Supplementary Appendix

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

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Additional Methods

Additional Information about the Bionic Pancreas

Meal "announcements" refer to the action taken by the user to inform the bionic pancreas (BP) through the device's graphical user interface that they are eating a meal. In traditional insulin pump therapy, as well as with hybrid closed-loop systems, the user counts the grams of carbohydrates to be eaten and then enters this number into their device's user interface. In contrast, the BP does not use quantitative, absolute counts of carbohydrates. Rather, the BP requires only that the user make a qualitative estimate of carbohydrate content that is not absolute but relative to what is usual for the user ("Usual For Me", "More", or "Less") compared to a typical meal of that type ("Breakfast", "Lunch", or "Dinner").

Users were told to announce carbohydrate-containing meals. They were trained to choose "Less" for meals that had about half of the carbohydrates as a "Usual For Me" meal and to choose "More" for meals that had the amount of carbohydrate in a "Usual For Me" meal plus about one half more. They could enter more than one meal announcement for meals that were larger than "More" meals. Users were instructed not to announce meals that were very low in carbohydrate content (i.e. less than half of a "Less" meal).

In response to meal announcements, the BP delivered ~75% of the autonomously estimated insulin need immediately, and then would autonomously add or refrain from additional basal or correction insulin dosing post-prandially, as necessary. If the user forgot to announce a meal but remembered within 30 minutes of starting to eat, they could announce the meal at that time. If more than 30 minutes had passed since they started to eat, they were told not to announce that meal because the BP would likely have started automatically dosing insulin in response to rising glucose. Users were told to expect that, if a meal announcement was missed, blood glucose would rise higher than if they had remembered to announce the meal.

With prolonged use, the BP will continuously adapt to the changing insulin needs of the user irrespective of the reason. It was recommended to the users that the weight entered into the system at initialization be updated if the weight increased or decreased by more than 15%. If the entered weight was increased, the algorithms were able to command larger doses at each time step, but never more than 3 units could be delivered by the BP at any given time step. Updating the weight did not reset the algorithms.

When CGM data were not available, the BP would continue to (i) dose insulin based on a basal insulin profile autonomously determined, continually updated, and stored by the BP when CGM data were available, (ii) give meal doses as usual in response to meal announcements, and (iii) give correction doses based on manually entered capillary blood glucose values from a blood glucose meter. Insulin dosing could be maintained, increased, or temporarily suspended autonomously by the BP in response to the entered blood-glucose values.

Additional Statistical Methods

1. Randomization was performed separately for adults and children on the trial website using a computer-generated sequence with a permuted block design and stratification according to site. Randomization to the 3 treatment groups was 2:2:1 for adult patients and randomization to the 2 treatment groups was 2:1 for pediatric patients. For each adult site, permuted random block sizes of 5 and 10 were used with equal probability. For each pediatric site, permuted random block sizes of 3 and 6 were used with equal probability.
2. The hierarchy of outcomes was tested in a hierarchical fashion with statistical testing continuing until a nonsignificant result was obtained to maintain a type I error rate of 5% included:
    - glycated hemoglobin

- percentage of time with glucose level <54 mg/dL testing for non-inferiority with a 1% margin
- mean glucose level
- percentage of time with glucose level in range 70-180 mg/dL
- percentage of time with glucose level >180 mg/dL
- percentage of time with glucose level >250 mg/dL
- glucose standard deviation
- percentage of time with glucose level <70 mg/dL
- percentage of time with glucose level <54 mg/dL testing for superiority
- glucose coefficient of variation

3. Additional secondary efficacy outcomes included:
    - additional CGM metrics
    - binary variables created from the glycated hemoglobin data
    - daily insulin doses
    - body mass index
4. Confidence intervals for additional secondary efficacy outcomes were adjusted for multiplicity using the adaptive Benjamini-Hochberg false discovery rate correction procedure (FDR)[1]. These confidence intervals should not be used in place of hypothesis testing as the family-wise error rate was not controlled.
5. Safety outcomes, which were not adjusted for multiple comparisons, included:
    - severe hypoglycemia *(defined as requiring assistance from another person to actively administer carbohydrate or glucagon due to altered consciousness)*
    - diabetic ketoacidosis *(as defined by the Diabetes Control and Complications Trial[2])*
    - other serious adverse events)
    - increase of glycated hemoglobin by >0.5% from baseline to week 13
6. Primary, key secondary, and other secondary hierarchical efficacy outcomes were tested using a linear mixed-effects regression model adjusting for the baseline value, age, and site (random effect). The upper bound of a 95% confidence interval for the time <54 mg/dL was compared to the noninferiority limit of 1.0%. Due to the skewed distribution, a rank normal transformation was applied to the key secondary outcome.
7. The safety outcome increase of glycated hemoglobin by >0.5% was tested using a marginal logistic regression model adjusting for age and the baseline value with a compound symmetry covariance structure to handle the patient dependence within site. Number of severe hypoglycemic events per patient was tested using a Poisson regression model adjusting for age, glycated hemoglobin at randomization, whether or not patient had at least 1 severe hypoglycemic event prior to randomization, and site (random effect). Number of other serious adverse events per patient was tested using a Poisson regression model adjusting for age, glycated hemoglobin at randomization, and site (random effect).
8. Quality of life was assessed with patient-reported outcome questionnaires, which will be reported separately.
9. For testing non-inferiority of time <54 mg/dL, statistical power was 99%, assuming no true difference in mean time <54 mg/dL between the BP and the SC groups with a non-inferiority margin of 1%, a standard deviation of 2.0%, a correlation between baseline and follow-up of 0.40, and one-sided type 1 error of 0.025%.

10. For the calculation of baseline CGM metrics, personal Dexcom G6 data were used for Dexcom G6 users who had ≥85% of possible CGM data during the 14 days prior to screening.
11. CGM data from randomization through the 13-week follow-up visit were included in the calculation of each metric.
12. Descriptive statistics include means with standard deviations and medians with interquartile ranges, depending on the distribution of data.
13. All P-values are two-sided.
14. Analyses were performed with SAS software, version 9.4 (SAS Institute).
15. A per-protocol analysis was performed, restricted to patients with:
    - Baseline and 13-week glycated hemoglobin central lab measurements available
    - No glucose-lowering medications used other than those acceptable in the protocol
    - No major protocol deviation that could impact outcome measures
    - For patients in the SC Group, at least 80% of CGM data available in the 13-week follow-up wear period
    - For patients in the BP Group, closed loop mode was active for at least 80% of the time during the 13 weeks and a meal bolus was announced on average at least 2 times per day when the system was being used
16. A 'while-on-treatment' analysis included all patients randomized. For patients who discontinued the iLet device in the BP group, glycated hemoglobin and CGM metrics only included data prior to iLet discontinuation
17. A subgroup analysis on glycated hemoglobin was performed for the following patient characteristics:
    - Age (6-12, 13-17, 18-25, 26-49, ≥50 years)
    - Diabetes duration (<20 years, ≥20 years)
    - Baseline glycated hemoglobin (<7.0%, 7.0 to 7.9%, 8.0 to 8.9%, 9.0 to 9.9%, ≥10.0%)
    - Baseline % time 70-180 mg/dL (<70%, ≥70%)
    - Baseline % time <70 mg/dL (<4%, ≥4%)
    - Baseline % time >180 mg/dL (<25%, ≥25%)
    - Baseline insulin and CGM device use
    - Sex
    - Race/Ethnicity
    - Body mass index
    - Education
    - C-peptide
    - Site
18. The primary and hierarchical secondary outcomes were also evaluated within the following subgroups:
    - Adult patients ≥ 18 years
    - Pediatric patients <18 years
    - Patients not using a hybrid closed-loop system before the trial

- Patients with a baseline glycated hemoglobin level >7.0%

19. The following sensitivity analyses were performed:

    - Covariate Adjustment: The primary analysis included a pre-specified list of covariates. As an additional sensitivity analysis, any baseline demographic or clinical characteristics observed to be imbalanced between treatment groups were added as covariates to the analyses of the primary endpoint. The determination of a meaningful baseline imbalance was based on clinical judgment and not a p-value.
    - Missing Data: All randomized patients were included in the primary and key secondary analyses according to ITT and any missing data were handled using direct likelihood. It is worth emphasizing that any statistical method for handling missing data makes a number of untestable assumptions. The goal was to minimize the amount of missing data in this study so that results and conclusions will not be sensitive to which statistical method is used. To that end, the following methods were performed:
        - Multiple imputation with a pattern mixture model assuming the dropout trajectory of the BP Group was that of the SC Group.
        - Available cases only.
    - The primary analysis was recalculated switching the non-randomized patient assigned to the BP Group due to a protocol deviation to the SC group.

Reference

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Table S1. Inclusion and Exclusion Criteria

Inclusion

1. Clinical diagnosis of T1D for at least one year and using insulin for at least 1 year
2. Diabetes managed using the same regimen (either pump or multiple daily injections, with or without CGM) for ≥ 3 months prior to collection of CGM data (either from personal Dexcom G6 device or blinded G6 device)
3. Age ≥ 6 years old
4. Current use of a CGM, or if not a CGM user, at least 3 blood glucose meter tests daily on average over the last 4 weeks (according to judgment of investigator if meter is not available).
5. Willingness not to start any new non-insulin glucose-lowering agent during the course of the trial.
6. For patients <18 years old, living with one or more parent/legal guardian knowledgeable about emergency procedures for severe hypoglycemia.
7. For patients ≥18 years old who live alone, patient has a relative or acquaintance who lives within 30 minutes of patient and is willing to be contacted to check on patient if study staff feel that patient may be experiencing a medical emergency and can't be reached.
8. Investigator believes that the patient can safely use the iLet and will follow the Protocol. The investigator will take into account the patient's glycated hemoglobin level, compliance with current diabetes management, and prior acute diabetic complications. For this reason, there is no upper limit on glycated hemoglobin specified for eligibility.
9. If a glucagon-like peptide 1 (GLP-1) agonist or pramlintide is being used, patient must be willing to discontinue use while the iLet BP system is being used.

Exclusion

1. Unable to provide informed consent (e.g. impaired cognition or judgment).
2. Unable to safely comply with study procedures and reporting requirements (e.g. impairment of vision or dexterity that prevents safe operation of the bionic pancreas, impaired memory)
3. Unable to speak and read English. For pediatric patients, both caregivers and patients must be able to speak and read English.
4. Plan to change usual diabetes regimen in the next 3 months. This would include changing from multiple daily injections to pump, pump to multiple daily injections, change in insulin automation delivery system, starting a CGM if not previously used, changes in drug therapy specifically for glucose control except for changes in one insulin analog to another. Changes in insulin dose, carb ratio, sensitivity factor and basal rate profile are allowed.
5. Current use of non-FDA approved closed-loop or hybrid closed-loop insulin delivery system.
6. Use of Apidra (Sanofi) as the pre-study rapid-acting insulin analog and unwilling to switch to insulin aspart or insulin lispro for the duration of the study.
7. Known hemoglobinopathy (sickle cell trait is not an exclusion).
8. Current participation in another diabetes-related clinical trial.
9. History of cystic fibrosis, pancreatitis, or other pancreatic disease, including pancreatic tumor or insulinoma, or history of complete pancreatectomy.

10. Electrically powered implants (e.g. cochlear implants, neurostimulators) that might be susceptible to radio frequency interference.
11. Established history of allergy or severe reaction to adhesive or tape that must be used in the study.
12. Current use of sodium glucose cotransporter 2 (SGLT2) inhibitors or a sulfonylurea drug (use more than 3 months prior to enrollment is acceptable).
13. If using GLP1 agonist, pramlintide, or metformin drugs must be on a stable dose for 3 months prior to enrollment (as per inclusion criterion #8, must be willing to discontinue use of GLP-1 agonist or pramlintide while using the iLet BP system during the randomized clinical trial).
14. Pregnant (positive urine human chorionic gonadotropin [hCG]), breast feeding, plan to become pregnant in the next 3 months, or sexually active without use of contraception. If the visit is conducted virtually, a pregnancy test will be provided to the patient and verbal report of the result will be acceptable.
15. For adults ≥18 years old, most recent (must be within the last 2 years) estimated glomerular filtration rate (eGFR) <30 ml/min OR currently in renal failure on dialysis. If no eGFR is available for an adult patient during the last 2 years, one must be obtained to confirm eligibility
16. Presence of a medical condition or use of a medication that, in the judgment of the investigator, clinical protocol chair, or medical monitor, could compromise the results of the study or the safety of the patient. Conditions to be considered by the investigator may include the following:
    - Alcohol or drug abuse
    - Use of prescription drugs that may dull the sensorium, reduce sensitivity to symptoms of hypoglycemia, or hinder decision making during the period of participation in the study
    - Coronary artery disease that is not stable with medical management, including unstable angina, angina that prevents moderate exercise (e.g. climbing a flight of stairs) despite medical management, or within the last 12 months before screening a history of myocardial infarction, percutaneous coronary intervention, enzymatic lysis of a presumed coronary occlusion, or coronary artery bypass grafting
    - Congestive heart failure with New York Heart Association (NYHA) Functional Classification III or IV
    - History of transient ischemic attack (TIA) or stroke in the last 12 months
    - Untreated or inadequately treated mental illness
    - History of eating disorder within the last 2 years, such as anorexia, bulimia, or diabulemia or omission of insulin to manipulate weight
    - History of intentional, inappropriate administration of insulin leading to severe hypoglycemia requiring treatment
17. Employed by, or having immediate family members employed by Beta Bionics, or being directly involved in conducting the clinical trial, 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.

Table S2. Patient Characteristics at Baseline

	BP Group (N=219)	SC Group (N=107)
Age (year)		
Mean (SD)	28 (19)	28 (20)
<18	112 (51%)	53 (50%)
18 to <25	16 (7%)	7 (7%)
25 to <45	38 (17%)	21 (20%)
45 to <60	33 (15%)	13 (12%)
≥60	20 (9%)	13 (12%)
Range	6 to 73	6 to 79
Diabetes Duration (year)		
Mean (SD)	16 (14)	18 (15)
Range	1 to 59	1 to 66
Glycated Hemoglobin at Randomization (%) [a]		
Mean (SD)	7.9 (1.2)	7.7 (1.1)
≤7.0	55 (25%)	30 (28%)
7.1 to 7.4	33 (15%)	13 (12%)
7.5 to 9.4	112 (51%)	56 (53%)
≥9.5	19 (9%)	7 (7%)
Range	5.5 to 13.1	5.5 to 11.3
Sex – Female *n (%)*	107 (49%)	41 (38%)
Race/Ethnicity Group *n (%)*		
White non-Hispanic	157 (72%)	83 (78%)
Black non-Hispanic	27 (12%)	5 (5%)
Hispanic or Latino	23 (11%)	11 (10%)
Asian	2 (<1%)	3 (3%)
American Indian/Alaskan Native	1 (<1%)	1 (<1%)
More than one race	7 (3%)	4 (4%)
Unknown/not reported	2 (<1%)	0 (0%)
Annual Household Income *n (%)*		
< $25,000	6 (3%)	2 (2%)
$25,000 - <$35,000	7 (3%)	6 (6%)
$35,000 - <$50,000	11 (5%)	4 (4%)
$50,000 - <$75,000	26 (12%)	9 (8%)
$75,000 - <$100,000	27 (12%)	16 (15%)
$100,000 - <$200,000	76 (35%)	29 (27%)
≥ $200,000	48 (22%)	23 (21%)
Unknown/Does not wish to provide	18 (8%)	18 (17%)
Education *n (%)*		
<Bachelor's	72 (33%)	37 (35%)
Bachelor's	76 (35%)	39 (36%)
>Bachelor's	68 (31%)	28 (26%)
Unknown/Does not wish to provide	3 (1%)	3 (3%)
Health Insurance *n (%)*		
Private	184 (84%)	85 (79%)
Medicare/Medicaid	25 (11%)	14 (13%)
Other Government Insurance	8 (4%)	6 (6%)
None	0 (0%)	1 (<1%)

Did not provide/Unknown	2 (<1%)	1 (<1%)
Body Mass Index [b]		
Value (age ≥18 yr; kg/m^2) *Mean (SD)*	28.9 (5.5)	29.1 (6.9)
Percentile (age <18 yr; %) *Mean (SD)*	74% (24%)	66% (27%)
Underweight *n (%)*	0 (0%)	4 (4%)
Normal Weight *n (%)*	93 (42%)	53 (50%)
Overweight *n (%)*	66 (30%)	22 (21%)
Obese *n (%)*	60 (27%)	28 (26%)
Insulin/CGM Device Use *n (%)*		
Multiple daily injections without CGM	20 (9%)	6 (6%)
Multiple daily injections with CGM	51 (23%)	33 (31%)
Pump without CGM	5 (2%)	4 (4%)
Pump with CGM (without automation)	66 (30%)	27 (25%)
Pump with predictive low glucose suspend feature	9 (4%)	5 (5%)
Hybrid Closed-Loop System [c]	68 (31%)	32 (30%)
Currently Using CGM *n (%)*	194 (89%)	97 (91%)
***c*-Peptide (ng/mL)** [d]		
Mean (SD)	0.043 (0.154)	0.025 (0.072)
<0.007 *n (%)*	154 (79%)	80 (82%)
Total Daily Insulin (Units per kg per day) *Median (IQR)*	0.75 (0.57, 1.00)	0.75 (0.56, 0.94)
Time Since Most Recent Severe Hypoglycemia Event *n (%)*		
Never had an event	141 (64%)	57 (53%)
<3 months ago	5 (2%)	0 (0%)
3 to <6 months ago	1 (<1%)	2 (2%)
≥6 months ago	72 (33%)	48 (45%)
Time Since Last Diabetic Ketoacidosis Event *n (%)*		
Never had an event	122 (56%)	51 (48%)
<3 months ago	1 (<1%)	1 (<1%)
3 to <6 months ago	1 (<1%)	0 (0%)
≥6 months ago	95 (43%)	55 (51%)
Non-insulin Blood Glucose Control Medications Taken *n (%)*		
None	209 (95%)	105 (98%)
Metformin	8 (4%)	2 (2%)
GLP1 Agonist	2 (<1%)	0 (0%)

Abbreviations: IQR, interquartile range; SD, standard deviation

a – Glycated hemoglobin at randomization missing for 1 patient in the SC group and no patients in the BP group.

b – The underweight, normal weight, overweight, and obese body mass index categories for patients aged ≥18 years are: <18.5, 18.5 to <25.0, 25.0 to <30.0, and ≥30.0 kg/m^2, respectively. The underweight, normal weight, overweight, and obese body mass index percentile categories for patients aged <18 years are: <5th percentile, 5th to <85th percentile, 85th to <95th percentile, and ≥95th percentile, respectively (calculated using the 2000 CDC growth charts).

c –Hybrid closed-loop systems used: BP group: 17 Medtronic 670G/770G and 51 Tandem Control-IQ. SC group: 12 Medtronic 670G/770G and 20 Tandem Control-IQ

d – C-Peptide at randomization missing for 23 patients in the BP group and 10 patients in the SC group.

