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Continuous Glucose Monitoring Versus Usual Care in Patients With Type 2 Diabetes Receiving Multiple Daily Insulin Injections

A Randomized Trial

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Background: Continuous glucose monitoring (CGM), which studies have shown is beneficial for adults with type 1 diabetes, has not been well-evaluated in those with type 2 diabetes receiving insulin.

Objective: To determine the effectiveness of CGM in adults with type 2 diabetes receiving multiple daily injections of insulin.

Design: Randomized clinical trial. (The protocol also included a type 1 diabetes cohort in a parallel trial and subsequent second trial.) (ClinicalTrials.gov: NCT02282397)

Setting: 25 endocrinology practices in North America.

Patients: 158 adults who had had type 2 diabetes for a median of 17 years (interquartile range, 11 to 23 years). Participants were aged 35 to 79 years (mean, 60 years [SD, 10]), were receiving multiple daily injections of insulin, and had hemoglobin A_{1c} (HbA_{1c}) levels of 7.5% to 9.9% (mean, 8.5%).

Intervention: Random assignment to CGM (n = 79) or usual care (control group, n = 79).

Measurements: The primary outcome was HbA_{1c} reduction at 24 weeks.

Results: Mean HbA_{1c} levels decreased to 7.7% in the CGM group and 8.0% in the control group at 24 weeks (adjusted difference in mean change, −0.3% [95% CI, −0.5% to 0.0%]; P = 0.022). The groups did not differ meaningfully in CGM-measured hypoglycemia or quality-of-life outcomes. The CGM group averaged 6.7 days (SD, 0.9) of CGM use per week.

Limitation: 6-month follow-up.

Conclusion: A high percentage of adults who received multiple daily insulin injections for type 2 diabetes used CGM on a daily or near-daily basis for 24 weeks and had improved glycemic control. Because few insulin-treated patients with type 2 diabetes currently use CGM, these results support an additional management method that may benefit these patients.

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Blood glucose meters have been used for home glucose monitoring by persons with diabetes for more than 30 years. In recent years, real-time continuous glucose monitoring (CGM) has become available. By providing glucose measurements as often as every 5 minutes, low and high glucose alerts, and glucose trend information, CGM can better inform diabetes management decisions than a relatively small number of daily glucose measurements, typically made with a blood glucose meter. A real-time CGM system consists of a small disposable sensor, a transmitter, and a receiver. The sensor is inserted by the patient about every 7 days into the subcutaneous fat and measures glucose concentrations in the interstitial fluid. A reusable transmitter is attached to the sensor and wirelessly transmits glucose values every 5 minutes to a receiver or smartphone, which displays the values. The receiver provides a graph with glucose trends and alerts the user when glucose concentrations exceed or fall below user-defined thresholds. Many studies have shown improved glycemic control with CGM use by adults with type 1 diabetes using an insulin pump (1–11). A recent randomized trial in adults with type 1 diabetes receiving multiple daily injections of insulin, done in parallel with the trial reported here, found that CGM use was associated with statistically significant reductions in hemoglobin A_{1c} (HbA_{1c}), hypoglycemia, hyperglycemia, and glucose variability (12).

Whether CGM could also benefit adults with type 2 diabetes receiving insulin has not been well-studied, although substantially more insulin users have type 2 than type 1 diabetes (13, 14), and glycemic control often remains suboptimal even with the use of insulin (15–18). In a randomized trial of adults with type 2 diabetes using treatment regimens other than prandial insulin, Vigersky and colleagues (19) found that 12 weeks of intermittent, real-time CGM was associated with significantly improved glycemic control compared with blood glucose meter testing. In contrast, Haak and colleagues' (20) randomized trial of insulin-using adults with poorly controlled type 2 diabetes found no HbA_{1c} benefit of the FreeStyle Libre Flash Glucose Monitoring System (Abbott Diabetes Care) compared with blood

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glucose meter testing. Aside from these trials, few data assess the benefit of CGM in persons with poorly controlled type 2 diabetes receiving insulin (21–23).

To evaluate the effectiveness of CGM in adults with type 2 diabetes receiving multiple daily injections of insulin, we did a 24-week, randomized, multicenter clinical trial comparing CGM with usual care.

METHODS

The trial was done at 25 endocrinology practices in North America (22 in the United States and 3 in Canada), of which 19 were community-based and 6 were academic centers (4 additional sites screened but did not enroll patients). The study is registered at Clinical Trials.gov (NCT02282397). The protocol and Health Insurance Portability and Accountability Act–compliant informed consent forms were approved by 1 central and multiple local institutional review boards. The protocol, provided in the **Supplement** (available at Annals.org), was identical to that of a parallel trial in patients with type 1 diabetes (12), which also had a second phase assessing insulin pump initiation. Key aspects of the protocol are summarized here.

Study Participants

We obtained written informed consent from each participant. Major eligibility criteria included age at least 25 years, type 2 diabetes treated with multiple daily injections of insulin for at least 1 year, central laboratory–measured HbA_{1c} levels of 7.5% to 10.0%, stable diabetes medication regimen and weight over the prior 3 months, self-reported blood glucose meter testing averaging 2 or more times per day, and estimated glomerular filtration rate of at least 45 mL/min/1.73 m^2. See **Appendix Table 1** (available at Annals.org) for a complete listing of inclusion and exclusion criteria.

Study Design

Informed consent was given by 253 participants. Twelve participants withdrew before screening was complete, and 71 were determined to be ineligible on initial screening at the clinic or after central laboratory measurement of HbA_{1c}. For 2 weeks before randomization, each participant used a CGM device that recorded glucose concentrations that were not visible to the participant (called a "blinded" CGM device). Eligibility, which was discussed on the consent form, required participants to wear the blinded CGM device on at least 85% of possible days, calibrate it at least twice per day, and do blood glucose meter testing at least twice per day on average. Ten participants did not meet these criteria and did not continue.

On the study Web site, after verification of eligibility from data entered, each participant was randomly assigned by a computer-generated sequence to either the CGM or control group in a 1:1 ratio, using a permuted block design (random block sizes of 2 and 4) stratified by HbA_{1c} level (<8.5% and ≥8.5%).

Participants in both groups were provided with a Contour Next USB meter (Ascensia Diabetes Care) and test strips. Participants in the CGM group were given a Dexcom G4 Platinum CGM System with an enhanced algorithm (software 505) (Dexcom), which measures glucose concentrations from interstitial fluid in the range of 2.22 to 22.2 mmol/L (40 to 400 mg/dL) every 5 minutes. Participants received general guidelines about using CGM, and their clinicians individualized recommendations about incorporating CGM trend information into their diabetes management. Participants used CGM as an adjunct to blood glucose monitoring, according to U.S. Food and Drug Administration labeling at the time of the study. The control group was asked to monitor their blood glucose at least 4 times daily. Specific insulin adjustments were not prescriptive in the protocol for either group but were made at the discretion of treating clinicians at the clinical sites.

Follow-up visits for both treatment groups occurred after 4, 12, and 24 weeks. The CGM group had an additional visit 1 week after randomization to troubleshoot potential use problems. The control group had 2 additional visits 1 week before the 12- and 24-week visits to initiate blinded CGM use for 1 week. Both groups were contacted by telephone 2 and 3 weeks after randomization. Staff at the Northwest Lipid Research Laboratories at the University of Washington (Seattle, Washington) measured HbA_{1c} levels at baseline, 12 weeks, and 24 weeks using the Diabetes Control and Complications Trial–standardized analyzer (Tosoh Bioscience).

Study Outcomes

Change in HbA_{1c} level from baseline to 24 weeks was the primary outcome. Prespecified secondary outcomes included the proportions of participants with HbA_{1c} levels below 7.0%, HbA_{1c} levels below 7.5%, relative reduction of at least 10%, reduction of at least 1%, reduction of at least 1% or HbA_{1c} level below 7.0%, and the CGM outcomes below. Researchers obtained CGM data in conjunction with the 12- and 24-week visits (blinded use in the control group and unblinded use in the CGM group for approximately 7 days each time) and used them to estimate the length of time per day the glucose concentration was hypoglycemic (<3.89, <3.33, and <2.78 mmol/L [<70, <60, and <50 mg/dL]), hyperglycemic (>9.99, >13.88, and >16.65 mmol/L [>180, >250, and >300 mg/dL]), and in the target range (3.89 to 9.99 mmol/L [70 to 180 mg/dL]). Glucose variability was assessed by computing the coefficient of variation. Additional outcomes included scores on the Clarke Hypoglycemia Unawareness Survey (24), 2 general quality-of-life measures (5-level EuroQol-5D and 5-item World Health Organization Well-Being Index) (25, 26), and 3 diabetes-specific quality-of-life measures (Hypoglycemia Fear Survey, Diabetes Distress Scale, and Hypoglycemic Confidence Scale) (27–29). The CGM group's satisfaction was assessed using the CGM Satisfaction Scale at 24 weeks (30). Health economic outcomes will be reported separately. Additional prespecified outcomes included insulin use,

body weight, and frequency of blood glucose meter testing. Preplanned exploratory subgroup analyses were defined on the basis of baseline HbA_{1c} level, age, CGM-measured hypoglycemia, frequency of blood glucose meter testing, education level, diabetes numeracy, Hypoglycemia Unawareness score, and Hypoglycemia Fear score. An outcome of HbA_{1c} level reduced at least 0.5% was computed post hoc.

