Supplementary Appendix

Supplement to: Wadwa RP, Reed ZW, Buckingham BA, et al. Trial of hybrid closed-loop control in young children with type 1 diabetes. N Engl J Med 2023;388:991-1001. DOI: 10.1056/NEJMoa2210834

This appendix has been provided by the authors to give readers additional information about the work.

SUPPLEMENT 2

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THE PEDAP TRIAL STUDY GROUP

Barbara Davis Center for Diabetes, University of Colorado, Anschutz Medical Campus, Aurora, CO: R. Paul Wadwa (PI), Gregory Forlenza (I), Robert Slover (I), Erin Cobry (I), Laurel Messer (I), Luke Geiser, Samantha Lange, Angela Karami, Cari Berget, Estella Escobar, Emily Jost, Lindsey Towers, Emily Boranian

Department of Pediatrics, Division of Pediatric Endocrinology and Diabetes, Stanford University School of Medicine: Bruce Buckingham (PI), Lisa Norlander(I), Laya Ekhlaspour (I), Korey Hood (I), Ryan Kingman, Bailey Suh, Marci Morgan, Aika Schneider-Utaka

University of Virginia, Center for Diabetes Technology, Charlottesville, VA: Marc Breton (Grant PI), Mark DeBoer (PI), Melissa Schoelwer (I), Emma Emory, Katie Krauthause, Katie Sullivan, Mary Oliveri, Dillon Cullipher

Jaeb Center for Health Research: John Lum, Roy Beck, Zachariah Reed, Craig Kollman, Amanda Morales, Shannon Hiser, Carlos Murphy, Heidi Strayer, Julie Davis, Amanda Hellmann

National Institute of Diabetes, Digestive, and Kidney Diseases (NIDDK): Guillermo Arreaza-Rubín (Project Scientist), Thomas Eggerman (Program Director), Neal Green (Project Manager)

PEDAP Steering Committee Members: Marc Breton, R. Paul Wadwa, Bruce Buckingham, Mark DeBoer, Guillermo Arreaza-Rubín, John Lum, Roy Beck

Central Laboratory - University of Minnesota Advanced Research and Diagnostic Laboratory: Robert Janicek, Deanna Gabrielson

Tandem Diabetes Care Pump Trainers: Gena Van Kirk, Katie Conschafter, Tracey Stamates-Roerty

DATA AND SAFETY MONITORING BOARD

Data Safety Monitoring Board (DSMB) Members: Steven H. Belle (Chair), Jessica Castle, Jennifer Green, Laurent Legault, Steven M. Willi, Carol Wysham, Thomas Eggerman (DSMB Executive Secretary for NIDDK)

ADDITIONAL METHODS

Additional Protocol Methods

1. Patients in the CLC group who had been receiving daily injections of insulin at the time of enrollment had an additional phone contact 3 days after initiation of the study pump.
2. Quality of life or treatment satisfaction questionnaires were completed at baseline and 13 weeks and will be reported separately.

Additional Statistical Methods

Calculation of CGM-measured outcomes

Baseline: For patients who were allowed to skip the run-in phase, baseline CGM-measured outcomes were calculated using the most recent 14 days of data prior to randomization. For the three patients who entered the run-in phase, baseline CGM-measured outcomes were calculated using the most recent 14 days of data between the beginning of the run-in phase and randomization. Since only patients who were already using a Dexcom sensor could skip the run-in phase, all baseline CGM data came from the same source.

Follow Up: CGM data from the fourth day after randomization through the 13-week visit were included in the calculation of each metric.

Analytic Model

For outcomes that were approximately normally distributed, analysis was done using the direct likelihood approach. Specifically, a longitudinal linear mixed effects regression model was fit with the outcome at baseline and follow-up as the dependent variable (2 observations per subject). The model adjusted for baseline by forcing the treatment groups to have the same mean value at baseline (sometimes referred to as a constrained longitudinal data analysis, cLDA). A separate treatment effect at follow-up was modelled by including a treatment by time interaction where time denotes either baseline or follow-up. The point estimate of the mean, 95% confidence interval, and p-value are reported for the treatment group difference at follow-up. The model included age, prior CGM use, and prior pump use as fixed effect covariates and site as a random effect. For skewed outcomes, robust regression with M-estimation was used to down-weight extreme values in the tail of the distribution. The displayed mean and standard deviation values for these outcomes were calculated from an intercept-only robust regression using M-estimation.

Plots of residual values were examined to assess model fit. The high compliance with closed loop usage in the treatment group indicated that the regression models produced accurate estimates of the marginal treatment effects in the intent-to-treat analysis.

Unless otherwise specified, all models and reported treatment group differences included adjustment for age, prior CGM and pump use, clinical center (random effect), and the baseline value of the response variable.

Tests for Interaction

Modification of the treatment effect (subgroup analyses) on percent time in range 70–180 mg per deciliter, percent time <70 mg per deciliter, and glycated hemoglobin by baseline variables was assessed in exploratory analyses by including an interaction term in the models described above.

Missing Data

There was very little missing CGM data: one patient was missing baseline data, and none were missing at follow-up. For the hierarchical outcomes, this patient was included in the model with one record in the dataset instead of two (see above description of the direct likelihood model). The direct likelihood method maximized the likelihood function integrated over possible values of the missing data. For skewed outcomes where robust regression was used (see above), the missing value was imputed by Rubin's method, assuming missing at random. For the secondary efficacy outcomes, differences and confidence intervals were estimated by including only patients who were not missing data.

Multiple Comparisons

A hierarchical testing procedure was used to preserve the overall type 1 error at 5% for the key endpoints. If the analysis of an outcome resulted in a statistically significant result ($p < 0.05$), then testing proceeded to the next outcome metric in the following order:

- CGM-measured % in range 70–180 mg/dl (primary outcome)
- CGM-measured % above 250 mg/dl
- CGM-measured mean glucose
- HbA1c at 13 weeks
- CGM-measured % below 70 mg/dl
- CGM-measured % below 54 mg/dl

This process continued iteratively, moving to the next variable down on the list unless/until a non-significant result ($p \geq 0.05$) was observed.

For the other outcomes, no p-values are given, and the confidence intervals were adjusted using the Benjamini-Hochberg method to control the false discovery rate (FDR).

TABLE S1. ELIGIBILITY AND EXCLUSION CRITERIA

Participant Inclusion Criteria

Individuals must meet all of the following inclusion criteria in order to be eligible to participate in the study.

1. Clinical diagnosis, based on investigator assessment, of type 1 diabetes for at least 6 months and using insulin for at least 6 months.
2. Familiarity and use of a carbohydrate ratio for meal boluses.
3. Age ≥2 and <6 years old.
4. Living with one or more parent/legal guardian knowledgeable about emergency procedures for severe hypoglycemia and able to contact emergency services and study staff.
5. Investigator has confidence that the parent can successfully operate all study devices and is capable of adhering to the protocol
6. Willingness to switch to lispro (Humalog) or aspart (Novolog) if not using already, and to use no other insulin besides lispro (Humalog) or aspart (Novolog) during the study for participants using a study-provided Tandem pump during the study.
    - *Study will not be providing insulin; therefore, participants will need to have access to either lispro or aspart*
7. Total daily insulin dose (TDD) at least 5 U/day.
8. Body weight at least 20 lbs.
9. Willingness not to start any new non-insulin glucose-lowering agent during the course of the trial.
10. Participant and parent(s)/guardian(s) willingness to participate in all training sessions as directed by study staff.
11. Parent/guardian proficient in reading and writing English.
12. Live in the United States, with no plans to move outside the United States during the study period[a]

Participant Exclusion Criteria

Individuals meeting any of the following exclusion criteria at baseline were excluded from study participation.

1. Concurrent use of any non-insulin glucose-lowering agent (including GLP-1 agonists, Symlin, DPP-4 inhibitors, SGLT-2 inhibitors, sulfonylureas).
2. Hemophilia or any other bleeding disorder
3. History of >1 severe hypoglycemic event with seizure or loss of consciousness in the last 3 months
4. History of >1 diabetic ketoacidosis event in the last 6 months not related to illness, infusion set failure, or initial diagnosis
5. History of chronic renal disease or currently on hemodialysis
6. History of adrenal insufficiency
7. Hypothyroidism that is not adequately treated
8. Use of oral or injectable steroids within the last 8 weeks
9. Known, ongoing adhesive intolerance
10. Plans to receive blood transfusions or erythropoietin injections during the course of the study

11. A condition, which in the opinion of the investigator or designee, would put the participant or study at risk (specified in the study procedure manual); the investigator will take into account the participant's HbA1c level, compliance with current diabetes management, and prior acute diabetic complications
12. Currently using any closed-loop system, or using an insulin pump that is incompatible with use of the study CGM
13. Participation in another pharmaceutical or device trial at the time of enrollment or during the study
14. Employed by, or having immediate family members employed by Tandem Diabetes Care, Inc., or having a direct supervisor at place of employment who is also directly involved in conducting the clinical trial (as a study investigator, coordinator, etc.); or having a first-degree relative who is directly involved in conducting the clinical trial.

a. U.S. residency criterion was added to protocol after study enrollment began; no non-U.S. residents were enrolled in the study.

