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Alarm Settings of Continuous Glucose Monitoring Systems and Associations to Glucose Outcomes in Type 1 Diabetes

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Context: Little evidence exists regarding the positive and negative impacts of continuous glucose monitor system (CGM) alarm settings for diabetes control in patients with type 1 diabetes (T1D).

Objective: Evaluate the associations between CGM alarm settings and glucose outcomes.

Design and Setting: A cross-sectional observational study in a single academic institution.

Patients and Main Outcome Measures: CGM alarm settings and 2-week CGM glucose information were collected from 95 T1D patients with > 3 months of CGM use and ≥ 86% active usage time. The associations between CGM alarm settings and glucose outcomes were analyzed.

Results: Higher glucose thresholds for *hypo*glycemia alarms (ie, ≥ 73 mg/dL vs < 73 mg/dL) were related to 51% and 65% less time with glucose < 70 and < 54 mg/dL, respectively ($P = 0.005$; $P = 0.016$), higher average glucose levels ($P = 0.002$) and less time-in-range ($P = 0.005$), but not more hypoglycemia alarms. The optimal alarm threshold for < 1% of time in hypoglycemia was 75 mg/dL.

Lower glucose thresholds for *hyper*glycemia alarms (ie, ≤ 205 mg/dL vs > 205 mg/dL) were related to lower average glucose levels and 42% and 61% less time with glucose > 250 and > 320 mg/dL ($P = 0.020$, $P = 0.016$, $P = 0.007$, respectively), without more hypoglycemia. Lower alarm thresholds were also associated with more alarms ($P < 0.0001$). The optimal alarm threshold for < 5% of time in hyperglycemia and hemoglobin A1c ≤ 7% was 170 mg/dL.

Conclusions: Different CGM glucose thresholds for hypo/hyperglycemia alarms are associated with various hypo/hyperglycemic outcomes. Configurations to the hypo/hyperglycemia alarm thresholds could be considered as an intervention to achieve therapeutic goals.

Key Words: type 1 diabetes, continuous glucose monitoring systems, hypoglycemia, hyperglycemia

Abbreviations: AUC, area under the curve; CGM, continuous glucose monitoring; COV, coefficient of variation; FPR, false positive rate; HbA1c, hemoglobin A1C; ROC, receiver operating characteristic; T1D, type 1 diabetes; TPR, true positive rate.

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Patients with type 1 diabetes (T1D) are bound to use exogenous insulin to control glucose, and thus face the challenge of avoiding and managing hypo- and hyperglycemia on a daily basis [1]. Continuous glucose monitoring (CGM) systems measure subcutaneous interstitial glucose to estimate blood glucose levels, and report glucose information to patients in real time. CGMs also generate audible alarms for low/high glucose levels, based on the settings made by patients or healthcare providers, to alert the patients to hypo/hyperglycemic events. CGMs have been demonstrated to improve hemoglobin A1C (HbA1c) and average glucose levels [2–4], as well as to reduce the percentages of time in hypoglycemia and severe hypoglycemia episodes [5–7] in patients with T1D.

An HbA1c of ≤ 7% (53 mmol/mol) has long been established as a treatment target for T1D patients [8, 9]. A recent international consensus [10] further proposed to target on the glucose time-in-range (defined as the time percentage with glucose levels between 70–180 mg/dL) by reducing the time in hypo/hyperglycemia. Specifically, < 4% and < 1% of time with glucose < 70 and <54 mg/dL, and < 25% and < 5% of time with glucose > 180 and > 250 mg/dL, respectively, were recommended as therapeutic goals. While multiple clinical trials have proven the utility of CGMs in reducing both hypo- and hyperglycemia [2, 3, 6, 7], retrospectively, many patients in these studies still failed to reach the recently proposed targets, and questions remain on how to improve glucose control in this population. In particular, while CGMs have hypo/hyperglycemia alerting systems, little evidence exists on how the alarm settings are associated with the glucose profiles. Such information can be used as a reference for alarm setting configurations to help improve glucose control as well as support future studies to further advance the utility of CGM alarms.

The alarms generated by CGMs for pending or ongoing hypo/hyperglycemic events can cause disruptions to daily life or sleep [11]. The consideration of alarm fatigue, that patients become overwhelmed by the number of alarms and thus fail to respond to them, has therefore been described [12]. However, little information exists on how CGM alarm settings are associated with the number of alarms, and whether the alarm numbers alter patients' responses and thus affect the time duration to recover from hypo/hyperglycemia.