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	A recruitment strategy was followed to enroll a cohort what would be broadly representative of the U.S. population of youth and adults with T1D. Age ranged from 6 to 79 years old. The study cohort was racially and ethnically diverse, with 26% of the cohort being of a racial or ethnicity minority. Baseline glycated hemoglobin levels ranged from 5.5% to 13.1%. About one-third of patients were using multiple daily injections of insulin, one-third an insulin pump without automation, and one-third a hybrid-closed loop system.

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 either the patient or for young children by their 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.

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Table S4. Reasons for and Timing of Discontinuation of Bionic Pancreas

Cohort	Study Day [a]	Pre-study Insulin Delivery Method [b]	Baseline Glycated Hemoglobin (%)	Baseline Mean Glucose (mg/dL)	Baseline Time <54 mg/dL	Reason for Discontinuing BP Use
Adult	3	HCL	6.5	162	0.30%	Hypoglycemia
Pediatric	7	HCL	6.4	154	0.44%	Hyperglycemia
Adult	15	HCL	8.6	206	0.00%	Issues with iLet pump
Adult	19	Pump without automation	8.3	198	0.07%	Dissatisfaction with glucose control (described as “erratic glucose levels and hypoglycemia”)
Adult	19	HCL	7.5	143	0.35%	Dissatisfaction with glucose control (described as “glycemic rollercoaster”)
Pediatric	20	Pump without automation	7.8	169	2.49%	Frequent hypoglycemia
Pediatric	30	HCL	8.6	211	0.05%	Investigator decision after attempted suicide
Adult	37	MDI	7.4	217	0.00%	Dissatisfaction with glucose control (described as “frequent high and low glucose levels”)
Adult *	42	HCL	6.6	139	0.44%	Withdrew from study due to family emergency
Adult *	42	HCL	6.5	124	1.41%	Dissatisfaction with glucose control (described as “frequent high and low glucose levels”)
Adult *	43	MDI	8.0	185	0.00%	Dissatisfaction with glucose control (described as “frequent post-meal hyperglycemia”)
Pediatric	50	MDI	11.5	290	0.00%	Investigator decision after intentional over delivery of insulin as an attempt to inflict self-harm
Adult	62	Pump without automation	7.9	169	0.05%	Multiple infusion set failures and hyperglycemia
Adult	70	HCL	6.3	172	0.07%	Frequent hypoglycemia

Pediatric	70	Pump without automation	8.9	191	0.30%	Frequent hypoglycemia
Adult	76	MDI	11.1	307	0.40%	Severe hypoglycemic event
Pediatric	85	Pump without automation	9.3	248	0.70%	iLet would not turn on and end of study imminent
Pediatric	86	MDI	8.1	179	0.65%	iLet would not turn on and end of study imminent
Pediatric	88	MDI	9.2	239	0.30%	iLet would not turn on and end of study imminent

a-Study Day is the last day with iLet data

b-MDI=multiple daily injections, HCL= hybrid closed loop system

*Patient withdrew from the study. All other patients discontinued the BP but remained in the trial through 13 weeks

Table S5. Summary of Device Use

A. Bionic Pancreas Use in Bionic Pancreas Group (N=219)

BASED ON 13 WEEKS OF POSSIBLE USE*	
Autonomous Dosing with or without CGM Input **	
Median (IQR)	96% (92%, 98%)
≥95% *n (%)*	124 (57%)
90-<95% *n (%)*	53 (24%)
80-<90% *n (%)*	22 (10%)
60-<80% *n (%)*	9 (4%)
<60% *n (%)*	11 (5%)
Autonomous Dosing with CGM Input	
Median (IQR)	89% (83%, 92%)
≥95% *n (%)*	9 (4%)
90 to <95% *n (%)*	82 (37%)
80 to<90% *n (%)*	89 (41%)
60 to <80% *n (%)*	24 (11%)
<60% *n (%)*	15 (7%)
BASED ON TIME WHEN BP WAS IN USE	
% Autonomous Dosing with or without CGM Input**	
Median (IQR)	97% (94%, 98%)
≥95% *n (%)*	142 (65%)
90 to <95% *n (%)*	58 (26%)
80 to <90% *n (%)*	19 (9%)
<80% *n (%)*	0 (0%)
Autonomous Dosing with CGM Input	
Median (IQR)	90% (86%, 93%)
≥95% *n (%)*	11 (5%)
90 to <95% *n (%)*	94 (43%)
80 to 90% *n (%)*	96 (44%)
60 to <80% *n (%)*	18 (8%)
<60% *n (%)*	0 (0%)

** Denominator is total possible time in which could have used the device. For patients who completed 13 weeks and did not discontinue the BP, this was the 13-week study follow-up period; for patients who dropped, the follow-up period ended at 13 weeks or latest contact date, whichever occurred earlier. The numerator is the total amount of time the iLet insulin-only feature was continuously on.*

***Reasons for autonomous dosing not occurring while iLet was on included empty cartridge, cartridge change in progress, occlusion alarm active, pause insulin active, motor alarm active.*

B. CGM Use in Standard Care Group (N=107)

% of Time CGM Used During 13 Weeks*	
Median (IQR)	96% (91%, 98%)
≥95% *n (%)*	62 (58%)
90 to <95% *n (%)*	23 (21%)
80 to <90% *n (%)*	17 (16%)
60 to <80% *n (%)*	4 (4%)
<60% *n (%)*	1 (<1%)

** Denominator is total possible time in which patient could have used the CGM. Sensor warmup time is included in the denominator, and thus the reported percentage is a conservative estimate of the percent time in which CGM is used.*

Table S6. Initial and During Use Glucose Target

Glucose Target	Initial glucose target %	During follow-up use glucose target [a] %
100 mg/dL	0%	3%
110 mg/dL	0%	20%
120 mg/dL	86%	60%
130 mg/dL	14%	17%

a – The glucose targets were described in the user interface as "Lower", "Usual", and "Higher", which by default were 110, 120, and 130 mg/dL, respectively. The study investigators had the option to offset the targets downward by 10 mg/dL if there was minimal hypoglycemia and the mean glucose was higher than desired when the "Lower" target was set to 110 mg/dL. This option required access by the investigator to a password protected screen that could not be accessed by the patients and was rarely used. A glucose target of 140 mg/dL was inadvertently set by a clinical site for two patients and was used for 0.4% of the time overall during follow-up.

Table S7. Estimated Carbohydrate Content Based on Type of Meal

	Estimate of Carbohydrate Content		
	Less	**Usual**	**More**
Breakfast (N=15,009)	19%	61%	19%
Lunch (N=20,138)	21%	59%	19%
Dinner (N=21,553)	21%	54%	25%

Table S8. Summary of Unscheduled Visits and Contacts in Randomized Clinical Trial Phase

	BP (N= 219)	**SC (N= 107)**
Total Number of Unscheduled Visits/Contacts	551	53
Number of unscheduled visits/contacts per patient *n (%)*		
0	45 (21%)	73 (68%)
1	57 (26%)	20 (19%)
2	44 (20%)	10 (9%)
3	30 (14%)	3 (3%)
4	11 (5%)	1 (<1%)
5-9	26 (12%)	0 (0%)
10-14	5 (2%)	0 (0%)
15-19	0 (0%)	0 (0%)
≥20	1 (<1%)	0 (0%)
Total Number of Unscheduled Visits	64	12
Number of unscheduled visits per patient *n (%)*		
0	166 (76%)	98 (92%)
1	44 (20%)	7 (7%)
2	7 (3%)	1 (<1%)
3	2 (<1%)	1 (<1%)
Total Number of Unscheduled Contacts	487	41
Number of unscheduled contacts per patient *n (%)*		
0	61 (28%)	76 (71%)
1	60 (27%)	22 (21%)
2	32 (15%)	8 (7%)
3	27 (12%)	1 (<1%)
4	11 (5%)	0 (0%)
5-9	23 (11%)	0 (0%)
10-14	4 (2%)	0 (0%)
15-19	0 (0%)	0 (0%)
≥20	1 (<1%)	0 (0%)

At least one unscheduled visit or contact occurred for 174 (79%) of 219 patients in the BP group and 34 (32%) of 107 in the SC group.

Table S9. Summary of Reasons for Unscheduled Visits and Contacts in Randomized Clinical Trial Phase

Counting number of contacts/visits, not number of patients.

	BP (N= 219)	SC (N= 107)
Unscheduled Visit Reason *		
Patient had a potential adverse event	5	0
Patient needed additional device training	3	0
Patient needed additional protocol training	4	0
Patient had a question or problem with diabetes management	5	0
Patient had a potential device deficiency/issue	28	0
Patient needed study supplies	26	7
Other	14	5
Unscheduled Contact Reason *		
Patient had a potential adverse event	81	6
Patient needed additional device training	45	1
Patient needed additional protocol training	25	2
Patient had a question or problem with diabetes management	179	4
Patient had a potential device deficiency/issue	141	8
Patient needed study supplies	34	5
Other	112	15

* Each unscheduled contact/visit may have had more than one reason

Table S10. Secondary Glycated Hemoglobin Outcomes

	BP (N=212)	SC (N=104)
Glycated hemoglobin <7.0%		
13 Weeks *n (%)*	65 (31%)	27 (26%)
13w Adjusted Risk Difference (95% CI)	8% (-1%, 17%)	
Glycated hemoglobin <7.0% for patients with baseline glycated hemoglobin >7.5%	N=115	N=56
13 Weeks *n (%)*	15 (13%)	2 (4%)
13w Adjusted Risk Difference (95% CI)	17% (1%, 33%)	
Glycated hemoglobin <7.5%		
13 Weeks *n (%)*	128 (60%)	40 (38%)
13w Adjusted Risk Difference (95% CI)	25% (19%, 30%)	
Glycated hemoglobin <8.0%		
13 Weeks *n (%)*	182 (86%)	73 (70%)
13w Adjusted Risk Difference (95% CI)	19% (12%, 26%)	
Glycated hemoglobin >9.0%		
13 Weeks *n (%)*	1 (0%)	13 (13%)
13w Adjusted Risk Difference (95% CI)	-13% (-20%, 14%)	
Glycated hemoglobin improvement from baseline >0.5%		
13 Weeks *n (%)*	100 (47%)	13 (13%)
13w Adjusted Risk Difference (95% CI)	30% (24%, 36%)	
Glycated hemoglobin improvement from baseline >1.0%		
13 Weeks *n (%)*	55 (26%)	5 (5%)
13w Adjusted Risk Difference (95% CI)	18% (10%, 23%)	
Glycated hemoglobin relative improvement from baseline >10%		
13 Weeks *n (%)*	72 (34%)	5 (5%)
13w Adjusted Risk Difference (95% CI)	26% (18%, 33%)	
Glycated hemoglobin improvement from baseline >1.0% or Glycated hemoglobin <7.0%		
13 Weeks *n (%)*	108 (51%)	30 (29%)
13w Adjusted Risk Difference (95% CI)	22% (10%, 34%)	

Adjusted risk difference computed from a marginal logistic regression model adjusting for central lab glycated hemoglobin at randomization and age at randomization with a compound symmetry covariance structure to handle the patient dependence within site. A 95% confidence interval for the treatment group adjusted risk difference (BP minus SC) was produced using parametric bootstrapping. Confidence intervals were adjusted using the Benjamini-Hochberg adaptive false discovery rate correction procedure, but confidence intervals should not be used in place of hypothesis testing as the family-wise error rate was not controlled.

Table S11. Secondary Binary CGM Outcomes and Composite Outcomes

	BP (N=218)	SC (N=107)
% Time in range 70-180 mg/dL >70%		
13 Weeks *n (%)*	56 (26%)	23 (21%)
13w Adjusted Risk Difference (95% CI)	5% (-1%, 11%)	
% Time in range 70-180 mg/dL improvement from baseline ≥5%		
13 Weeks *n (%)*	159 (73%)	55 (51%)
13w Adjusted Risk Difference (95% CI)	23% (14%, 33%)	
% Time in range 70-180 mg/dL improvement from baseline ≥10%		
13 Weeks *n (%)*	146 (67%)	43 (40%)
13w Adjusted Risk Difference (95% CI)	29% (18%, 40%)	
% Time <70 mg/dL <4%		
13 Weeks *n (%)*	194 (89%)	86 (80%)
13w Adjusted Risk Difference (95% CI)	10% (3%, 17%)	
% Time <54 mg/dL <1%		
13 Weeks *n (%)*	190 (87%)	88 (82%)
13w Adjusted Risk Difference (95% CI)	7% (0%, 14%)	
Improvement in glycated hemoglobin > 0.5% without an increase in time < 54 mg/dL by > 0.5% OR improvement in time < 54 mg/dL by > 0.5% without an increase in glycated hemoglobin by > 0.5%	N=212	N=103
13 Weeks *n (%)*	104 (49%)	15 (15%)
13w Adjusted Risk Difference (95% CI)	30% (21%, 37%)	
Improvement in time 70–180 mg/dL by >10% without an increase in time < 54 mg/dL by > 0.5% OR improvement in time < 54 mg/dL by > 0.5% without a decrease in time 70–180 mg/dL by > 10%		
13 Weeks *n (%)*	120 (55%)	25 (23%)
13w Adjusted Risk Difference (95% CI)	31% (21%, 40%)	
Mean glucose <154 mg/dL and % time <54 mg/dL <1%		
13 Weeks *n (%)*	46 (21%)	17 (16%)
13w Adjusted Risk Difference (95% CI)	6% (0%, 11%)	
% Time in range 70-180 mg/dL >70% and % time <54 mg/dL <1%		
13 Weeks *n (%)*	52 (24%)	16 (15%)
13w Adjusted Risk Difference (95% CI)	10% (4%, 16%)	

Adjusted risk difference computed from a marginal logistic regression model adjusting for the baseline version of the outcome and age at randomization with a compound symmetry covariance structure to handle the patient dependence within site. A 95% confidence interval for the treatment group adjusted risk difference (BP minus SC) was produced using parametric bootstrapping. Confidence intervals were adjusted using the Benjamini-Hochberg

adaptive false discovery rate correction procedure, but confidence intervals should not be used in place of hypothesis testing as the family-wise error rate was not controlled.