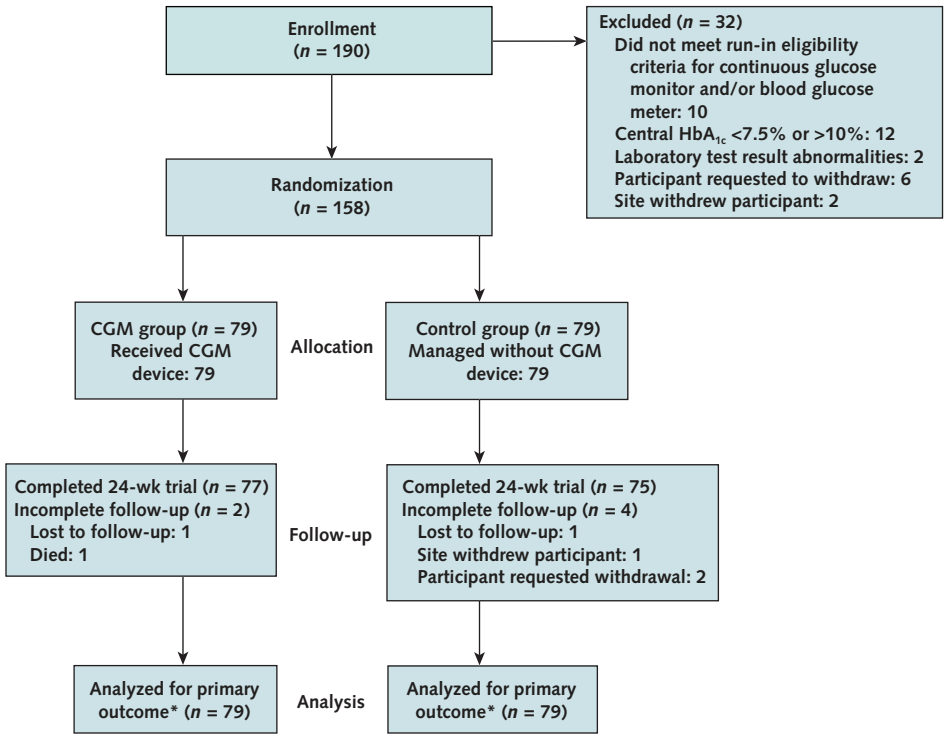
Reportable adverse events included all device or study-related adverse events, severe hypoglycemia (defined as an event that required assistance from another person to administer carbohydrates or other re-

Table 1. Baseline Participant Characteristics in the CGM and Usual Care Groups*

Characteristic	CGM Group (*n* = 79)	Control Group (*n* = 79)
Age		
25–44 y	9 (11)	4 (5)
45–59 y	27 (34)	36 (46)
≥60 y	43 (54)	39 (49)
Mean (SD), *y*	60 (11)	60 (9)
Range, *y*	35–77	42–79
Median diabetes duration (interquartile range), *y*	17 (11–23)	18 (12–23)
Female	49 (62)	40 (51)
Race/ethnicity†		
White non-Hispanic	43 (54)	57 (73)
Black non-Hispanic	11 (14)	7 (9)
Hispanic or Latino	14 (18)	12 (15)
Other	11 (14)	2 (3)
Highest education‡		
Less than bachelor's degree	45 (58)	49 (66)
Bachelor's degree	19 (24)	17 (23)
Graduate/professional degree	14 (18)	8 (11)
Mean BMI (SD), kg/m^2	35 (8)	37 (7)
Mean weight (SD), *kg*	98 (23)	105 (25)
Preexisting conditions		
Hypertension	61 (77)	65 (82)
Hyperlipidemia	54 (68)	50 (63)
Myocardial infarction	4 (5)	3 (4)
Stroke	1 (1)	1 (1)
HbA_{1c} level (measured at central laboratory)		
7.5%–<8.5%	39 (49)	38 (48)
8.5%–≤9.9%	40 (51)	41 (52)
Mean (SD), %	8.5 (0.6)	8.5 (0.7)
Range, %	7.5–9.9	7.5–9.9
Mean self-reported number of blood glucose tests per day (SD), *n*	3.3 (1.2)	3.2 (1.2)
Used CGM in past	6 (8)	4 (5)
Mean total daily insulin dose (SD), *units/kg/d*	1.2 (0.6)	1.0 (0.5)
Number of long-acting insulin injections per day		
0§	0 (0)	1 (1)
1	55 (70)	54 (68)
2	23 (29)	23 (29)
3	1 (1)	1 (1)
Number of rapid-acting insulin injections per day		
0§	1 (1)	0 (0)
2	4 (5)	9 (11)
3	68 (86)	60 (76)
4	5 (6)	8 (10)
5	1 (1)	2 (3)
Use of noninsulin glucose-lowering medication‖	56 (71)	52 (66)
≥1 severe hypoglycemia event in previous 12 mo	2 (3)	2 (3)
≥1 diabetic ketoacidosis event in previous 12 mo	0 (0)	0 (0)
C-peptide level¶		
<0.2 ng/mL	9 (11)	4 (5)
≥0.2 ng/mL	70 (89)	75 (95)
Hypoglycemia unawareness**		
Reduced awareness	9 (11)	9 (11)
Uncertain	16 (20)	8 (10)
Aware	54 (68)	62 (78)

BMI = body mass index; CGM = continuous glucose monitoring; HbA_{1c} = hemoglobin A_{1c}.
* Values are numbers (percentages) unless otherwise stated.
† Missing data for 1 participant from the control group.
‡ Missing data for 1 participant from the CGM group and 5 participants from the control group.
§ Participant was ineligible and should not have been randomly assigned.
‖ Noninsulin medications for CGM group/control group were metformin, 44/41; glucagon-like peptide-1, 11/8; dipeptidyl peptidase-4, 6/4; sodium-glucose cotransporter-2, 15/15; and other, 7/10.
¶ Measured at local laboratories. To convert from ng/mL to nmol/L, multiply values by 0.331.
** Measured with the Clarke Hypoglycemia Unawareness Survey.

Figure. Study flow diagram.



All enrolled participants started the run-in phase; 32 did not proceed to randomization for the reasons indicated in the figure. CGM = continuous glucose monitoring; HbA_{1c} = hemoglobin A_{1c}.
* Multiple imputation used for HbA_{1c} value for 2 participants in the CGM group and 4 in the control group.

suscitative action), diabetic ketoacidosis or severe hyperglycemia if treatment was received at a health care facility, and serious adverse events regardless of causality.

Statistical Analysis

We calculated that a sample size of 132 was necessary to provide at least 90% power to detect a difference in mean HbA_{1c} level between treatment groups, assuming a population difference of 0.4%, effective SD of 0.7 for the 24-week values after adjustment for the correlation between baseline and 24-week values, and a 2-sided α level of 0.05. Sample size was initially set at 169 to account for potential loss to follow-up and to mirror the sample size in a parallel type 1 diabetes trial.

Table 2. Comparison of HbA_{1c} Outcomes at 12 and 24 Weeks in the CGM and Usual Care Groups*

Outcome	12 wk		
	CGM Group (*n* = 77)	Control Group (*n* = 75)	Adjusted Difference (95% CI); *P* Value†
Primary outcome			
Mean HbA_{1c} level (95% CI), %	7.5 (7.4 to 7.7)	7.9 (7.7 to 8.1)	–
Mean change in HbA_{1c} level from baseline (95% CI), %	−1.0 (−1.2 to −0.8)	−0.6 (−0.8 to −0.4)	−0.3 (−0.6 to −0.1); 0.005
Secondary outcomes‡			
HbA_{1c} level <7.0%, *n (%)*	17 (22)	9 (12)	10% (−2% to 23%); 0.26
HbA_{1c} level <7.5%, *n (%)*	35 (45)	22 (29)	17% (−3% to 37%); 0.054
Relative reduction in HbA_{1c} level ≥10%, *n (%)*	44 (57)	26 (35)	25% (3% to 46%); 0.016
Reduction in HbA_{1c} level ≥1%, *n (%)*	40 (52)	25 (33)	20% (−1% to 41%); 0.044
Reduction in HbA_{1c} level ≥1% or HbA_{1c} level <7.0%, *n (%)*	41 (53)	25 (33)	22% (0% to 43%); 0.034
Reduction in HbA_{1c} level ≥0.5%, *n (%)*	61 (79)	38 (51)	31% (5% to 57%); 0.002

CGM = continuous glucose monitoring; HbA_{1c} = hemoglobin A_{1c}.
* Mean baseline HbA_{1c} level was 8.5% in each group.
† *P* value for change in HbA_{1c} level is from a mixed-effects linear model adjusting for baseline HbA_{1c} level and accounting for clinical site. For the binary outcomes, *P* values are from mixed-effects logistic regression models adjusting for baseline HbA_{1c} level and accounting for clinical site. Confidence bounds for adjusted differences for the binary outcomes were calculated using bootstrap methods.
‡ At 24 wk, *n* = 77 for the CGM group and *n* = 75 for the control group. All analyses were prespecified except for reduction in HbA_{1c} level ≥0.5%, which was done post hoc.

When the coordinating center recognized that the trial completion rate was higher than anticipated, the recruitment goal was changed to a minimum of 150.

