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Time spent outside of target glucose range for young children with type 1 diabetes: a continuous glucose monitor study

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Abstract

Aim—To assess the associations between demographic and clinical characteristics and sensor glucose metrics in young children with type 1 diabetes, using masked, continuous glucose monitoring data from children aged 2 to < 8 years.

Research design and methods—The analysis included 143 children across 14 sites in the USA, enrolled in a separate clinical trial. Eligibility criteria were: age 2 to <8 years; type 1 diabetes duration 3 months; no continuous glucose monitoring use for past 30 days; and HbA_{1c} concentration 53 to <86 mmol/mol (7.0 to <10.0%). All participants wore masked continuous glucose monitors up to 14 days.

Results—On average, participants spent the majority (13 h) of the day in hyperglycaemia (>10.0 mmol/l) and a median of ~1 h/day in hypoglycaemia (<3.9 mmol/l). Participants with minority race/ethnicity and higher parent education levels spent more time in target range, 3.9–10.0 mmol/l, and less time in hyperglycaemia. More time in hypoglycaemia was associated with minority race/ ethnicity and younger age at diagnosis. Continuous glucose monitoring metrics were similar in pump and injection users.

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Ethical approval statement None.

Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Conclusions—Given that both hypo- and hyperglycaemia negatively impact neurocognitive development, strategies to increase time in target glucose range for young children are needed.

Introduction

Traditional type 1 diabetes management in young children has focused on avoiding hypoglycaemia, even at the expense of hyperglycaemia. This approach has been based on data on adverse central nervous system outcomes related to recurrent hypoglycaemic seizure/coma [1–5] and parental fear of hypoglycaemia in young children, especially at night [6]. There is increasing recognition, however, that hyperglycaemia also negatively impacts central nervous system structure and function in very young children [1,7–11].

Most paediatric studies examining glucose profiles using continuous glucose monitoring (CGM) have enrolled few, if any, very young children [12,13] and have primarily used unmasked CGM (glucose values visible to individual with diabetes/caregiver). Tansey *et al.* [14] examined time in range using masked CGM in a cohort of 135 children with type 1 diabetes with a mean (range) age of 7 (4–10) years; however, that group used older-generation CGM devices, enrolled a predominately non-Hispanic white cohort, and did not report on factors associated with time in range [14].

In the present study, we used masked CGM data (glucose values not visible to individual with diabetes), collected at baseline for a trial evaluating the benefits of CGM in a large cohort of children aged 2 to <8 years with type 1 diabetes in order to assess glucose profiles and identify demographic and clinical factors associated with time spent in glycaemic ranges.

Research design and methods

The SENCE (Strategies to Encourage New CGM use in Early Childhood) study is a randomized clinical trial evaluating the efficacy and safety of CGM use in children aged 2 to <8 years with type 1 diabetes. This report includes baseline data from participants enrolled at 14 paediatric endocrinology clinics in the T1D Exchange Clinic Network in the USA (Appendix S1).

Children were eligible for the SENCE study if they met the following criteria: clinical diagnosis of type 1 diabetes for at least 3 months; age 2 to <8 years; total daily insulin 0.3 units per kg of body weight per day; HbA_{1c} 53 to <86 mmol/mol (7.0 to <10.0%) within 30 days prior to consent or at time of screening; use of either an insulin pump or multiple daily injections of insulin; no use of real-time CGM in the 30 days prior to enrolment; and self-report or meter download of at least three fingerstick blood glucose checks per day.