TABLE S2. ADDITIONAL CHARACTERISTICS OF PATIENTS AT BASELINE

	CLC (N=68)	SC (N=34)
Age (years)		
2 to <4	31 (46%)	16 (47%)
4 to <6	37 (54%)	18 (53%)
Mean ± SD	3.84 ± 1.23	4.06 ± 1.25
Range	2.00 to 5.98	2.02 to 5.90
Sex – Female	33 (49%)	19 (56%)
Race/Ethnicity		
White non-Hispanic	50 (74%)	25 (74%)
Black/African-American	4 (6%)	2 (6%)
Hispanic or Latino	11 (16%)	5 (15%)
Asian	1 (1%)	1 (3%)
More than one race	2 (3%)	1 (3%)
Parent Education		
≤H.S. diploma	6 (9%)	3 (9%)
Technical/Vocational	2 (3%)	1 (3%)
Associates Degree or Some College but no Degree	6 (9%)	5 (15%)
Bachelor's Degree	22 (32%)	13 (38%)
Advanced Degree (e.g. Master's, PhD, MD)	32 (47%)	12 (35%)
Annual Household Income[a]		
$25,000 to <$35,000	2 (3%)	2 (6%)
$35,000 to <$50,000	6 (9%)	4 (13%)
$50,000 to <$75,000	8 (13%)	5 (16%)
$75,000 to <$100,000	11 (17%)	7 (22%)
$100,000 to <$200,000	22 (34%)	10 (31%)
≥$200,000	15 (23%)	4 (13%)
Health Insurance[a]		
Private[b]	52 (76%)	26 (79%)
Medicare	2 (3%)	1 (3%)
Medicaid[c]	8 (12%)	3 (9%)
Other Government Insurance	5 (7%)	3 (9%)
No Coverage	1 (1%)	0 (0%)
Diabetes Duration (years)		
0.5 to <1	29 (43%)	10 (29%)
1 to <2	24 (35%)	15 (44%)
2 to <4	11 (16%)	7 (21%)
≥4	4 (6%)	2 (6%)
Median (Quartiles)	1.04 (0.71, 1.85)	1.40 (0.91, 2.11)
Range	0.50 to 4	0.51 to 5
Body Mass Index Percentile[a]		

Median (Quartiles)	81 (57, 94)	77 (56, 94)
Glycated Hemoglobin at Randomization[a]		
<7.0%	23 (36%)	8 (25%)
7.0% to <8.0%	20 (31%)	8 (25%)
8.0% to <9.0%	15 (23%)	15 (47%)
≥9.0%	6 (9%)	1 (3%)
Mean ± SD	7.5 ± 1.2	7.7 ± 0.9
Range	5.2 to 11.5	6.0 to 9.7
Pre-study Insulin Modality		
Insulin Pump	42 (62%)	24 (71%)
Multiple Daily Injections	26 (38%)	10 (29%)
Pre-study Continuous Glucose Monitor Use	66 (97%)	34 (100%)
Diabetic Ketoacidosis Events in Last 12 Months		
None	57 (84%)	31 (91%)
1	10 (15%)	2 (6%)
2	1 (1%)	1 (3%)
Severe Hypoglycemia Events in Last 12 Months		
None	64 (94%)	32 (94%)
1	4 (6%)	2 (6%)

a. Missing data (CLC/SC): annual household income 4/2, health insurance 0/1, BMI percentile 2/0, glycated hemoglobin 4/2. All other variables have no missing data.
b. For patients with private insurance, 7 patients also had Medicaid, 1 patient also had Medicare, and 1 patient also had other government insurance.
c. For patients with Medicaid, 1 patient also had other government insurance.

TABLE S3. REPRESENTATIVENESS OF STUDY PATIENTS

Disease under investigation	Type 1 Diabetes (T1D)
Special considerations related to:	
Sex and gender	The incidence and prevalence of T1D is similar in males and females.[1,2]
Age	T1D can develop at any age from <1 years to >65 years old. It has been estimated that there are about 64,000 new cases of T1D each year in the U.S.[3] Based on prevalence data from the National Health Interview Survey (NHIS) in 2016–2017,[4] it is estimated that there are about 1.2 million adults ≥20 years old with T1D in the U.S. From the Search for Diabetes in Youth Study (SEARCH) data, it is estimated that there are ~200,000 youth with T1D in the U.S.[2,5]
Race or ethnic group	In the most recent data from the SEARCH study on the prevalence of T1D in youth, Non-Hispanic white youth had the highest prevalence (2.79/1,000), followed by non-Hispanic black (2.18/1,000), Hispanic (1.56/1,000), Asian or Pacific Islander (0.76/1,000), and American Indian or Alaska Native youth (0.56/1,000).[2] It is presumed that a similar pattern is present in adults with T1D.
Geography	There is considerable variation in the incidence of T1D internationally among countries.[6] The incidence may be higher in Finland and Norway than other countries. The U.S. incidence is similar to the United Kingdom.[5]
Other considerations	T1D represents about 5% of cases of diabetes overall: 98% of cases in children <10 years old and 87% of cases in youth 10–19 years old.[5] The incidence appears to have been increasing during the last 20 years.[2,3]
Overall representativeness of this trial	The recruitment strategy that allowed for enrollment of patients who were remote from a study site enabled the enrollment of a cohort that was broadly representative of the U.S. population of young children 2–<6 years old with T1D. The study cohort was racially and ethnically diverse, with 26% of the cohort being of a racial or ethnicity minority. Baseline glycated hemoglobin levels covered a wide range from 5.2% to 11.5%. An insulin pump was being used by 65% and multiple daily injections of insulin by 35%, a distribution very similar to that reported for this age group in the T1D Exchange Clinic Registry.[7]

Note: Sex, race, and ethnicity were collected on an electronic case report form completed by the study sites at enrollment. Race and ethnicity were reported by the patient's legally authorized representative (typically a parent). Race was reported as White, Black/African American, Asian, Native Hawaiian/Other Pacific Islander, American Indian/Alaskan Native, or more than one race. Ethnicity was reported as Hispanic/Latino or not Hispanic/Latino.

TABLE S4. VISITS ACCORDING TO WHETHER THEY WERE VIRTUAL

	Overall		CLC		SC	
Visit	**Completed**	**Virtual**	**Completed**	**Virtual**	**Completed**	**Virtual**
Screening	105	97 (92%)	68	60 (88%)	34	34 (100%)
CGM Training [a]	3	2 (67%)	2	2 (100%)	1	0 (0%)
Run-in Review [a]	3	3 (100%)	2	2 (100%)	1	1 (100%)
Randomization	102	98 (96%)	68	65 (96%)	34	33 (97%)
Study Device Training	102	88 (86%)	68	55 (81%)	34	33 (97%)
2 Week Visit	99	97 (98%)	66	64 (97%)	33	33 (100%)
6 Week Visit	99	96 (97%)	66	63 (95%)	33	33 (100%)
13 Week Visit	101	89 (88%)	67	61 (91%)	34	28 (82%)
Total	614	570 (93%)	407	372 (91%)	204	195 (96%)

a. Only for patients completing run-in

TABLE S5. UNSCHEDULED CONTACTS AND VISITS

	CLC (N=209 contacts/ visits)	SC (N=21 contacts/ visits)
Reason for Contact or Visit [a,b]		
Additional device training	9	1
Additional protocol/procedural training	5	1
Question or problem with diabetes management	80	1
Potential adverse event	19	5
Potential device deficiency/issue	14	1
Study supplies needed	12	1
Review/change device configuration setting	25	10
Site notified patient of a potential device deficiency/issue [c]	42	0
Visit/call scheduling	3	0
Issue related to device data	3	0
Patient had a consent-related issue	2	1
Related to medication or medical condition not associated with an adverse event	3	0

a. All but 4 interactions were remote contacts (text, email, phone call, videoconference) rather than in-clinic visits.
b. More than one reason possible for each contact or visit.
c. Contacts mandated by study DSMB after an Adverse Event involving inappropriate insulin boluses delivered by a child participant's pushing buttons on the pump. The DSMB required study staff to encourage participant caregivers to enable the optional security PIN feature and to ensure that the maximum bolus threshold of the pump was not set inappropriately high.

TABLE S6. SENSITIVITY ANALYSES FOR PRIMARY ENDPOINT TIME IN RANGE 70–180 MG/DL

	CLC	SC
Primary Analysis	N=68	N=34
Change from baseline to 13 weeks	12.5% ± 11.8%	1.0% ± 6.6%
Adjusted treatment difference *Mean (95% CI)*[c]	12.4% (9.5%, 15.3%)	
P-value	<0.001	
Additional Covariates[b] **Included in the Model**	N=64	N=32
Adjusted treatment difference *Mean (95% CI)*[c]	11.7% (8.9%, 14.6%)	
P-value	<0.001	
Exclude First 2 Weeks of CGM Data	N=68	N=34
Change from baseline to 13 weeks	12.7% ± 11.9%	1.1% ± 6.7%
Adjusted treatment difference *Mean (95% CI)*[c]	12.4% (9.4%, 15.4%)	
P-value	<0.001	
Available Cases Only	N=67[a]	N=34
Change from baseline to 13 weeks	12.5% ± 11.8%	1.0% ± 6.6%
Adjusted treatment difference *Mean (95% CI)*[c]	12.1% (9.1%, 15.1%)	
P-value	<0.001	
Rubin's MI with Treatment Group in the Imputation Model	N=68	N=34
Adjusted treatment difference *Mean (95% CI)*[c]	12.2% (9.2%, 15.1%)	
P-value	<0.001	
MI with Pattern Mixture Model	N=68	N=34
Adjusted treatment difference *Mean (95% CI)*[c]	12.1% (9.2%, 15.1%)	
P-value	<0.001	
Per-protocol Analysis [d]	N=60	N=30
Change from baseline to 13 weeks	13.5% ± 11.5%	1.4% ± 6.8%
Adjusted treatment difference *Mean (95% CI)*[c]	12.5% (9.6%, 15.3%)	
P-value	<0.001	

a. One patient in the CLC group was missing baseline CGM data.
b. Potentially confounding variables observed to be slightly out of balance at baseline were added to the primary model as covariates: glycated hemoglobin and number of diabetic ketoacidosis events in the 12 months prior to enrollment.
c. Difference is CLC – SC.
d. Patients were included in the per-protocol analyses if they were in the CLC group and closed-loop mode was active for at least 80% of the follow-up period, or if they were in the SC group and provided CGM data for at least 80% of the follow-up period.