The current study evaluated the associations between CGM alarm settings and glucose outcomes by: (1) determining how CGM alarm settings are related to the time in hypo/hyperglycemia; (2) assessing the associations between alarm settings, the alarm numbers and the time duration to recover from hypo/hyperglycemia; and (3) identifying the optimal alarm thresholds associated with various percentages of time in hypo/hyperglycemia.

1. Methods

A. Participants and Measurements

An observational study was conducted at the University of Utah between May 2018 and December 2018. The eligibility criteria were T1D, ongoing real-time CGM use for longer than 3 months [6], and active CGM usage time ≥ 86% [2, 13]. The active usage time was defined by the time percentages with glucose records in the preceding 2 weeks on CGM download reports. Candidates using insulin pumps linked to CGMs with programmed automated insulin adjustments/suspension were excluded.

Nighty-five participants met the eligibility criteria and were included in the data analyses (Table 1). All participants were using Dexcom CGMs (sensor G4, G5, and G6 in 7, 74, and 14 participants, respectively). All study participants completed a study survey to document their duration of T1D history and CGM use, as well as insulin programs (multiple daily injections vs continuous subcutaneous insulin infusion). Medical records were reviewed to confirm the diagnosis of T1D and to collect the participant data for age, sex, and the most recent HbA1c values. The CGM glucose data in the preceding 2 weeks were downloaded through Dexcom Clarity software, including the single glucose values, as well as the average glucose levels, time-in-range, and glucose coefficients of variation (COVs). Algorithms constructed by biomedical informatics were used to analyze the single glucose values to

Table 1. Demographics, CGM Glucose Characteristics, and Alarm Settings

Demographics	
Age, years	44.8 ± 15.8
Sex (female/male), n (%)	51/44 (54/46)
HbA1c, % (mmol/mol)	7.4 ± 1.2 (57.4)
Duration of diabetes, years	22.4 ± 15.3
Duration of CGM usage, months	31.9 ± 25.4
Insulin regimen (MDI/CSII), n (%)	30/65 (32/68)
Active CGM usage time, %	94.4 ± 4.4
CGM Glucose Characteristics	
Average glucose, mg/dL	163 ± 34
Percentage of time spent in hypoglycemia, with glucose levels	
<70 mg/dL	3.58 ± 4.18
<54 mg/dL	1.05 ± 1.98
Percentage of time spent in hyperglycemia, with glucose levels	
>180 mg/dL	33.6 ± 19.4
>250 mg/dL	11.2 ± 11.9
>320 mg/dL	3.33 ± 5.33
Glucose time-in-range, %	62.8 ± 18.1
Glucose COV, %	35.6 ± 6.3
Hypoglycemia Alarm Settings	
Hypoglycemia alarm turned on, n (%)	86 (91)
Repeat alarm turned on, n (%)	32 (34)
Glucose threshold for hypoglycemia alarm, mg/dL	
Day	72.9 ± 10.7
Night	72.8 ± 10.7
Glucose fall alarm turned on, n (%)	35 (37)
Hyperglycemia Alarm Settings	
Hyperglycemia alarm turned on, n (%)	83 (87)
Repeat alarm turned on, n (%)	30 (32)
Glucose threshold for hyperglycemia alarm[1], mg/dL	205 ± 45
Glucose rise alarm turned on, n (%)	29 (31)

Data presented as mean ± standard deviation or proportion. Abbreviations: CGM, continuous glucose monitoring; COV, coefficient of variation; CSII, continuous subcutaneous insulin infusion; HbA1c, hemoglobulin A1C; MDI, multiple daily injections.
[1]Based on the 83 participants who turned on their hyperglycemia alarm; for both day and nighttime.

study the glucose profiles. Specifically, the percentages of time spent in hypo/hyperglycemia were determined by the number of points below/above the hypoglycemia (ie, 70 or 54 mg/dL) or hyperglycemia (ie, 180, 250, and 320 mg/dL) glucose cutoffs over the total available glucose points, respectively [2, 13]. The CGM alarm settings, including the hypo/hyperglycemia alarm, repeat hyper/hypoglycemia alarm, and glucose rise/fall alarm, were recorded. For those who turned off the hypoglycemia alarm, a glucose level of 55 mg/dL (the factory setting of glucose threshold for urgent low glucose alarm that could not be changed nor turned off) was documented as the glucose threshold for hypoglycemia alarm. There was no significant difference between the day and nighttime glucose thresholds for hypo/hyperglycemia alarms ($P = 0.946$ and $P = 0.945$, respectively) (Table 1).