After enrolment, participants used masked (glucose values not visible) CGM (DexcomTM G4 Platinum CGM System® with the enhanced 505 software algorithm; Dexcom, Inc., San Diego, CA, USA) for 14–21 days, with daily calibrations of the sensor with a blood glucose meter as per the manufacturer's instructions. The Dexcom G4 continuous glucose monitor involves insertion of a subcutaneous sensor under the skin with an attached transmitter that sends a glucose reading every 5 min to a downloadable receiver; each

sensor can be used for glucose readings for up to 7 days before a new insertion is needed. Only participants who wore the CGM sensor for at least 200 h (equivalent to 8.3 days) and performed at least three blood glucose measurements per day with a home blood glucose meter were included. Whole blood samples were collected for HbA_{1c} after the successful completion of blinded CGM data collection. These samples were analysed at the University of Minnesota Advanced Research and Diagnostics Laboratory using a Diabetes Control and Complications Trial (DCCT)-standardized analyser (Tosoh Automated Analyser HLC-723G8).

Statistical analysis

Masked CGM data were used to calculate glucose metrics, including percent time in range, defined as 3.9-10.0 mmol/l, percent time below 3.9 mmol/l, percent time above 10.0 mmol/l, percent time above 13.9 mmol/l, and coefficient of variation (defined as standard deviation divided by the mean, to assess glucose variability) for each participant [15,16]. Percent time in range 3.9-10.0 mmol/l and percent time below 3.0 mmol/l were also calculated separately for daytime (06:00 to <22:00 h) and nighttime (22:00 to <06:00 h). For HbA_{1c} assessment, the central laboratory value was used where available; for two participants who were missing a central laboratory value, the local laboratory/point-of-care value (obtained on a DCCT-standardized device) at screening was used.

The following demographic and clinical characteristics were assessed for associations with the above CGM glycaemic metrics and with HbA_{1c}: child age; sex; self-reported race/ethnicity; BMI percentile for age; age at diagnosis; type 1 diabetes duration; total daily insulin in units per kg; insulin delivery method (via an insulin pump or multiple daily injections); history of previous CGM use; average number of blood glucose meter checks per day; annual household income; highest level of parent education; and health insurance type. Race/ethnicity was evaluated as non-minority (non-Hispanic white) vs minority (Hispanic, non-Hispanic black, and other) because the sample was not large enough to consider each of the minority races separately.

First, a univariable regression model was fit to assess the unadjusted association of each characteristic with each outcome. Then a multivariable linear regression model with stepwise selection of factors was fit for each glycaemic outcome to determine the subset of factors associated with the outcome when considered together. A threshold of 0.20 was used to enter factors into the model and only factors with *P* values <0.10 were retained. The stepwise selection procedure was run before adjusting for multiple comparisons. For all models, multiple imputations based on fully conditional specification were used for missing data so that all participants were included. No formal statistical analyses to assess interactions were performed because of the small sample sizes in each combined category.

Analyses were performed using sAs software version 9.4 (SAS Institute Inc., Cary, NC, USA). Metrics that had a reasonably normal distribution were summarized using means \pm SD. Skewed metrics were summarized using median [interquartile range (IQR)] values and were modelled using ranks. *P* values were corrected for multiple comparisons using the adaptive Benjamini–Hochberg procedure to control the false discovery rate, with a false

discovery rate value <0.05 considered statistically significant [17–19]. All reported P values are two-sided.

Ethics

The protocol and consent forms were approved by a central institutional review board or local institutional review boards, as required. Written informed consent was obtained from the parent/legal guardian prior to enrolment. Child assent also was obtained as applicable.

Results

The cohort included 143 participants with a median (IQR) of 305 (278, 352) masked CGM hours per participant collected over 14 to 21 days between February 2017 and August 2018. The median (IQR) age of participants was 5.9 (4.2–7.3) years, 50% of participants were girls and 68% were non-Hispanic white. Thirty-five percent of the participants were pump users. Only 12% of participants had ever used real-time CGM in the past. Participant demographic and clinical characteristics are shown in Table 1.