Table S12. Secondary Continuous CGM Outcomes

	BP	SC
Hours of CGM data		
Baseline (N=219 BP, 107 SC) *median (IQR)*	329 (315, 336)	332 (315, 336)
Follow Up (13 weeks; N=218 BP, 107 SC) *median (IQR)*	1990 (1887, 2056)	2090 (1984, 2130)
% Time in range 70-140 mg/dL		
Baseline *mean (SD)*	30% (15%)	30% (16%)
Follow-Up (13 weeks) *mean (SD)*	39% (8%)	33% (13%)
13w Adjusted Group Difference (95% CI) [c]	6% (4%, 8%)	
% Time in range 70-120 mg/dL		
Baseline *mean (SD)*	19% (11%)	19% (12%)
Follow-Up (13 weeks) *mean (SD)*	23% (6%)	21% (10%)
13w Adjusted Group Difference (95% CI) [c]	2% (1%, 4%)	
% Time <60 mg/dL		
Baseline *median (IQR)*	0.4% (0.1%, 1.2%)	0.4% (0.1%, 1.0%)
Follow-Up (13 weeks) *median (IQR)*	0.7% (0.4%, 1.1%)	0.6% (0.3%, 1.3%)
13w Adjusted Group Difference (95% CI) [c]	-0.0% (-0.1%, 0.1%)	
Area over the curve 70 mg/dL		
Baseline *median (IQR)*	0.13 (0.03, 0.32)	0.12 (0.03, 0.25)
Follow-Up (13 weeks) *median (IQR)*	0.18 (0.10, 0.29)	0.16 (0.07, 0.34)
13w Adjusted Group Difference (95% CI) [c]	-0.00 (-0.03, 0.02)	
Low blood glucose index (LBGI)		
Baseline *median (IQR)*	0.43 (0.19, 0.84)	0.42 (0.21, 0.83)
Follow-Up (13 weeks) *median (IQR)*	0.54 (0.38, 0.76)	0.52 (0.31, 0.88)
13w Adjusted Group Difference (95% CI) [c]	-0.00 (-0.06, 0.06)	
Hypoglycemic event rate per week [a]		
Baseline *median (IQR)*	0.50 (0.00, 1.10)	0.00 (0.00, 1.00)
Follow-Up (13 weeks) *median (IQR)*	0.68 (0.26, 1.19)	0.48 (0.22, 1.31)
13w Adjusted Group Difference (95% CI) [c]	0.00 (-0.12, 0.08)	
Hyperglycemic event rate per week (≥15 min >300 mg/dL) [b]		
Baseline *median (IQR)*	4.5 (2.0, 8.9)	5.1 (1.5, 8.5)
Follow-Up (13 weeks) *median (IQR)*	2.8 (1.4, 5.7)	4.6 (1.7, 8.5)
13w Adjusted Group Difference (95% CI) [c]	-0.9 (-1.4, -0.4)	
Hyperglycemic event rate per week (≥90 min >300 mg/dL in 120 minutes) [d]		
Baseline *median (IQR)*	2.1 (0.5, 4.6)	2.0 (0.5, 5.1)
Follow-Up (13 weeks) *median (IQR)*	0.9 (0.4, 2.0)	2.1 (0.6, 4.2)
13w Adjusted Group Difference (95% CI) [c]	-0.7 (-1.0, -0.4)	

	BP	SC
% Time > 300 mg/dL		
Baseline *median (IQR)*	5.5% (1.4%, 13.2%)	6.4% (1.3%, 16.3%)
Follow-Up (13 weeks) *median (IQR)*	2.4% (1.2%, 4.7%)	6.0% (1.6%, 11.6%)
13w Adjusted Group Difference (95% CI) [c]	-1.9% (-2.8%, -1.2%)	
Area under the curve 180 mg/dL		
Baseline *median (IQR)*	28.7 (14.1, 45.5)	30.0 (13.2, 52.2)
Follow-Up (13 weeks) *median (IQR)*	17.2 (11.5, 23.1)	26.2 (13.1, 42.2)
13w Adjusted Group Difference (95% CI) [c]	-7.7 (-10.2, -5.6)	
High blood glucose index (HBGI)		
Baseline *median (IQR)*	10.7 (6.8, 15.4)	10.9 (6.1, 17.0)
Follow-Up (13 weeks) *median (IQR)*	7.4 (5.9, 9.1)	10.0 (6.4, 14.3)
13w Adjusted Group Difference (95% CI) [c]	-2.3 (-3.0, -1.7)	
Mean of daily difference		
Baseline *mean (SD)*	30 (12)	31 (13)
Follow-Up (13 weeks) *mean (SD)*	20 (7)	30 (11)
13w Adjusted Group Difference (95% CI) [c]	-9 (-11, -8)	
Blood glucose risk index (BGRI = LBGI + HBGI)		
Baseline *median (IQR)*	11.1 (7.7, 15.8)	11.6 (7.6, 17.4)
Follow-Up (13 weeks) *median (IQR)*	8.0 (6.7, 9.7)	10.7 (6.9, 14.9)
13w Adjusted Group Difference (95% CI) [c]	-2.4 (-3.0, -1.8)	

a – A CGM-measured hypoglycemic event is defined as ≥15 consecutive minutes with a CGM sensor value <54 mg/dL. The event ends when there is ≥15 consecutive minutes with a CGM sensor value ≥70 mg/dL, at which point the patient becomes eligible for another hypoglycemic event.

b - A CGM-measured hyperglycemic event is defined as ≥15 consecutive minutes with a CGM glucose value >300 mg/dL. The hyper event ends when there are ≥15 consecutive minutes with a CGM glucose value ≤250 mg/dL, at which point the patient becomes eligible for another hyper event.

c –Adjusted group differences computed from mixed effect models adjusting for baseline value, age at randomization, and site (random effect). Missing data were handled using direct likelihood analyses. Confidence intervals were adjusted using the Benjamini-Hochberg adaptive false discovery rate correction procedure, but confidence intervals should not be used in place of hypothesis testing as the family-wise error rate was not controlled.

d – A CGM-measured hyperglycemic event is defined as ≥90 cumulative minutes with a CGM sensor value >300 mg/dL within a 120-minute period. The event ends when there is ≥15 consecutive minutes with a CGM sensor value ≤180 mg/dL, at which point the patient becomes eligible for another hyperglycemic event.

Table S13. CGM Outcomes According to Time of Day

	Daytime (06:00 to 23:59)		Nighttime (00:00 to 05:59)	
	BP (N=218)	**SC (N=107)**	**BP (N=218)**	**SC (N=107)**
Hours of CGM Data *median (IQR)*	1481 (1400, 1526)	1568 (1501, 1592)	515 (485, 530)	521 (495, 536)
Mean Glucose mg/dL *mean (SD)*	168 (16)	182 (33)	156 (19)	177 (33)
% Time 70-180 mg/dL *mean (SD)*	62% (9%)	53% (17%)	71% (13%)	56% (19%)
% Time >180 mg/dL *mean (SD)*	36% (10%)	44% (18%)	26% (13%)	41% (20%)
% Time >250 mg/dL *median (IQR)*	9.9% (5.9%, 14.4%)	15.3% (6.9%, 27.6%)	4.5% (2.2%, 8.1%)	14.3% (4.6%, 25.0%)
Glucose SD *mean (SD)*	62 (11)	67 (16)	53 (13)	64 (16)
% Time <70 mg/dL *median (IQR)*	1.8% (1.0%, 3.0%)	1.5% (0.8%, 3.1%)	1.7% (0.9%, 2.8%)	1.6% (0.7%, 3.3%)
% Time <54 mg/dL *median (IQR)*	0.32% (0.12%, 0.57%)	0.23% (0.09%, 0.61%)	0.35% (0.14%, 0.65%)	0.26% (0.07%, 0.58%)
Glucose Coefficient of Variation *mean (SD)*	37% (5%)	37% (5%)	34% (6%)	36% (6%)

Table S14. CGM Outcomes by 4-week Intervals

	Weeks 1-4		Weeks 5-8		Weeks 9-12	
	BP (N=218)	**SC (N=107)**	**BP (N=218)**	**SC (N=107)**	**BP (N=215)**	**SC (N=107)**
Hours of CGM Data *median (IQR)*	624 (590, 641)	652 (620, 661)	617 (585, 638)	652 (620, 660)	617 (580, 634)	647 (613, 657)
Mean Glucose mg/dL *mean (SD)*	164 (15)	179 (31)	165 (17)	182 (34)	166 (18)	182 (35)
% Time 70-180 mg/dL *mean (SD)*	65% (10%)	55% (17%)	64% (10%)	53% (18%)	64% (11%)	54% (18%)
% Time >180 mg/dL *mean (SD)*	33% (9%)	43% (18%)	34% (10%)	44% (18%)	34% (11%)	44% (18%)
% Time >250 mg/dL *median (IQR)*	8.4% (4.8%, 12.7%)	14.3% (6.0%, 24.3%)	8.6% (5.4%, 13.5%)	14.9% (6.2%, 27.6%)	8.7% (5.2%, 13.0%)	14.9% (6.1%, 27.5%)
Glucose SD *mean (SD)*	59 (11)	66 (15)	61 (12)	67 (16)	61 (13)	67 (16)
% Time <70 mg/dL *median (IQR)*	1.7% (0.9%, 2.9%)	1.7% (0.8%, 3.0%)	1.7% (0.9%, 2.9%)	2.0% (0.9%, 3.1%)	1.8% (1.1%, 3.0%)	1.7% (0.9%, 3.4%)
% Time <54 mg/dL *median (IQR)*	0.26% (0.09%, 0.55%)	0.24% (0.08%, 0.65%)	0.33% (0.12%, 0.63%)	0.27% (0.07%, 0.63%)	0.32% (0.15%, 0.68%)	0.27% (0.08%, 0.73%)
Glucose Coefficient of Variation *mean (SD)*	36% (5%)	37% (5%)	36% (5%)	37% (6%)	36% (5%)	37% (5%)

Table S15. Efficacy Outcomes Excluding Pre-Study Users of a Hybrid Closed-loop System

Metric	BP	SC
Glycated Hemoglobin (%)		
Baseline (N=151 BP, 74 SC) *mean (SD)*	8.0 (1.3)	7.8 (1.2)
Follow-Up (13 weeks; N=147 BP, 73 SC) *mean (SD)*	7.3 (0.6)	7.8 (1.1)
Change from baseline to week 13 (N=147 BP, 72 SC) *mean (SD)*	-0.7 (1.0)	-0.1 (0.6)
13w Adjusted Group Difference (95% CI) [a]	-0.6 (-0.7, -0.4)	
Hours of CGM Data		
Baseline (N=151 BP, 75 SC) *median (IQR)*	328 (316, 336)	333 (318, 336)
Follow Up (13 weeks; N=151 BP, 75 SC) *median (IQR)*	1982 (1878, 2057)	2093 (1984, 2130)
Mean Glucose mg/dL		
Baseline *mean (SD)*	193 (43)	193 (43)
Follow-Up (13 weeks) *mean (SD)*	165 (15)	184 (34)
13w Adjusted Group Difference (95% CI) [a]	-19 (-24, -15)	
Glucose SD mg/dL		
Baseline *mean (SD)*	70 (16)	70 (18)
Follow-Up (13 weeks) *mean (SD)*	61 (12)	70 (15)
13w Adjusted Group Difference (95% CI) [a]	-8 (-11, -6)	
Glucose Coefficient of Variation (%)		
Baseline *mean (SD)*	37% (6%)	36% (6%)
Follow-Up (13 weeks) *mean (SD)*	37% (5%)	38% (5%)
13w Adjusted Group Difference (95% CI) [a]	-1.0% (-2.0%, 0.0%)	
% Time 70-180 mg/dL		
Baseline *mean (SD)*	47% (19%)	48% (20%)
Follow-Up (13 weeks) *mean (SD)*	64% (9%)	51% (17%)
13w Adjusted Group Difference (95% CI) [a]	13% (11%, 16%)	
% Time >180 mg/dL		
Baseline *mean (SD)*	50% (20%)	49% (21%)
Follow-Up (13 weeks) *mean (SD)*	34% (9%)	46% (18%)
13w Adjusted Group Difference (95% CI) [a]	-13% (-15%, -10%)	
% Time >250 mg/dL		
Baseline *median (IQR)*	19.2% (9.2%, 30.7%)	19.6% (8.5%, 33.8%)
Follow-Up (13 weeks) *median (IQR)*	9.2% (5.8%, 13.7%)	18.2% (8.8%, 26.9%)
13w Adjusted Group Difference (95% CI) [a]	-7.6% (-9.6%, -5.7%)	
% Time <70 mg/dL		
Baseline *median (IQR)*	1.7% (0.5%, 3.5%)	1.5% (0.5%, 2.9%)
Follow-Up (13 weeks) *median (IQR)*	1.7% (1.0%, 3.0%)	2.1% (0.8%, 3.9%)
13w Adjusted Group Difference (95% CI) [a]	-0.3% (-0.6%, 0.1%)	
% Time <54 mg/dL		
Baseline *median (IQR)*	0.25% (0.03%, 0.66%)	0.22% (0.03%, 0.46%)
Follow-Up (13 weeks) *median (IQR)*	0.32% (0.15%, 0.61%)	0.28% (0.14%, 0.73%)
Change from Baseline to Week 13 (N=151 BP, 75 SC) *median (IQR)*	0.07% (-0.24%, 0.27%)	0.10% (-0.01%, 0.39%)
13w Adjusted Group Difference (95% CI) [a]	-0.03% (-0.11%, 0.03%)	

a –Adjusted group differences computed from mixed effect models adjusting for baseline value, age at randomization, and site (random effect). Missing data were handled using direct likelihood analyses. Due to skewness in the distributions, % time >250, <70, and <54 mg/dL were transformed using a rank normal transformation. Confidence intervals were adjusted using the Benjamini-Hochberg adaptive false discovery rate correction procedure, but confidence intervals should not be used in place of hypothesis testing as the family-wise error rate was not controlled.

Table S16. Efficacy Outcomes for Patients with Baseline Glycated Hemoglobin >7.0%

Metric	BP	SC
Glycated Hemoglobin (%)		
Baseline (N=164 BP, 76 SC) *mean (SD)*	8.3 (1.1)	8.2 (0.9)
Follow-Up (13 weeks; N=161 BP, 74 SC) *mean (SD)*	7.5 (0.6)	8.1 (0.8)
Change from baseline to week 13 (N=161 BP, 74 SC) *mean (SD)*	-0.8 (0.9)	-0.1 (0.6)
13w Adjusted Group Difference (95% CI) [a]	-0.7 (-0.9, -0.5)	
Hours of CGM Data		
Baseline (N=164BP, 76 SC) *median (IQR)*	327 (312, 336)	333 (318, 336)
Follow Up (13 weeks; N=164 BP, 76 SC) *median (IQR)*	1982 (1892, 2055)	2084 (1979, 2117)
Mean Glucose mg/dL		
Baseline *mean (SD)*	199 (38)	207 (37)
Follow-Up (13 weeks) *mean (SD)*	168 (14)	194 (28)
13w Adjusted Group Difference (95% CI) [a]	-24 (-28, -20)	
Glucose SD mg/dL		
Baseline *mean (SD)*	72 (14)	75 (15)
Follow-Up (13 weeks) *mean (SD)*	63 (11)	73 (13)
13w Adjusted Group Difference (95% CI) [a]	-9 (-12, -7)	
Glucose Coefficient of Variation (%)		
Baseline *mean (SD)*	37% (6%)	36% (6%)
Follow-Up (13 weeks) *mean (SD)*	37% (5%)	38% (5%)
13w Adjusted Group Difference (95% CI) [a]	-0.8% (-1.8%, 0.1%)	
% Time 70-180 mg/dL		
Baseline *mean (SD)*	45% (16%)	42% (16%)
Follow-Up (13 weeks) *mean (SD)*	62% (8%)	47% (14%)
13w Adjusted Group Difference (95% CI) [a]	15% (12%, 17%)	
% Time >180 mg/dL		
Baseline *mean (SD)*	53% (17%)	56% (17%)
Follow-Up (13 weeks) *mean (SD)*	36% (9%)	51% (14%)
13w Adjusted Group Difference (95% CI) [a]	-15% (-17%, -12%)	
% Time >250 mg/dL		
Baseline *median (IQR)*	21.3% (12.1%, 33.7%)	25.9% (15.1%, 39.8%)
Follow-Up (13 weeks) *median (IQR)*	10.2% (7.3%, 14.0%)	22.6% (12.1%, 27.8%)
13w Adjusted Group Difference (95% CI) [a]	-8.9% (-10.9%, -7.0%)	
% Time <70 mg/dL		
Baseline *median (IQR)*	1.2% (0.3%, 2.5%)	1.0% (0.3%, 2.1%)
Follow-Up (13 weeks) *median (IQR)*	1.8% (1.0%, 2.7%)	1.4% (0.6%, 2.4%)
13w Adjusted Group Difference (95% CI) [a]	0.1% (-0.1%, 0.4%)	
% Time <54 mg/dL		
Baseline *median (IQR)*	0.18% (0.00%, 0.50%)	0.12% (0.00%, 0.33%)
Follow-Up (13 weeks) *median (IQR)*	0.33% (0.16%, 0.60%)	0.19% (0.11%, 0.53%)
Change from Baseline to Week 13 (N=164 BP, 76 SC) *median (IQR)*	0.13% (-0.02%, 0.33%)	0.10% (-0.01%, 0.24%)
13w Adjusted Group Difference (95% CI) [a]	0.03% (-0.01%, 0.08%)	

a –Adjusted group differences computed from mixed effect models adjusting for baseline value, age at randomization, and site (random effect). Missing data were handled using direct likelihood analyses. Due to a skewed distribution, % time >250, <70, and <54 mg/dL were transformed using a rank normal transformation. Confidence intervals were adjusted using the Benjamini-Hochberg adaptive false discovery rate correction procedure, but confidence intervals should not be used in place of hypothesis testing as the family-wise error rate was not controlled.