TABLE S7. SELECTED CGM-MEASURED OUTCOMES BY DAYTIME AND NIGHTTIME

	Baseline		13 Weeks	
	CLC	SC	CLC	SC
Daytime (06:00–21:59)				
N	67[a]	33[a]	68	34
% Time 70–180 mg/dl	58 ± 18	55 ± 15	67 ± 11	56 ± 13
% Time >250 mg/dl [b]	14.4 ± 15.2	16.1 ± 14.7	9.3 ± 8.1	15.1 ± 12.2
Mean Glucose (mg/dl)	172 ± 37	177 ± 28	157 ± 21	174 ± 24
% Time <70 mg/dl [b]	3.1 ± 2.7	2.3 ± 1.2	3.3 ± 2.1	2.9 ± 1.8
Glucose CV (%)	38 ± 6	38 ± 6	39 ± 5	39 ± 5
Nighttime (22:00–05:59)				
N	67[a]	34	68	34
% Time 70–180 mg/dl	55 ± 20	56 ± 16	74 ± 12	56 ± 14
% Time >250 mg/dl [b]	14.7 ± 16.0	13.6 ± 12.2	6.6 ± 6.5	14.6 ± 11.8
Mean Glucose (mg/dl)	174 ± 37	171 ± 25	149 ± 20	174 ± 25
% Time <70 mg/dl [b]	3.0 ± 3.7	3.3 ± 4.0	2.4 ± 2.1	3.0 ± 2.6
Glucose CV (%)	36 ± 7	38 ± 8	37 ± 6	38 ± 5

Values are mean ± standard deviation

a - One patient in the CLC group was missing baseline CGM data. One patient in the SC group did not provide enough CGM data during daytime hours to be included in the baseline tabulation.
b - For outcomes with a skewed distribution, the mean and standard deviation were calculated by robust regression using an M-estimator.

TABLE S8. CHANGE IN PERCENT TIME IN TARGET RANGE 70–180 MG/DL FROM BASELINE ACCORDING TO SUBGROUPS

	CLC			SC		
	N	**Baseline**	**Change from Baseline**	**N**	**Baseline**	**Change from Baseline**
Overall	67[a]	57 ± 18	12.5 ± 11.8	34	55 ± 15	1.0 ± 6.6
Site						
A	22	53 ± 21	12.7 ± 12.5	11	53 ± 15	2.1 ± 7.4
B	22	56 ± 18	13.0 ± 13.9	12	58 ± 14	−1.9 ± 6.7
C	23	61 ± 14	11.7 ± 9.2	11	53 ± 16	3.1 ± 4.8
Age at Enrollment						
2 to <4 years	31	54 ± 16	15.0 ± 11.4	16	56 ± 12	−1.9 ± 4.9
4 to <6 years	36	59 ± 19	10.3 ± 11.9	18	53 ± 17	3.6 ± 6.9
Diabetes Duration at Enrollment						
<1.5 years	42	58 ± 19	12.4 ± 13.0	18	61 ± 13	−0.6 ± 7.1
≥1.5 years	25	55 ± 16	12.6 ± 9.8	16	48 ± 14	2.9 ± 5.5
Gender						
Female	32	60 ± 17	10.0 ± 11.4	19	51 ± 14	−0.2 ± 5.5
Male	35	54 ± 18	14.7 ± 11.8	15	60 ± 14	2.5 ± 7.7
Race/Ethnicity						
White non-Hispanic	50	57 ± 17	12.1 ± 11.9	25	55 ± 15	1.6 ± 7.0
Other	17	55 ± 20	13.4 ± 11.9	9	54 ± 14	−0.6 ± 5.2
BMI Z-Score		**N=65**				
<0.5	23	53 ± 17	12.9 ± 11.7	15	58 ± 14	0.0 ± 6.5
≥0.5	42	58 ± 19	12.6 ± 12.1	19	53 ± 15	1.8 ± 6.7
Family Income		**N=63**			**N=32**	
<$100,000	27	49 ± 18	15.9 ± 13.1	18	51 ± 14	1.4 ± 6.8
≥$100,000	36	62 ± 17	10.1 ± 10.6	14	60 ± 15	0.1 ± 6.8
Parent Education						
≤Bachelor's Degree	36	51 ± 18	14.4 ± 12.8	22	52 ± 15	2.1 ± 6.4
>Bachelor's Degree	31	63 ± 16	10.2 ± 10.3	12	60 ± 13	−1.0 ± 6.6
Health Insurance					**N=33**	
Private	51	59 ± 18	12.3 ± 11.3	26	58 ± 14	−0.2 ± 5.8
Not Private	16	51 ± 18	13.0 ± 13.7	7	47 ± 16	5.3 ± 8.4
Baseline HbA1c		**N=63**			**N=32**	
<7.0%	22	73 ± 13	6.4 ± 9.8	8	73 ± 6	−0.4 ± 5.6
7.0% to <8.0%	20	57 ± 10	11.8 ± 9.4	8	56 ± 6	−0.4 ± 5.5
≥8.0%	21	41 ± 12	19.4 ± 12.4	16	45 ± 12	2.6 ± 6.9
Baseline % Time 70–180 mg/dl						
<40%	11	30 ± 7	29.4 ± 10.0	7	35 ± 4	6.1 ± 4.7
40% to <60%	28	49 ± 5	14.5 ± 8.4	14	50 ± 7	1.9 ± 6.4
≥60%	28	75 ± 8	3.8 ± 5.9	13	70 ± 6	−2.6 ± 5.8
Baseline % Time >250 mg/dl						
<20%	44	66 ± 13	8.0 ± 8.9	22	63 ± 10	−0.3 ± 6.7
≥20%	23	39 ± 10	21.1 ± 12.0	12	40 ± 7	3.4 ± 5.8

Baseline % Time <70 mg/dl						
<2%	24	48 ± 17	19.6 ± 13.1	13	55 ± 15	2.6 ± 8.9
2% to <4%	22	60 ± 16	9.0 ± 9.0	12	56 ± 15	1.4 ± 3.7
≥4%	21	64 ± 18	7.9 ± 9.2	9	53 ± 16	−1.8 ± 5.2
Baseline % Time <54 mg/dl						
<1%	51	55 ± 19	13.8 ± 12.5	27	55 ± 15	1.5 ± 7.0
≥1%	16	62 ± 15	8.3 ± 8.3	7	54 ± 14	−0.9 ± 4.7
Insulin Modality before Enrollment						
Pump	41	62 ± 16	9.4 ± 10.4	24	55 ± 14	0.4 ± 6.0
MDI	26	48 ± 18	17.2 ± 12.4	10	55 ± 17	2.6 ± 7.9
CGM Use before Enrollment						
Yes	65	58 ± 17	11.9 ± 11.5	34	55 ± 15	1.0 ± 6.6
No	2	20 ± 2	31.3 ± 0.0	0	NA	NA
Pump and CGM Use before Enrollment						
CGM only	24	50 ± 16	16.1 ± 12.2	10	55 ± 17	2.6 ± 7.9
Pump + CGM	41	62 ± 16	9.4 ± 10.4	24	55 ± 14	0.4 ± 6.0
None	2	20 ± 2	31.3 ± 0.0	0	NA	NA
Severe Hypoglycemia Events in the 12 Months before Enrollment						
None	63	57 ± 18	12.8 ± 11.9	32	55 ± 15	1.4 ± 6.6
≥1	4	52 ± 15	6.7 ± 8.5	2	54 ± 14	−4.8 ± 1.2
Diabetic Ketoacidosis Events in the 12 Months before Enrollment						
None	56	58 ± 17	11.4 ± 11.4	31	54 ± 15	1.4 ± 6.7
≥1	11	48 ± 19	17.8 ± 13.0	3	61 ± 7	−2.7 ± 4.3

Values are mean ± standard deviation. NA = not applicable.

a - One patient in the CLC group was missing baseline CGM data.

TABLE S9. ADDITIONAL SECONDARY GLYCATED HEMOGLOBIN OUTCOMES

	Baseline		13 Weeks		Difference[a] (95% CI)
	CLC (N=64)	SC (N=32)	CLC (N=62)	SC (N=33)	
HbA1c <7.0%[b]	23 (36%)	8 (25%)	30 (48%)	10 (30%)	+13% (−2%, +30%)
HbA1c <7.5%[c]	34 (53%)	14 (44%)	47 (76%)	16 (48%)	+25% (+11%, +42%)
			N=59	**N=31**	
Absolute Reduction >0.5% from Baseline[c]	NA	NA	29 (49%)	7 (23%)	+28% (+10%, +46%)
Absolute Reduction >1.0% from Baseline[d]	NA	NA	11 (19%)	0 (0%)	+16% (+8%, +27%)
Relative Reduction >10% from Baseline[d]	NA	NA	16 (27%)	0 (0%)	+26% (+16%, +38%)
Absolute Reduction >1.0% from Baseline or HbA1c <7.0%[c]	NA	NA	38 (64%)	9 (29%)	+28% (+9%, +48%)

Values are n (%). NA = not applicable.

a. Difference is CLC − SC. Confidence interval was FDR-adjusted.
b. Model adjusted for baseline glycated hemoglobin, age, prior CGM and pump use, and site as a random effect.
c. Model adjusted for baseline glycated hemoglobin, age, and prior CGM and pump use.
d. Model adjusted for baseline glycated hemoglobin.

TABLE S10. COMPARISON OF BINARY CGM OUTCOMES

	Baseline		13 Weeks		Difference[b] (95% CI)
	CLC (N=67)[a]	SC (N=34)	CLC (N=68)	SC (N=34)	
% CGM in Range 70–180 mg/dl >70% and % CGM <70 mg/dl <4%[c]	9 (13%)	4 (12%)	21 (31%)	2 (6%)	+25% (+12%, +37%)
			N=67[a]	**N=34**	
% CGM in Range 70–180 mg/dl Improvement ≥5% from Baseline[d]	NA	NA	43 (64%)	8 (24%)	+42% (+26%, +57%)
% CGM in Range 70–180 mg/dl Improvement ≥10% from Baseline[d]	NA	NA	37 (55%)	2 (6%)	+49% (+36%, +62%)

Values are n (%). NA = not applicable.

a. One patient in the CLC group was missing baseline CGM data.
b. Difference is CLC − SC. Confidence interval was FDR-adjusted.
c. Model adjusted for baseline CGM in range 70–180 mg/dl, age, and prior CGM and pump use.
d. Model adjusted for baseline CGM in range 70–180 mg/dl, age, prior CGM and pump use, and site as a random effect.