Analyses followed the intention-to-treat principle. The primary analysis was a treatment group comparison of the change in HbA_{1c} level from baseline to 24 weeks in a mixed-effects linear model with baseline HbA_{1c} level as a fixed effect and clinical site as a random effect. The analysis was repeated post hoc with clinical site as a fixed effect. We assessed confounding by including baseline variables imbalanced between treatment groups as covariates. Multiple imputation was used to replace missing 24-week HbA_{1c} data (31, 32) when both central laboratory and local values were missing. If the central laboratory measurement was missing but the local measurement was known, the value used in the analysis was imputed using a regression line based on the site's local HbA_{1c} measurements. We also did the analysis using a repeated-measures mixed-effects linear model (see **Supplement** for more details). To assess for interaction between baseline factors and treatment effect on the change in HbA_{1c} level from baseline to 24 weeks, we included interaction terms in the mixed-effects models. Binary HbA_{1c} outcomes were evaluated in mixed-effects logistic regression models with baseline HbA_{1c} level as a fixed effect and clinical site as a random effect using an adaptive quadrature estimation routine. We calculated adjusted differences for the binary outcomes using Kleinman and Norton's method (33) and CIs using bootstrapping. Frequency of blood glucose self-monitoring according to meter download was compared between groups by using the Wilcoxon rank-sum test.

Analyses were done using SAS, version 9.4 (SAS Institute). All *P* values are 2-sided.

Role of the Funding Source

Dexcom funded the trial. A Dexcom employee (D.P.) participated on the steering committee and, as a coauthor of the manuscript, provided comments for the other authors, but Dexcom had no approval authority for the manuscript before submission. Data management, monitoring, and analysis were the responsibility of the coordinating center, the Jaeb Center for Health Research (Tampa, Florida), and were independent of the sponsor. Dexcom staff participated in onsite audit visits.

Table 2–Continued

24 wk		
CGM Group (*n* = 79)	**Control Group (*n* = 79)**	**Adjusted Difference (95% CI); *P* Value†**
7.7 (7.5 to 7.8)	8.0 (7.8 to 8.2)	–
−0.8 (−1.0 to −0.7)	−0.5 (−0.7 to −0.3)	−0.3 (−0.5 to 0.0); 0.022
11 (14)	9 (12)	3% (−9% to 14%); 0.88
27 (35)	21 (28)	8% (−11% to 26%); 0.63
40 (52)	24 (32)	22% (0% to 42%); 0.028
30 (39)	21 (28)	12% (−7% to 30%); 0.21
33 (43)	22 (29)	15% (−5% to 34%); 0.146
56 (73)	37 (49)	26% (0% to 50%); 0.007

RESULTS

Between October 2014 and March 2016, we assigned 158 participants to the CGM group (*n* = 79) or control group (*n* = 79). The number per site ranged from 1 to 27 (**Supplement Table 1**, available at Annals.org). Mean age was 60 years (SD, 10; range, 35 to 79 years, with 52% of participants ≥60 years), median diabetes duration was 17 years (interquartile range, 11 to 23 years), and mean baseline HbA_{1c} level was 8.5% (SD, 0.6%; range, 7.5% to 9.9%). Participant characteristics according to treatment group are shown in **Table 1**.

The 24-week primary outcome visit was completed by 77 participants (97%) in the CGM group and 75 (95%) in the control group (**Figure** and **Appendix Figure 1**, available at Annals.org). In the CGM group, CGM use was high across the age range of participants. Among the 77 participants completing the trial, mean CGM use was 6.9 days per week (SD, 0.4) in month 1 (weeks 1 to 4), 6.7 days per week (SD, 1.0) in month 3 (weeks 9 to 12), and 6.7 days per week (SD, 1.0) in month 6 (weeks 21 to 24). Only 1 participant discontinued CGM before the 24-week visit (**Appendix Table 2**, available at Annals.org). In month 6, the 42 participants aged at least 60 years completing the trial had mean CGM use of 6.7 days per week (SD, 1.3) and the 17 participants with baseline HbA_{1c} levels of at least 9.0% completing the trial had mean CGM use of 6.8 days per week (SD, 0.4). No participant in the control group initiated unblinded CGM use before the primary outcome visit (except for 1 who used an unblinded CGM for the first few days because of a protocol deviation by the site). Two participants (3%) in each group started a new noninsulin diabetes medication during follow-up.

Based on meter downloads, frequencies of blood glucose self-monitoring averaged 4.1 tests per day (SD, 1.1) in the CGM group and 4.0 tests per day (SD, 1.2) in the control group during the baseline period of blinded CGM use. At 24 weeks, frequencies averaged 2.9 tests per day (SD, 1.1) in the CGM group and 3.8 tests per day (SD, 1.5) in the control group ($P < 0.001$).

Glycemic Control and Other Outcomes

Mean HbA_{1c} levels, which at baseline were 8.5% (SD, 0.6%) in the CGM group and 8.5% (SD, 0.7%) in the control group, decreased to 7.5% (SD, 0.7%) and 7.9% (SD, 0.8%), respectively, at 12 weeks (adjusted difference in mean change in HbA_{1c} level, −0.3% [95% CI, −0.6% to −0.1%]; $P = 0.005$). In both groups, mean HbA_{1c} levels increased slightly between 12 and 24 weeks (mean HbA_{1c} level at 24 weeks, 7.7% [SD, 0.7%] in the CGM group vs. 8.0% [SD, 0.9%] in the control

Table 3. CGM Metrics at Baseline, 12 Weeks, and 24 Weeks in the CGM and Usual Care Groups*

Variable	CGM Group			Control Group		
	Baseline (*n* = 79)	12 wk (*n* = 77)†	24 wk (*n* = 74)†	Baseline (*n* = 78)†	12 wk (*n* = 74)†	24 wk (*n* = 72)†
Data collected, *h*	311 (294–319)	161 (152–165)	159 (153–163)	312 (293–318)	150 (140–154)	149 (137–156)
Mean glucose concentration, *mg/dL*	177 (154–191)	166 (149–187)	171 (149–195)	175 (155–191)	172 (155–199)	171 (156–199)
Time per day in range of 70–180 mg/dL, *min*	802 (604–974)	937 (664–1083)	882 (647–1077)	794 (665–976)	822 (537–1025)	836 (551–965)
Hyperglycemia						
Time per day >180 mg/dL, *min*	612 (411–809)	501 (323–746)	549 (353–789)	607 (392–775)	560 (382–818)	571 (422–883)
Time per day >250 mg/dL, *min*	150 (68–265)	100 (37–180)	105 (37–246)	154 (66–281)	137 (53–251)	118 (48–288)
Time per day >300 mg/dL, *min*	33 (9–77)	19 (0–56)	23 (0–66)	42 (9–96)	33 (1–95)	18 (0–83)
Area under curve 180 mg/dL	22 (13–32)	14 (7–26)	16 (8–30)	21 (11–33)	18 (11–34)	18 (12–34)
Hypoglycemia						
Time per day <70 mg/dL, *min*	11 (1–33)	9 (1–25)	4 (0–17)	12 (3–39)	11 (0–37)	12 (0–34)
Time per day <60 mg/dL, *min*	3 (0–15)	1 (0–7)	0 (0–6)	4 (0–17)	1 (0–12)	2 (0–12)
Time per day <50 mg/dL, *min*	0 (0–8)	0 (0–0)	0 (0–1)	0 (0–7)	0 (0–3)	0 (0–5)
Area above curve of 70 mg/dL	0.1 (0.0–0.3)	0.0 (0.0–0.1)	0.0 (0.0–0.1)	0.1 (0.0–0.3)	0.0 (0.0–0.3)	0.1 (0.0–0.2)
Glucose variability: coefficient of variation, %	31 (27–38)	30 (26–34)	30 (26–33)	32 (27–37)	30 (25–37)	29 (25–36)

CGM = continuous glucose monitoring.
* Values are medians (interquartile ranges). To convert glucose values from mg/dL to mmol/L, multiply the values by 0.0555.
† CGM metrics were not calculated for participants with <72 h of data: 1 control participant at baseline, 1 CGM and 3 control participants at 12 wk, and 3 CGM and 3 control participants at 24 wk.

group). The adjusted difference in mean change in HbA_{1c} level from baseline to 24 weeks was −0.3% (CI, −0.5% to 0.0%) (P = 0.022) (Table 2 and Appendix Figure 2, available at Annals.org). In a post hoc analysis including clinical site as a fixed effect, the adjusted difference was −0.2% (CI, −0.5% to 0.0%) (P = 0.072). In the repeated measures model, the adjusted difference was −0.2% (CI, −0.3% to −0.1%) (P = 0.022). Secondary HbA_{1c} outcomes tended to favor the CGM group, although none of the prespecified secondary outcomes reached statistical significance (Table 2). In subgroup analyses, HbA_{1c} results favored the CGM group in all subgroups, including older and younger age, higher and lower education levels, and higher and lower scores on a diabetes numeracy test (Appendix Table 3, available at Annals.org).