Time in range and hyperglycaemia

Participants spent a mean 40% of time (9.6 h/day) in the target glucose range of 3.9–10.0 mmol/l and 55% of time (13.1 h/day) above 10.0 mmol/l, including 30% of time (7.3 h/day) above 13.9 mmol/l (Fig. 1a). Participants with parents with lower education levels spent less time in range (P = 0.014) and more time in hyperglycaemia above both 10.0 mmol/l (P = 0.014) and 13.9 mmol/l (P = 0.014). Similarly, non-Hispanic white participants spent less time in range (P = 0.031), more time above 10.0 mmol/l (P = 0.014) and tended to spend more time above 13.9 mmol/l (P = 0.050). No other assessed factors, including pump use (vs multiple daily injections), were significantly associated with these CGM metrics (Table 2).

Participants spent a mean of 40% of time in the target glucose range of 3.9-10.0 mmol/l during both the daytime and nighttime. Participants with parents with lower education levels spent less time in range during both daytime (P = 0.020) and nighttime (P = 0.020) hours. A lower age was associated with lower daytime time in range (P = 0.021), but age was not associated with nighttime time in range. Minority race/ethnicity was associated with a higher nighttime time in range (P = 0.031), but was not significantly associated with daytime time in range. No other factors were associated with time in range when considering daytime and nighttime hours separately (Table S1).

Hypoglycaemia

Participants spent a median of 4.1% of time (59 min/day) in hypoglycaemia below 3.9 mmol/l, and 1.4% of time (20 min/day) below 3.0 mmol/l (Fig. 1b). Pump use was not associated with less time spent in hypoglycaemia. Younger age at diagnosis was significantly associated with more time spent in hypoglycaemia both below 3.9 mmol/l (P = 0.002) and below 3.0 mmol/l (P = 0.005). Non-Hispanic white participants spent less time below 3.9 mmol/l than did other participants (median 3.4% vs 6.7%, respectively; P = 0.011). Time spent below 3.0 mmol/l also tended to be lower in non-Hispanic white participants (P = 0.040; Table 3)

Participants spent a median 1.1% of time below 3.0 mmol/l during the daytime and 1.4% of time below 3.0 mmol/l during the nighttime. Younger age at diagnosis was significantly associated with more time spent below 3.0 mmol/l during both the daytime (P= 0.002) and nighttime (P= 0.030) hours. No other factors were associated with time below 3.0 mmol/l when considering daytime and nighttime hours separately (Table S2).

Glucose variability

Overall, participants had highly variable glucose levels, with a mean (SD/mean) coefficient of variation of 44 (\pm 7)%. No factors were significantly associated with glycaemic variability (Table S3).

HbA_{1c}

Overall participants had a mean HbA_{1c} of $66 \pm 8 \text{ mmol/mol} (8.2 \pm 0.7\%)$. Mean HbA_{1c} was 71 mmol/mol (8.6%) among participants with parent education of high school or less vs 65 mmol/mol (8.1%) among those with parent education of some college or more (P=0.018). No other factors were associated with HbA_{1c} (Table S4).

Discussion

We found that children aged 2 to <8 years with type 1 diabetes not using CGM as part of daily diabetes management spent only a minority of the day in the glycaemic target range of 3.9-10.0 mmol/l. Half of these children had glucose values > 10.0 mmol/l for at least 12 h/ day, as well as a substantial amount of time, a median of almost 1 h/day, in hypoglycaemia. CGM metrics were similar in pump and multiple daily injection users.

These data obtained in children who were not using CGM at baseline are similar to those reported previously by Tansey *et al.* [14] in their cohort with type 1 diabetes with a mean (range) age of 7 (4–10) years and a mean HbA_{1c} of 63 mmol/mol (7.9%), 56% of whom were using insulin pumps [14]. Although 41% of their population used unmasked, real-time CGM, the children still spent >50% of time in hyperglycaemia and 4.6% of time below 3.9 mmol/l. That cohort also had substantial glucose variability with a coefficient of variation for glucose values (43%) that was similar to that observed in our participants (44%).