To determine the number of hypo/hyperglycemia alarms that were generated by CGMs, each count of hypo/hyperglycemia alarms was determined based on a glucose value being below or above the glucose thresholds for hypoglycemia or hyperglycemia alarms, respectively. The recovery duration from hypo/hyperglycemia was defined by the time periods between the first and the preceding last glucose value below/above the glucose thresholds for hypo/hyperglycemia, respectively.

The University of Utah Institutional Board Review Committee approved the conduct of the current study. Informed consent was completed by all study participants. The current study is an extension of a prior study reporting the diabetes characteristics of T1D CGM users [14].

B. Statistical Analysis

The demographics and CGM glucose and alarm setting information were reported as mean ± standard deviation or proportion. Student *t*-test was used to assess the differences in the percentages of time in hypo/hyperglycemia, average glucose levels, time-in-range, and glucose COVs between the participants, with the alarm thresholds set above and below the mean hypo/hyperglycemia alarm thresholds. Logistic regression analyses were conducted to evaluate the correlations of the CGM glucose profiles with the statuses of hypo/hyperglycemia alarms, repeat alarms, and glucose fall/rise alarms. Linear regression analyses were conducted to evaluate the correlations between the number of alarms and the time-to-recover from hypo/hyperglycemia.

Receiver operating characteristic (ROC) analyses and Youden Index (*J*) calculations were conducted to determine the optimal cutoffs of hypo/hyperglycemia alarm thresholds to maximize the true positive rate (TPR) and false positive rate (FPR) for < 1%, < 2%, and < 4% of time with glucose levels < 70 mg/dL, <5 %, < 15%, and < 25% of time with glucose > 180 mg/dL and HbA1c ≤ 7%.

All study participants were included in the hypoglycemia alarm setting analyses. For the analyses evaluating hyperglycemia alarms (ie, the glucose thresholds for hyperglycemia alarms, and the alarm numbers and duration recovering from hyperglycemia), only the 83 participants who turned on their hyperglycemia alarms were included. For day/nighttime analyses, 6:00 AM to 10:00 PM was considered day-time, and 10:01 PM to 5:59 AM was considered nighttime. Sex was not considered as a factor in the data analysis for the purpose of the current study. *P* values < 0.05 were considered statistically significant and *P* values between ≥ 0.05 and < 0.10 were noted as trends.

2. Results

A. Hypoglycemia Alarm Thresholds and Glucose Outcomes

The participants with glucose thresholds for hypoglycemia alarms set at ≥ 73 mg/dL (ie, at or above the study cohort's mean threshold for hypoglycemia alarms) spent lower percentages of time with glucose levels < 70 and < 54 mg/dL (2.29% ± 2.35% and 0.53% ± 0.68%) compared with those who had the alarm set at < 73 mg/dL (4.70% ± 5.03% and 1.50% ± 2.55%; $P = 0.005$ and $P = 0.016$, respectively) (Fig. 1). Similar patterns were also observed for the day and nighttime analyses (Table 2). The participants with alarm threshold ≥ 73 mg/dL also had higher average glucose levels (175 ± 32 mg/dL) and less time-in-range (57.3% ± 18.7%)

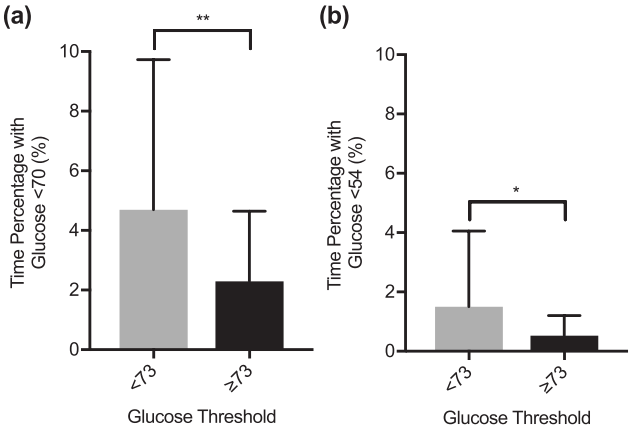

Figure 1. Bar graphs showing the means and standard deviations of the percentages of time spent with glucose (a) <70 and (b) <54 mg/dL with CGM glucose thresholds <73 and ≥73 mg/dL for hypoglycemia alarms.