Median CGM-measured time in the range of 3.89 to 9.99 mmol/L (70 to 180 mg/dL) increased more in the CGM group than in the control group (from 802 minutes per day at baseline to 882 minutes per day at 24 weeks in the CGM group and from 794 to 836 minutes per day in the control group), reflecting a greater reduction in time above 9.99 mmol/L (180 mg/dL) in the CGM group than in the control group (Table 3). Treatment group differences in both metrics favoring the CGM group were present during daytime and nighttime (Appendix Tables 4 and 5, available at Annals.org). The groups did not differ meaningfully in changes in CGM-measured mean glucose concentrations or glycemic variability (coefficient of variation). The amount of CGM-measured hypoglycemia was extremely low at baseline (median time below 3.89 mmol/L [70 mg/dL], 11 minutes per day in the CGM group and 12 minutes per day in the control group), which limited our ability to assess the effect of CGM on reducing hypoglycemia in this cohort.

At 24 weeks, change from baseline in total daily insulin dose per kilogram of body weight was 0.1 units (SD, 0.3) in the CGM group and 0.0 units (SD, 0.3) in the control group. The groups did not differ meaningfully in the ratio of basal–bolus daily insulin dose or number of injections per day of rapid-acting insulin (Appendix Table 6, available at Annals.org). New noninsulin diabetes medications were added during follow-up for 2 participants (3%) in the CGM group and 2 (3%) in the control group. Mean weight change from baseline to 24 weeks was 1.3 kg (SD, 3.6) in the CGM group and −0.2 kg (SD, 4.5) in the control group (Appendix Table 6). The group did not differ meaningfully in Clarke Hypoglycemia Unawareness scores at 24 weeks.

Severe Hypoglycemia and Other Adverse Events

Severe hypoglycemia or diabetic ketoacidosis did not occur in either group. In the CGM group, 1 participant died of a myocardial infarction and 2 others were hospitalized for chest pain and fully recovered, all considered to be unrelated to CGM use. No serious adverse events occurred in the control group.

CGM Satisfaction and Quality-of-Life Measures

The treatment groups did not differ meaningfully in any of the 5 quality-of-life measures (Table 4). However, the CGM group had high satisfaction with use of CGM, as indicated by the mean score of 4.3 (SD, 0.4) on the CGM Satisfaction Scale (score range, 1 to 5). Mean scores were 4.4 (SD, 0.5) on the benefits subscale and 1.8 (SD, 0.5) on the hassles subscale, indicating that perceived benefits were high and perceived hassles low (Appendix Table 7, available at Annals.org). On almost all items, most participants responded with scores indicating high satisfaction.

DISCUSSION

In this trial of patients with type 2 diabetes receiving multiple daily injections of insulin, HbA_{1c} improvement at 24 weeks was significantly greater in partici-

pants using CGM than in a control group using only a blood glucose meter for monitoring. Exploratory analyses suggested that an HbA_{1c} difference favoring the CGM group was present across the age range of 35 to 79 years, the baseline HbA_{1c} level range of 7.5% to 9.9%, all education levels, and all diabetes numeracy scores. The greater HbA_{1c} improvement in the CGM group was reflected in a greater increase in time with glucose concentrations in the range of 3.89 to 9.99 mmol/L (70 to 180 mg/dL) and a greater reduction in time with glucose concentrations above 9.99 mmol/L (180 mg/dL). Biochemical hypoglycemia, measured with CGM, was infrequent, limiting the trial's ability to assess the effect of CGM on reducing hypoglycemia. No cases of severe hypoglycemia occurred in either group. The observed benefits of CGM occurred even though the CGM group decreased testing during the study more than the control group. A small weight gain was seen in the CGM group compared with the control group, the significance of which is not known.

Because few studies of CGM in type 2 diabetes have been done, we did not know whether persons with type 2 diabetes would sustain daily use of CGM over 6 months. However, the amount of CGM use after 24 weeks exceeded our expectations. All but 1 participant in the CGM group who completed the trial were still using CGM after 24 weeks, with more than 90% averaging 6 or more days of CGM use per week. The treatment groups did not differ meaningfully on the quality-of-life measures. However, the participant-completed CGM Satisfaction Scale at the end of the trial indicated high satisfaction with CGM, which likely contributed to the high frequency of use, particularly because the protocol had only 1 visit after week 4 before the 24-week primary outcome visit and no scheduled visits or phone contacts between weeks 12 and 24.

Mean improvements in HbA_{1c} level at 24 weeks were 0.8% in the CGM group and 0.5% in the control group, both of which are substantial reductions. A mean HbA_{1c} level reduction of 0.3% is a meaningful improvement on a patient level, particularly because it was achieved without a pharmacologic change. In the CGM group, 73% of participants achieved an HbA_{1c} level reduction of at least 0.5% at 24 weeks, compared with 49% in the control group. Fifty-two percent and 32%, respectively, achieved a relative HbA_{1c} level reduction of at least 10%. The latter outcome is clinically meaningful according to the Diabetes Control and Complications Trial, which showed that for each 10% relative decrease in HbA_{1c} level (for example, 8.0% to 7.2%), risk for progression of diabetic retinopathy decreases approximately 40% and risk for progression of renal disease decreases 25% (34). Of note, the treatment effect was greater (HbA_{1c} level reduction of 1.4% in the CGM group vs. 0.7% in the control group) in participants with the highest baseline HbA_{1c} values (at least 9.0%), who are at greatest risk for complications.

In contrast to the findings in our trial, the REPLACE randomized trial in an insulin-using type 2 diabetes population with similar characteristics to ours found no HbA_{1c} benefit of the FreeStyle Libre Flash Glucose Monitoring System (20). Unlike the Dexcom G4 Platinum CGM System, the FreeStyle Libre requires the patient to actively scan the system for glucose concentrations and does not provide hypoglycemia or hyperglycemia alerts. This finding suggests that the

Table 4. Quality-of-Life Measures at Baseline and 24 Weeks in the CGM and Usual Care Groups*

Measure	Baseline		24 wk	
	CGM Group (*n* = 79)	Control Group (*n* = 79)	CGM Group (*n* = 77)	Control Group (*n* = 73)
General measures				
EQ-5D-5L overall index†	0.82 (0.15)	0.82 (0.14)	0.82 (0.14)	0.82 (0.16)
WHO-5 total score‡	16 (4)	17 (4)	16 (5)	17 (4)
Diabetes-specific measures				
Diabetes Distress Scale overall mean score§	1.9 (0.8)	2.0 (0.8)	1.8 (0.9)	1.8 (0.6)
Emotional burden mean score	2.3 (1.2)	2.3 (1.1)	2.2 (1.2)	2.1 (1.0)
Clinician-related distress mean score	1.3 (0.6)	1.3 (0.8)	1.3 (0.9)	1.1 (0.3)
Regimen-related distress mean score	2.2 (0.9)	2.4 (1.0)	2.0 (0.9)	2.1 (0.9)
Diabetes-related interpersonal distress mean score	1.8 (1.0)	2.0 (1.2)	1.7 (1.1)	1.7 (0.8)
Hypoglycemia Fear Survey, worry subscale, mean score‖	0.8 (0.7)	0.8 (0.6)	0.8 (0.6)	0.7 (0.5)
Hypoglycemic Confidence Scale mean score¶	3.2 (0.7)	3.4 (0.6)	3.3 (0.6)	3.4 (0.6)

CGM = continuous glucose monitoring; EQ-5D-5L = 5-level EuroQol-5D; WHO-5 = 5-item World Health Organization Well-Being Index.
* Values are means (SDs).
† 5 items on the patient's health status. Calculated using the U.S. weights and time–tradeoff valuation technique. Scores range from 0 to 1, with higher scores denoting fewer health problems. Missing for 1 CGM and 1 control participant at baseline and 1 CGM and 3 control participants at 24 wk.
‡ 5 items (scale of 0–5) on how the patient has been feeling over the past 2 wk. Total score calculated if all questions are answered. Scores range from 0 to 25, with higher scores denoting better well-being. Missing for 1 CGM and 4 control participants at 24 wk.
§ 17 items on diabetes distress factors. Mean score calculated if ≥75% of the questions are answered. Scores range from 1 to 6, with lower scores denoting less of a problem or less distress. Missing for 3 control participants at 24 wk.
‖ 18 items on what the patient worries about related to their diabetes. Mean score calculated if ≥75% of the questions are answered. Scores range from 0 to 4, with lower scores denoting less fear. Missing for 2 control participants at 24 wk.
¶ 9 items on the patient's general confidence related to hypoglycemia. Mean score calculated if ≥75% of the questions are answered. Scores range from 1 to 4, with higher scores denoting more confidence. Missing for 2 control participants at 24 wk.

alerts with CGM may help improve glycemic control in patients with type 2 diabetes.

Improvement in HbA_{1c} has also been shown in insulin-using patients with type 2 diabetes who used a different technology, switching from injections to an insulin pump. In the OpT2mise randomized trial, a treatment effect of 0.7% was found when a group using insulin pumps was compared with a control group that continued to use injections (35). The greater treatment effect in the OpT2mise trial than in ours may have been related to a coordinated treat-to-target strategy; more frequent titration visits; and of importance, higher baseline HbA_{1c} levels (mean, 9.0%).

The strengths of this randomized trial included very high treatment adherence and participant retention, protocol and study processes that can be replicated in real-world clinical practice, and measurement of HbA_{1c} levels at a central laboratory. With broad eligibility criteria and participation by both community-based and academic sites, the trial results should be generalizable to most patients with type 2 diabetes who are 35 to 79 years of age, have HbA_{1c} levels of 7.5% to 9.9%, and are being treated with multiple daily injections of insulin. A limitation of the trial is that follow-up was only 6 months.