Contrary to previous studies, we found differences in CGM profiles by race/ethnicity, with non-Hispanic black or Hispanic children in this cohort spending more time in target range, less time in hyperglycaemia, and more time in hypoglycaemia than non-Hispanic white participants. Earlier research has generally reported higher HbA_{1c} values, indicating higher mean glucose levels and less optimal glycaemic control in racial/ethnic minority groups [20,21]. By contrast, children of parents with higher levels of education had greater time in range and lower HbA_{1c}, which is in agreement with prior research [22,23]. Higher parental education may be associated with more optimal recognition and fewer overcorrections of low glucose levels, as compared to families who may be challenged with basic understanding of management of hypoglycaemia due to educational background. Alternatively, fear of hypoglycaemia may be associated with overtreatment of low glucose levels.

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We observed better glycaemic control in children from minority groups despite their families having lower parent education levels (23% minority parent with college degree vs 51% in non-Hispanic white parents). Given our inclusion criteria, our cohort was composed of young children with type 1 diabetes who were not currently using CGM, very few of whom had any past experience with CGM (12%), raising the issue as to whether these families had easy access to CGM prior to enrolment in our study. Thus, the differences in association of ethnic and minority race and time in range compared to previous studies may be attributable to a larger population of relatively late CGM adopters, even among non-Hispanic white children in our cohort compared with cohorts in other studies of CGM [1,24]. Although this study had high representation of children from minority groups, the minority families who chose to have their child with type 1 diabetes participate in the study may not be representative of other children with type 1 diabetes from minorities in the USA.

Intensive insulin therapy in children requires a complex orchestration of insulin dosing and diet while accounting for other variables such as physical activity and illness, which may help explain why the overwhelming majority of children with type 1 diabetes currently have suboptimal glycaemic control and why only 17% of young children aged < 6 years, with type 1 diabetes achieve an HbA_{1c} <58 mmol/mol (<7.5%) [25]. Further, overall underutilization and suboptimal utilization of advanced diabetes technologies (including insulin pumps, CGM, sensor-augmented pump therapy, and automated insulin delivery systems) in this age group remains [1,25–28]. Given that both hypo- and hyperglycaemia may negatively impact cognitive development in young children, further research and development of clinical strategies to successfully incorporate and sustain optimal use of new technologies that are readily employable by families and care providers are urgently needed.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Competing interests

R.P.W. reports grants and personal fees from Dexcom, outside the submitted work. J.C.W. reports grants from Dexcom, Inc, outside the submitted work and is a volunteer on the Medical Advisory Board of Tidepool. The remaining authors have no competing interests to declare.

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What's new?

- Traditional type 1 diabetes management in young children has focused on avoiding hypoglycaemia even at the expense of hyperglycaemia.
- There are limited glucose profile data available for very young children with type 1 diabetes.
- Very young children with type 1 diabetes spend the majority of the day outside of the target glucose range.
- Given that both hypo- and hyperglycaemia negatively impact paediatric neurocognitive development, strategies to increase time in target glucose range are needed.

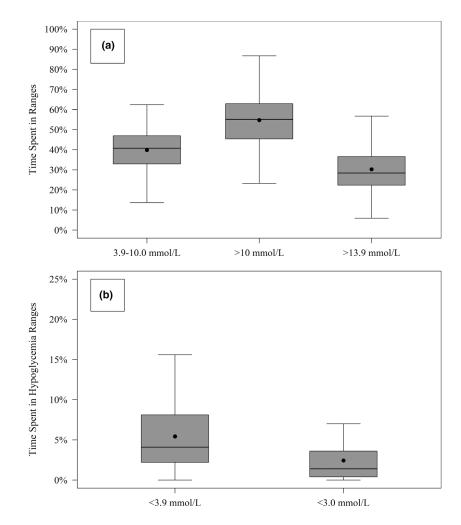


FIGURE 1.

Time in ranges based on glucose targets. (a) Time in target range (3.9-10.0 mmol/l) and time in hyperglycaemia (>10.0 and >13.9 mmol/l). (b) Time spent in hypoglycaemia (<3.9 and <3.0 mmol/l). Top and bottom portions of the boxes denote the 25th and 75th percentile, the line represents the median and the dot the mean. Whiskers represent the minimum and maximum after removing outliers.