TABLE S11. ADDITIONAL CGM-MEASURED OUTCOMES

Outcome	Baseline		13 Weeks		Difference [b] (95% CI)
	CLC (N=67) [a]	SC (N=34)	CLC (N=68)	SC (N=34)	
% CGM in Range 70–140 mg/dl	37 ± 16	34 ± 12	48 ± 11	35 ± 11	+11.4 (+8.7, +14.2)
% CGM >180 mg/dl	40 ± 19	42 ± 15	28 ± 11	41 ± 13	−12.0 (−15.2, −8.9)
% CGM >300 mg/dl [c]	5.6 ± 7.0	6.2 ± 7.2	3.0 ± 3.4	5.8 ± 6.2	−1.9 (−2.8, −1.1)
% CGM <60 mg/dl [c]	1.2 ± 1.0	1.0 ± 1.1	1.1 ± 0.7	1.1 ± 1.1	−0.02 (−0.3, +0.2)
Coefficient of Variation (%)	37 ± 6	39 ± 6	39 ± 5	39 ± 5	+0.3 (−0.9, +1.5)
Standard Deviation (mg/dl)	65 ± 17	68 ± 15	60 ± 14	68 ± 14	−5.5 (−8.3, −2.8)
Low Blood Glucose Index [c]	0.83 ± 0.58	0.76 ± 0.49	0.85 ± 0.37	0.81 ± 0.46	+0.01 (−0.10, +0.12)
High Blood Glucose Index [c]	9.4 ± 6.2	10.2 ± 6.1	6.5 ± 3.5	9.8 ± 4.5	−2.8 (−3.7, −2.0)
CGM-measured hypoglycemia Event Rate/Week [c, d]	1.4 ± 2.0	0.7 ± 1.1	1.1 ± 0.9	0.9 ± 1.1	−0.03 (−0.38, +0.32)
CGM-measured hyperglycemia Event Rate/Week [c, e]	1.9 ± 2.7	2.2 ± 2.6	1.0 ± 1.2	2.1 ± 2.4	−0.66 (−1.00, −0.33)

Values are mean ± standard deviation

a - One patient in the CLC group was missing baseline CGM data.

b - Difference is CLC − SC. For approximately normally distributed outcomes, a direct likelihood model was used. This model adjusted for the baseline value of the metric, age, prior CGM and pump use, and site as a random effect. Confidence interval was FDR-adjusted.

c - For outcomes with a skewed distribution, the mean, standard deviation, and difference were calculated by robust regression using an M-estimator. The model used to calculate the adjusted difference and its confidence interval adjusted for the same effects as the direct likelihood model, though site was treated as a fixed effect.

d - A hypoglycemia event is defined as 15 consecutive minutes with a sensor glucose value below 54 mg/dl.

e - A hyperglycemia event is defined as 90 consecutive minutes with a sensor glucose value above 300 mg/dl.

TABLE S12. CHANGE IN GLYCATED HEMOGLOBIN FROM BASELINE ACCORDING TO SUBGROUPS

	CLC			SC		
	N	**Baseline**	**Change from Baseline**	**N**	**Baseline**	**Change from Baseline**
Overall	59	7.5 ± 1.2	−0.58 ± 0.71	31	7.7 ± 0.9	−0.20 ± 0.39
Site						
A	22	7.9 ± 1.4	−0.62 ± 0.84	11	8.0 ± 0.9	−0.25 ± 0.52
B	17	7.4 ± 1.3	−0.52 ± 0.71	10	7.5 ± 0.8	−0.18 ± 0.40
C	20	7.3 ± 0.8	−0.60 ± 0.55	10	7.6 ± 1.0	−0.17 ± 0.22
Age at Enrollment						
2 to <4 years	24	7.8 ± 0.9	−0.80 ± 0.64	16	7.8 ± 0.9	−0.08 ± 0.44
4 to <6 years	35	7.4 ± 1.3	−0.44 ± 0.72	15	7.5 ± 1.0	−0.33 ± 0.29
Diabetes Duration at Enrollment						
<1.5 years	35	7.5 ± 1.3	−0.66 ± 0.76	17	7.5 ± 0.9	−0.15 ± 0.44
≥1.5 years	24	7.6 ± 1.1	−0.47 ± 0.61	14	7.9 ± 0.9	−0.26 ± 0.32
Gender						
Female	30	7.5 ± 1.3	−0.49 ± 0.74	17	8.1 ± 0.9	−0.14 ± 0.41
Male	29	7.6 ± 1.1	−0.68 ± 0.67	14	7.2 ± 0.7	−0.28 ± 0.37
Race/Ethnicity						
White non-Hispanic	45	7.4 ± 1.1	−0.51 ± 0.59	23	7.7 ± 1.0	−0.23 ± 0.38
Other	14	7.9 ± 1.6	−0.81 ± 0.99	8	7.8 ± 0.9	−0.12 ± 0.44
BMI Z-Score		**N=57**				
<0.5	18	7.8 ± 1.3	−0.69 ± 0.85	15	7.7 ± 0.9	−0.25 ± 0.40
≥0.5	39	7.5 ± 1.1	−0.54 ± 0.66	16	7.7 ± 0.9	−0.15 ± 0.39
Family Income		**N=57**			**N=29**	
<$100,000	21	8.1 ± 1.3	−0.91 ± 0.86	17	7.9 ± 0.9	−0.15 ± 0.43
≥$100,000	36	7.2 ± 1.0	−0.41 ± 0.55	12	7.5 ± 1.0	−0.28 ± 0.32
Parent Education						
≤Bachelor's Degree	30	7.9 ± 1.4	−0.76 ± 0.87	20	7.7 ± 1.0	−0.20 ± 0.39
>Bachelor's Degree	29	7.2 ± 0.9	−0.40 ± 0.42	11	7.6 ± 0.9	−0.20 ± 0.40
Health Insurance					**N=30**	
Private	49	7.5 ± 1.2	−0.54 ± 0.67	24	7.6 ± 0.9	−0.20 ± 0.41
Not Private	10	7.9 ± 1.2	−0.78 ± 0.87	6	8.0 ± 0.9	−0.30 ± 0.30
Baseline HbA1c						
<7.0%	21	6.4 ± 0.5	−0.08 ± 0.33	8	6.5 ± 0.3	−0.18 ± 0.37
7.0% to <8.0%	19	7.5 ± 0.3	−0.51 ± 0.34	8	7.4 ± 0.2	−0.01 ± 0.36
≥8.0%	19	8.9 ± 0.9	−1.22 ± 0.81	15	8.5 ± 0.4	−0.31 ± 0.40
Baseline % Time 70–180 mg/dl		**N=58**				
<40%	9	9.3 ± 1.3	−1.52 ± 1.01	7	8.7 ± 0.6	−0.24 ± 0.28
40% to <60%	23	7.9 ± 0.6	−0.67 ± 0.45	12	7.9 ± 0.5	−0.16 ± 0.41
≥60%	26	6.7 ± 0.7	−0.20 ± 0.40	12	7.0 ± 0.8	−0.22 ± 0.45
Baseline % Time >250 mg/dl		**N=58**				
<20%	40	7.1 ± 0.9	−0.33 ± 0.45	21	7.4 ± 0.8	−0.20 ± 0.42
≥20%	18	8.7 ± 1.1	−1.18 ± 0.83	10	8.4 ± 0.7	−0.19 ± 0.33

Baseline % Time <70 mg/dl	**N=58**					
<2%	22	8.0 ± 1.1	−0.95 ± 0.77	12	7.5 ± 0.7	−0.10 ± 0.42
2% to <4%	17	7.6 ± 1.4	−0.48 ± 0.65	12	7.6 ± 0.9	−0.22 ± 0.40
≥4%	19	7.0 ± 0.8	−0.28 ± 0.51	7	8.2 ± 1.1	−0.33 ± 0.30
Baseline % Time <54 mg/dl	**N=58**					
<1%	44	7.7 ± 1.2	−0.68 ± 0.73	25	7.6 ± 0.9	−0.18 ± 0.41
≥1%	14	7.0 ± 0.9	−0.31 ± 0.57	6	8.0 ± 1.0	−0.30 ± 0.32
Insulin Modality before Enrollment						
Pump	40	7.2 ± 1.0	−0.36 ± 0.46	21	7.7 ± 0.9	−0.19 ± 0.41
MDI	19	8.3 ± 1.3	−1.06 ± 0.90	10	7.7 ± 1.1	−0.22 ± 0.37
CGM Use before Enrollment						
Yes	57	7.5 ± 1.1	−0.52 ± 0.64	31	7.7 ± 0.9	−0.20 ± 0.39
No	2	10.0 ± 0.4	−2.25 ± 0.21	0	NA	NA
Pump and CGM Use before Enrollment						
CGM only	17	8.0 ± 1.2	−0.92 ± 0.84	10	7.7 ± 1.1	−0.22 ± 0.37
Pump + CGM	40	7.2 ± 1.0	−0.36 ± 0.46	21	7.7 ± 0.9	−0.19 ± 0.41
None	2	10.0 ± 0.4	−2.25 ± 0.21	0	NA	NA
Severe Hypoglycemia Events in the 12 Months before Enrollment						
None	57	7.5 ± 1.2	−0.59 ± 0.72	29	7.7 ± 0.9	−0.19 ± 0.38
≥1	2	8.3 ± 0.4	−0.40 ± 0.00	2	8.2 ± 0.0	−0.35 ± 0.64
Diabetic Ketoacidosis Events in the 12 Months before Enrollment						
None	50	7.4 ± 1.2	−0.49 ± 0.65	28	7.6 ± 0.9	−0.19 ± 0.37
≥1	9	8.3 ± 1.0	−1.12 ± 0.79	3	8.6 ± 0.3	−0.27 ± 0.68

Values are mean ± standard deviation. NA = not applicable.