CGM, continuous glucose monitoring. *$P < 0.05$; **$P < 0.01$. *P*-values were determined by Student *t*-test. All glucose information is presented in mg/dL.

compared with those who had alarm thresholds < 73 mg/dL (153 ± 32 mg/dL; $P = 0.002$ and 67.6% ± 16.2%; $P = 0.005$, respectively).

B. Hyperglycemia Alarm Thresholds and Glucose Outcomes

Among the 83 participants who turned on their hyperglycemia alarms, those with hyperglycemia alarm thresholds ≤ 205 mg/dL (ie, at or below the cohort's mean threshold of hyperglycemia alarms) had lower average glucose levels (155 ± 26.8 mg/dL) compared with those who had alarm thresholds > 205 mg/dL (172 ± 39 mg/dL; $P = 0.020$). These participants also tended to have lower percentages of time with glucose levels >180 mg/dL (30.0% ± 16.4%), and spent significantly less time with glucose levels > 250 and > 320 mg/dL (8.36% ± 8.08%; 2.02% ± 3.21%), compared with those who had alarms set at > 205 mg/dL (37.1 ± 22.5%, 14.5 ± 14.8%, 5.13 ± 7.02%; $P = 0.099$, $P = 0.016$, $P = 0.007$, respectively) (Fig. 2). Similar findings were also identified for both the day and nighttime analyses (Table 2). The time percentages with glucose levels < 70 and < 54 mg/dL and time-in-range between the groups with hyperglycemia alarm thresholds ≤ 205 and > 205 mg/dL were statistically indistinguishable ($P = 0.141$, $P = 0.588$, $P = 0.171$, respectively).

There were no significant differences in glucose COVs between the participants with *hypo*glycemia alarm thresholds ≥ 73 mg/dL and < 73 mg/dL ($P = 0.973$), as well as between those with *hyper*glycemia alarm thresholds ≤ 205 mg/dL and > 205 mg/dL ($P = 0.543$).

C. ROC and Youden Index Analysis to Determine Optimal Alarm Thresholds for Various Time Percentages in Hypo/Hyperglycemia

An alarm threshold of 75 mg/dL was the optimal hypoglycemia alarm cutoff for both < 2% (TPR, 0.63; FPR, 0.67; $J = 0.30$) and < 1% (TPR, 0.64; FPR, 0.60; $J = 0.24$) of time with glucose levels < 70 mg/dL (Fig. 3). No optimal alarm threshold was associated with < 4% of time with glucose levels < 70 mg/dL. For hyperglycemia, 170 mg/dL was the optimal

Table 2. The Relationships Between CGM Glucose Thresholds for Hypo/Hyperglycemia Alarms and Percentages of Time Spent in Hypo/Hyperglycemia During the Day and Nighttime

	Percentage of Time in Hypoglycemia (%)		
	Thresholds <73 mg/dL	**Thresholds ≥73 mg/dL**	***P* Value**
<70 mg/dL			
Day	4.69 ± 5.57	2.37 ± 2.50	0.012
Night	4.55 ± 4.85	2.13 ± 2.55	0.004
<54 mg/dL			
Day	1.41 ± 2.60	0.59 ± 0.88	0.049
Night	1.64 ± 2.98	0.40 ± 0.61	0.009
	Percentage of time in hyperglycemia (%)		
	Thresholds >205 mg/dL	**Thresholds ≤205 mg/dL**	***P* Value**
>180 mg/dL			
Day	36.9 ± 22.3	30.1 ± 16.6	0.116
Night	37.7 ± 25.5	29.7 ± 18.3	0.108
>250 mg/dL			
Day	14.3 ± 15.1	8.55 ± 8.33	0.027
Night	15.2 ± 17.3	7.98 ± 8.98	0.015
>320 mg/dL			
Day	5.04 ± 7.40	2.01 ± 3.45	0.013
Night	5.46 ± 8.52	2.04 ± 3.91	0.015

Data presented as mean ± standard deviation and analyzed by Student *t*-test. Abbreviations: CGM, continuous glucose monitoring.