By design, the study protocol approximated usual practice and did not include a structured protocol to more aggressively titrate insulin dosing or have structured review of glucose patterns seen on CGM tracings. We wanted to avoid biasing the results by providing more aggressive management to the CGM group than to the control group. Although time in the target range increased and time in hyperglycemia decreased, most participants in the CGM group still had substantial daily hyperglycemia and most did not achieve the HbA_{1c} goal of 7.0% recommended by American Diabetes Association (36). The minimal increase in daily insulin dose suggests that clinicians did not often make substantial insulin adjustments, despite persistent hyperglycemia and infrequent hypoglycemia. In contrast to patients with type 1 diabetes, patients with type 2 diabetes may have less advanced diabetes management skills (such as carbohydrate counting, insulin sensitivity factors, and appropriate correction timing) and less patient autonomy, which would limit their ability to use CGM to improve glycemic control. Our finding of high CGM use and high satisfaction with CGM suggests that even greater glycemic benefits could be obtained if clinicians incorporate traditional insulin titration algorithms or expand shared decision making and other decision support based on CGM data.

In conclusion, this randomized trial demonstrates that CGM can be beneficial for adults with type 2 diabetes treated with basal–bolus insulin therapy, as has been shown in prior studies for adults with type 1 diabetes. A high percentage of the study participants used CGM on a daily or near-daily basis over 6 months with a limited number of visits and phone contacts, none after 3 months prior to the 24-week primary outcome visit. Use of CGM was associated with a high degree of patient satisfaction, reduced hyperglycemia and consequently HbA_{1c} levels, and increased time in the target glucose range. Because few insulin-treated patients with type 2 diabetes are currently prescribed CGM, the study results indicate an additional management method that may be beneficial for these patients.

From Jaeb Center for Health Research, Tampa, Florida; Oregon Health & Science University, Portland, Oregon; Diabetes & Glandular Disease Clinic, San Antonio, Texas; Henry Ford Medical Center, Detroit, Michigan; Washington University in St. Louis, St. Louis, Missouri; Behavioral Diabetes Institute and Dexcom, San Diego, California; Research Institute of Dallas, Dallas, Texas; LMC Diabetes & Endocrinology, Toronto, Ontario, Canada; Joslin Diabetes Center, Boston, Massachusetts; and Park Nicollet International Diabetes Center, St. Louis Park, Minnesota.

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sures can also be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M16-2855.

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Statistical expertise: R.W. Beck, T.D. Riddlesworth, C. Kollman.
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Appendix: DIAMOND Study Group

Participating Clinical Sites

Personnel are listed as (I) for study investigator and (C) for study coordinator. Sites are listed in order by number of participants randomly assigned to a group. The number of participants is noted in parentheses preceded by the site location and site name. All listed clinical staff were contributors to data collection and study visit completion.

Diabetes & Glandular Disease Clinic, San Antonio, Texas (27): Mark Kipnes† (I), Stacie Haller* (C), and Terri Ryan† (C)

Accent Clinical Trials, Las Vegas, Nevada (16): Quang Nguyen† (I), Alejandra Martinez† (C), and Cathy Duran† (C)

Research Institute of Dallas, Dallas, Texas (12): Stephen Aronoff* (I), Satanya Brooks† (C), Gloria Martinez† (C), Angela Mendez† (C), and Theresa Dunnam† (C)

Henry Ford Medical Center Division of Endocrinology, Detroit, Michigan (10): Davida Kruger* (I), Shiri Levy† (I), Arti Bhan† (I), Terra Cushman† (C), and Heather Remtema† (C)

LMC Diabetes & Endocrinology–Toronto, Ontario, Canada (10): Ronnie Aronson* (I) and Jana Nathan† (C)

LMC Diabetes & Endocrinology–Barrie, Ontario, Canada (9): Hani Alasaad† (I), Suzan Abdel-Salam† (I), Katherine Buckley† (C), Laura Pidgen† (C), and Lydia Frost† (C)

Rocky Mountain Diabetes and Osteoporosis Center, Idaho Falls, Idaho (8): David Liljenquist† (I), Heather Judge† (C), and Jean Halford† (C)

Iowa Diabetes & Endocrinology Research Center, Des Moines, Iowa (6): Anuj Bhargava† (I), Kathy Fitzgerald† (I), Diana Wright† (I), Teck Khoo† (I), Pierre Theuma† (I), Tara Herrold† (C), and Debra Thomsen† (C)

International Diabetes Center–HealthPartners Institute, Minneapolis, Minnesota (6): Richard Bergenstal* (I), Marcia Madden† (I), Kathleen McCann† (C), Arlene Monk† (C), and Char Ashanti† (C)

Columbus Regional Research Institute, Endocrine Consultants, Columbus, Georgia (6): Steven Leichter† (I) and Emily Evans† (C)

Advanced Research Institute, Ogden, Utah (6): Jack Wahlen† (I), Jon Winkfield† (I), Hilary Wahlen† (C), Emily Hepworth† (C), David Winkfield† (C), and Sue Owens† (C)

LMC Diabetes & Endocrinology–Thornhill, Ontario, Canada (6): Ronald Goldenberg† (I), Sarah Birch† (C), and Danielle Porplycia† (C)

Oregon Health & Science University, Portland, Oregon (5): Andrew Ahmann* (I), Bethany Klopfenstein† (I), Farahnaz Joarder† (I), Kathy Hanavan† (I), Jessica Castle† (I), Diana Aby-Daniel† (I), Victoria Morimoto† (I), Donald DeFrang† (C), and Bethany Wollam† (C)

Amarillo Medical Specialists LLP, Amarillo, Texas (4): William Biggs† (I), Lorena Sandoval† (C), Robin Eifert† (C), and Becky Cota† (C)

Washington University in St. Louis, St. Louis, Missouri (4): Janet McGill* (I), Olivia Jordan† (C), and Carol Recklein† (C)

Mountain Diabetes and Endocrine Center, Asheville, North Carolina (4): Wendy Lane† (I), Stephen Weinrib† (I), Kaitlin Ramsey† (C), Lynley Farmer† (C), and Mindy Buford† (C)

NorthShore University HealthSystem, Skokie, Illinois (4): Liana K. Billings† (I), Cheryl Auston† (C), and Janet Yoo† (C)

Atlanta Diabetes Associates, Atlanta, Georgia (3): Bruce Bode† (I), Jennifer Boyd† (I), Joseph Johnson† (I), Nitin Rastogi† (C), and Katherine Lindmark† (C)

Portland Diabetes & Endocrinology Center, Portland, Oregon (2): Fawn Wolf† (I), James Neifing† (I), Jennifer Murdoch† (I), Susan Staat† (C), and Tamara Mayfield† (C)

East Coast Institute for Research, Jacksonville, Florida (2): Scott Segel† (I), David Sutton† (I), Miguel Roura† (I), Rebecca Rosenwasser† (C), Jennifer McElveen† (C), Emily Knisely† (C), and Anne Johnson† (C)

Diabetes & Endocrine Associates, Omaha, Nebraska (2): Sarah Konigsberg† (I) and Jennifer Rahman† (C)

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Appendix Table 1. Inclusion and Exclusion Criteria

Inclusion criteria

- Age ≥25 y
- Diagnosis of type 2 diabetes
- Followed regularly by a physician or diabetes educator for diabetes management, with ≥2 office visits in last year as documented by clinical history
- Use of multiple daily injections of insulin for ≥12 mo before study entry
- Suboptimal glycemic control, defined as persistent hyperglycemia, confirmed initially by historical or local laboratory (POC or site's laboratory) HbA_{1c} level of ≥7.7% to ≤10%, then followed with a confirmatory result by central laboratory of ≥7.5% to ≤10%
- Desire to lower HbA_{1c} level, such as a goal of 7%
- Stable control of diabetes, as determined by investigator assessment
- Stable diabetes medication regimen for 3 mo before study entry
- Stable weight maintained for 3 mo before study entry, per investigator's assessment, and not planning any structured weight reduction interventions, such as prescription weight loss medications, bariatric surgery, or protein-sparing modified fast during the study
- Willingness to use a CGM device
- Willingness to avoid use of acetaminophen medications throughout the study
- Currently performing self-monitoring blood glucose testing (by history) an average of ≥2 times per day
- Ability to speak, read, and write English

