributable to hypoglycemia (GRADE%Hypoglycemia), and Hypoglycemia Index.

A limitation of COGI is the pragmatic decision related to the weight of the three components: TIR 50%, TBR 35%, and GV 15%. We allocated the most substantial weight to the time in range with 50% contribution to the index as this is likely to be the parameter most likely to relate to HbA1c and hence to capture the risk of long-term complications. We allocated 35% of weight to time below range, more than the 15% weight for GV to account for the importance of avoiding hypoglycemia as it remains one of the biggest barriers to achieving near normal glucose control. Other potential limitations include the use of SD instead of CV (see above) and use of 70 mg/dl as a cut off for time below range. Until recently, HbA1c remains to date the only clinically validated prognostic marker of diabetes complications. However two recent publications, have demonstrated a link with time in range and long term diabetes complications.[23,24] This further supports our allocation of highest weight to time in range. There is a need to evaluate whether COGI can provide prognostic indications for future risk of macro and microvascular complications. Future studies will also need to evaluate the utility of COGI in type 2 diabetes or hospitalized patients and the relationship between COGI and patient-reported outcomes such as diabetes distress or low mood. COGI does not contain mean glucose and this may be viewed as a potential limitation. However, there is a strong correlation between mean glucose and TIR as well as mean glucose and SD.

In conclusion, we have presented a novel composite CGM index consisting of three clinically meaningful parameters of glucose control representing euglycemia, hypoglycemia, and GV. We demonstrated, using four randomized studies involving adults with type 1 diabetes in diverse settings, that COGI may be utilized as an index of quality of glucose control specifically in the context of novel technology using CGM. Future studies evaluating its impact on real world data as well as clinical and patient-related outcomes are needed.

Abbreviations

CGM, continuous glucose monitoring; CI, confidence interval; COGI, continuous glucose monitoring index; CSII, continuous subcutaneous insulin infusion; GRADE, Glycemic Risk Assessment in Diabetes Equation; GV, glucose variability; HCL, hybrid closed loop; MDI, multiple daily injections; MODD, mean of daily difference; RCT, randomized controlled trial; SD, standard deviation; TBR, time below range; TIR, time in range.

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Declaration of Conflicting Interests

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