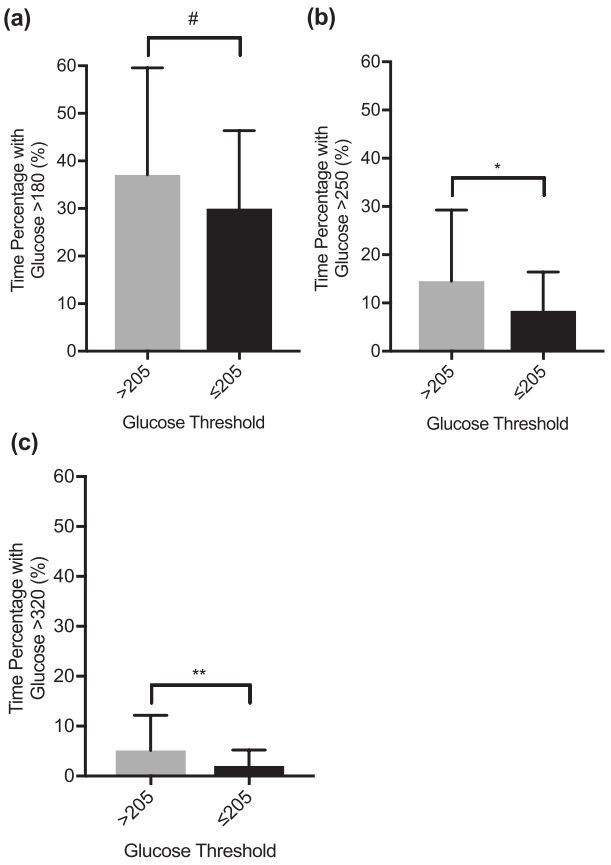

Figure 2. Bar graphs showing the means and standard deviations of the percentages of time spent with glucose levels (a) >180 mg/dL, (b) >250 mg/dL and (c) >320 mg/dL with CGM glucose thresholds ≤205 and >205 mg/dL for hyperglycemia alarms.

Abbreviations: CGM, continuous glucose monitoring. #0.05≤*P* < *0.1;* **P* < 0.05*;* ***P* < 0.01. *P*-values were determined by Student *t*-test. All glucose information is presented in mg/dL.

hyperglycemia alarm threshold for < 15% (TPR, 0.64; FPR, 0.78; $J = 0.43$) and < 5% (TPR, 0.80; FPR, 0.74; $J = 0.54$) of time with glucose > 180 mg/dL, as well as for HbA1c ≤ 7% (TPR, 0.49; FPR, 0.87; $J = 0.37$). No optimal alarm threshold was determined for < 25% of time with glucose levels > 180 mg/dL.

D. Other CGM Alarm Settings and Glucose Outcomes

Between the participants who turned on and off their hypo/hyperglycemia alarms, repeat hypo/hyperglycemia alarms and glucose fall/rise alarms, there were no significant differences in the time percentages in hypo/hyperglycemia, average glucose levels, time-in-range and COVs (Table 3).

E. Hypo/Hyperglycemia Alarm Numbers and Recovery Duration

Over the 2-week period, 33 ± 18.5 alarms were generated for each participant (~1.4 alarms/day), with 42.0% ± 30.1% of them being hypoglycemia alarms. There was no difference in the number of hypoglycemia alarms between the participants with hypoglycemia alarm thresholds ≥ 73 mg/dL and < 73 mg/dL ($P = 0.895$). Additionally, the number of hypoglycemia alarms did not correlate with longer duration to recover from hypoglycemia ($P = 0.812$). In contrast, participants with hyperglycemia alarm thresholds ≤ 205 mg/dL had more hyperglycemia alarms (30.9 ± 11.1) than those with alarm thresholds > 205 mg/dL (14.2 ± 9.9;