Exclusion criteria

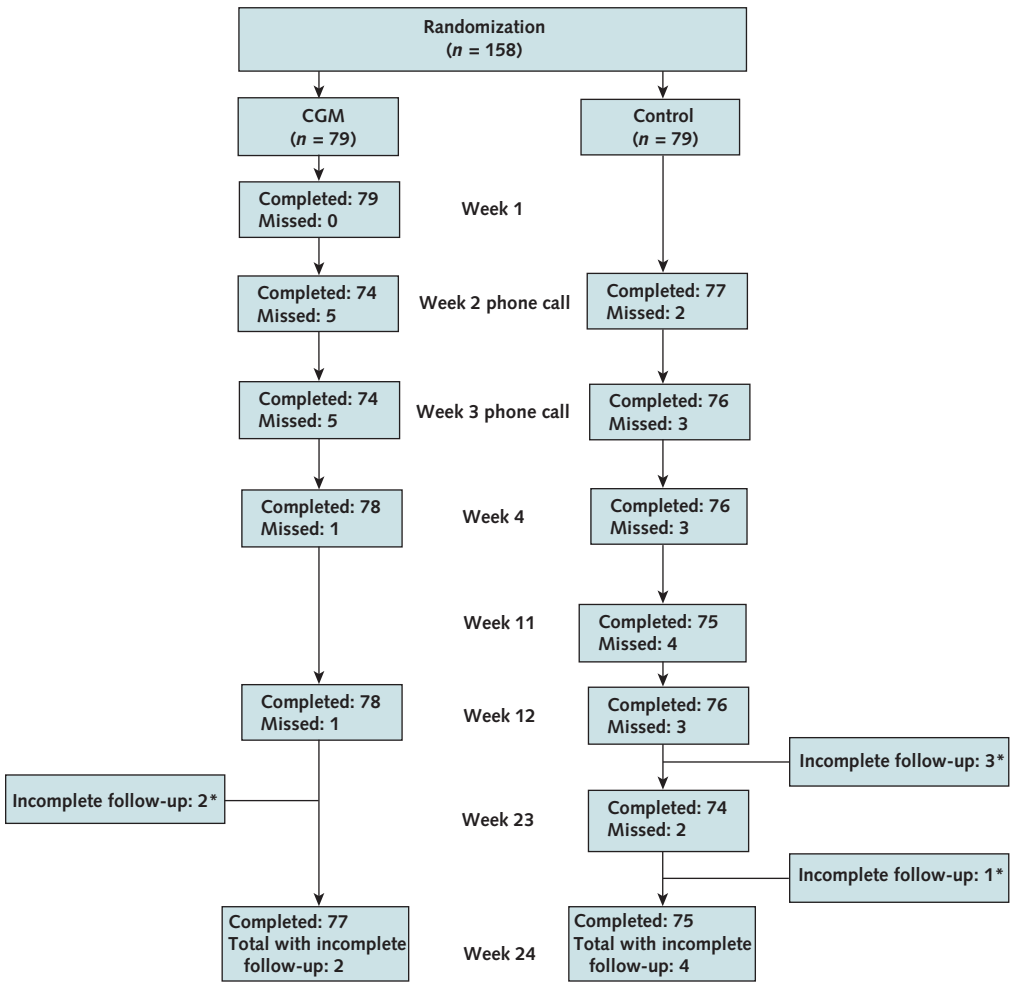
- Use of personal real-time CGM ≤3 mo before study entry (professional CGM use, blinded or unblinded, is acceptable)
- Use of CSII ≤3 mo before study entry (including patch pumps)
- Plan to use personal CGM device and/or pump during study
- Addition of any new oral or injectable hypoglycemic agents (including GLP-1 analogues, pramlintide, and SGLT-2 inhibitors) <3 mo before study entry. (Use of these agents does not affect eligibility if used ≥3 mo before study entry.) For GLP-1 medications, must be on stable dose and the GLP-1 medication will be maintained throughout the study. Note: These agents should not be added or modified during course of the study. If use of this class medication is planned, the patient is not eligible
- Use of premixed insulin (e.g., 70/30 or 50/50) ≤6 mo before study entry
- Current or anticipated short-term uses of glucocorticoids (oral, injectable, or intravenous) that will affect glycemic control and HbA_{1c} levels, such as frequent steroid bursts required for inflammatory arthritis or inflammatory bowel disease, recurrent lumbar epidural steroid injections, etc. (Long-term stable glucocorticoid doses are allowed, such as when used for the treatment of rheumatoid arthritis or Addison disease.)
- Pregnancy (as demonstrated by a positive test result) at time of screening or plan to become pregnant during study
- Medical conditions that, per investigator determination, make it inappropriate or unsafe to target an HbA_{1c} level of <7%; conditions may include but are not limited to unstable recent cardiovascular disease, recent myocardial infarction, significant heart failure, ventricular rhythm disturbances, recent transient ischemic attack or cerebrovascular accident, significant malignancy, other conditions resulting in physical or cognitive decline, or recurrent severe hypoglycemia
- History of visual impairment that would hinder patient's ability to participate in the study and perform all study procedures safely, as determined by investigator
- History of psychiatric, psychological, or psychosocial issues that could limit adherence to required study tasks
- Renal disease, defined as estimated glomerular filtration rate <45 mL/min/1.73 m^2
- Extensive skin changes/disease that preclude wearing the sensor on normal skin (e.g., extensive psoriasis, recent burns or severe sunburn, extensive eczema, extensive scarring, extensive tattoos, or dermatitis herpetiformis)
- Known allergy to medical-grade adhesives
- Current participation in another investigational study (must have completed any previous studies ≥30 d before being enrolled in this study)
- Hospitalization or emergency department visit ≤6 mo before screening resulting in a primary diagnosis of uncontrolled diabetes
- Currently abusing illicit drugs, alcohol, or prescription drugs
- Any condition, per investigator assessment, that could impact reliability of the HbA_{1c} measurement, such as (but not limited to) hemoglobinopathy, hemolytic anemia, chronic liver disease, chronic gastrointestinal blood loss, red blood cell transfusion, or erythropoietin administration <3 mo before screening

Changes made during the study to expand eligibility

- Currently performing self-monitoring blood glucose testing (by history) an average of ≥3 times per day; *changed to:* Currently performing self-monitoring blood glucose testing (by history) an average of ≥2 times per day
- Use of personal real-time CGM ≤6 mo before study entry (professional CGM, blinded or unblinded, is acceptable); *changed to:* Use of personal real-time CGM ≤3 mo before study entry (professional CGM use, blinded or unblinded, is acceptable)
- Use of CSII ≤6 mo before study entry; *changed to:* Use of CSII ≤3 mo before study entry (including patch pumps)
- Addition of any new oral hypoglycemic agent <3 mo before study entry. Use of any oral hypoglycemic agent (including SGLT-2 inhibitors) does not affect eligibility if used ≥3 mo before study entry. Note: SGLT-2 inhibitors should not be added during course of the study; if use of this class medication is planned, the patient is not eligible. *Changed to:* Addition of any new oral or injectable hypoglycemic agents (including GLP-1 analogues, pramlintide, and SGLT-2 inhibitors) <3 mo before study entry. (Use of these agents does not affect eligibility if used ≥3 mo before study entry.) For GLP-1 medications, must be on stable dose and the GLP-1 medication will be maintained throughout the study. Note: These agents should not be added or modified during course of the study. If use of this class medication is planned, the patient is not eligible
- Currently taking or planning to take long-term oral, injectable, or intravenous steroids 12 wk before screening visit or planning to take any oral, injectable, or intravenous steroids during the study. *Changed to:* Current or anticipated short-term uses of glucocorticoids (oral, injectable, or intravenous) that will affect glycemic control and HbA_{1c} levels, such as frequent steroid bursts required for inflammatory arthritis or inflammatory bowel disease, recurrent lumbar epidural steroid injections, etc. (Long-term stable glucocorticoid doses are allowed, such as when used for the treatment of rheumatoid arthritis or Addison disease.)

CGM = continuous glucose monitoring; CSII = continuous subcutaneous insulin infusion; GLP-1 = glucagon-like peptide-1; HbA_{1c} = hemoglobin A_{1c}; POC = point of care; SGLT-2 = sodium-glucose cotransporter-2.

Appendix Figure 1. Flow chart of study visits.



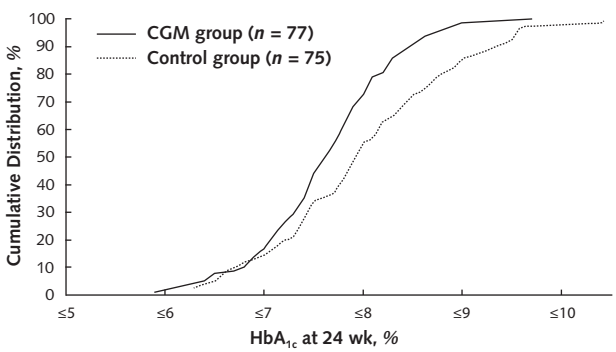
CGM = continuous glucose monitoring.
Two participants from the CGM group and 4 from the control group did not complete the final study visit for the reasons indicated in Figure 1.

Appendix Table 2. CGM Use in the CGM Group*

Variable	Week-4 Visit (*n* = 78)	Week-12 Visit (*n* = 77)†	Week-24 Visit (*n* = 76)†	Overall (*n* = 77)‡
Average CGM use per week				
Mean (SD), *d*	6.9 (0.4)	6.7 (1.0)	6.7 (1.0)	6.7 (0.9)
Median (interquartile range), *d*	7.0 (7.0–7.0)	7.0 (7.0–7.0)	7.0 (7.0–7.0)	7.0 (6.8–7.0)
Zero use, *n (%)*	0 (0)	1 (1)	1 (1)	1 (1)
2–<3 d/wk, *n (%)*	0 (0)	1 (1)	1 (1)	0 (0)
3–<4 d/wk, *n (%)*	1 (1)	0 (0)	0 (0)	0 (0)
4–<5 d/wk, *n (%)*	0 (0)	2 (3)	1 (1)	1 (1)
5–<6 d/wk, *n (%)*	1 (1)	1 (1)	2 (3)	5 (6)
6–<7 d/wk, *n (%)*	5 (6)	7 (9)	7 (9)	16 (21)
7 d/wk, *n (%)*	71 (91)	65 (84)	64 (84)	54 (70)
<6 d/wk, *n (%)*	2 (3)	5 (6)	5 (7)	7 (9)
≥6 d/wk, *n (%)*	76 (97)	72 (94)	71 (93)	70 (91)
Percentage of possible CGM readings§				
Mean (SD), %	95 (7)	92 (16)	91 (16)	92 (13)
Median (interquartile range), %	97 (95–99)	97 (92–99)	96 (91–98)	96 (92–98)

CGM = continuous glucose monitoring.
* Based on most recent 28 d from CGM device download at each visit.
† One participant at week 12 and 1 participant at week 24 who used the device but whose CGM download was unavailable were considered to have missing data.
‡ Average of weeks 4, 12, and 24. Includes participants with missing data (average over nonmissing data).
§ Excludes 2 h after each new sensor insertion.