Table 1

Participant characteristics

Characteristic	Overall, N = 143
Age, years	
Median (Q1, Q3)	5.9 (4.2, 7.3)
Range	2.0-8.0
Girls, <i>n</i> (%)	72 (50)
Race/ethnicity, n (%)	
Non-Hispanic white	95 (68)
Non- Hispanic black	21 (15)
Hispanic or Latino	16 (11)
Asian	1 (<1)
Other/more than one race	7 (5)
Median (Q ₁ , Q ₃) BMI percentile	74 (53, 92)
BMI category, n (%)	
Underweight (BMI percentile <5)	4 (3)
Normal weight: 5 BMI percentile <85	90 (63)
Overweight: 85 BMI percentile <95	25 (17)
Obese: 95 BMI percentile	24 (17)
Median (Q ₁ , Q ₃) age at diagnosis, years	3.1 (1.8, 4.8)
Median (Q1, Q3) duration of diabetes, years	1.9 (0.7, 3.9)
Mean \pm SD HbA _{1c}	
mmol/mol	66 ± 8
%	8.2 ± 0.7
Median (Q_1, Q_3) total daily insulin units per kg	0.7 (0.5, 0.8)
Insulin pump use, <i>n</i> (%)	50 (35)
Prior CGM use, $n(\%)$	
In past, but not current	17 (12)
Never	126 (88)
1 Severe hypoglycaemic event † in the past 12 months, $n(\%)$	14 (10)
1 diabetic ketoacidosis event ^{$\frac{1}{2}$} in the past 12 months, <i>n</i> (%)	34 (24)
Median (Q_1, Q_3) average blood glucose meter checks/day	6 (5, 7)
Annual household income, n (%)	
<\$35,000	25 (19)
\$35,000 to <\$75,000	54 (41)
\$75,000	52 (40)
Highest level of parent education, $n(\%)$	
High school or less	32 (24)
Some college/associate degree	47 (35)
Bachelor's or higher	57 (42)
Health insurance, n(%)	

Characteristic	Overall, $N = 143^*$
Private	87 (62)
Medicaid/other	52 (37)
None	2 (1)

CGM, continuous glucose monitoring.

* Missing: race/ethnicity, 3 (2%); total daily insulin, 1 (<1%); income, 12 (8%); parent education, 7 (5%); health insurance, 2 (1%). All other variables have no missing data.

 † Defined as an event that required assistance from another person to administer carbohydrate, glucagon, or other resuscitative actions due to altered consciousness.

 ‡ Defined as an episode when the participant had diabetic ketoacidosis that necessitated treatment in a healthcare facility. Ketoacidosis events in the past 12 months could include ketoacidosis at onset of type 1 diabetes for participants with disease duration <1 year.