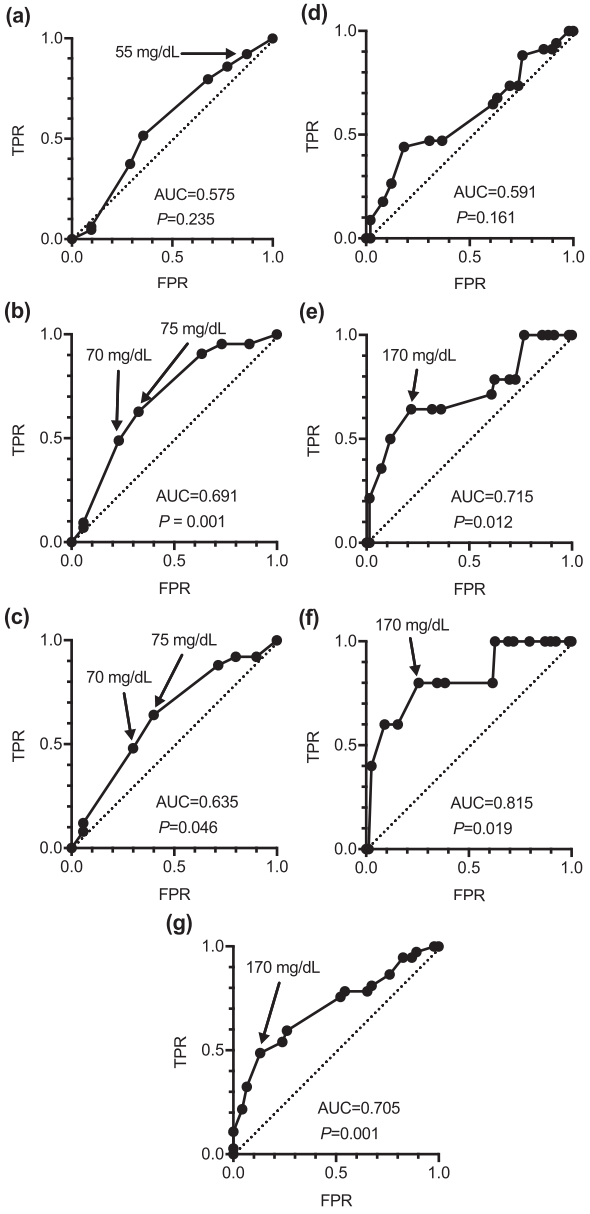

Figure 3. Receiver operating characteristic analyses for the associations of (a) <4%, (b) <2% and (c) <1% of time spent with glucose <70 mg/dL with glucose thresholds for hypoglycemia alarms, and (d) <25%, (e) <15%, (f) <5% of time spent with glucose >180 mg/dL and (g) HbA1c levels with glucose thresholds for hyperglycemia alarms.

Abbreviations: HbA1c, hemoglobin A1C; TPR, true positive rate; FPR, false positive rate; AUC, area under the curve.

$P < 0.0001$). Furthermore, the number of hyperglycemia alarms correlated with longer duration to recover from hyperglycemia (R = 0.277; $P = 0.010$).

3. Discussion

In the current study, participants with higher glucose thresholds for *hypo*glycemia alarms spent about 50% and 65% less time in hypoglycemia with glucose levels < 70 and < 54 mg/dL, respectively, accompanied with higher average glucose levels and less time-in-range.

Table 3. CGM Settings for Hypo/Hyperglycemia and Glucose Fall/Rise Alarms and Glucose Outcomes

CGM Settings	*P* Value
Hypoglycemia Alarm Settings	
Hypoglycemia alarm On vs Off	
Percentage of time with glucose <70 mg/dL	0.537
Percentage of time with glucose <54 mg/dL	0.630
Time-in-range	0.384
Glucose COV	0.873
Hypoglycemia repeat alarm On vs Off	
Percentage of time with glucose <70 mg/dL	0.954
Percentage of time with glucose <54 mg/dL	0.918
Time-in-range	0.429
Glucose COV	0.876
Hyperglycemia Alarm *Settings*	
Hyperglycemia alarm On vs Off	
Average glucose level	0.397
Percentage of time with glucose >180 mg/dL	0.207
Percentage of time with glucose >250 mg/dL	0.283
Percentage of time with glucose >320 mg/dL	0.475
Time-in-range	0.384
Glucose COV	0.873
Hyperglycemia repeat alarm On vs Off	
Average glucose level	0.503
Percentage of time with glucose >180 mg/dL	0.174
Percentage of time with glucose >250 mg/dL	0.126
Percentage of time with glucose >320 mg/dL	0.184
Time-in-range	0.156
Glucose COV	0.302
Glucose Fall/Rise Settings	
Glucose fall alarm On vs Off	
Percentage of time with glucose <70 mg/dL	0.729
Percentage of time with glucose <54 mg/dL	0.810
Time-in-range	0.785
Glucose COV	0.883
Glucose rise alarm On vs Off	
Average glucose level	0.233
Percentage of time with glucose >180 mg/dL	0.282
Percentage of time with glucose >250 mg/dL	0.324
Percentage of time with glucose >320 mg/dL	0.721
Time-in-range	0.785
Glucose COV	0.883

P value determined by logistic regression analyses. Abbreviations: CGM, continuous glucose monitoring; COV, coefficient of variation.