TABLE S13. CHANGE IN PERCENT TIME <70 MG/DL FROM BASELINE ACCORDING TO SUBGROUPS

	CLC			SC		
	N	**Baseline**	**Change from Baseline**	**N**	**Baseline**	**Change from Baseline**
Overall	67[a]	3.0 ± 2.2	−0.2 ± 1.8	34	2.7 ± 2.0	0.2 ± 1.0
Site						
A	22	3.7 ± 2.7	−0.4 ± 2.1	11	2.7 ± 1.3	0.4 ± 1.0
B	22	2.3 ± 2.6	0.3 ± 1.4	12	2.4 ± 2.3	0.2 ± 1.1
C	23	3.4 ± 2.8	−0.4 ± 2.0	11	3.2 ± 3.0	0.2 ± 1.2
Age at Enrollment						
2 to <4 years	31	2.7 ± 2.0	−0.1 ± 1.5	16	2.5 ± 1.5	0.2 ± 0.9
4 to <6 years	36	3.1 ± 1.9	−0.3 ± 2.3	18	2.8 ± 2.2	0.2 ± 1.1
Diabetes Duration at Enrollment						
<1.5 years	42	2.7 ± 2.0	−0.1 ± 1.3	18	2.4 ± 1.4	0.3 ± 0.9
≥1.5 years	25	3.5 ± 3.2	−0.5 ± 2.5	16	2.9 ± 2.2	0.1 ± 1.3
Gender						
Female	32	2.9 ± 1.7	−0.3 ± 1.8	19	3.3 ± 1.9	−0.1 ± 1.2
Male	35	3.1 ± 2.9	−0.1 ± 1.8	15	2.0 ± 1.6	0.6 ± 0.8
Race/Ethnicity						
White non-Hispanic	50	3.1 ± 2.6	−0.3 ± 1.9	25	2.4 ± 1.8	0.4 ± 1.0
Other	17	3.2 ± 1.1	0.2 ± 1.5	9	3.7 ± 2.7	−0.2 ± 0.8
BMI Z-Score		**N=65**				
<0.5	23	2.9 ± 1.6	0.1 ± 1.2	15	3.1 ± 2.5	0.1 ± 1.3
≥0.5	42	3.3 ± 3.5	−0.3 ± 2.1	19	2.4 ± 1.8	0.3 ± 0.8
Family Income		**N=63**			**N=32**	
<$100,000	27	2.9 ± 2.0	−0.1 ± 1.8	18	2.6 ± 1.6	0.3 ± 0.9
≥$100,000	36	3.1 ± 3.2	−0.2 ± 1.9	14	3.0 ± 2.8	0.1 ± 1.3
Parent Education						
≤Bachelor's Degree	36	2.3 ± 2.4	0.3 ± 0.9	22	2.5 ± 1.4	0.4 ± 0.8
>Bachelor's Degree	31	4.1 ± 2.6	−0.7 ± 2.4	12	3.3 ± 3.4	−0.2 ± 1.2
Health Insurance					**N=33**	
Private	51	3.0 ± 2.2	−0.2 ± 2.0	26	2.4 ± 1.7	0.3 ± 1.0
Not Private	16	2.8 ± 2.3	−0.1 ± 1.4	7	4.6 ± 5.2	−0.6 ± 2.7
Baseline HbA1c		**N=63**			**N=32**	
<7.0%	22	4.1 ± 2.1	−0.8 ± 2.2	8	2.6 ± 1.5	0.8 ± 1.2
7.0% to <8.0%	20	3.3 ± 2.7	−0.5 ± 1.6	8	1.6 ± 1.0	0.4 ± 0.8
≥8.0%	21	1.9 ± 1.6	0.6 ± 1.9	16	3.3 ± 2.3	−0.04 ± 1.1
Baseline % Time 70–180 mg/dl						
<40%	11	1.1 ± 0.9	1.1 ± 1.0	7	2.5 ± 3.0	0.4 ± 0.9
40% to <60%	28	3.0 ± 1.7	−0.02 ± 1.8	14	2.8 ± 2.5	0.3 ± 0.9
≥60%	28	3.9 ± 2.7	−0.9 ± 1.9	13	2.8 ± 1.4	0.2 ± 1.4
Baseline % Time >250 mg/dl						
<20%	44	3.9 ± 2.8	−0.7 ± 2.2	22	2.5 ± 1.8	0.1 ± 1.2
≥20%	23	1.9 ± 1.6	0.7 ± 1.6	12	2.9 ± 1.9	0.5 ± 0.7

Baseline % Time <70 mg/dl						
<2%	24	0.9 ± 0.8	0.9 ± 0.8	13	1.0 ± 0.8	0.3 ± 0.7
2% to <4%	22	3.1 ± 0.7	0.02 ± 0.9	12	2.7 ± 0.6	0.5 ± 0.8
≥4%	21	6.9 ± 3.8	−2.4 ± 2.2	9	6.3 ± 2.7	−0.6 ± 2.5
Baseline % Time <54 mg/dl						
<1%	51	2.2 ± 2.0	0.4 ± 1.2	27	2.0 ± 1.4	0.4 ± 0.8
≥1%	16	7.5 ± 3.2	−2.8 ± 2.8	7	6.7 ± 3.5	−0.7 ± 3.3
Insulin Modality before Enrollment						
Pump	41	3.6 ± 1.9	−0.5 ± 2.2	24	3.1 ± 2.7	0.1 ± 1.1
MDI	26	2.2 ± 1.9	0.4 ± 1.1	10	2.2 ± 1.3	0.6 ± 0.9
CGM Use before Enrollment						
Yes	65	3.0 ± 2.2	−0.2 ± 1.9	34	2.7 ± 2.0	0.2 ± 1.0
No	2	1.3 ± 0.6	−0.1 ± 1.3	0	NA	NA
Pump and CGM Use before Enrollment						
CGM only	24	2.3 ± 2.0	0.4 ± 1.1	10	2.2 ± 1.3	0.6 ± 0.9
Pump + CGM	41	3.6 ± 1.9	−0.5 ± 2.2	24	3.1 ± 2.7	0.1 ± 1.1
None	2	1.3 ± 0.6	−0.1 ± 1.3	0	NA	NA
Severe Hypoglycemia Events in the 12 Months before Enrollment						
None	63	3.0 ± 2.4	−0.2 ± 2.0	32	2.5 ± 1.7	0.2 ± 1.0
≥1	4	2.9 ± 0.7	0.2 ± 1.1	2	4.1 ± 0.03	0.3 ± 1.9
Diabetic Ketoacidosis Events in the 12 Months before Enrollment						
None	56	3.1 ± 2.2	−0.3 ± 1.8	31	2.6 ± 1.9	0.3 ± 1.0
≥1	11	2.2 ± 1.5	0.3 ± 2.4	3	3.5 ± 4.3	−0.3 ± 0.8

Values are mean ± standard deviation calculated by robust regression using an M-estimator. NA = not applicable.

a - One patient in the CLC group was missing baseline CGM data.

TABLE S14. INSULIN RECEIVED BY TREATMENT GROUP

	Baseline		13 Weeks		Difference [b] (95% CI)
	CLC (N=68)	SC (N=34)	CLC (N=63) [a]	SC (N=26) [a]	
Total Daily Insulin (U/kg/day) [c]	0.66 ± 0.17	0.66 ± 0.23	0.70 ± 0.16	0.74 ± 0.29	−0.03 (−0.09, +0.04)
% of Total Daily Insulin Delivered via Basal	40 ± 14	39 ± 11	39 ± 9	38 ± 11	+1.2 (−4.1, +6.4)

Values are mean ± standard deviation of the patients' mean daily intake for the 7 days preceding the visit. Data from the screening visit were used for the baseline calculation.

a. Missing data (CLC/SC): 5/8. In the CLC group, 1 patient withdrew, 2 patients failed to provide insulin data, 1 patient had a missing value for weight, and 1 patient's data were out-of-window. In the SC group, 5 patients failed to provide insulin data, 1 patient had a missing value for weight, and 2 patients' data were out-of-window.
b. Difference is CLC − SC. For approximately normally distributed outcomes, a direct likelihood model was used. This model adjusted for the baseline value of the metric, age, prior CGM and pump use, and site as a random effect. Confidence interval was FDR-adjusted.
c. Skewed outcome—the mean, standard deviation, and difference were calculated by robust regression using an M-estimator. The model used to calculate the adjusted difference and its confidence interval adjusted for the same effects as the direct likelihood model, though site was treated as a fixed effect.

TABLE S15. DAILY INSULIN DOSES FOR PUMP AND INJECTION USERS

A. Daily Insulin in Units per Kilogram

	Baseline		13 Weeks [a]	
	CLC	**SC**	**CLC**	**SC**
Pump Users [b]	**N=42**	**N=24**	**N=62**	**N=18**
Total Daily Insulin (U/kg/day)	0.65 (0.54, 0.76)	0.69 (0.60, 0.81)	0.68 (0.59, 0.80)	0.73 (0.64, 0.91)
Total Daily Basal Insulin (U/kg/day)	0.26 (0.20, 0.34)	0.27 (0.26, 0.31)	0.27 (0.22, 0.33)	0.28 (0.21, 0.37)
Total Daily Bolus Insulin (U/kg/day)	0.39 (0.28, 0.49)	0.40 (0.30, 0.50)	0.41 (0.35, 0.52)	0.41 (0.35, 0.50)
Injection Users [b]	**N=26**	**N=10**		**N=8**
Total Daily Insulin (U/kg/day)	0.67 (0.56, 0.85)	0.52 (0.45, 0.60)	NA	0.65 (0.50, 0.97)
Total Daily Basal Insulin (U/kg/day)	0.23 (0.16, 0.38)	0.15 (0.14, 0.20)	NA	0.20 (0.17, 0.32)
Total Daily Bolus Insulin (U/kg/day)	0.42 (0.35, 0.53)	0.38 (0.30, 0.45)	NA	0.45 (0.36, 0.65)
Number of Daily Short-Acting Injections (n/day)	4 (3, 5)	4 (3, 4)	NA	4 (4, 5)

Values are median (quartiles) of the patients' mean daily intake for the 7 days preceding the visit. Data from the screening visit were used for the baseline calculation. NA = not applicable.

a. Missing data (CLC/SC): 6/8. In the CLC group, 1 patient withdrew, 2 patients failed to provide insulin data, 1 patient had a missing value for weight, 1 patient's data were out-of-window, and 1 patient was excluded because they were using insulin injections instead of CLC during the final week of the study. In the SC group, 5 patients failed to provide insulin data, 1 patient had a missing value for weight, and 2 patients' data were out-of-window.

b. For pump users, data were downloaded from the pump. For injection users, data were from a case report form estimated from patient reports or logs mostly as integer values.