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Table 2

Continuous glucose monitor-measured time in range and in hyperglycaemia

		% Time in r	% Time in range 3.9–10.0 mmol/1	10l/1	% Time abov	% Time above 10.0 mmol/1		% Time abo	% Time above 13.9 mmol/1	
	Z	Mean ± SD	Univarible P^*	Multivariable $P^{*, \mathring{T}}$	Mean ± SD	Univarible P*	Multivariable P*,†	Mean ± SD	Univarible P*	Multivariable $P^{*,\mathring{\tau}}$
Overall	143	40 ± 11	I	I	55 ± 13	I	I	30 ± 12	I	I
${ m Age}^{{ m {\it I}}}$			0.124	0.059		0.470			0.079	0.068
<5 years	49	37 ± 12			57 ± 15			34 ± 15		
5 years	94	41 ± 10			54 ± 12			28 ± 10		
Sex			0.470	ı		0.497			0.394	
Girls	72	39 ± 11			56 ± 13			32 ± 13		
Boys	71	41 ± 11			53 ± 13			29 ± 12		
Race/ethnicity			0.170	0.031		0.050	0.014		0.190	0.050
Non-minority	95	39 ± 10			57 ± 12			32 ± 12		
Minority	45	42 ± 12			50 ± 14			27 ± 14		
Annual household income			0.550	I		0.741	ı		0.616	ı
< \$35,000	25	40 ± 9			52 ± 12			28 ± 10		
\$35,000 to <\$75,000	54	37 ± 12			58 ± 14			33 ± 15		
\$75,000	52	41 ± 10			53 ± 12			28 ± 11		
Highest level of parent education			0.024	0.014		0.043	0.014		0.030	0.014
High school or less	32	35 ± 11			60 ± 13			37 ± 14		
Some college/associate degree	47	40 ± 10			55 ± 12			30 ± 11		
Bachelor's or higher	57	42 ± 11			52 ± 14			28 ± 12		
Health insurance			0.574	I		0.751	ı		0.735	
Not private/no insurance	54	39 ± 11			55 ± 13			31 ± 13		
Private	87	41 ± 11			54 ± 13			30 ± 13		
BMI category ${}^{\not{I}}$			0.800	ı		0.809	ı		0.729	ı
Normal/underweight	94	40 ± 10			54 ± 13			31 ± 12		
Overweight	25	39 ± 12			56 ± 15			32 ± 15		
Obese	24	41 ± 11			55 ± 13			28 ± 10		

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		% Time in ra	% Time in range 3.9–10.0 mmol/1	10J/1	% Time above 10.0 mmol/1	: 10.0 mmol/1		% Time abo	% Time above 13.9 mmol/1	
	N	Mean ± SD	Univarible <i>P</i> *	Multivariable $m{P}^{*, \mathring{T}}$	Mean ± SD	Univarible P^*	Multivariable ${m p}^{*, \dot{T}}$	Mean ± SD	Univarible P*	Multivariable $P^{*, \mathring{T}}$
Type 1 diabetes duration \ddagger			0.738			0.607			0.557	
<2 years	76	40 ± 12			55 ± 14			31 ± 14		
2 years	67	40 ± 9			54 ± 12			30 ± 11		
Age at diagnosis \ddagger			0.190			0.741			0.455	
<3 years	68	38 ± 10			55 ± 13			31 ± 13		
3 years	75	41 ± 11			54 ± 13			29 ± 12		
Insulin delivery method			0.839	,		0.989	ı		0.659	
Injections	93	40 ± 12			55 ± 14			31 ± 14		
Pump	50	40 ± 9			55 ± 11			29 ± 10		
Total daily insulin units per kg^{\ddagger}			0.638	ı		0.923	ı		0.741	
0.3 to <0.7	LL	40 ± 12			55 ± 15			30 ± 14		
0.7	65	40 ± 8			55 ± 11			30 ± 10		
Prior CGM use			0.587	0.234		0.716	ı		0.735	
Prior CGM use	17	38 ± 11			56 ± 14			31 ± 12		
No prior CGM use	126	40 ± 11			55 ± 13			30 ± 13		
Average blood glucose meter checks/day \ddagger			0.859	I		0.850	1		0.557	ı
9>	62	39 ± 13			55 ± 15			31 ± 15		
6	81	40 ± 9			54 ± 12			29 ± 11		
CGM, continuous glucose monitoring. *	oring.									
Pvalues have been adjusted for multiple comparisons using the adaptive Benjamini-Hochberg procedure to control the false discovery rate.	multiple	comparisons us	ing the adaptive B	enjamini-Hochberg	procedure to cont	rol the false disc	covery rate.			

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⁴Age, BMI percentile, type 1 diabetes duration, age at diagnosis, total daily insulin per kg, and blood glucose meter checks/day were entered in the models as continuous variables. Parent education and

annual household income were considered ordinal, with seven and five levels, respectively. Categories for these variables are for display only.