An alarm threshold of 75 mg/dL was the optimal cutoff for hypoglycemia alarms for < 1% of time with glucose levels < 70 mg/dL. Higher hypoglycemia alarm thresholds were not associated with more hypoglycemia alarms, and greater numbers of hypoglycemia alarms also did not correlate with longer durations to recover from hypoglycemia. For *hyper*glycemia alarms, participants with lower alarm thresholds experienced lower average glucose levels, and about 40% and 60% less time with glucose levels > 250 and > 320 mg/dL, respectively, without more time in hypoglycemia. An alarm threshold of 170 mg/dL was the optimal cutoff for hyperglycemia alarms for < 5% of time with glucose levels > 180 mg/dL and HbA1c ≤ 7%. Lower hyperglycemia alarm thresholds were associated with greater alarm numbers, and also correlated with longer durations to recover from hyperglycemia. As the average glucose threshold for hyperglycemia alarms was greater than 180 mg/dL, a comment cannot be made on how the alarm threshold affects the time percentage spent > 180 mg/dL when comparing the group with hyperglycemia alarm threshold above vs the group below the average glucose thresholds.

While prior studies have demonstrated the benefits of initiating CGMs to improve glucose control [2–7], little evidence exists on whether the configurations of CGM alarm settings can further reduce hypo/hyperglycemia. One study assessed the use of hypoglycemia alarms with thresholds set at 108 mg/dL together with other hypoglycemia avoidance programs, and demonstrated an improvement in the epinephrine responses to hypoglycemia in an adolescent population [15]. However, this study was limited by its single-arm design and the small sample size nature of clamp studies. The HypoCOMPaSS group reported certain CGM features that were considered by the participants to be useful in preventing hypoglycemia [5], yet this observation was limited by the low active CGM usage time and subjectivity of the reports.

A. Observations for the Hypoglycemia Alarm

The current study suggests that even slightly higher glucose thresholds for hypoglycemia alarms (eg, 75 mg/dL instead of 70 mg/dL) were associated significantly less hypoglycemia (Fig 3b and 3c). An alarm threshold of 70 mg/dL is one of the most common settings used for hypoglycemia alarms, likely reflecting the physiological definition of hypoglycemia [16]. However, T1D patients, who rely on exogenous insulin and often lack alpha cell responses to hypoglycemia, have at least some deficits in counterregulatory mechanisms [17]. Thus, these patients often rely on external treatments, which require time for access, and to administer and absorb, in order to recover from or prevent the development of hypoglycemic events. Higher hypoglycemia alarm thresholds, even with small increments, may help inform patients sufficiently early to allow lead time for treatments.

In the current cohort, no particular alarm threshold was identified for < 4% of time in hypoglycemia. This may suggest that techniques to avoid or manage hypoglycemia (eg, following with CGM glucose regularly and administer treatments before the occurrence of hypoglycemia), or physiology helping to recover from such events (eg, with better catecholamine responses) are still critical to accomplish this therapeutic goal despite using CGM alarms. On the other hand, optimal alarm thresholds were identified for lower percentages of time (eg, < 1%), implying that CGM alarms become more important to further lower the time in hypoglycemia, although the rather low TPRs and FPRs suggest that the other behavioral and physiological factors continue to be essential. Clinically, up-titration of alarm thresholds for hypoglycemia may be used for high-risk patients (eg, older or high-risk T1D patients) who require stricter avoidance of hypoglycemia and have higher HbA1c and less time-in-range treatment goals [8, 10].