Appendix Figure 2. Cumulative distribution of 24-week HbA_{1c} values.



For any given 24-week HbA_{1c} level, the percentage of cases in each treatment group with HbA_{1c} at that level or lower can be determined from the figure. CGM = continuous glucose monitoring; HbA_{1c} = hemoglobin A_{1c}.

Appendix Table 3. Change in HbA_{1c} Level from Baseline to 24 Weeks in the CGM and Usual Care Groups, According to Baseline Factors

Baseline Factor	CGM Group (n = 77)		Control Group (n = 75)		*P* Value for Interaction*
	Participants, *n*	Mean Change in HbA_{1c} Level From Baseline (SD), %	Participants, *n*	Mean Change in HbA_{1c} Level From Baseline (SD), %	
HbA_{1c} level					0.35
<8.5%	38	−0.6 (0.7)	36	−0.3 (0.8)	
≥8.5%	39	−1.1 (0.6)	39	−0.7 (0.9)	
Age					0.89
≤44 y	9	−1.0 (0.6)	4	−0.3 (1.2)	
45 to 59 y	26	−0.7 (0.7)	32	−0.5 (0.9)	
≥60 y	42	−0.9 (0.7)	39	−0.5 (0.8)	
Percentage of CGM time <70 mg/dL†					0.55
<5%	67	−0.8 (0.7)	63	−0.6 (0.8)	
≥5%	10	−0.9 (0.8)	11	−0.1 (0.8)	
Frequency of blood glucose self-monitoring before enrollment					0.78
≥3 times per day	51	−0.9 (0.7)	52	−0.6 (0.8)	
≤4 times per day	26	−0.7 (0.6)	23	−0.3 (0.9)	
Education‡					0.64
Less than bachelor's degree	43	−0.8 (0.7)	46	−0.5 (0.9)	
Bachelor's degree or higher	33	−0.9 (0.7)	24	−0.6 (0.7)	
Hypoglycemia Unawareness Survey score§					0.031
Reduced awareness or uncertain (≥3)	24	−0.8 (0.7)	16	−0.2 (1.0)	
Aware (≤2)	53	−0.9 (0.7)	59	−0.6 (0.8)	
Diabetes numeracy test score‖					0.39
≤3 of 5 correct	27	−0.8 (0.8)	34	−0.5 (0.9)	
≥4 of 5 correct	50	−0.9 (0.6)	41	−0.5 (0.8)	
Hypoglycemia Fear Survey score¶					0.72
0 to 13	44	−0.8 (0.8)	41	−0.5 (0.9)	
14 to 77	33	−0.9 (0.6)	34	−0.5 (0.8)	

CGM = continuous glucose monitoring; HbA_{1c} = hemoglobin A_{1c}.
* Obtained by including interaction term in each mixed effects model with baseline HbA_{1c} level as a fixed effect and clinical site as a random effect. Continuous variable used for all models other than the model for education.
† To convert glucose values from mg/dL to mmol/L, multiply them by 0.0555. Missing for 1 participant in the control group due to insufficient CGM data.
‡ Missing for 1 participant in the CGM group and 5 in the control group.
§ 8 items, with a total score from 0 to 7. Higher score denotes more unawareness.
‖ 5 items testing the participant's knowledge of calculations related to diabetes management.
¶ 18 items on what the participant worries about related to their diabetes. Higher score denotes more fear.

Appendix Table 4. Daytime CGM Metrics at Baseline, 12 Weeks, and 24 Weeks in the CGM and Usual Care Groups*

Variable	CGM Group			Control Group		
	Baseline (*n* = 79)	**12 wk (*n* = 77)†**	**24 wk (*n* = 74)†**	**Baseline (*n* = 78)†**	**12 wk (*n* = 74)†**	**24 wk (*n* = 72)†**
Data collected, *h*	206 (196–213)	107 (100–109)	105 (99–108)	208 (195–213)	100 (94–105)	100 (91–105)
Mean glucose concentration, *mg/dL*	176 (157–196)	170 (149–185)	167 (154–193)	175 (153–195)	173 (152–194)	173 (161–200)
Percentage of time in range of 70–180 mg/dL, %	55 (43–67)	61 (47–76)	64 (46–74)	55 (43–70)	57 (41–74)	56 (39–66)
Hyperglycemia						
Percentage of time >180 mg/dL, %	42 (29–55)	38 (23–50)	35 (24–54)	41 (29–55)	41 (23–58)	40 (30–61)
Percentage of time >250 mg/dL, %	9 (4–19)	6 (2–12)	7 (3–15)	10 (5–17)	10 (2–18)	8 (4–20)
Percentage of time >300 mg/dL, %	2 (<1–6)	<1 (0–4)	1 (0–5)	3 (<1–6)	2 (0–6)	2 (0–6)
Area under curve of 180 mg/dL	19 (11–32)	17 (8–24)	16 (7–29)	21 (11–31)	18 (10–30)	19 (12–36)
Hypoglycemia						
Percentage of time <70 mg/dL, %	0.6 (0.0–2.0)	0.3 (0.0–1.5)	0.3 (0.0–1.0)	0.6 (0.0–2.6)	0.6 (0.0–2.3)	0.3 (0.0–2.3)
Percentage of time <60 mg/dL, %	0.1 (0.0–0.9)	0.0 (0.0–0.5)	0.0 (0.0–0.4)	0.1 (0.0–0.9)	0.0 (0.0–0.9)	0.0 (0.0–0.9)
Percentage of time <50 mg/dL, %	0.0 (0.0–0.2)	0 (0–0)	0 (0–0)	0.0 (0.0–0.2)	0 (0–0)	0.0 (0.0–0.3)
Area above curve of 70 mg/dL	0.0 (0.0–0.2)	0.0 (0.0–0.1)	0.0 (0.0–0.1)	0.0 (0.0–0.2)	0.0 (0.0–0.2)	0.0 (0.0–0.2)
Glucose variability: coefficient of variation, %	31 (26–36)	28 (25–34)	29 (25–33)	31 (27–37)	30 (25–36)	30 (25–35)

CGM = continuous glucose monitoring.
* Values are medians (interquartile ranges). Daytime defined as 6:00 a.m. to <10:00 p.m. To convert glucose values from mg/dL to mmol/L, multiply them by 0.0555.
† CGM metrics were not calculated for participants with <48 h of daytime data: 1 control participant at baseline, 1 CGM and 3 control participants at 12 wk, and 3 CGM and 3 control participants at 24 wk.

Appendix Table 5. Nighttime CGM Metrics at Baseline, 12 Weeks, and 24 Weeks in the CGM and Usual Care Groups*

Variable	CGM Group			Control Group		
	Baseline (*n* = 79)	**12 wk (*n* = 77)†**	**24 wk (*n* = 74)†**	**Baseline (*n* = 78)†**	**12 wk (*n* = 74)†**	**24 wk (*n* = 72)†**
Data collected, *h*	105 (98–106)	55 (54–56)	55 (50–56)	105 (97–106)	50 (47–50)	49 (46–50)
Mean glucose concentration, *mg/dL*	172 (153–193)	161 (148–188)	172 (143–199)	168 (146–195)	173 (152–204)	168 (146–200)
Percentage of time in range of 70–180 mg/dL, %	55 (42–71)	66 (45–78)	63 (39–78)	59 (36–75)	55 (35–72)	57 (38–73)
Hyperglycemia						
Percentage of time >180 mg/dL, %	41 (26–55)	33 (20–50)	37 (18–61)	38 (22–63)	43 (25–63)	37 (22–62)
Percentage of time >250 mg/dL, %	10 (2–19)	7 (<1–15)	6 (<1–19)	7 (2–19)	7 (1–23)	5 (<1–18)
Percentage of time >300 mg/dL, %	2 (0–6)	<1 (0–4)	<1 (0–5)	1 (0–7)	<1 (0–8)	0 (0–4)
Area under curve of 180 mg/dL	20 (10–34)	14 (6–25)	15 (5–33)	18 (8–35)	18 (7–39)	14 (7–35)
Hypoglycemia						
Percentage of time <70 mg/dL, %	0.6 (0.0–3.4)	0.2 (0.0–1.8)	0.0 (0.0–1.6)	1.0 (0.0–3.2)	0.0 (0.0–1.8)	0.0 (0.0–2.9)
Percentage of time <60 mg/dL, %	0.0 (0.0–1.6)	0.0 (0.0–0.1)	0.0 (0.0–0.2)	0.2 (0.0–1.1)	0.0 (0.0–0.3)	0.0 (0.0–<0.1)
Percentage of time <50 mg/dL, %	0.0 (0.0–0.2)	0 (0–0)	0 (0–0)	0.0 (0.0–0.4)	0 (0–0)	0 (0–0)
Area above curve of 70 mg/dL	0.0 (0.0–0.4)	0.0 (0.0–0.1)	0.0 (0.0–0.1)	0.1 (0.0–0.3)	0.0 (0.0–0.1)	0.0 (0.0–0.2)
Glucose variability: coefficient of variation, %	31 (25–39)	29 (24–34)	28 (23–32)	30 (25–36)	27 (23–34)	27 (22–35)

CGM = continuous glucose monitoring.
* Values are medians (interquartile ranges). Nighttime defined as 10:00 p.m. to <6:00 a.m. To convert glucose values from mg/dL to mmol/L, multiply them by 0.0555.
† CGM metrics were not calculated for participants with <24 h of nighttime data: 1 control participant at baseline, 1 CGM and 2 control participants at 12 wk, and 3 CGM and 3 control participants at 24 wk.