 ${}^{\dagger}P$ values are only given for variables that were selected in the final model.

Table 3

Continuous glucose monitor-measured hypoglycaemia

		% Time 3.9 mmol/			% Time 3.0 mmol/		
	Ν	Median (Q1, Q3)	Univariable <i>P</i> value [*]	Multivariable P value $^{*, \dagger}$	Median (Q1, Q3)	Univariable <i>P</i> value [*]	Multivariable P value $^{*, \mathring{\tau}}$
Overall	143	4.1 (2.2, 8.1)	1	1	1.4 (0.4, 3.6)	1	
${ m Age}^{{\mathcal I}}$			0.260	1		0.140	
<5 years	49	4.5 (2.3, 8.1)			1.8 (0.5, 3.6)		
5 years	94	3.6 (2.1, 7.1)			1.2 (0.4, 3.2)		
Sex			0.578			0.789	ı
Girls	72	4.3 (1.9, 7.5)			1.5(0.4, 3.5)		
Boys	71	3.7 (2.3, 8.1)			1.4 (0.5, 3.6)		
Race/ethnicity			0.011	0.011		0.019	0.040
Non-minority	95	3.4 (1.6, 6.5)			1.0 (0.4, 2.4)		
Minority	45	6.7 (2.9, 10.2)			3.1 (0.9, 4.9)		
Annual household income			0.223			0.080	
< \$35,000	25	4.5 (2.9, 9.9)			2.4 (1.0, 4.9)		
\$35,000 to <\$75,000	54	3.7 (1.3, 7.4)			1.3 (0.4, 2.8)		
\$75,000	52	3.4 (2.2, 7.9)			1.0 (0.4, 3.4)		
Highest level of parent education			0.516	ı		0.956	I
High school or less	32	3.9 (1.8, 7.6)			1.4 (0.4, 3.9)		
Some college/associate degree	47	4.2 (2.4, 7.4)			1.4 (0.5, 3.6)		
Bachelor degree or higher	57	3.7 (2.2, 8.6)			1.2 (0.4, 2.9)		
Health insurance			0.170	ı		0.040	0.127
Not private/no insurance	54	5.6 (2.7, 8.6)			2.0 (0.9, 3.9)		
Private	87	3.4 (2.0, 7.1)			1.0 (0.4, 2.8)		
BMI category ${}^{\!\mathcal{X}}$			0.815	1		0.806	1
Normal/underweight	94	4.2 (2.4, 8.6)			1.4 (0.5, 3.7)		
Overweight	25	3.7 (1.6, 7.1)			$1.6\ (0.5,\ 3.5)$		
Obese	24	3.7 (2.1, 5.2)			$1.0\ (0.4,\ 1.8)$		
Type 1 diabetes duration \mathring{x}			0.074			0.170	ı