Table S17. Glycated Hemoglobin According to Baseline Subgroups

	Baseline				13 Weeks			
	BP		SC		BP		SC	
	N	*Mean (SD)*	*N*	*Mean (SD)*	*N*	*Mean (SD)*	*N*	*Mean (SD)*
Age								
6-12 years	63	7.9 (1.0)	27	7.9 (1.0)	63	7.5 (0.6)	26	8.0 (0.9)
13-17 years	49	8.4 (1.4)	26	7.7 (1.2)	47	7.5 (0.7)	25	7.6 (1.2)
18-25 years	17	8.6 (1.8)	7	7.1 (1.1)	16	7.2 (0.7)	6	6.9 (1.0)
26-49 years	49	7.5 (1.1)	27	7.6 (1.2)	48	7.0 (0.6)	28	7.5 (1.0)
≥50 years	41	7.3 (0.9)	19	7.8 (1.2)	38	7.1 (0.6)	19	7.7 (0.7)
Diabetes Duration								
<20 years	154	8.1 (1.3)	68	7.7 (1.1)	148	7.4 (0.7)	65	7.7 (1.1)
≥20 years	65	7.4 (0.8)	38	7.6 (1.1)	64	7.1 (0.5)	39	7.6 (0.8)
Baseline Glycated Hemoglobin								
<7.0%	49	6.4 (0.3)	27	6.3 (0.4)	45	6.7 (0.5)	26	6.5 (0.5)
7.0 to 7.9%	73	7.4 (0.3)	39	7.5 (0.3)	73	7.2 (0.5)	39	7.5 (0.4)
8.0 to 8.9%	58	8.4 (0.3)	27	8.3 (0.3)	57	7.5 (0.6)	26	8.1 (0.6)
9.0 to 9.9%	28	9.3 (0.3)	10	9.4 (0.3)	28	7.9 (0.6)	10	9.5 (0.8)
≥10.0%	11	11.1 (1.0)	3	10.7 (0.5)	9	7.7 (0.3)	2	9.3 (0.3)
Baseline % Time 70-180 mg/dL								
<70%	180	8.1 (1.2)	81	8.1 (1.0)	175	7.4 (0.7)	80	7.9 (0.9)
≥70%	39	6.7 (0.6)	25	6.4 (0.6)	37	7.0 (0.6)	24	6.7 (0.6)
Baseline % Time <70 mg/dL								
<4%	184	8.0 (1.3)	91	7.8 (1.1)	179	7.3 (0.7)	88	7.7 (1.0)
≥4%	35	7.3 (0.9)	15	7.1 (0.9)	33	7.2 (0.6)	16	7.4 (0.8)
Baseline % Time >180 mg/dL								
<25%	34	6.6 (0.5)	21	6.3 (0.5)	31	7.0 (0.4)	20	6.6 (0.6)
≥25%	185	8.1 (1.2)	85	8.0 (1.0)	181	7.4 (0.7)	84	7.9 (0.9)
Baseline insulin and CGM device use [a]								
MDI without CGM	20	8.6 (1.5)	6	8.5 (1.5)	20	7.2 (0.6)	6	7.7 (0.9)
MDI with CGM	51	8.2 (1.2)	33	7.9 (1.2)	49	7.4 (0.6)	33	8.0 (1.1)
Pump without CGM	5	9.1 (2.4)	3	8.9 (0.7)	4	7.2 (0.8)	4	8.8 (0.8)
Pump with CGM	66	7.8 (1.1)	27	7.5 (1.0)	65	7.3 (0.6)	25	7.4 (0.9)
Pump with CGM and Predictive Low Glucose Suspend Feature	9	6.8 (0.6)	5	7.5 (1.4)	9	7.1 (0.7)	5	7.5 (1.1)
Hybrid Closed Loop System	68	7.5 (0.9)	32	7.4 (1.0)	65	7.3 (0.7)	31	7.3 (0.8)
Sex								
Female	107	7.9 (1.3)	40	7.5 (1.1)	102	7.3 (0.7)	38	7.4 (0.9)
Male	112	7.8 (1.2)	66	7.8 (1.1)	110	7.3 (0.7)	66	7.8 (1.0)
Race/Ethnicity								
Not white non-Hispanic	62	8.3 (1.5)	24	7.9 (0.9)	59	7.5 (0.6)	23	7.9 (0.9)
White non-Hispanic	157	7.7 (1.1)	82	7.6 (1.2)	153	7.2 (0.7)	81	7.6 (1.0)
Body Mass Index [b]								
Underweight	0	NA	4	6.7 (0.8)	0	NA	0	NA
Normal weight	93	7.9 (1.3)	53	7.7 (1.2)	81	7.3 (0.6)	50	7.7 (1.1)
Overweight	66	7.8 (1.3)	22	7.7 (1.2)	61	7.2 (0.7)	23	7.7 (0.9)
Obese	60	8.0 (1.1)	27	7.8 (1.0)	66	7.5 (0.6)	26	7.7 (0.9)
Education								
<Bachelor's	72	8.3 (1.5)	36	7.9 (1.2)	69	7.4 (0.7)	35	7.9 (1.1)
≥Bachelor's	147	7.7 (1.0)	70	7.6 (1.1)	143	7.2 (0.6)	69	7.6 (1.0)
***c*-peptide**								
<0.01 ng/mL	155	7.8 (1.2)	81	7.6 (1.1)	150	7.3 (0.7)	81	7.6 (0.9)
≥0.01 ng/mL	41	8.2 (1.5)	15	8.0 (1.4)	41	7.2 (0.7)	15	8.2 (1.5)

a – MDI=multiple daily injections

b – The underweight, normal weight, overweight, and obese body mass index categories for patients aged ≥18 years are: <18.5, 18.5 to <25.0, 25.0 to <30.0, and ≥30.0 kg/m^2, respectively. The underweight, normal weight, overweight, and obese body mass index percentile categories for patients aged <18 years are: <5th percentile, 5th to <85th percentile, 85th to <95th percentile, and ≥95th percentile, respectively (calculated using the 2000 CDC growth charts).

Table S18. Per-Protocol Analysis: Glycated Hemoglobin Primary Outcome

	BP	SC
Baseline*	N=158	N=99
Glycated Hemoglobin % *mean (SD)*	7.7 (1.0)	7.6 (1.1)
6 weeks	N=157	N=99
Glycated Hemoglobin % *mean (SD)*	7.3 (0.7)	7.5 (1.0)
Change from Baseline (N=157 BP, 99 SC) *mean (SD)*	-0.3 (0.6)	-0.1 (0.3)
13 weeks	N=158	N=99
Glycated Hemoglobin % *mean (SD)*	7.2 (0.6)	7.6 (0.9)
Change from Baseline (N=158 BP, 99 SC) *mean (SD)*	-0.4 (0.8)	-0.0 (0.5)
13w Adjusted Difference (95% CI) [a]	-0.4 (-0.5, -0.3)	

*3 patients had late glycated hemoglobin sample collections at randomization, max collection delay of 9 days after randomization date.

a – Adjusted group difference computed from a mixed effect model adjusting for baseline value, age at randomization, and site (random effect). Missing data were handled using direct likelihood analyses.

Inclusion Criteria for Per-Protocol Analysis

a) Baseline and 13-week glycated hemoglobin central lab measurements available
b) No glucose-lowering medications used other than those acceptable in the protocol
c) No major protocol deviation that could impact outcome measures
d) For patients in the SC group, at least 80% of CGM data available in the 13-week follow-up wear period
e) For patients in the BP group, closed-loop mode was active for at least 80% of the time during the 13 weeks and a meal bolus was announced on average at least 2 times per day when the system was being used.

Table S19. While-On-Treatment Analysis: Primary, Key Secondary, and Hierarchical Outcomes

Metric	BP	SC
Glycated Hemoglobin (%)	N=219	N=106
Baseline (N=219 BP, 106 SC) *mean (SD)*	7.9 (1.2)	7.7 (1.1)
Follow-Up (13 weeks; N=197 BP, 104 SC) *mean (SD)*	7.2 (0.6)	7.7 (1.0)
Change from baseline to week 13 (N=197 BP, 103 SC) *mean (SD)*	-0.6 (0.9)	-0.0 (0.6)
13w Adjusted Group Difference (95% CI) [a]	-0.5 (-0.7, -0.4)	
Hours of CGM Data		
Baseline (N=219 BP, 107 SC) *median (IQR)*	329 (315, 336)	332 (315, 336)
Follow Up (13 weeks; N=217 BP, 107 SC) *median (IQR)*	1992 (1888, 2056)	2090 (1984, 2130)
% Time <54 mg/dL		
Baseline *median (IQR)*	0.21% (0.02%, 0.57%)	0.20% (0.00%, 0.44%)
Follow-Up (13 weeks) *median (IQR)*	0.32% (0.16%, 0.60%)	0.24% (0.13%, 0.63%)
Change from Baseline to Week 13 (N=217 BP, 107 SC) *mean (SD)*	0.09% (-0.12%, 0.31%)	0.10% (-0.05%, 0.31%)
13w Risk-Adjusted Difference (95% CI) [a]	0.00% (-0.05%, 0.04%)	
Mean Glucose mg/dL		
Baseline *mean (SD)*	187 (40)	190 (42)
Follow-Up (13 weeks) *mean (SD)*	164 (14)	181 (32)
13w Adjusted Group Difference (95% CI) [a]	-16 (-20, -13)	
% Time 70-180 mg/dL		
Baseline *mean (SD)*	51% (19%)	51% (20%)
Follow-Up (13 weeks) *mean (SD)*	65% (9%)	54% (17%)
13w Adjusted Group Difference (95% CI) [a]	11% (9%, 13%)	
% Time >180 mg/dL		
Baseline *mean (SD)*	46% (20%)	47% (21%)
Follow-Up (13 weeks) *mean (SD)*	33% (9%)	44% (18%)
13w Adjusted Group Difference (95% CI) [a]	-11% (-13%, -9%)	
% Time >250 mg/dL		
Baseline *median (IQR)*	16.0% (7.0%, 27.3%)	17.8% (6.0%, 33.5%)
Follow-Up (13 weeks) *median (IQR)*	8.3% (5.3%, 12.6%)	14.9% (6.3%, 25.3%)
13w Adjusted Group Difference (95% CI) [a]	-5.3% (-6.9%, -3.8%)	
Glucose SD mg/dL		
Baseline *mean (SD)*	67 (16)	68 (18)
Follow-Up (13 weeks) *mean (SD)*	60 (11)	67 (16)
13w Adjusted Group Difference (95% CI) [a]	-7 (-9, -5)	
% Time <70 mg/dL		
Baseline *median (IQR)*	1.5% (0.5%, 2.8%)	1.4% (0.4%, 2.9%)
Follow-Up (13 weeks) *median (IQR)*	1.8% (1.1%, 2.9%)	1.8% (0.8%, 3.1%)
13w Adjusted Group Difference (95% CI) [a]	-0.0% (-0.3%, 0.2%)	
Glucose Coefficient of Variation (%)		
Baseline *mean (SD)*	36% (6%)	36% (6%)

Metric	BP	SC
Follow-Up (13 weeks) *mean (SD)*	36% (5%)	37% (5%)
13w Adjusted Group Difference (95% CI) [a]	-0.7% (-1.5%, 0.1%)	

a – Adjusted group difference computed from a mixed effect model adjusting for baseline value, age at randomization, and site (random effect). Missing data were handled using direct likelihood analyses. Due to a skewed distribution, % time >250, <70, and <54 mg/dL were transformed using a rank normal transformation.

Table S20. Sensitivity Analyses: Glycated Hemoglobin Primary Outcome

	Glycated Hemoglobin (%)
Covariate Adjustment for Race [a]	
13w Adjusted Group Difference *mean (95% CI)*	-0.5 (-0.6, -0.3)
Covariate Adjustment for Race and Insulin Delivery [a]	
13w Adjusted Group Difference *mean (95% CI)*	-0.5 (-0.6, -0.3)
Complete Case [b]	
Change from Baseline to Week 13, BP versus SC (N=212 BP, 103 SC) *mean (SD)*	-0.6 (1.0) versus -0.0 (0.6)
13w Adjusted Group Difference *mean (95% CI)*	-0.4 (-0.6, -0.3)
Multiple Imputation with Pattern Mixture Model [c]	
13w Adjusted Group Difference *mean (95% CI)*	-0.5 (-0.6, -0.3)
Treatment Group Switched for Non-randomized Patients [d]	
13w Adjusted Group Difference *mean (95% CI)*	-0.5 (-0.6, -0.3)

a – Due to the treatment group imbalance on race, indicator of White non-Hispanic was added as a covariate to the primary analysis model. A separate sensitivity analysis added indicator of White non-Hispanic and pre-study insulin modality as covariates to the primary analysis model. Missing data were handled using direct likelihood analyses.

b – Complete case analysis was assessed through a mixed effect model adjusting for baseline value, central lab glycated hemoglobin at randomization, age at randomization, and site (random effect).

c – Multiple imputations with pattern mixture model imputed missing data based on age and glycated hemoglobin utilizing sequential regression assuming dropout trajectory is the same as the SC trajectory. The imputed datasets were analyzed through a mixed effect model adjusted for central lab glycated hemoglobin at randomization, age at randomization, and site (random effect).

d – One non-randomized patients assigned to BP group due to a protocol deviation was re-analyzed as part of SC group. Adjusted group difference computed from a mixed effect model adjusting for baseline value, age at randomization, and site (random effect). Missing data were handled using direct likelihood analyses.

Table S21. Glycated Hemoglobin by Site

Site	Baseline				Week 13			
	BP-A/L		SC		BP-A/L		SC	
	N	*Mean (SD)*	*N*	*Mean (SD)*	*N*	*Mean (SD)*	*N*	*Mean (SD)*
A	18	8.5 (1.7)	9	7.8 (1.0)	17	7.3 (0.7)	9	7.7 (0.8)
B	17	7.3 (0.8)	9	7.4 (1.1)	17	6.9 (0.5)	9	7.4 (1.2)
C	16	8.2 (1.4)	8	8.1 (1.2)	14	7.4 (0.5)	6	8.0 (0.6)
D	15	7.9 (0.6)	7	7.8 (1.2)	15	7.6 (0.5)	7	8.0 (0.9)
E	15	8.6 (0.9)	7	8.0 (1.3)	15	7.4 (0.7)	6	7.8 (1.4)
F	14	7.6 (1.5)	7	7.1 (0.8)	12	7.0 (0.5)	7	7.4 (1.1)
G	14	7.5 (0.7)	7	7.5 (1.1)	14	7.4 (0.4)	7	7.2 (0.8)
H	14	8.0 (0.8)	7	7.9 (1.1)	14	7.3 (0.5)	7	7.7 (0.9)
I	13	8.1 (0.9)	6	8.2 (1.2)	13	7.7 (0.7)	6	7.9 (0.9)
J	12	7.3 (1.0)	5	7.6 (1.3)	12	7.1 (0.7)	6	7.8 (1.0)
K	13	9.3 (1.4)	5	7.1 (0.7)	13	7.6 (0.7)	5	7.2 (0.6)
L	12	8.0 (1.3)	6	7.5 (0.9)	12	7.6 (0.6)	6	7.7 (0.8)
M	11	7.1 (1.0)	6	8.2 (1.0)	11	7.3 (0.8)	6	8.4 (1.7)
N	12	7.1 (0.9)	5	7.7 (0.7)	12	6.8 (0.6)	5	7.2 (0.5)
O	9	8.4 (1.1)	4	8.4 (0.9)	9	7.6 (0.9)	4	8.4 (1.0)
P	8	7.1 (0.5)	4	8.0 (2.4)	8	7.0 (0.5)	4	7.6 (1.3)
Q	6	6.8 (0.7)	4	6.3 (0.7)	4	6.7 (0.7)	4	6.7 (0.8)

Table S22. Percent Time <54 mg/dL by Site

	Baseline				Week 13			
	BP-A/L		SC		BP-A/L		SC	
Site	*N*	*Median (IQR)*	*N*	*Median (IQR)*	*N*	*Median (IQR)*	*N*	*Median (IQR)*
A	18	0.04% (0.00%, 0.23%)	9	0.25% (0.13%, 0.45%)	18	0.24% (0.14%, 0.51%)	9	0.20% (0.18%, 0.48%)
B	17	0.08% (0.00%, 0.36%)	9	0.00% (0.00%, 0.07%)	17	0.23% (0.11%, 0.47%)	9	0.17% (0.14%, 0.58%)
C	16	0.29% (0.12%, 0.92%)	8	0.22% (0.06%, 0.31%)	16	0.49% (0.32%, 0.91%)	8	0.20% (0.14%, 0.58%)
D	15	0.08% (0.00%, 0.24%)	7	0.34% (0.11%, 1.57%)	15	0.27% (0.14%, 0.48%)	7	1.10% (0.23%, 1.76%)
E	15	0.29% (0.05%, 0.89%)	7	0.03% (0.00%, 1.52%)	15	0.36% (0.22%, 1.39%)	7	0.54% (0.28%, 0.63%)
F	14	0.11% (0.00%, 0.44%)	7	0.00% (0.00%, 0.37%)	13	0.22% (0.12%, 0.41%)	7	0.18% (0.04%, 0.35%)
G	14	0.20% (0.05%, 0.57%)	7	0.09% (0.00%, 0.30%)	14	0.46% (0.19%, 0.80%)	7	0.32% (0.05%, 0.66%)
H	14	0.52% (0.36%, 2.88%)	7	0.07% (0.02%, 0.23%)	14	0.42% (0.13%, 0.52%)	7	0.17% (0.08%, 0.94%)
I	13	0.05% (0.00%, 0.75%)	6	0.25% (0.00%, 0.46%)	13	0.32% (0.08%, 0.75%)	6	0.34% (0.14%, 0.73%)
J	12	0.36% (0.14%, 0.77%)	6	0.07% (0.02%, 0.52%)	12	0.46% (0.26%, 1.08%)	6	0.19% (0.14%, 1.05%)
K	13	0.05% (0.00%, 0.20%)	5	0.21% (0.15%, 0.41%)	13	0.25% (0.15%, 0.39%)	5	0.26% (0.18%, 0.44%)
L	12	0.39% (0.15%, 0.76%)	6	0.15% (0.08%, 0.51%)	12	0.41% (0.24%, 0.57%)	6	0.25% (0.16%, 0.48%)
M	11	0.40% (0.02%, 1.44%)	6	0.71% (0.00%, 0.87%)	11	0.19% (0.16%, 0.58%)	6	0.27% (0.15%, 0.87%)
N	12	0.15% (0.04%, 0.42%)	5	0.58% (0.00%, 0.99%)	12	0.35% (0.25%, 0.93%)	5	0.35% (0.07%, 0.58%)
O	9	0.23% (0.00%, 0.44%)	4	0.01% (0.00%, 0.15%)	9	0.49% (0.12%, 0.93%)	4	0.28% (0.02%, 0.53%)
P	8	0.74% (0.24%, 1.15%)	4	0.26% (0.13%, 2.12%)	8	0.25% (0.12%, 0.46%)	4	0.20% (0.05%, 1.08%)
Q	6	0.13% (0.00%, 1.41%)	4	0.35% (0.18%, 0.95%)	6	0.31% (0.10%, 2.15%)	4	0.20% (0.11%, 0.79%)

Table S23. Daily Insulin Delivery

	Baseline		13 Weeks		13w Adjusted Group Difference (95% CI) [a]
	BP	SC	BP	SC	
Total Daily Insulin Units per Kg *mean (SD)*	0.82 (0.34) (N=219)	0.79 (0.32) (N=107)	0.86 (0.33) (N=217)	0.81 (0.34) (N=107)	–
Change from Baseline *mean (SD)*			0.04 (0.21) (N=217)	0.02 (0.19) (N=107)	0.04 (-0.02, 0.11)

Based on weight at randomization and week 13. Baseline insulin data for the BP and SC groups and Week 13 insulin data for the SC group only are reported from case report forms. Week 13 insulin data for the BP group only are from iLet data and any reported manual injections during 13-week iLet wear period. The mean (SD) of total daily insulin per kg for insulin solely delivered by the iLet (i.e., without any manual injections) was 0.86 (0.33).
a –Adjusted group difference computed from a mixed effect model adjusting for baseline value, age at randomization, and site (random effect). Missing data were handled using direct likelihood analyses. Confidence intervals were adjusted using the Benjamini-Hochberg adaptive false discovery rate correction procedure, but confidence intervals should not be used in place of hypothesis testing as the family-wise error rate was not controlled.