Appendix Table 6. Insulin Use, Body Weight, Noninsulin Diabetes Medications, and Hypoglycemia Unawareness at Baseline and 24 Weeks in the CGM and Usual Care Groups

Variable	Baseline		24 wk	
	CGM Group (*n* = 79)	**Control Group (*n* = 79)**	**CGM Group (*n* = 77)**	**Control Group (*n* = 75)**
Mean total daily insulin dose (SD), *units/kg/d**	1.2 (0.6)	1.0 (0.5)	1.3 (0.7)	1.1 (0.5)
Mean change in total daily insulin dose from baseline to 24 wk (SD), *units/kg/d**	–	–	0.1 (0.3)	0.0 (0.3)
Mean ratio of basal–bolus units of insulin per day (SD)*	1.3 (0.8)	1.4 (1.1)	1.2 (0.6)	1.3 (0.9)
Mean change in ratio of basal–bolus units of insulin per day from baseline to 24 wk (SD)*	–	–	−0.1 (0.6)	−0.1 (0.8)
Number of boluses per day, *n (%)*				
0	1 (1)	0 (0)	2 (3)	0 (0)
1	0 (0)	0 (0)	0 (0)	0 (0)
2	4 (5)	9 (11)	4 (5)	6 (8)
3	68 (86)	60 (76)	55 (71)	56 (75)
4	5 (6)	8 (10)	13 (17)	12 (16)
≥5	1 (1)	2 (3)	3 (4)	1 (1)
Change in number of boluses per day from baseline to 24 wk, *n (%)*				
≤−1	–	–	5 (6)	4 (5)
0	–	–	57 (74)	62 (83)
≥1	–	–	15 (19)	9 (12)
Mean body weight (SD), *kg**	98.2 (23.1)	105.5 (24.7)	99.4 (22.8)	104.9 (23.5)
Mean change in body weight (SD), *kg**	–	–	1.3 (3.6)	−0.2 (4.5)
Patients who added ≥1 noninsulin diabetes medication after randomization, *n (%)*†	–	–	2 (3)	2 (3)
Mean Clarke Hypoglycemia Unawareness total score (SD)*	1.8 (1.4)	1.6 (1.3)	2.0 (1.5)	1.7 (1.4)
Mean change in Clarke Hypoglycemia Unawareness total score from baseline (SD)*	–	–	0.1 (1.5)	0.2 (1.7)

CGM = continuous glucose monitoring.
* Total daily insulin dose missing for 1 participant in the control group at 24 wk due to unknown weight. Ratio of basal–bolus units of insulin not calculated for 1 CGM participant at baseline and 2 at 24 wk due to them reporting 0 boluses per day. Weight missing for 1 participant in the control group at 24 wk. Clarke Hypoglycemia Unawareness total score missing at 24 wk for 4 participants in the CGM group and 6 in the control group.
† 1 participant in the control group added exenatide, and another added canagliflozin; 2 participants in the CGM group added metformin.

Appendix Table 7. CGM Satisfaction Questionnaire at 24 Weeks in the CGM Group (n = 77)*

Using the Continuous Glucose Monitor:	Mean Score†	Agree Strongly, %	Agree, %	Neutral, %	Disagree, %	Disagree Strongly, %
1. Causes me to be more worried about controlling blood sugars.	3.2	19	19	10	19	31
2. ▶Makes adjusting insulin easier.	4.5	58	32	4	3	1
3. ▶Helps me to be sure about making diabetes decisions.	4.6	61	34	1	3	0
4. Causes others to ask too many questions about diabetes.	3.5	8	16	19	31	26
5. Makes me think about diabetes too much.	3.7	1	12	27	39	21
6. ▶Helps to keep low blood sugars from happening.	4.3	55	29	10	5	0
7. ▶Has taught me new things about diabetes that I didn't know before.	4.5	57	32	9	1	0
8. Causes too many hassles in daily life.	4.3	3	1	13	34	49
9. ▶Teaches me how eating affects blood sugar.	4.6	64	35	1	0	0
10. ▶Helps me to relax, knowing that unwanted changes in blood sugar will be detected quickly.	4.5	55	36	6	1	0
11. ▶Has helped me to learn about how exercise affects blood sugar.	4.3	48	35	16	1	0
12. ▶Helps with keeping diabetes under control on sick days.	4.2	40	42	17	0	0
13. ▶Has shown me that blood sugar is predictable and orderly.	3.8	26	47	9	12	4
14. Sometimes gives too much information to work with.	3.9	3	8	14	44	30
15. ▶Has made it easier to accept doing blood sugar tests.	4.3	45	42	5	5	0
16. Is uncomfortable or painful.	4.1	1	5	17	32	44
17. ▶Has helped me to learn how to treat low sugars better.	4.3	51	36	9	4	0
18. Is more trouble than it is worth.	4.5	3	0	6	26	65
19. ▶Has helped my family to get along better about diabetes.	3.9	27	38	30	4	1
20. ▶Shows patterns in blood sugars that we didn't see before.	4.5	56	43	1	0	0
21. ▶Helps prevent problems rather than fixing them after they've happened.	4.4	52	39	8	1	0
22. ▶Allows more freedom in daily life.	4.1	38	43	16	4	0
23. ▶Makes it clearer how some everyday habits affect blood sugar levels.	4.5	52	43	3	0	0
24. ▶Makes it easier to complete other diabetes self-care duties.	4.4	43	51	6	0	0
25. Has caused more family arguments.	4.4	0	5	8	23	62
26. Is too hard to get it to work right.	4.4	0	1	9	36	52
27. Has been harder or more complicated than expected.	4.3	0	4	9	36	51
28. ▶Has helped to control diabetes better even when not wearing it.	3.6	25	32	26	10	6
29. Causes our family to talk about blood sugars too much.	3.9	1	4	21	45	26
30. Makes it harder for me to sleep.	4.2	1	4	12	35	47
31. Causes more embarrassment about feeling different from others.	4.5	1	0	3	38	58
32. Shows more "glitches" and "bugs" than it should.	4.1	3	4	10	43	40
33. Interferes a lot with sports, outdoor activities, etc.	4.3	0	1	10	42	47
34. Skips too many readings to be useful.	4.4	0	1	3	49	47
35. Gives a lot of results that don't make sense.	4.3	3	3	8	40	47
36. Causes too many interruptions during the day.	4.4	0	1	8	43	48
37. Alarms too often for no good reason.	4.4	0	3	3	45	48
38. ▶Has helped to adjust premeal insulin doses.	4.2	45	35	12	8	0
39. The feedback from the device is not easy to understand or useful.	4.3	1	3	4	47	44
40. I don't recommend this for others with diabetes.	4.7	1	3	4	10	82
41. ▶Has made me worry less about having low blood sugars.	4.2	48	31	14	4	3
42. ▶If possible, I want to use this device when the research study is over.	4.5	68	21	4	4	3
43. ▶Helps in adjusting doses of insulin needed through the night.	4.2	45	36	14	4	0
44. ▶Makes me feel safer knowing that I will be warned about low blood sugar before it happens.	4.6	73	21	4	3	0

CGM = continuous glucose monitoring.

* 44 items on how satisfied the participant is with using CGM. Scale, 1 to 5. Responses were missing from 1 participant for items 2, 3, 6, 10, 12, 14, 25, 26, 30, 37, 39, and 42 and from 2 participants for items 13, 15, 23, and 29. Percentages may not sum to 100 because of rounding.

† Overall mean score, 4.3 (SD, 0.4). Items with a ▶ symbol are positively worded (agreeing corresponds to more satisfaction), and those without the symbol are negatively worded (agreeing corresponds to less satisfaction). To calculate the mean value for each item and the overall mean value, the scores for the positively worded items were reversed so that a higher score always corresponds to greater satisfaction. For example, a value of 5 corresponds to "Agree Strongly" with a positively worded item, or "Disagree Strongly" with a negatively worded item. To calculate the subscale mean values, scores for all questions were reversed so that a higher score on the benefits subscale denotes greater satisfaction and a higher score on the hassles subscale denotes less satisfaction. Benefits subscale mean score, 4.4 (SD, 0.5) (items 2, 3, 6, 7, 9, 10, 11, 12, 17, 20, 21, 22, 23, 24, 38, 41, 42, 43, and 44). Hassles subscale mean score, 1.8 (SD, 0.5) (items 4, 5, 8, 14, 16, 18, 25, 26, 27, 29, 30, 31, 32, 33, 34, 35, 36, 37, 39, and 40).