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NMetanolicyMetanolicyMultivariable $P \operatorname{value}^{4}$ Multivariable $P \operatorname{value}^{4}$ <			% Time 3.9 mmol/l			% Time 3.0 mmol/l	I	
$ \begin{array}{llllllllllllllllllllllllllllllllllll$	N	•	Median (Q1, Q3)	Univariable <i>P</i> value [*]	Multivariable P value $^{*, \dagger}$	Median (Q1, Q3)	Univariable <i>P</i> value [*]	Multivariable P value $^{*, \dot{f}}$
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$			3.4 (1.4, 7.5)			1.1 (0.3, 3.6)		
$ \begin{array}{llllllllllllllllllllllllllllllllllll$			4.2 (2.7, 8.6)			1.5 (0.7, 3.6)		
$ \begin{array}{llllllllllllllllllllllllllllllllllll$	Age at diagnosis t			0.002	0.002		0.002	0.005
$ \begin{array}{ccccccc} 75 & 29 (13, 7.1) & & & & & & & & & & & & & & & & & & &$						$1.9\ (0.9,\ 3.7)$		
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$						$0.9\ (0.3,\ 3.1)$		
$ \begin{array}{ccccc} & 33 & 4.2 & (2.2, 8.1) \\ & 50 & 3.9 & (2.3, 7.4) & & & & & & & & & & & & & & & & & & &$	Insulin delivery method		_	0.570			0.738	
$ \begin{array}{ccccc} 50 & 3.9 (2.3, 7.4) & & & & & & & & & & & & & & & & & & &$			4.2 (2.2, 8.1)			$1.4\ (0.5, 3.6)$		
$\begin{array}{c cccc} 0.040 & 0.072 & & \\ \hline 77 & 3.8 (1.4, 8.1) & & & \\ 65 & 4.2 (2.6, 7.4) & & & \\ 17 & 4.4 (2.5, 7.4) & & & \\ 17 & 4.4 (2.5, 7.4) & & & \\ 126 & 3.9 (2.1, 8.1) & & & \\ 126 & 3.9 (2.1, 8.1) & & & \\ 126 & 3.9 (2.1, 8.1) & & & \\ 126 & 3.9 (1.7, 7.1) & & & \\ \end{array} $			3.9 (2.3, 7.4)			1.4 (0.4, 3.2)		
$\begin{array}{ccccc} 77 & 3.8 (1.4, 8.1) \\ 65 & 4.2 (2.6, 7.4) \\ & & & & & & \\ 17 & 4.4 (2.5, 7.4) \\ & & & & & & & \\ 17 & 4.4 (2.5, 7.4) \\ & & & & & & & \\ 126 & 3.9 (2.1, 8.1) \\ & & & & & & & \\ & & & & & & \\ $	Total daily insulin units per kg^\sharp			0.040	0.072		0.040	0.080
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$			3.8 (1.4, 8.1)			$1.1\ (0.5, 3.6)$		
se 17 $4.4(2.5, 7.4)$ - $2.4(0.7, 3.5)$ M use 17 $4.4(2.5, 7.4)$ $2.4(0.7, 3.5)$ M use 126 $3.9(2.1, 8.1)$ $1.4(0.4, 3.6)$ splucose meter checks/day [‡] - 0.666 - $1.2(0.4, 3.1)$			4.2 (2.6, 7.4)			1.7~(0.4, 3.6)		
17 4.4 (2.5, 7.4) 2.4 (0.7, 3.5) 126 3.9 (2.1, 8.1) 1.4 (0.4, 3.6) 62 3.9 (1.7, 7.1) 1.2 (0.4, 3.1)	Prior CGM use		_	0.605			0.474	
126 3.9 (2.1, 8.1) 1.4 (0.4, 3.6) 0.666 - 1.2 (0.4, 3.1) 62 3.9 (1.7, 7.1) 1.2 (0.4, 3.1)			4.4 (2.5, 7.4)			2.4 (0.7, 3.5)		
0.666 - 0.666 - 0.666 - 0.666 - 0.67.7.1) - 0.2 (0.4, 3.1)			3.9			$1.4 \ (0.4, 3.6)$		
62 3.9 (1.7, 7.1)	Average blood glucose meter checks/day ‡			0.666	ı		0.839	
		62	3.9 (1.7, 7.1)			1.2 (0.4, 3.1)		
6 81 4.1 (2.5, 8.1) 1.4 (0.5, 3.6)			4.1 (2.5, 8.1)			$1.4\ (0.5, 3.6)$		

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* Pvalues have been adjusted for multiple comparisons using the adaptive Benjamini–Hochberg procedure to control the false discovery rate.

 $\stackrel{f}{\succ} P$ values are only given for variables that were selected in the final model.

⁴Age, BMI percentile, type 1 diabetes duration, age at diagnosis, total daily insulin per kg, and blood glucose meter checks/day were entered in the models as continuous variables. Parent education and annual household income were considered ordinal, with seven and five levels, respectively. Categories for these variables are for display only.