Table S24. Body Weight and Body Mass Index

	Baseline		13 Weeks		13w Adjusted Group Difference (95% CI) [a]
	BP	SC	BP	SC	
Body Weight (kg) *mean (SD)*	68 (24) (N=219)	69 (28) (N=107)	69 (24) (N=215)	70 (27) (N=107)	–
Change from Baseline *mean (SD)*			1.3 (2.8) (N=215)	0.9 (2.5) (N=107)	-0.2 (-4.8, 4.4)
Body Mass Index (kg/m^2) *mean (SD)*	25.2 (6.2) (N=219)	25.0 (7.3) (N=107)	25.5 (6.3) (N=211)	25.2 (7.5) (N=102)	–
Change from Baseline *mean (SD)*			0.4 (1.1) (N=211)	0.2 (0.9) (N=102)	0.6 (-0.7, 1.9)

a –Adjusted group differences computed from mixed effect models adjusting for baseline value, age at randomization, and site (random effect). Missing data were handled using direct likelihood analyses. Confidence intervals were adjusted using the Benjamini-Hochberg adaptive false discovery rate correction procedure, but confidence intervals should not be used in place of hypothesis testing as the family-wise error rate was not controlled.

Table S25. Presumed Infusion Set Failures with Comparison to Published Data for the Tandem t:slim X2 insulin pump with Control-IQ Technology

Age Group					
Age 6-13		Age 14-17		Age ≥18	
# of presumed infusion set failures within 72 hrs/# of infusion sets worn					
BP	Control-IQ	BP	Control-IQ	BP	Control-IQ
88/1544 (5.7%)	115/2105 (5.5%)	60/808 (7.4%)	189/2731 (6.9%)	55/2407 (2.3%)	143/6216 (2.3%)

The BP columns refer to the current study. The Control-IQ columns refer to data from a published analysis assessing the frequency of potential infusion set failures in clinical trials in which patients used the Tandem t:slim X2 insulin pump with Control-IQ Technology, with a variety of infusion sets.[1] Since only infusion sets with a 90 degree insertion were used with the BP in the current study, for this comparison, the Control-IQ data were limited to 90 degree insertion infusion sets. Data are stratified by age group since failure rates varied by age.

The denominator in each cell is the number of infusion sets worn and the numerator is the number of infusion sets which were removed prior to 72 hours preceded by prolonged hyperglycemia. Prolonged hyperglycemia was defined as (1) CGM >300 mg/dL immediately before infusion set removal, (2) CGM continuously >250 mg/dL in the 2-hour period before the infusion set removal, and (3) CGM >300 mg/dL for at least 90 minutes of the 2-hour period before the infusion set removal.

1. Kanapka LG, Lum JW, Beck RW. Insulin Pump Infusion Set Failures Associated with Prolonged Hyperglycemia: Frequency and Relationship to Age and Type of Infusion Set During 22,741 Infusion Set Wears. Diabetes Technol Ther 2022;24:396-402.

Table S26. Summary of BP Group Device Issues

Counting number of events, not patients. "ADE" stands for adverse device effect.

Device	Issue Type	Device Issues with Adverse Event (N=98 pts with ≥1 device issue from 219 randomized)	Device Issues without Adverse Events (N=103 pts with ≥1 device issue from 219 randomized)
Dexcom G6	Dexcom G6 Applicator Release	0	7
	Dexcom G6 Sensor Accuracy	1	1
	Dexcom G6 Sensor Failure	1	15
	Dexcom G6 Transmitter Issue	1	15
iLet	iLet Alarm Issue	2	1
	iLet Algorithm-related Issue	4	0
	iLet Algorithm-related Issue User Error	1	3
	iLet Case Issue	0	1
	iLet Connectivity Issue	0	3
	iLet Infusion Set Issue	132	26
	iLet Infusion Set Skin Irritation	2	1
	iLet Screen Issue	0	22
	iLet battery/charging issue	5	23
	iLet cartridge issue	16	26
	iLet motor issue	3	10
	iLet waking issue	0	6
Other	Cell phone for G6 Clarity App	0	2
	Dexcom Clarity Issue	1	1
Total		169	163

Figure S1. Ketone Action Plan

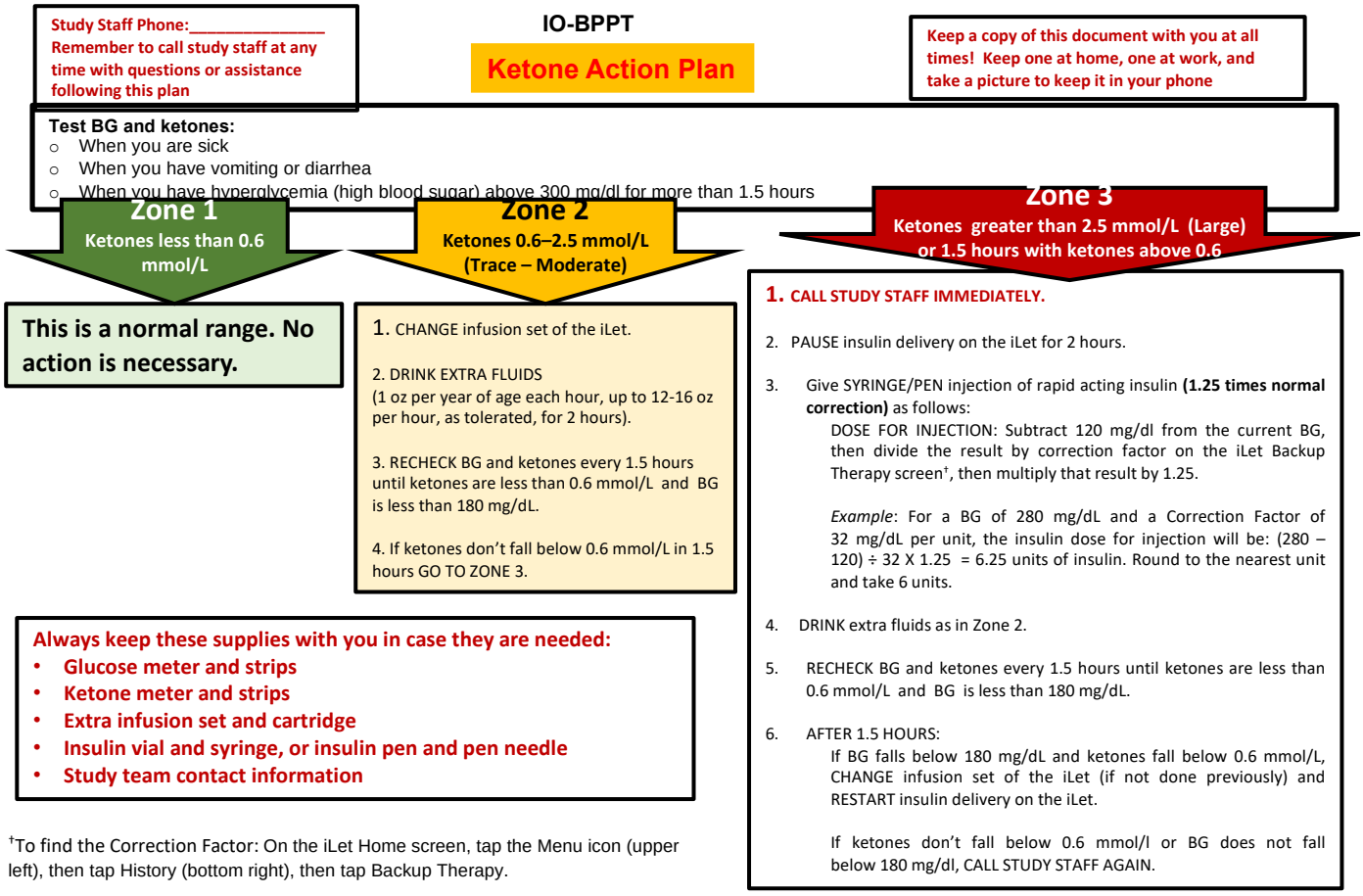

Figure S1. Ketone Action Plan. The plan was provided to patients in the BP group, along with a glucometer and glucose test strips and a ketone meter and ketone test strips, which they were instructed to carry with them at all times.

Figure S2. Flowchart of Study Completion

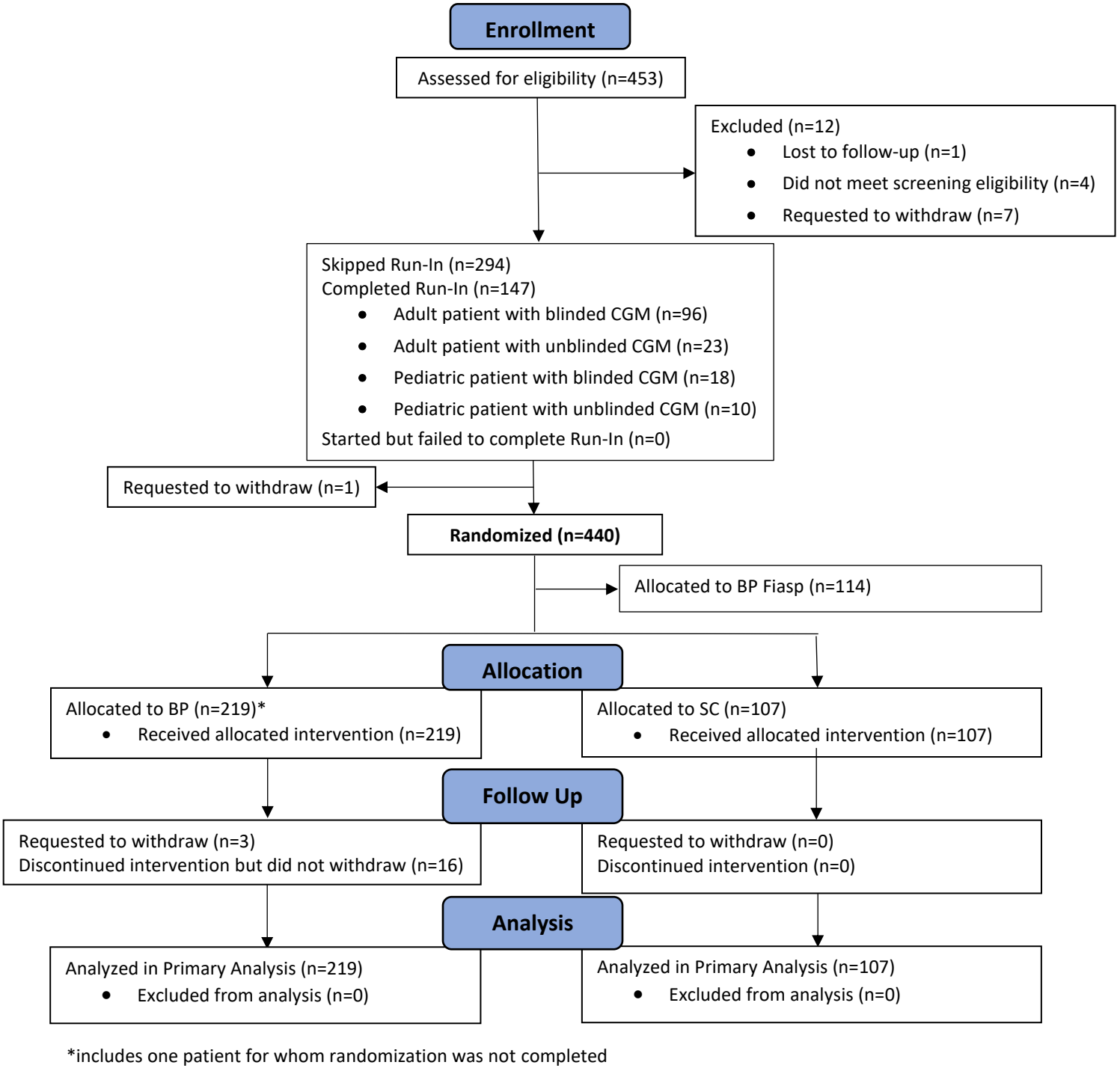

Figure S2. Flowchart of Study Completion. The flow of patients is shown from initial assessment through analysis.

Figure S3. Cumulative Distribution of Glycated Hemoglobin at Week 13

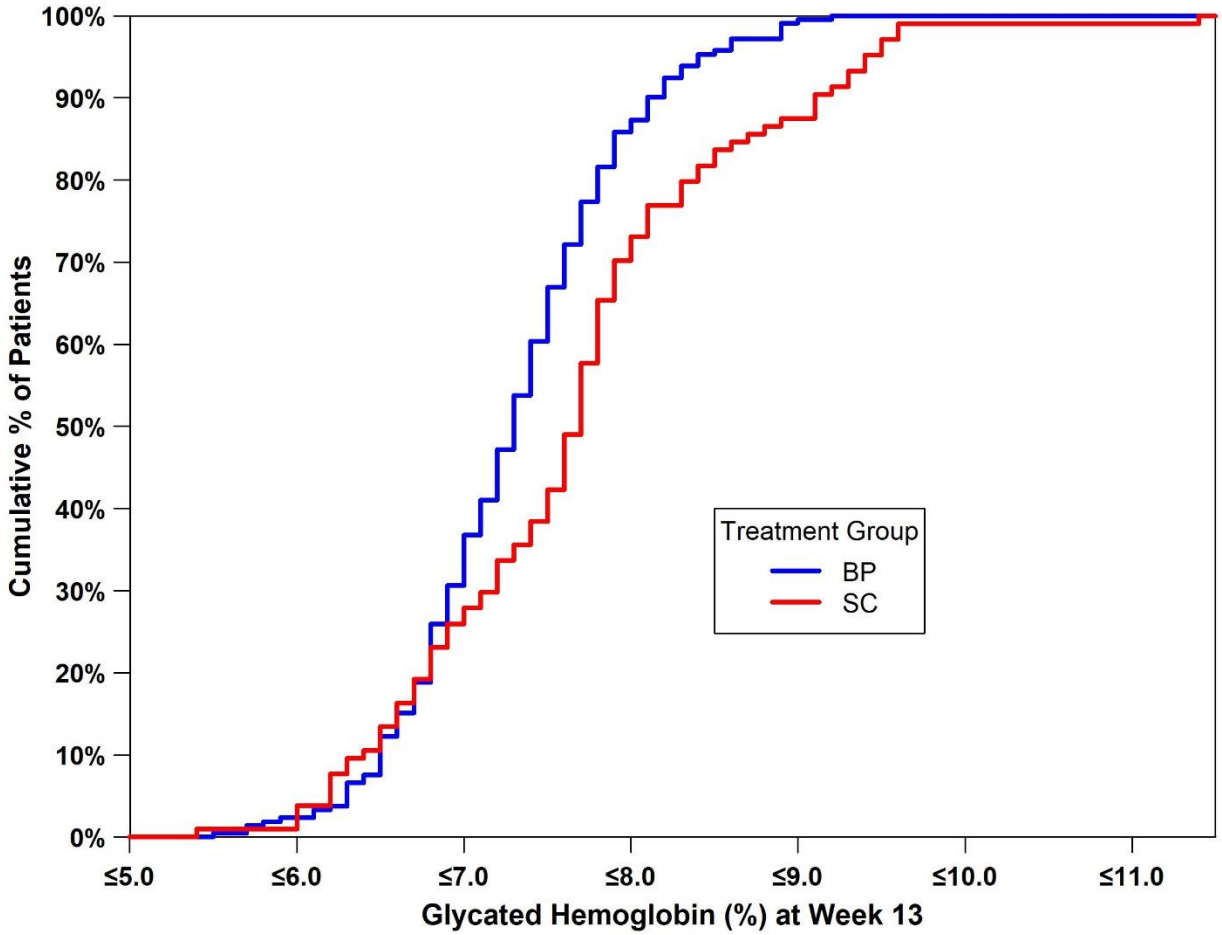

Figure S3. Cumulative Distribution of Glycated Hemoglobin at Week 13. The cumulative distribution plot of the percentage of patients versus the glycated hemoglobin at week 13 is shown. The distribution for the BP group is represented by blue curve and the distribution of the SC group is represented by the red curve.