B. Daily Insulin in Units

	Baseline		13 Weeks [a]	
	CLC	**SC**	**CLC**	**SC**
Pump Users [b]	**N=42**	**N=24**	**N=63**	**N=18**
Total Daily Insulin (U/day)	10.85 (9.00, 14.40)	13.85 (9.75, 15.40)	12.48 (9.85, 15.41)	14.63 (8.90, 17.31)
Total Daily Basal Insulin (U/day)	4.50 (3.50, 6.00)	4.90 (3.50, 7.35)	4.81 (3.77, 6.00)	4.98 (3.20, 7.10)
Total Daily Bolus Insulin (U/day)	6.75 (4.50, 8.50)	7.45 (5.70, 9.20)	7.76 (5.84, 9.20)	7.83 (5.00, 9.40)
Injection Users [b]	**N=26**	**N=10**		**N=9**
Total Daily Insulin (U/day)	10 (9, 13)	10 (8, 10)	NA	11 (9, 20)
Total Daily Basal Insulin (U/day)	4 (3, 6)	3 (2, 4)	NA	3 (3, 5)
Total Daily Bolus Insulin (U/day)	7 (6, 8)	6 (6, 8)	NA	8 (7, 12)
Number of Daily Short-Acting Injections (n/day)	4 (3, 5)	4 (3, 4)	NA	4 (4, 5)

Values are median (quartiles) of the patients' mean daily intake for the 7 days preceding the visit. Data from the screening visit were used for the baseline calculation. NA = not applicable.

a. Missing data (CLC/SC): 5/7. In the CLC group, 1 patient withdrew, 2 patients failed to provide insulin data, 1 patient's data were out-of-window, and 1 patient was excluded because they were using insulin injections instead of CLC during the final week of the study. In the SC group, 5 patients failed to provide insulin data and 2 patients' data were out-of-window.

b. For pump users, data were downloaded from the pump. For injection users, data were from a case report form estimated from patient reports or logs mostly as integer values.

TABLE S16. WEIGHT AND BODY MASS INDEX

	Baseline [a]		13 Weeks [b]		Difference [c] (95% CI)
	CLC (N=68)	SC (N=34)	CLC (N=66)	SC (N=32)	
Body Weight (kg) [d]	17.3 ± 3.4	17.8 ± 3.5	18.3 ± 3.6	18.4 ± 3.5	+0.2 (−0.2, +0.5)
	N=66	N=34	N=62	N=31	
BMI Z-Score	0.73 ± 1.28	0.69 ± 0.86	0.95 ± 1.04	0.53 ± 1.03	+0.40 (−0.09, +0.90)

Values are mean ± standard deviation. Data from the screening visit were used for the baseline calculation.

a – Missing data (CLC/SC): 2/0 for BMI; In the CLC group, 2 patients had missing values for height.

b – Missing data (CLC/SC): 2/2 for body weight; 6/3 for BMI; In the CLC group, 1 patient withdrew and 1 patient had a missing value for weight. In the SC group, 2 patients had missing values for weight and for one of these, the measurement would have been out-of-window. BMI could not be calculated for an additional 4 patients in the CLC group and 1 patient in the SC group who had missing values for height.

c – Difference is CLC – SC. For approximately normally distributed outcomes, a direct likelihood model was used. This model adjusted for the baseline value of the metric, age, prior CGM and pump use, and site as a random effect. Confidence interval was FDR-adjusted.

d – Since body weight had a skewed distribution, the mean, standard deviation, and difference were calculated by robust regression using an M-estimator. The model used to calculate the adjusted difference and its confidence interval adjusted for the same effects as the direct likelihood model, though site was treated as a fixed effect.

TABLE S17. REASONS FOR AND TIMING OF DISCONTINUATION OF STUDY HYBRID CLOSED-LOOP SYSTEM

Study Day[a]	Age at Enrollment	Pre-study Insulin Delivery Method [b]	Baseline Glycated Hemoglobin (%)	Reason for Discontinuing Hybrid Closed-Loop Use
0	5.47	MDI	8.8	Following study pump training, patient refused to wear the pump
0	4.99	Pump	5.7	Approximately concurrent with study pump training, patient contracted COVID and refused to wear the pump
8	5.04	MDI	6.9	Issues with pump infusion set insertion
19	4.36	Pump	7.6	Site discontinued patient after patient pushed buttons on pump resulting in insulin delivery and hypoglycemia
22*	4.67	Pump	6.0	Severe hypoglycemia event and patient unhappy with study pump

a-Study Day is the last day with hybrid-closed loop data
b-MDI = multiple daily injections

*Patient withdrew from the study. All other patients discontinued the hybrid-closed loop system but remained in the trial through 13 weeks.

TABLE S18. FREQUENCY OF CLOSED LOOP USE IN THE CLC GROUP

	Overall (N=68)	**Weeks 1–4 (N=68)**	**Weeks 5–8 (N=67)**	**Weeks 9–13 (N=67)**
% Time Closed Loop Use *Median (Quartiles*)	94% (90%, 95%)	92% (87%, 95%)	95% (93%, 97%)	95% (92%, 97%)
≥90%	52 (76%)	42 (62%)	57 (85%)	52 (78%)
80% to <90%	9 (13%)	14 (21%)	5 (7%)	8 (12%)
70% to <80%	2 (3%)	3 (4%)	1 (1%)	1 (1%)
60% to <70%	1 (1%)	1 (1%)	0 (0%)	1 (1%)
50% to <60%	0 (0%)	4 (6%)	0 (0%)	0 (0%)
<50%	2 (3%)	2 (3%)	0 (0%)	1 (1%)
0%	2 (3%)	2 (3%)	4 (6%)	4 (6%)

Denominator is the number of days between the beginning of the fourth day after randomization and the end of the day before the 13-week visit, or the end of the day before the last contact date for the patient who dropped out.

TABLE S19. DEVICE ISSUES IN CLOSED-LOOP CONTROL GROUP

Device	Issue Type	Number of Issues that were Associated with an Adverse Event	Number of Issues that were not Associated with an Adverse Event
Tandem t:slim X2 with Control-IQ technology	Various pump failure modes that required replacement of pump	1	8
	User error/inappropriate use	2	0
Infusion Set	Infusion set failure	38	3
	Pain/infection related to infusion set	4	0
Dexcom G6 CGM sensor	Infection related to CGM sensor	1	0
Dexcom G6 CGM transmitter	Component failure requiring replacement	0	1
Total		46	12

TABLE S20. FREQUENCY OF CONTINUOUS GLUCOSE MONITOR USE IN THE SC GROUP

	Overall (N=34)	**Weeks 1–4 (N=34)**	**Weeks 5–8 (N=34)**	**Weeks 9–13 (N=34)**
% Time CGM Use ***Median (Quartiles*****)**	96% (89%, 98%)	95% (87%, 98%)	98% (91%, 98%)	97% (91%, 99%)
≥90%	25 (74%)	24 (71%)	27 (79%)	26 (76%)
80% to <90%	5 (15%)	4 (12%)	3 (9%)	5 (15%)
70% to <80%	2 (6%)	2 (6%)	1 (3%)	1 (3%)
60% to <70%	1 (3%)	3 (9%)	2 (6%)	0 (0%)
50% to <60%	0 (0%)	0 (0%)	0 (0%)	0 (0%)
<50%	1 (3%)	1 (3%)	1 (3%)	2 (6%)
0%	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Denominator is the number of days between the beginning of the fourth day after randomization and the end of the day before the 13-week visit.