B. Observations for the Hyperglycemia Alarm

The participants with lower hyperglycemia alarm thresholds (ie, ≤ 205 mg/dL) experienced less time with glucose levels > 250 and > 320 mg/dL than the group with higher alarm thresholds. However, the differences in the time with glucose levels > 180 mg/dL and the time-in-range (ie, time with glucose levels 70–180 mg/dL) between these 2 groups were not as robust. These observations could be explained by the fact that some participants in the lower alarm threshold group still had their alarms set at ≥ 180 mg/dL, and thus might not have received alarms sufficiently early for treatments to prevent hyperglycemia and increase the time-in-range. Indeed, the ROC analysis demonstrated that participants with alarm thresholds ≤ 170 mg/dL experienced lower percentages of time with glucose > 180 mg/dL. These observations together evidence the positive correlation between the hyperglycemia alarm thresholds and the time spent below these threshold levels.

While there was no optimal glucose threshold identified for < 25% of time spent with glucose > 180 mg/dL, an alarm threshold at 170 mg/dL was associated with both < 15% and < 5% of time in hyperglycemia, as well as HbA1c ≤ 7%. Similar to the observations on the hypoglycemia alarms, other factors, such as behavioral or physiological components (eg, early intervention or residual beta-cell mass with significant endogenous insulin production) [18],

likely still play major roles in achieving < 25% of time in hyperglycemia. On the other hand, the high FPRs (ie, the proportion of participants not setting the alarm to ≤ 170 mg/dL and not achieving the targets) also reinforce the need for hypoglycemia alarms to accomplish the goals of lower time percentages in hyperglycemia and HbA1c ≤ 7%.

The negative impacts of lowering hyperglycemia alarm thresholds appeared to be greater numbers of alarms, together with the alarm fatigue reflected by the positive correlation between the hyperglycemia alarm numbers and the duration recovering from hyperglycemia. Thus, clinically, down-titration of the hyperglycemia alarm thresholds could be considered for CGM users who need to further lower HbA1c or reduce the time in hyperglycemia, without major concerns for increasing the time in hypoglycemia. However, assessments on the overall decrease in hyperglycemia may be required during the follow-up encounters: When no further improvements in hyperglycemia are observed, alarm fatigue and the increased glucose recovery duration may have overridden the benefits of alarm adjustments.

C. Other Alarm Features

It may seem counterintuitive that there were no differences in the hypo/hyperglycemia outcomes between the participants who turned on and off their hypo/hyperglycemia alarms. The participants who turned off their alarms may, again, be a subcohort with stronger mechanisms to prevent or recover from hypo/hyperglycemia. Indeed, nearly 10% of the participants with hypoglycemia alarm thresholds of 55 mg/dL still achieve the goal of < 4% of time in hypoglycemia (reflected by the TPR in the ROC analysis, Fig. 3a). Identifying the behavioral advantages of these participants may be of clinical interest to further develop hypo/hyperglycemia prevention/management programs.

The current study has several strengths but also some limitations. To our knowledge, the observations made in the current analyses are the first to report on how CGM settings are positively and negatively associated with glucose control. The observational design allows the current study to avoid the confounding effects (eg, strict recruitment criteria or additional patient education) of interventional studies. Also, only patients with high active CGM usage time (ie, more than 6 out of 7 days) [2] and a reasonable amount of time to learn how to implement CGM technology (> 4 weeks) [6] were recruited. We used the duration to recover from hypo/hyperglycemia as an objective and clinically meaningful way to evaluate patients' alarm fatigue. On the other hand, the cross-sectional nature of the study also does not allow to assess the actual responses and tolerance of the CGM setting changes. Furthermore, the current results were solely determined based on Dexcom CGMs, even though this homogeneity also allows to minimize the variability between CGM systems [7]. How the Dexcom G6 predictive low alert function affects the hypo/hyperglycemia profiles, and whether the receiver device type (ie, CGM receiver vs personal phone) influences the glucose outcomes or not, were not evaluated in the current study. Finally, the data were derived from a single academic center, and thus may not fully represent other patient populations.

In conclusion, CGM glucose thresholds for hypo/hyperglycemia alarms are associated with both positive and negative impacts on glucose control. When needed, modifications to hypo/hyperglycemia alarm thresholds could be considered as a potential approach to help achieve glucose control or HbA1c goals. The variability observed across the current cohort also reinforces the need for future studies that take into account individuals' behavioral and physiological characteristics to further the goal of a more personalized approach of configuring hypo/hyperglycemia alarm settings.

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Additional Information

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Disclosure Summary: The authors have nothing to disclose.

References and Notes

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