Figure S4. Scatterplot of Glycated Hemoglobin at Week 13 Versus Baseline

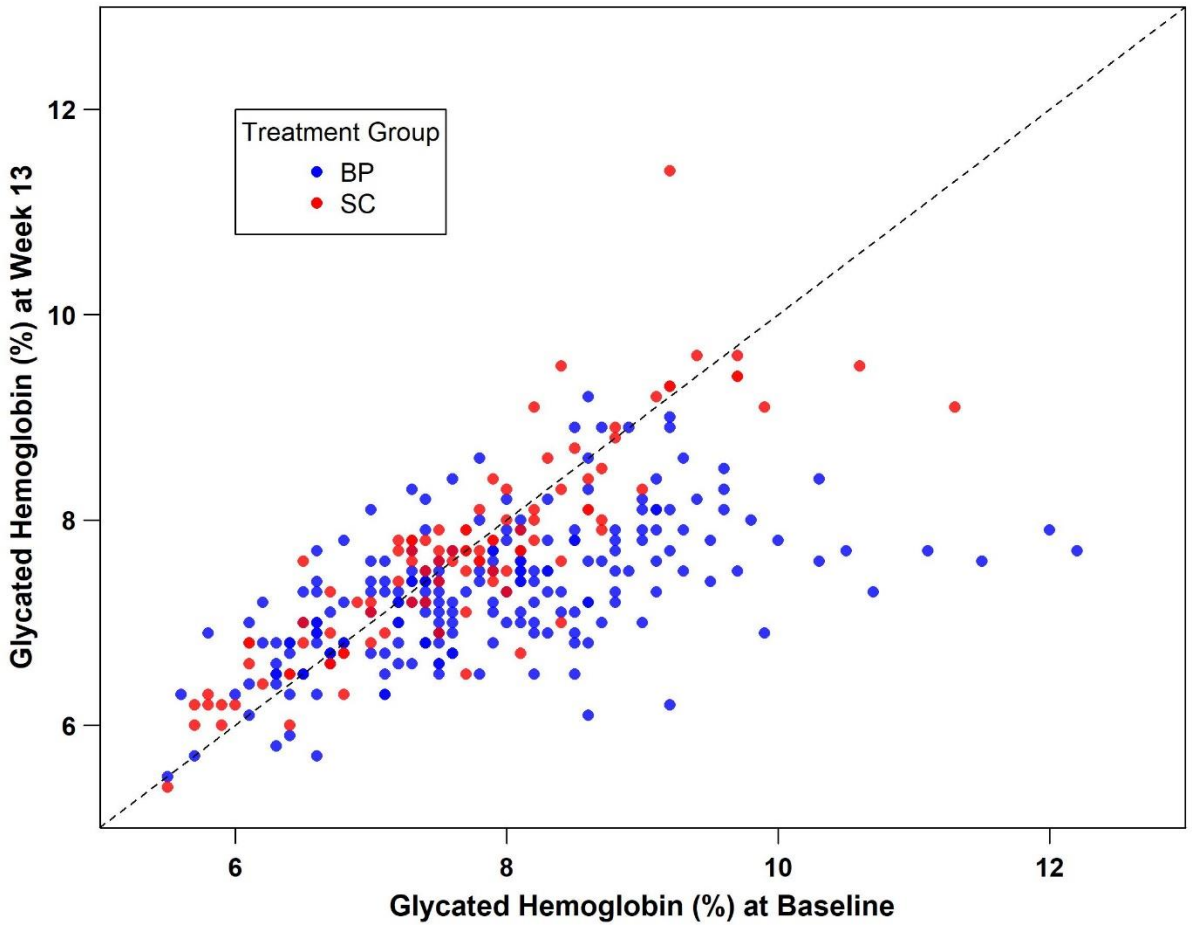

Figure S4. Scatterplot of Glycated Hemoglobin at Week 13 Versus Baseline. A scatterplot of the glycated hemoglobin at week 13 versus the baseline glycated hemoglobin is shown. Each point represents an individual patient, with those randomized to the BP group being represented by blue points and those randomized to the SC group being represented by red points. Patients plotted on the dashed line of identity had no difference in glycated hemoglobin at 13 weeks versus at baseline.

Figure S5. Boxplots of Glycated Hemoglobin at Baseline, Week 6, and Week 13

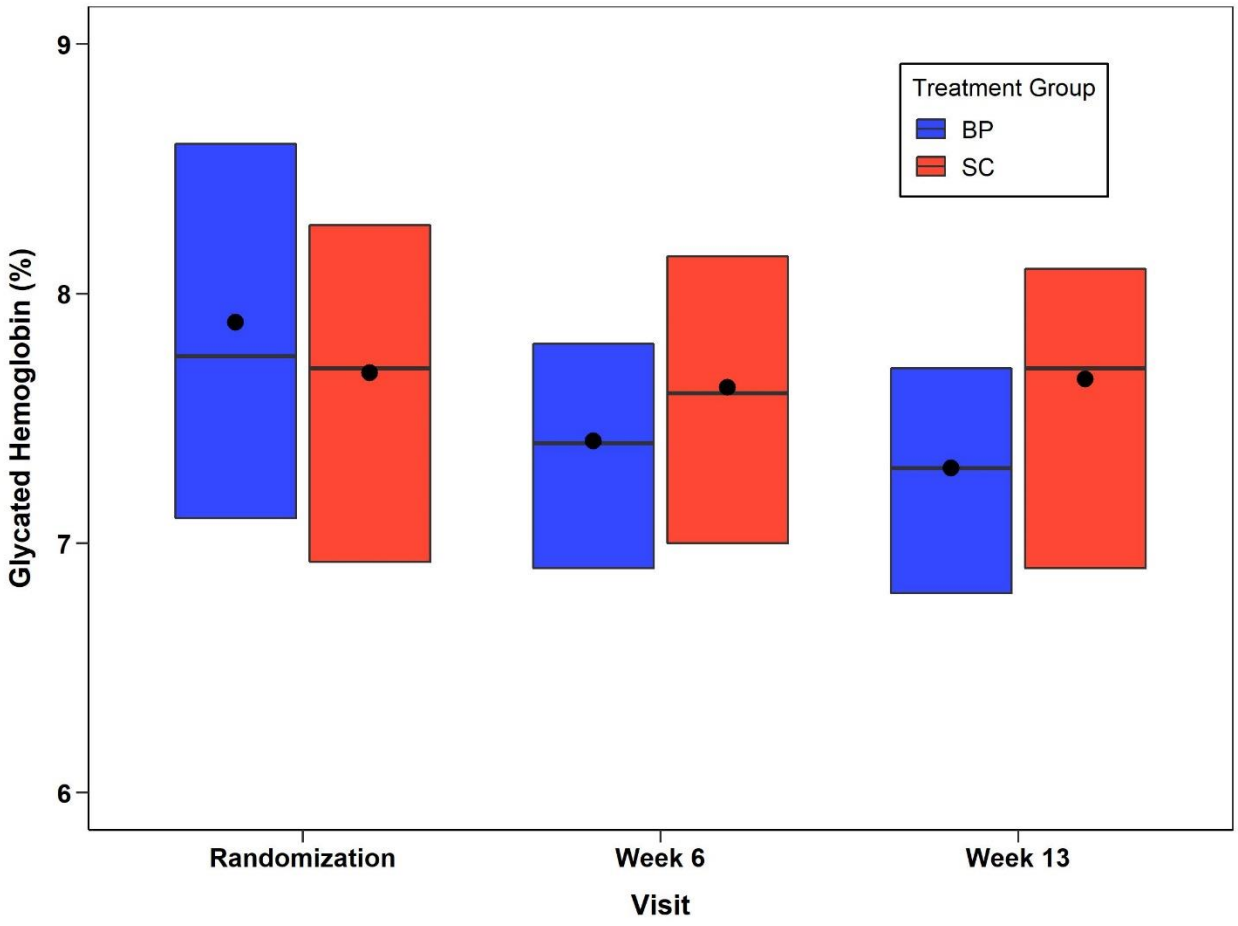

Figure S5. Boxplots of Glycated Hemoglobin at Baseline, Week 6, and Week 13. Box plots of glycated hemoglobin at baseline, week 6, and week 3 are shown. Those randomized to the BP group are represented by blue boxes and those randomized to the SC group are represented by red boxes. Black dots indicate the mean values, horizontal bars in the boxes indicate the medians, and the bottom and top of each box represent the 25th and 75th percentiles, respectively.

Figure S6. Scatterplot of Time <54 mg/dL Over 13 Weeks Versus Baseline

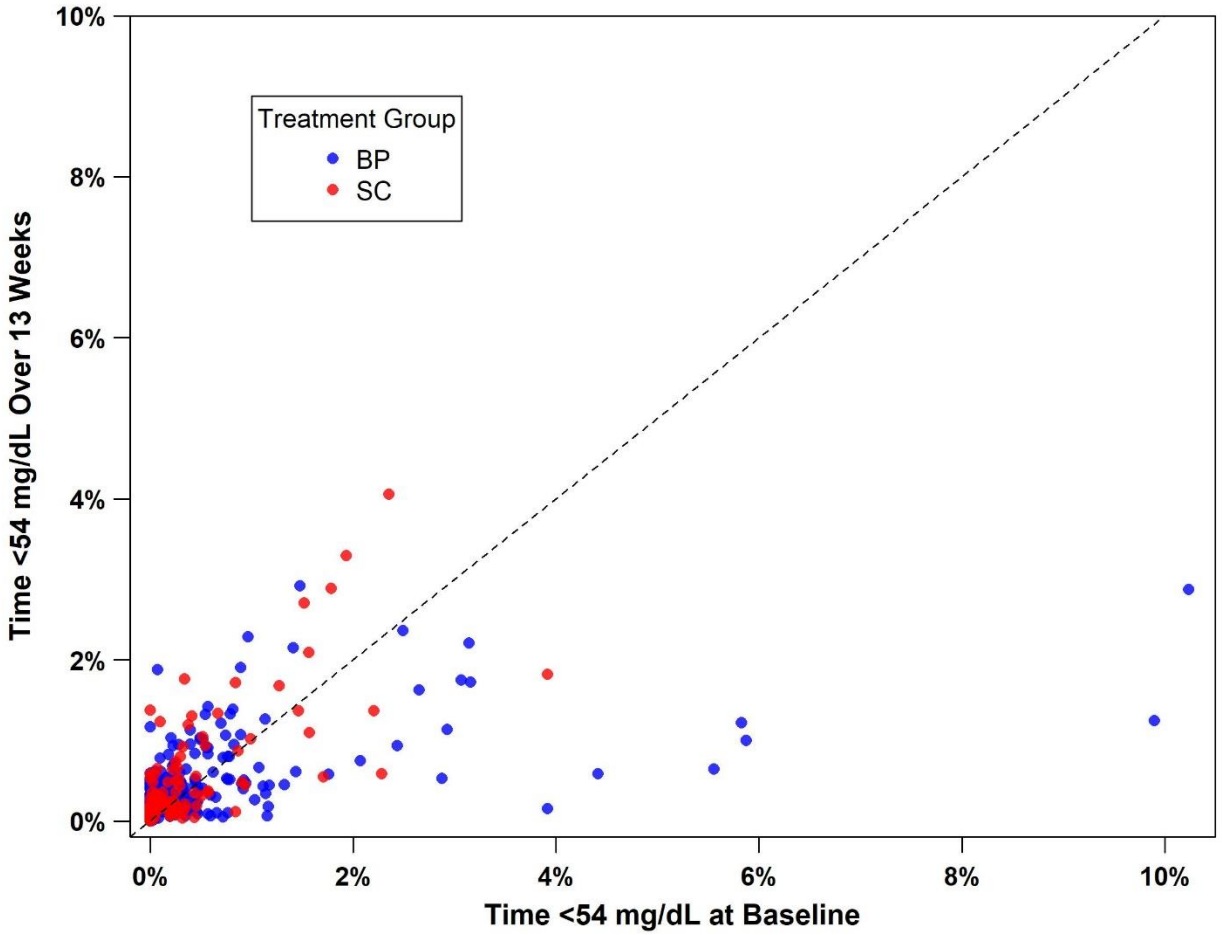

Figure S6. Scatterplot of Time <54 mg/dL Over 13 Weeks Versus Baseline. A scatterplot of percentage of time with glucose <54 mg/dL measured by CGM from baseline to week 13 versus percentage of time with glucose <54 mg/dL at baseline is shown. Each point represents an individual patient, with those randomized to the BP group being represented by blue points and those randomized to the SC group being represented by red points. Patients plotted on the dashed line of identity had no difference in percentage of time with glucose <54 mg/dL over 13 weeks versus at baseline.

Figure S7. Boxplots of Time <54 mg/dL at Baseline and Over 13 Weeks

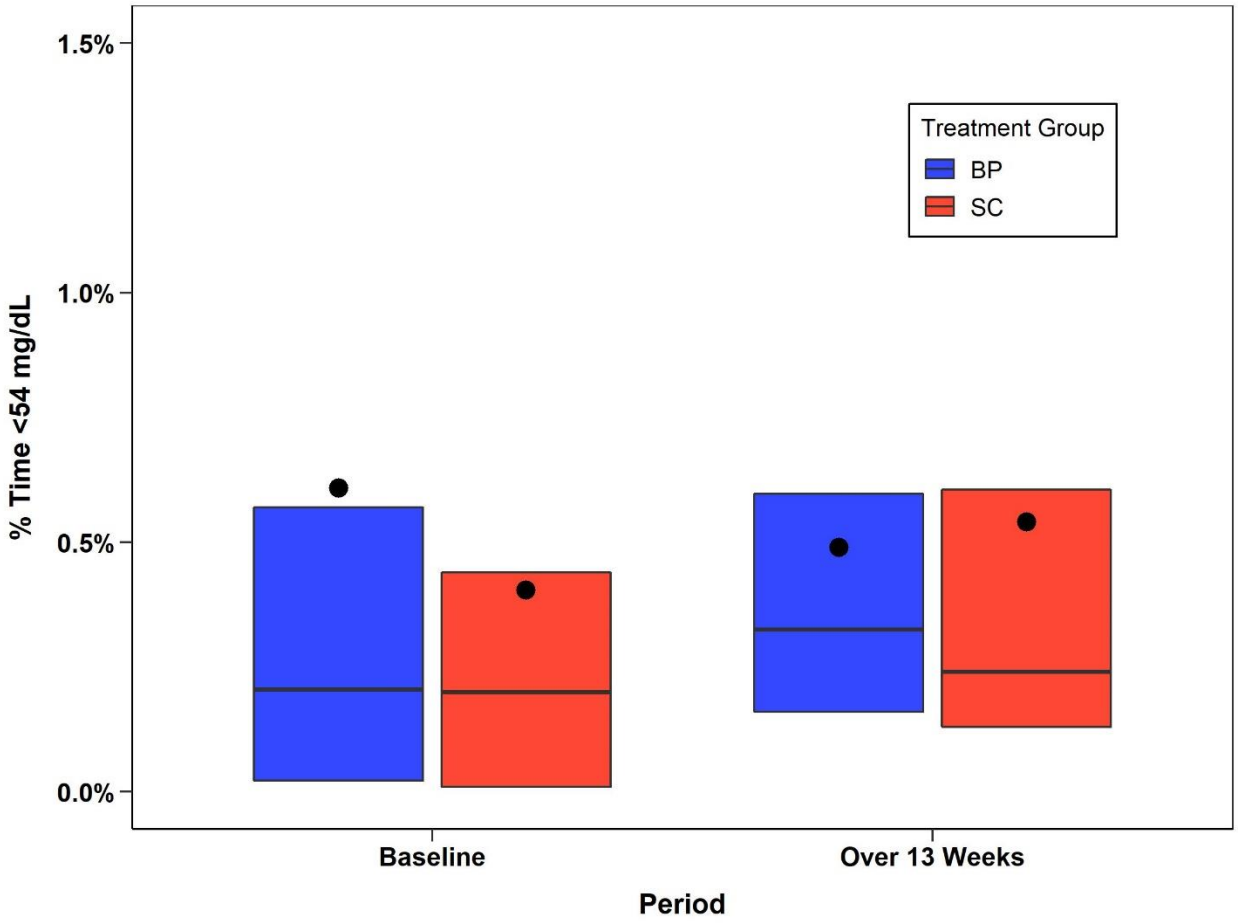

Figure S7. Boxplots of Time <54 mg/dL at Baseline and Over 13 Weeks. Box plots of percentage of time with glucose <54 mg/dL measured by CGM at baseline and over 13 weeks are shown. Those randomized to the BP group are represented by blue boxes and those randomized to the SC group are represented by red boxes. Black dots indicate the mean values, horizontal bars in the boxes indicate the medians, and the bottom and top of each box represent the 25th and 75th percentiles, respectively.

Figure S8. Scatterplot of Mean Glucose Over 13 Weeks Versus Baseline

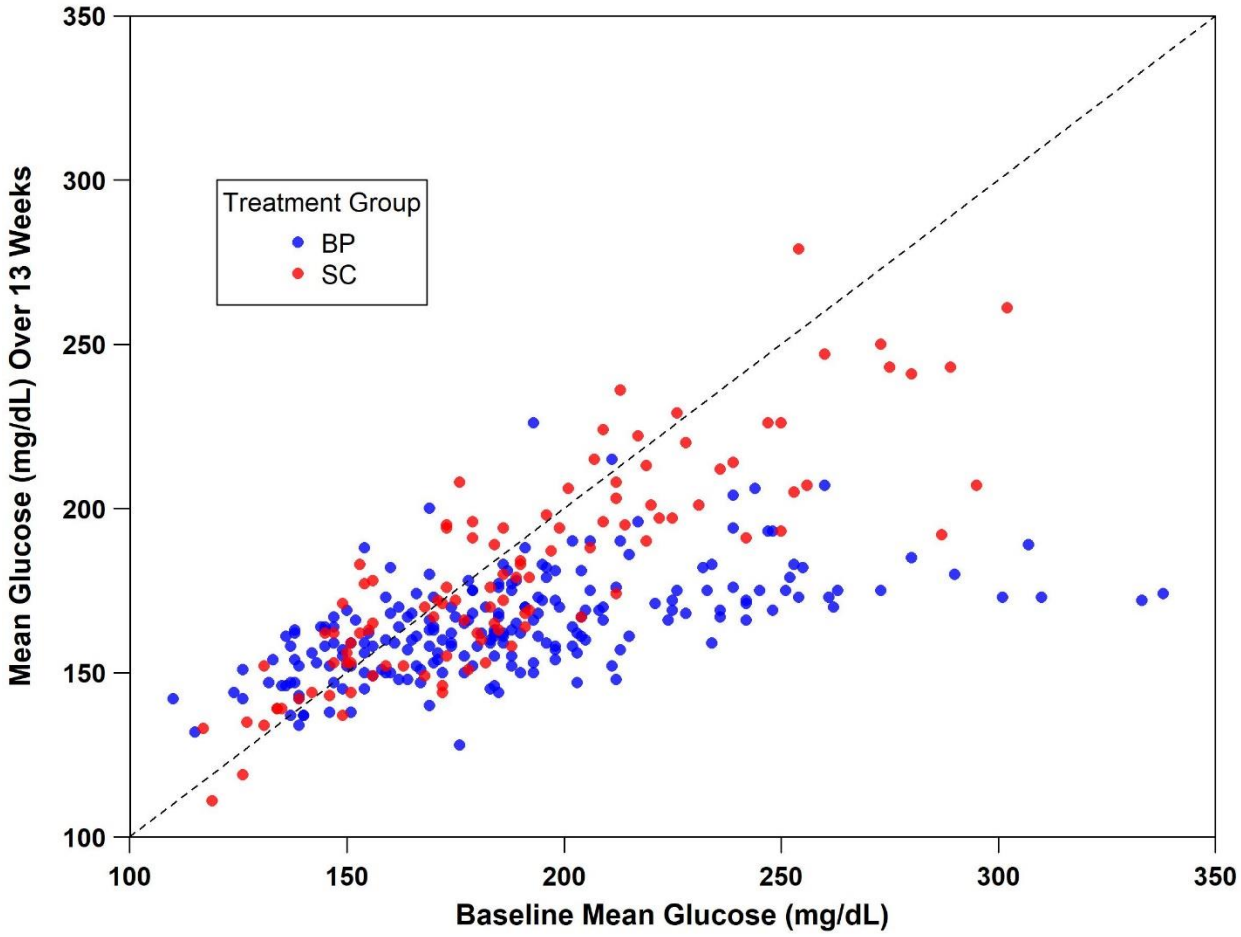

Figure S8. Scatterplot of Mean Glucose Over 13 Weeks Versus Baseline. A scatterplot of mean glucose measured by CGM from baseline to week 13 versus mean glucose at baseline is shown. Each point represents an individual patient, with those randomized to the BP group represented by blue points and those randomized to the SC group represented by red points. Patients plotted on the dashed line of identity had no difference in mean glucose over 13 weeks versus at baseline.