FIGURE S1. FLOWCHART OF STUDY COMPLETION

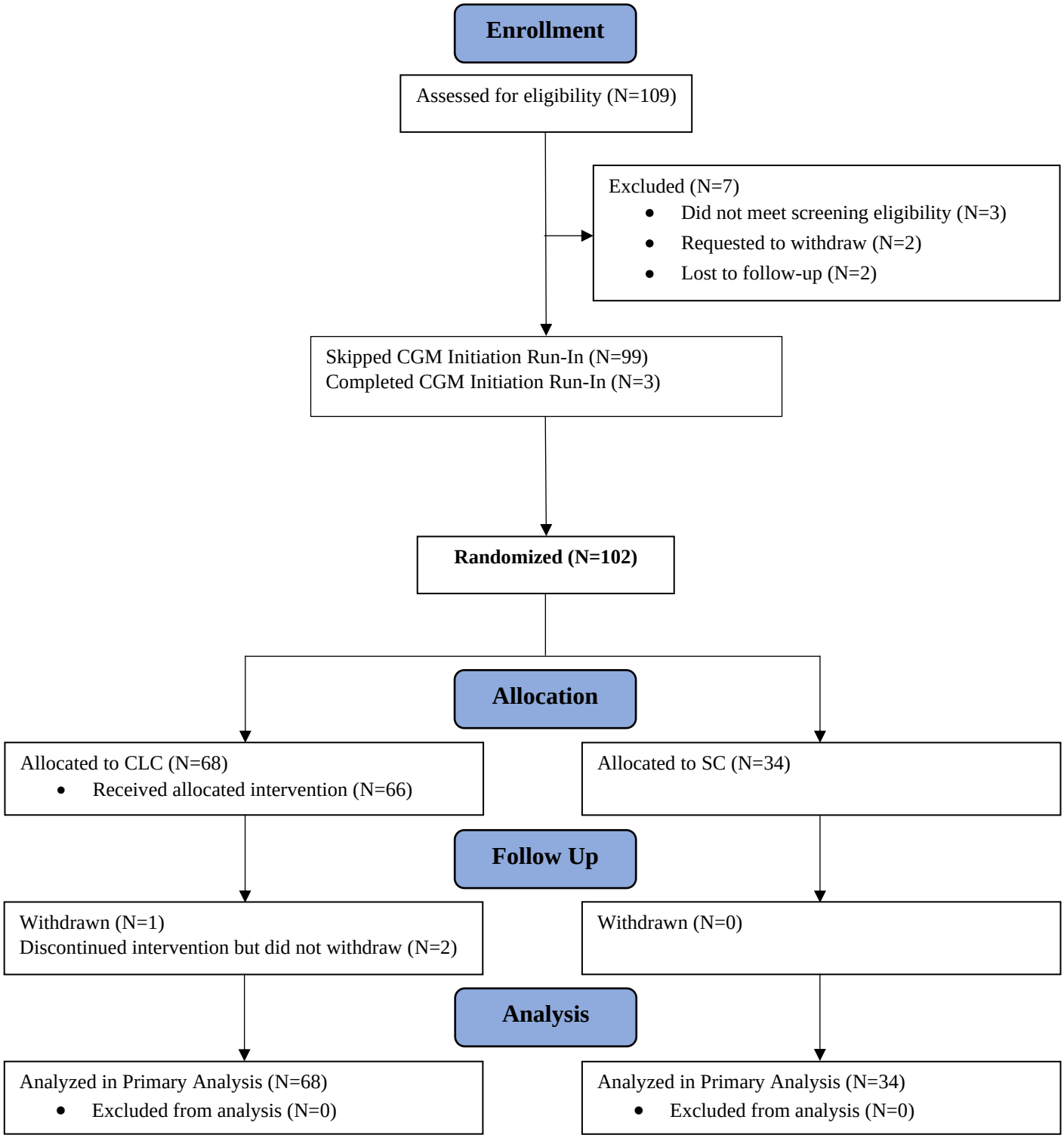
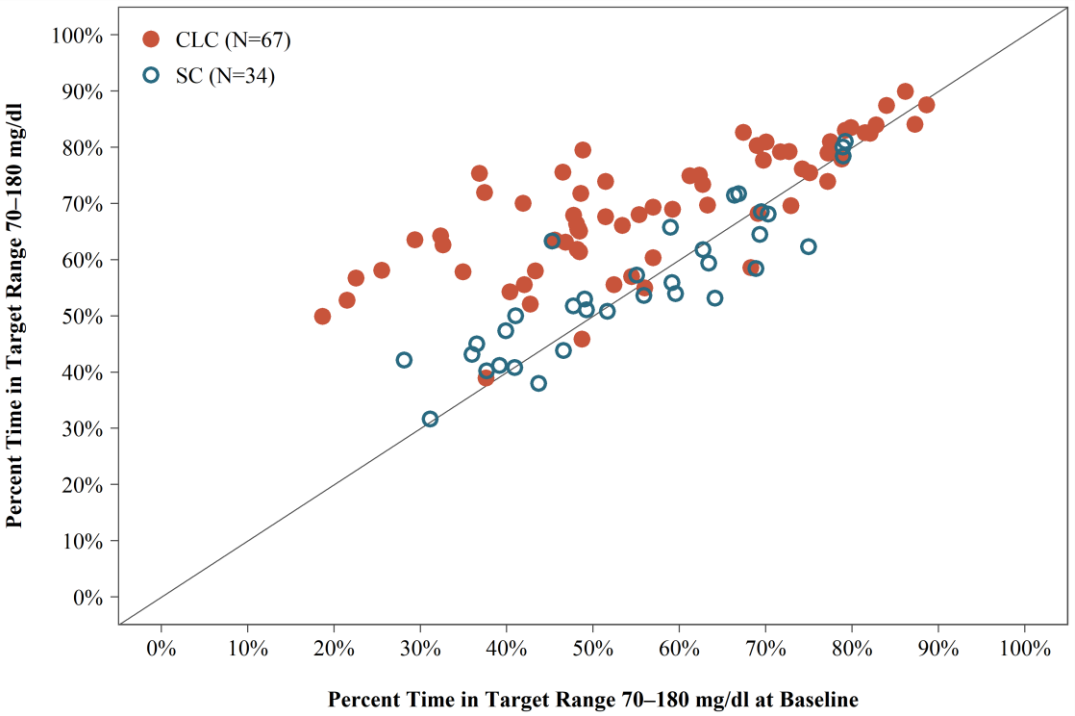


FIGURE S2. SCATTER PLOT FOR PERCENT TIME IN RANGE 70–180 MG/DL BY TREATMENT GROUP

A. Time in Range Over 13 Weeks Versus Baseline Time in Range



B. Change in Time in Range Over 13 Weeks Versus Baseline Time in Range

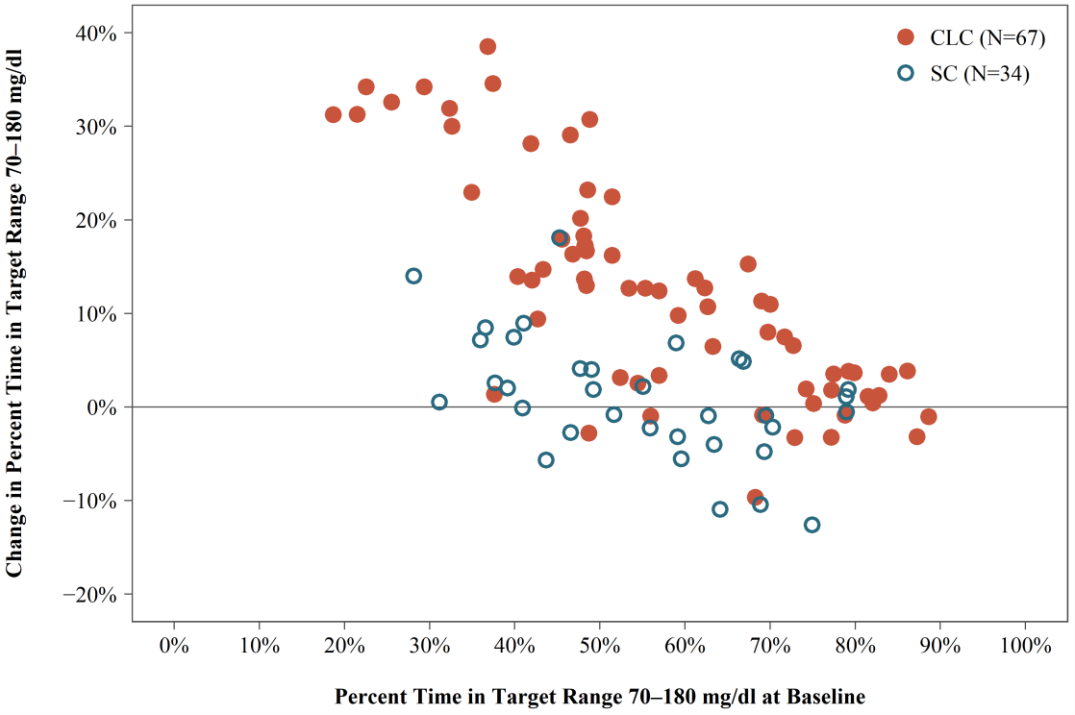


Figure S2. Scatterplots for Percent Time in Range by Treatment Group. Panel A shows time in target range 70–180 mg/dl calculated over 13 weeks versus baseline time in range. Panel B shows change in time in range from

baseline versus baseline time in range. The solid lines in each panel represent no change. Each point represents an individual patient, with those in the CLC group represented by red points and those in the SC group represented by open circle points.