Figure S9. Scatterplot of Time in Range 70-180 mg/dL Over 13 Weeks Versus Baseline

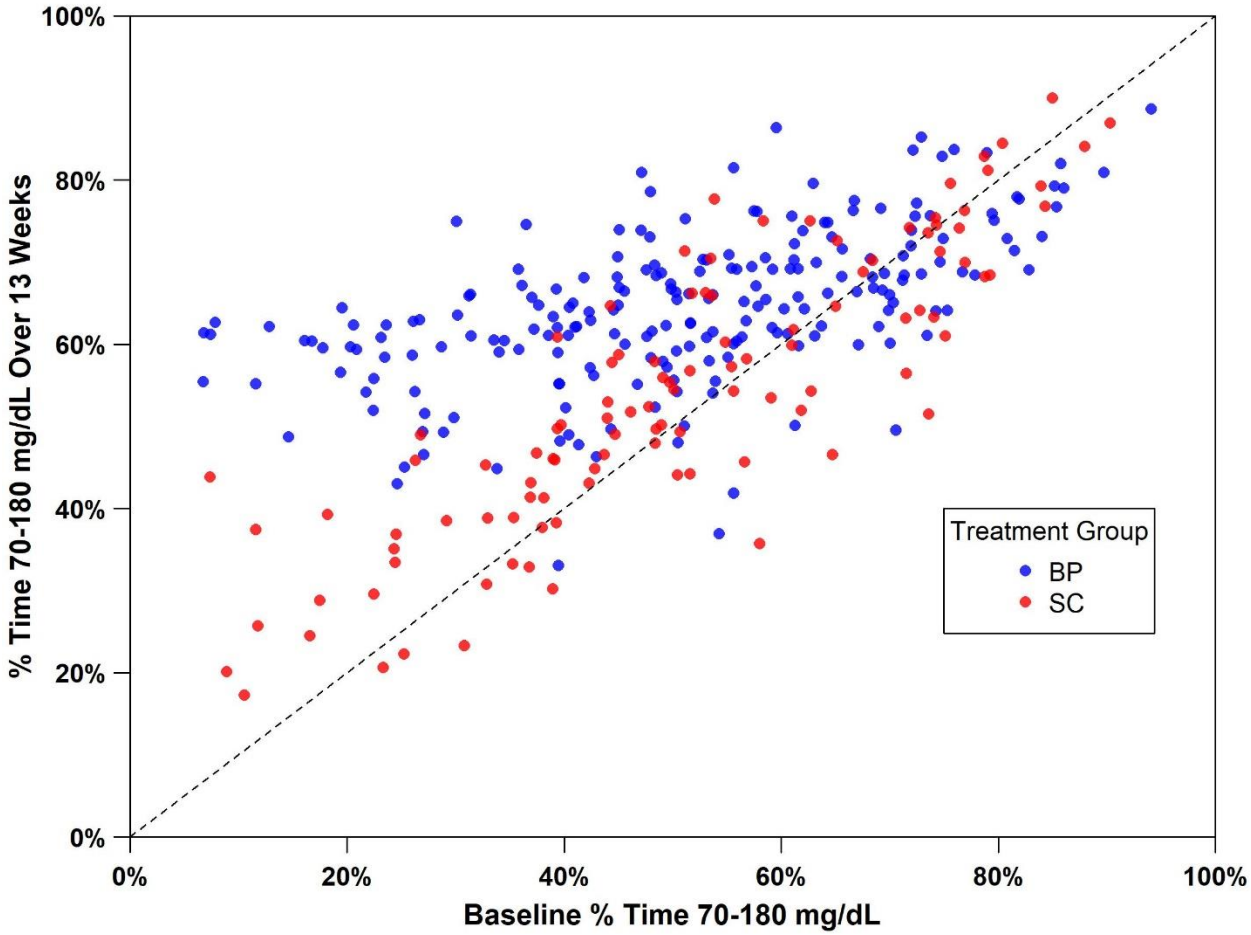

Figure S9. Scatterplot of Time in Range 70-180 mg/dL Over 13 Weeks Versus Baseline. A scatterplot of percentage time in the range of 70-180 mg/dL measured by CGM from baseline to week 13 versus percentage time in range at baseline is shown. Each point represents an individual patient, with those randomized to the BP group being represented by blue points and those randomized to the SC group being represented by red points. Patients plotted on the dashed line of identity had no difference in percentage time in the range of 70-180 mg/dL over 13 weeks versus at baseline.

Figure S10. Scatterplot of Time >180 mg/dL Over 13 Weeks Versus Baseline

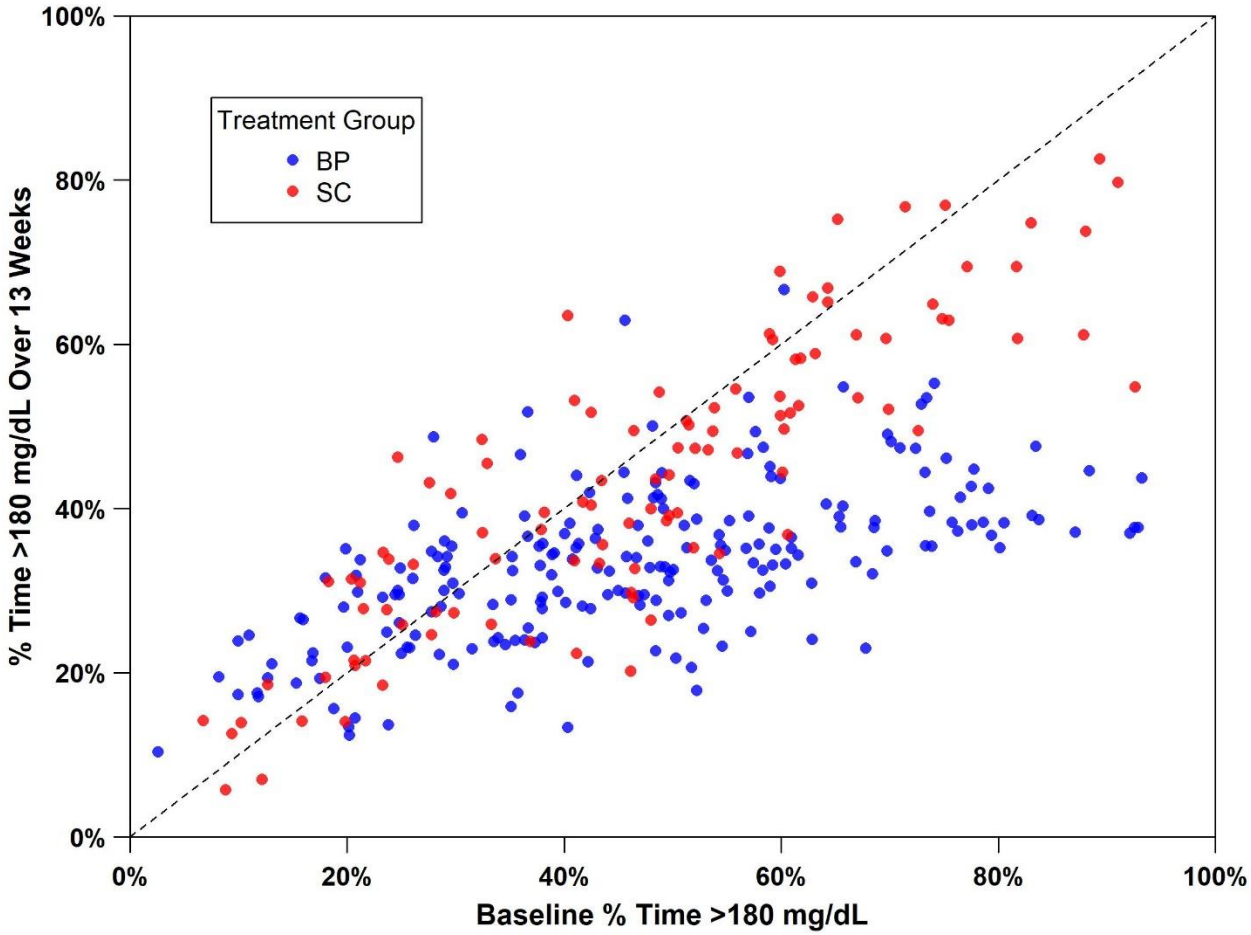

Figure S10. Scatterplot of Time >180 mg/dL Over 13 Weeks Versus Baseline. A scatterplot of percentage of time >180 mg/dL measured by CGM from baseline to week 13 versus percentage of time >180 mg/dL at baseline is shown. Each point represents an individual patient, with those randomized to the BP group being represented by blue points and those randomized to the SC group being represented by red points. Patients plotted on the dashed line of identity had no difference in percentage of time >180 mg/dL over 13 weeks versus at baseline.

Figure S11. Scatterplot of Time >250 mg/dL Over 13 Weeks Versus Baseline

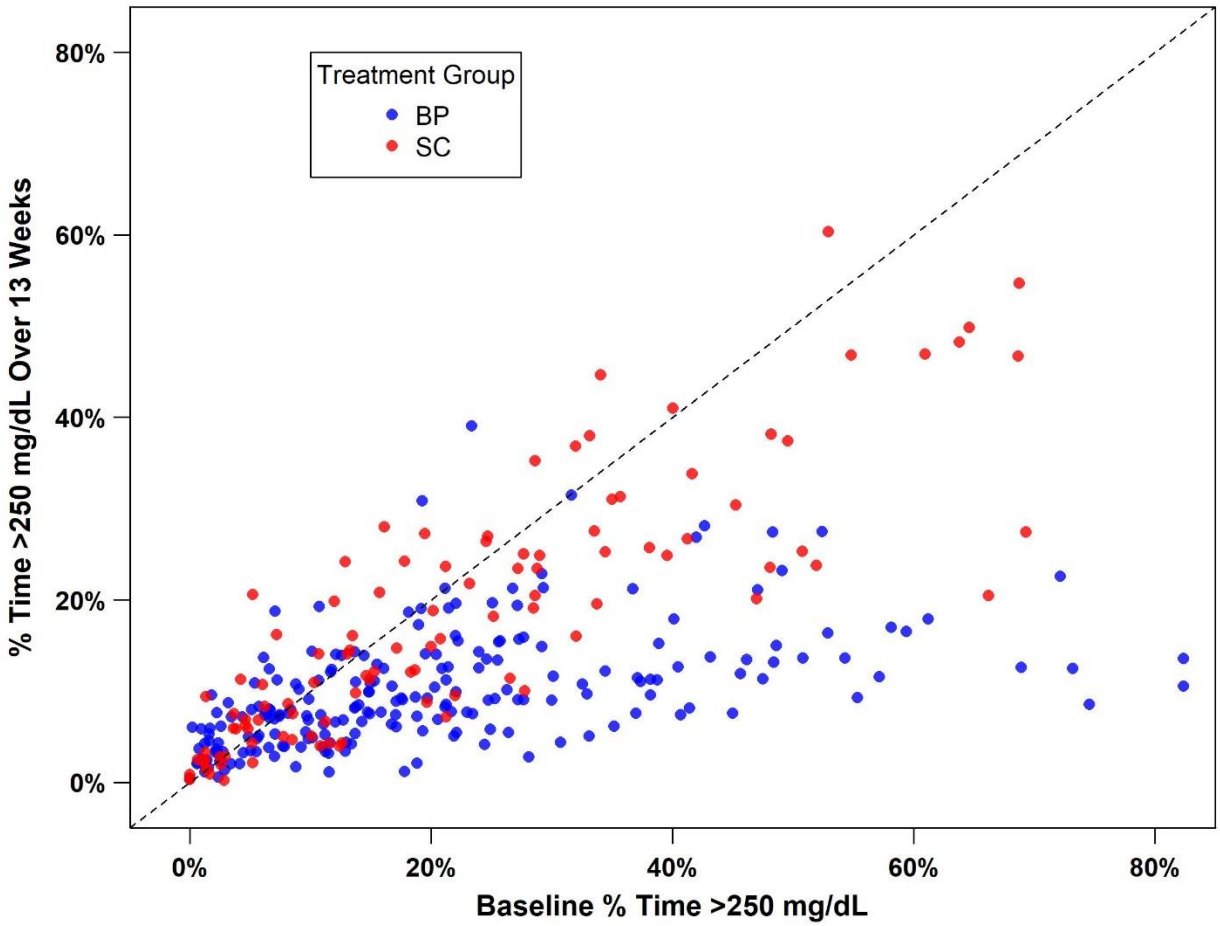

Figure S11. Scatterplot of Time >250 mg/dL Over 13 Weeks Versus Baseline. A scatterplot of percentage of time >250 mg/dL measured by CGM from baseline to week 13 versus percentage of time >250 mg/dL at baseline is shown. Each point represents an individual patient, with those randomized to the BP group being represented by blue points and those randomized to the SC group being represented by red points. Patients plotted on the dashed line of identity had no difference in percentage of time >250 mg/dL over 13 weeks versus at baseline.

Figure S12. Scatterplot of Glucose SD Over 13 Weeks Versus Baseline

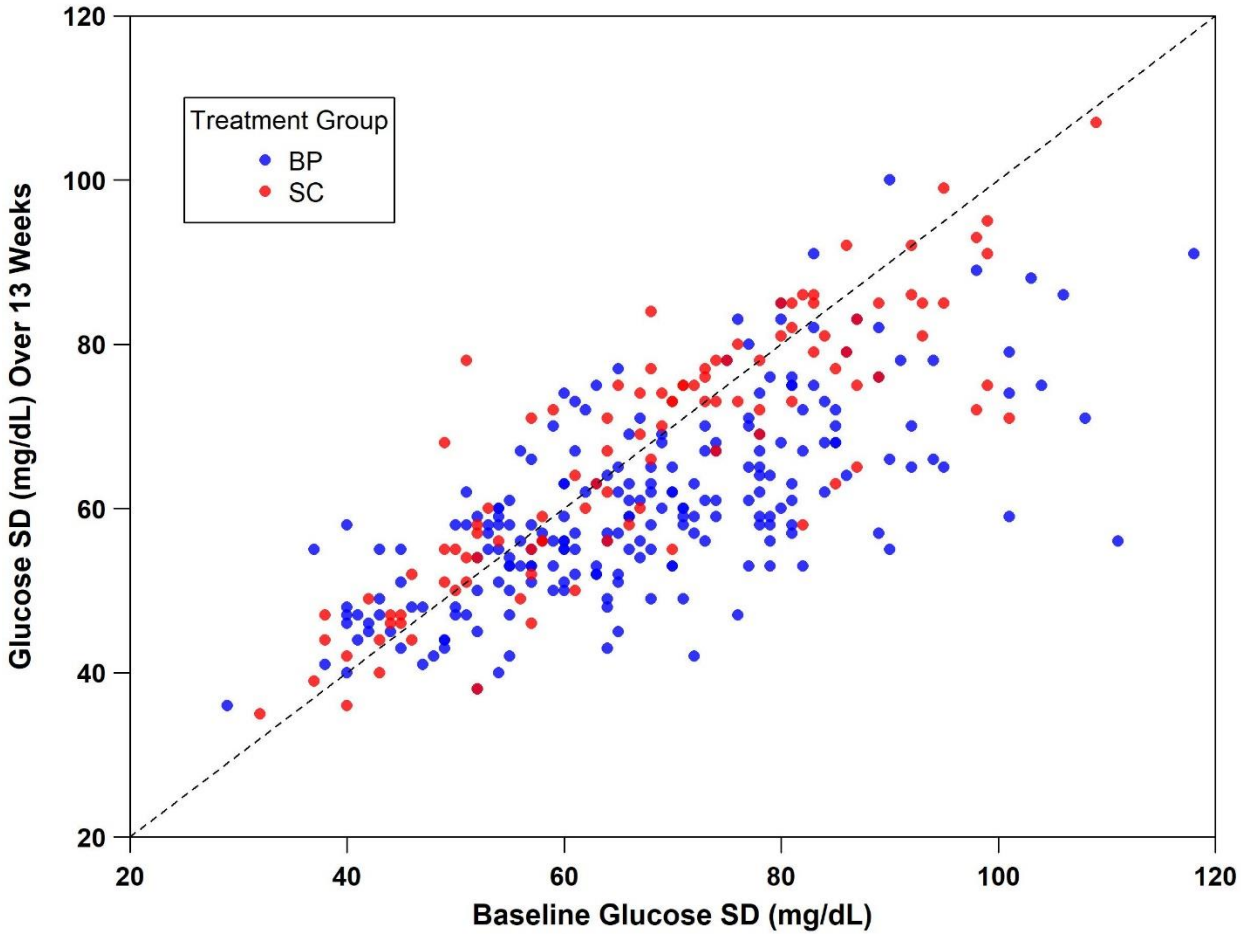

Figure S12. Scatterplot of Glucose SD Over 13 Weeks Versus Baseline. A scatterplot of glucose standard deviation (SD) measured by CGM from baseline to week 13 versus glucose SD at baseline is shown. Each point represents an individual patient, with those randomized to the BP group being represented by blue points and those randomized to the SC group being represented by red points. Patients plotted on the dashed line of identity had no difference in glucose SD over 13 weeks versus at baseline.