FIGURE S3. CUMULATIVE DISTRIBUTION OF TIME IN RANGE 70–180 MG/DL OVER 13 WEEKS

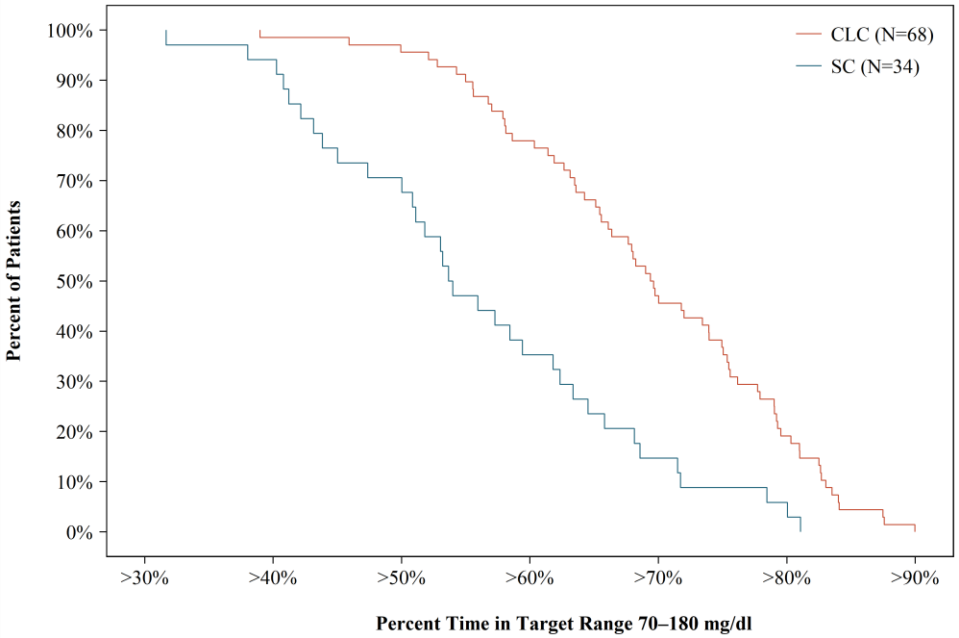
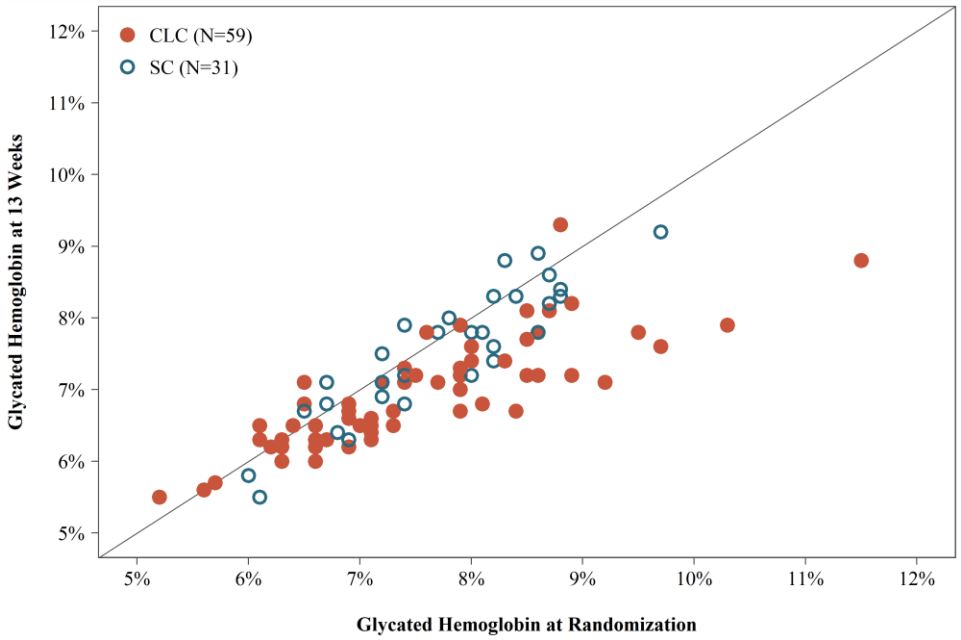


Figure S3. Cumulative Distribution of Time in Target Range 70-180 mg/dl Over 13 Weeks The figure shows the cumulative distribution plot of the percentage of patients vs. the percentage of time that the glucose level was within the range of 70–180 mg/dl, as measured by continuous glucose monitoring over 13 weeks. The distribution for the CLC group is represented by red curve and the distribution of the SC group is represented by the blue curve.

FIGURE S4. SCATTER PLOT FOR GLYCATED HEMOGLOBIN BY TREATMENT GROUP

A. Glycated hemoglobin at 13 weeks Versus Baseline Glycated Hemoglobin



B. Change in Glycated Hemoglobin from Baseline to 13 Weeks Versus Baseline Glycated Hemoglobin

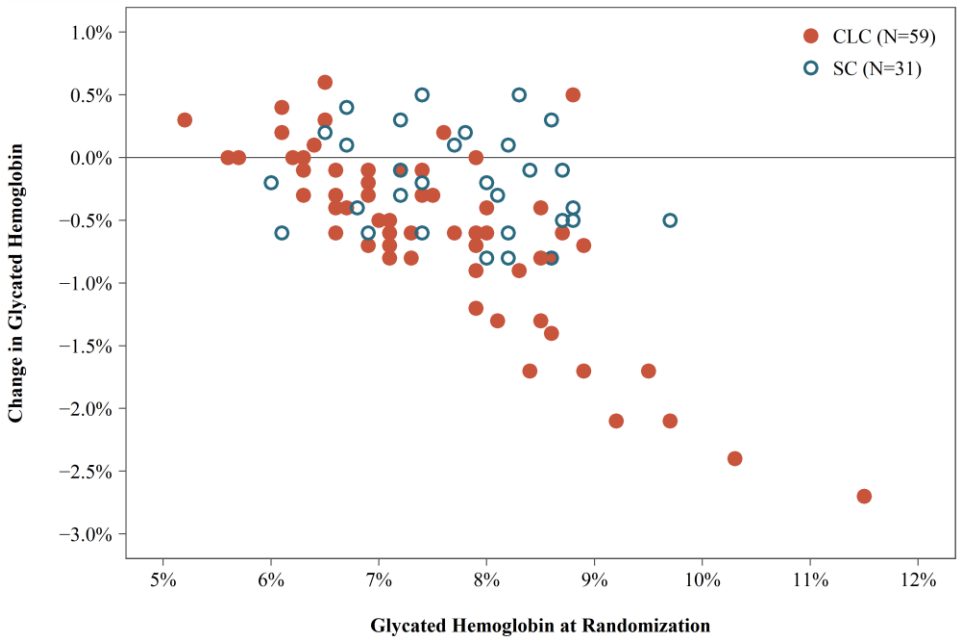
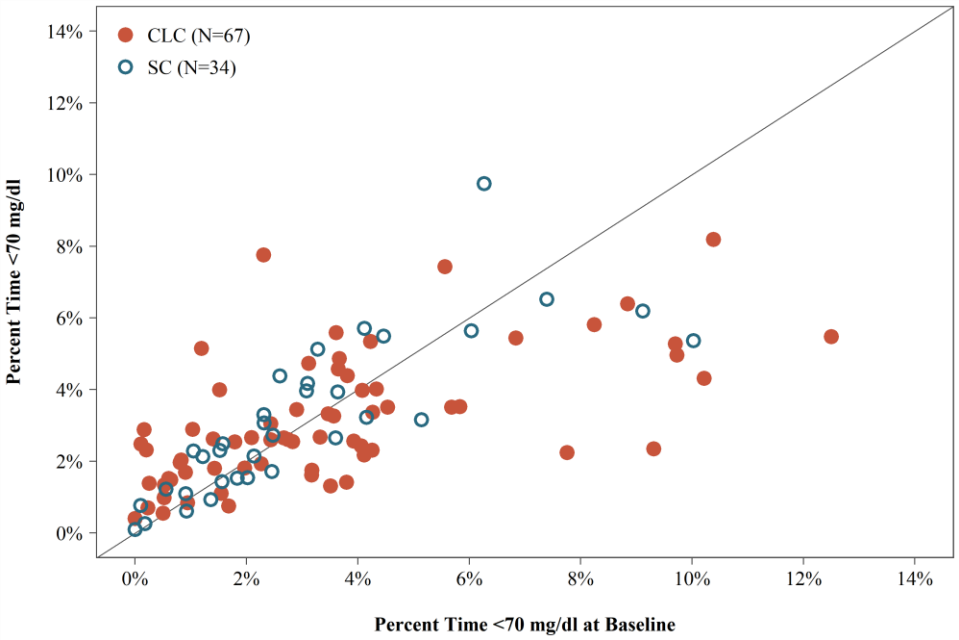


Figure S4. Scatterplots for Glycated Hemoglobin by Treatment Group. Panel A shows glycated hemoglobin values at 13 weeks versus baseline glycated hemoglobin for each patient. Panel B shows change in glycated hemoglobin from baseline versus baseline glycated hemoglobin. The solid lines in each panel represent no change. Each point represents an individual patient, with those in the CLC group represented by red points and those in the SC group represented by open circle points.

FIGURE S5. SCATTER PLOT FOR PERCENT TIME <70 MG/DL BY TREATMENT GROUP

A. Percent Time <70 mg/dl Over 13 Weeks Versus Baseline Time in Range



B. Change in Percent Time <70 mg/dl Over 13 Weeks Versus Baseline Time in Range

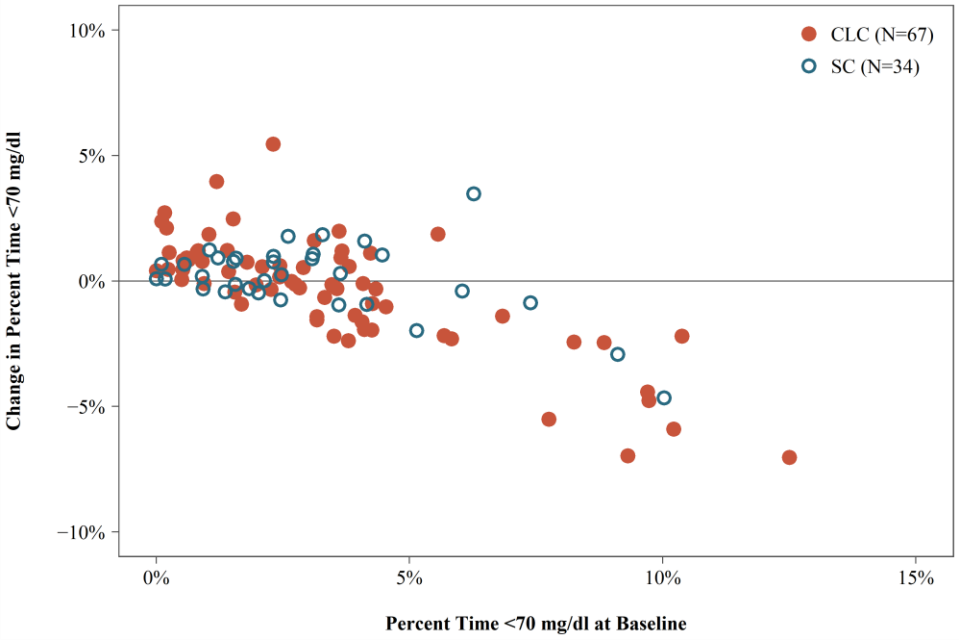


Figure S5. Scatterplots for Percent Time <70 mg/dl by Treatment Group. Panel A shows time in target <70 mg/dl calculated over 13 weeks versus baseline time <70 mg/dl. Panel B shows change in time <70 mg/dl from baseline versus baseline time <70 mg/dl. The solid lines in each panel represent no change. Each point represents an individual patient, with those in the CLC group represented by red points and those in the SC group represented by open circle points.

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