Figure S13. Scatterplot of Time <70 mg/dL Over 13 Weeks Versus Baseline

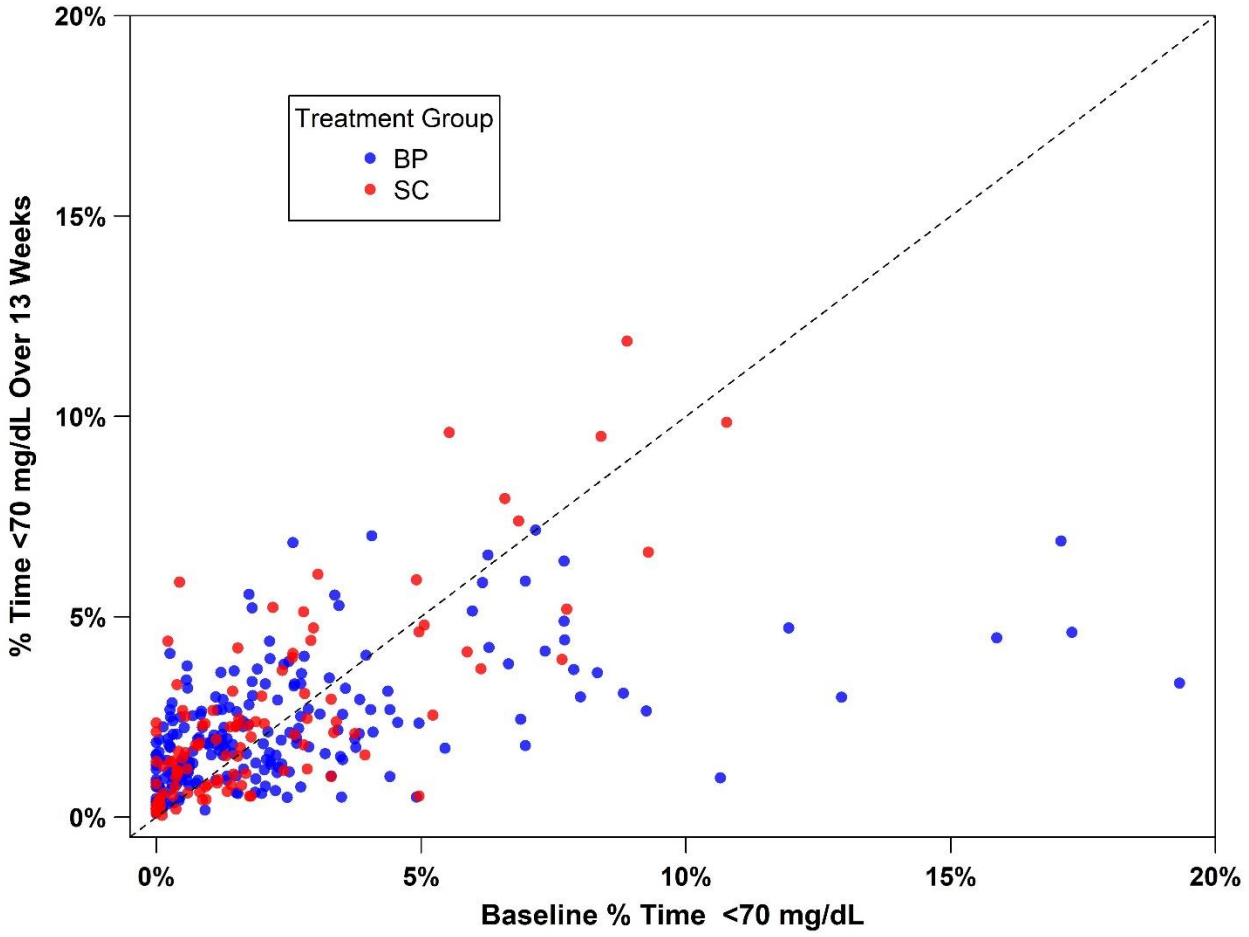

Figure S13. Scatterplot of Time <70 mg/dL Over 13 Weeks Versus Baseline. A scatterplot of percentage of time <70 mg/dL measured by CGM from baseline to week 13 versus percentage of time <70 mg/dL at baseline is shown. Each point represents an individual patient, with those randomized to the BP group being represented by blue points and those randomized to the SC group being represented by red points. Patients plotted on the dashed line of identity had no difference in percentage of time <70 mg/dL over 13 weeks versus at baseline.

Figure S14. Scatterplot of Glucose Coefficient of Variation Over 13 Weeks Versus Baseline

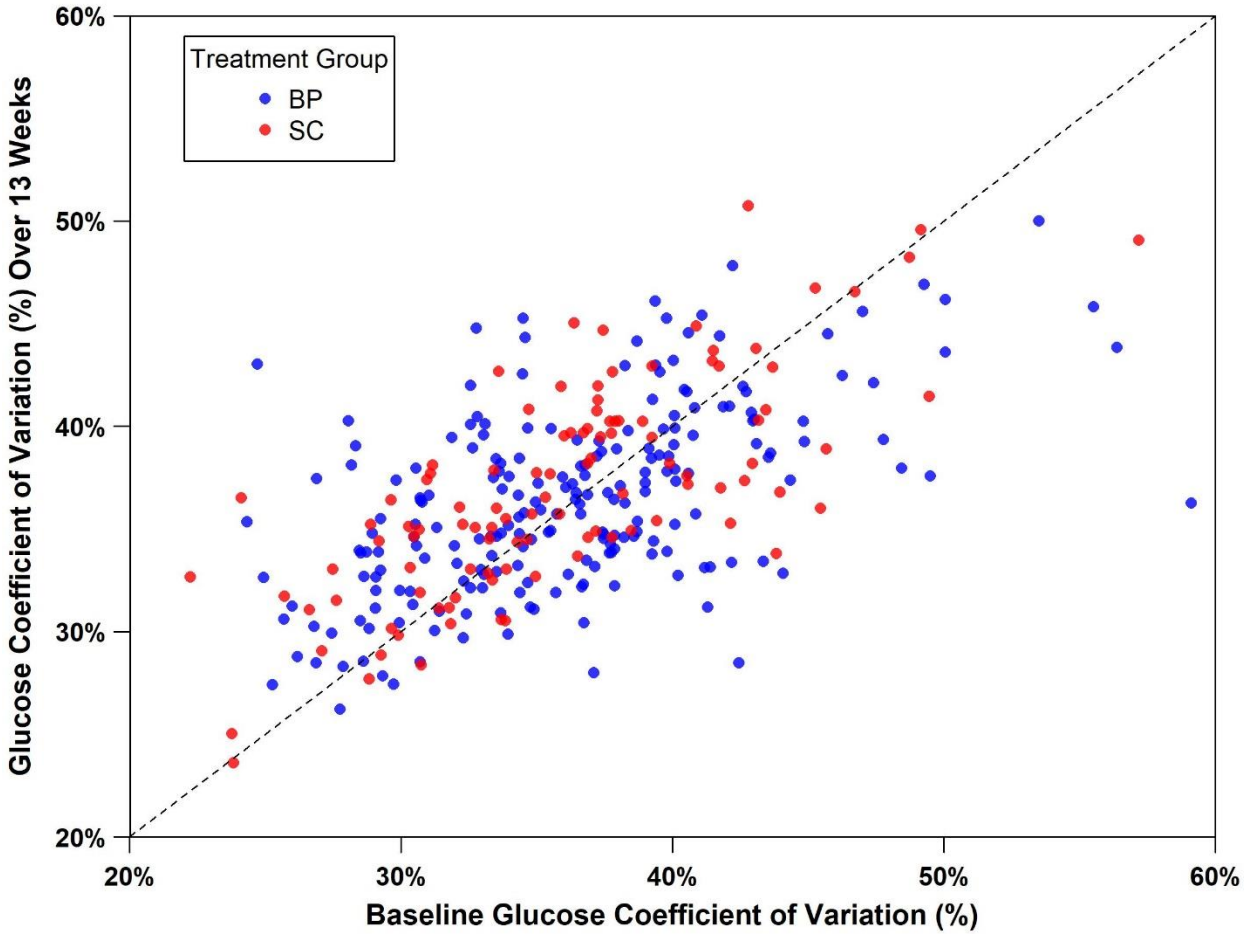

Figure S14. Scatterplot of Glucose Coefficient of Variation Over 13 Weeks Versus Baseline. A scatterplot of coefficient of variation (CV) measured by CGM from baseline to week 13 versus CV at baseline is shown. Each point represents an individual patient, with those randomized to the BP group being represented by blue points and those randomized to the SC group being represented by red points. Patients plotted on the dashed line of identity had no difference in CV over 13 weeks versus at baseline.

Figure S15. Boxplots of Time 70-180 mg/dL by Time of Day

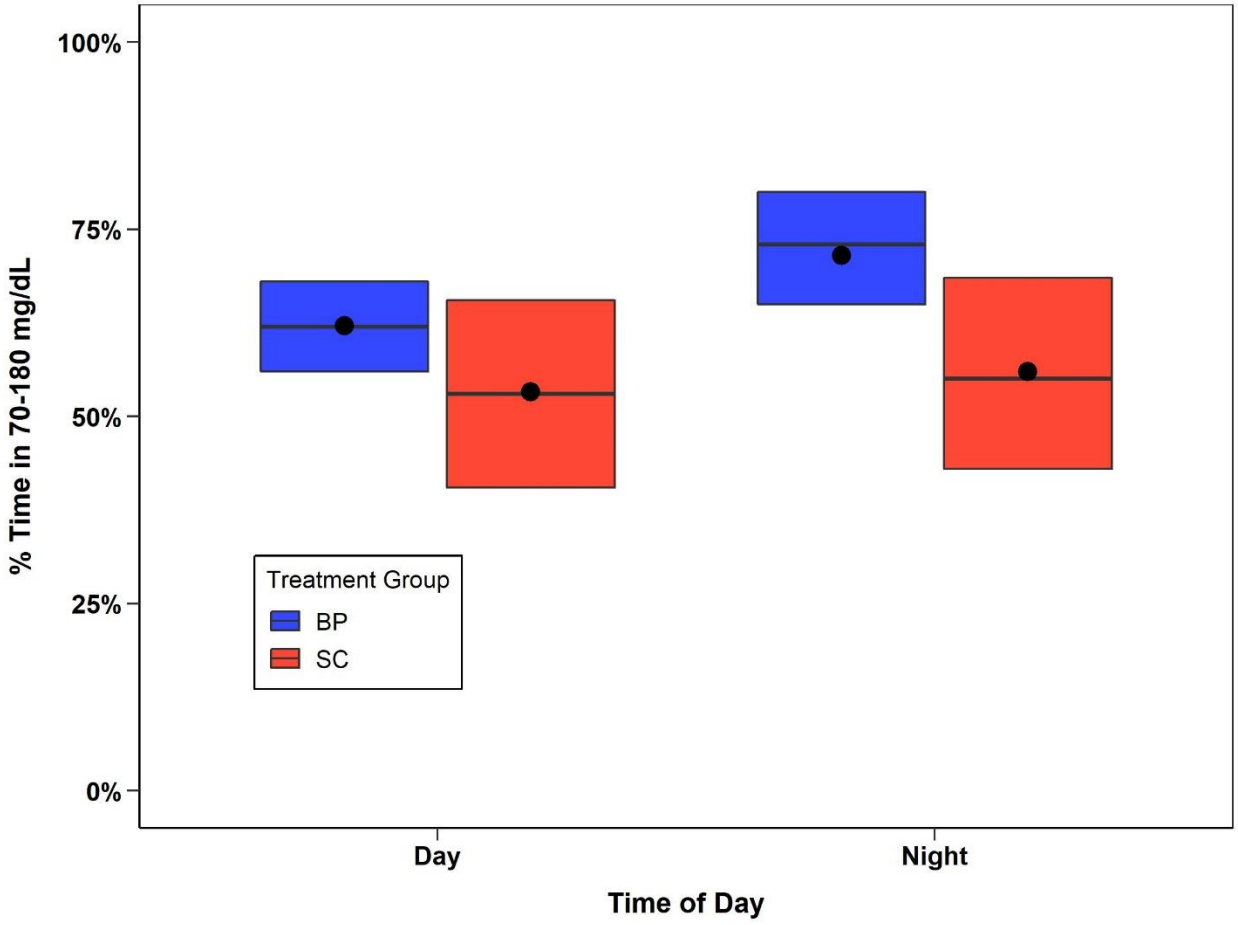

Figure S15. Boxplots of Time 70-180 mg/dL by Time of Day. Box plots of percentage of time with glucose 70-180 mg/dL measured by CGM in the BP and SC groups during the day (06:00 to 23:59) and night (00:00 to 05:59) are shown. Those randomized to the BP group are represented by blue boxes and those randomized to the SC group are represented by red boxes. Black dots indicate the mean values, horizontal bars in the boxes indicate the medians, and the bottom and top of each box represent the 25th and 75th percentiles, respectively.

Figure S16. Boxplots of Time <54 mg/dL by Time of Day

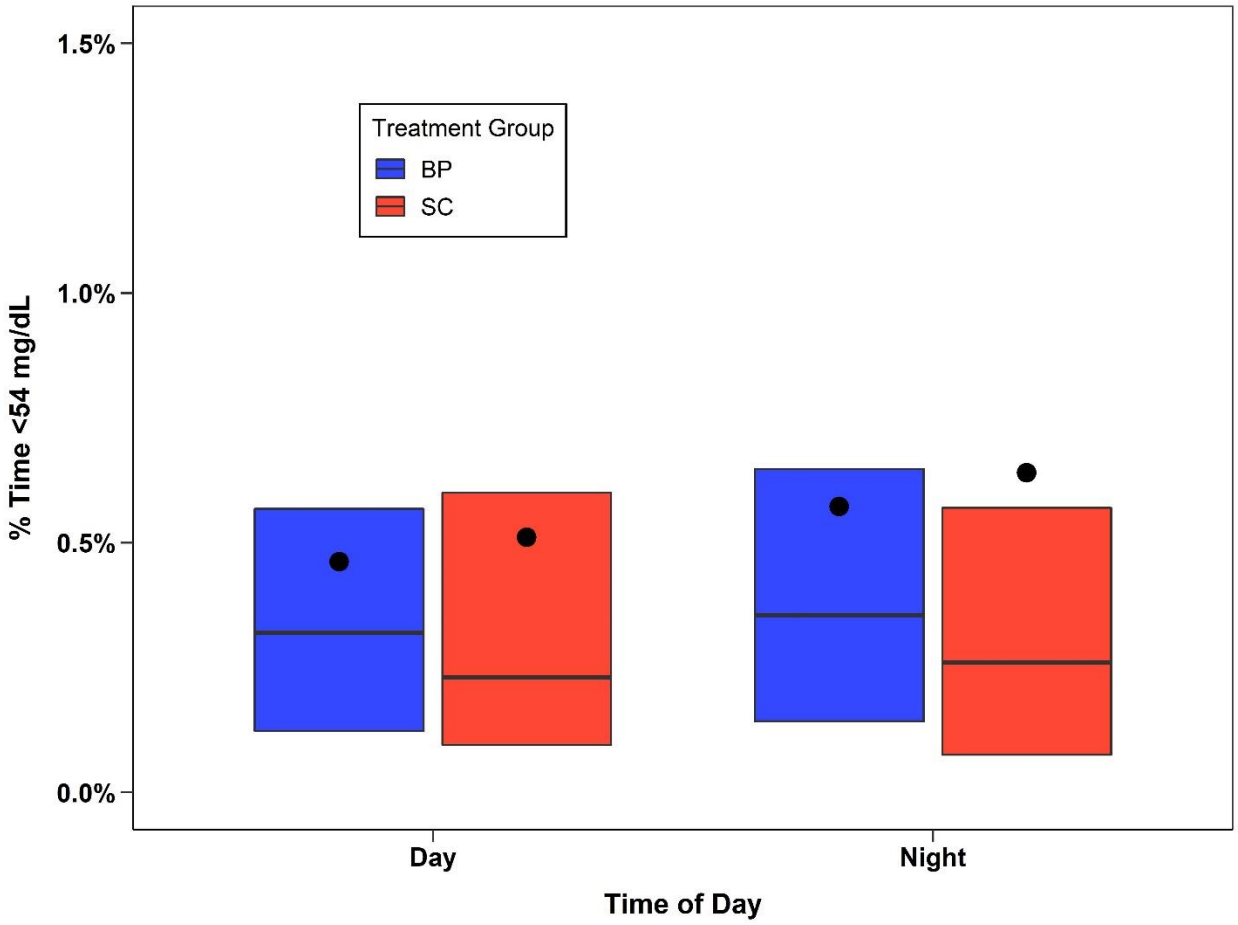

Figure S16. Boxplots of Time <54 mg/dL by Time of Day. Box plots of percentage of time with glucose <54 mg/dL measured by CGM in the BP and SC groups during the day (06:00 to 23:59) and night (00:00 to 05:59) are shown. Those randomized to the BP group are represented by blue boxes and those randomized to the SC group are represented by red boxes. Black dots indicate the mean values, horizontal bars in the boxes indicate the medians, and the bottom and top of each box represent the 25th and 75th percentiles, respectively.

Figure S17. Boxplots of Time 70-180 mg/dL by 4-week Interval

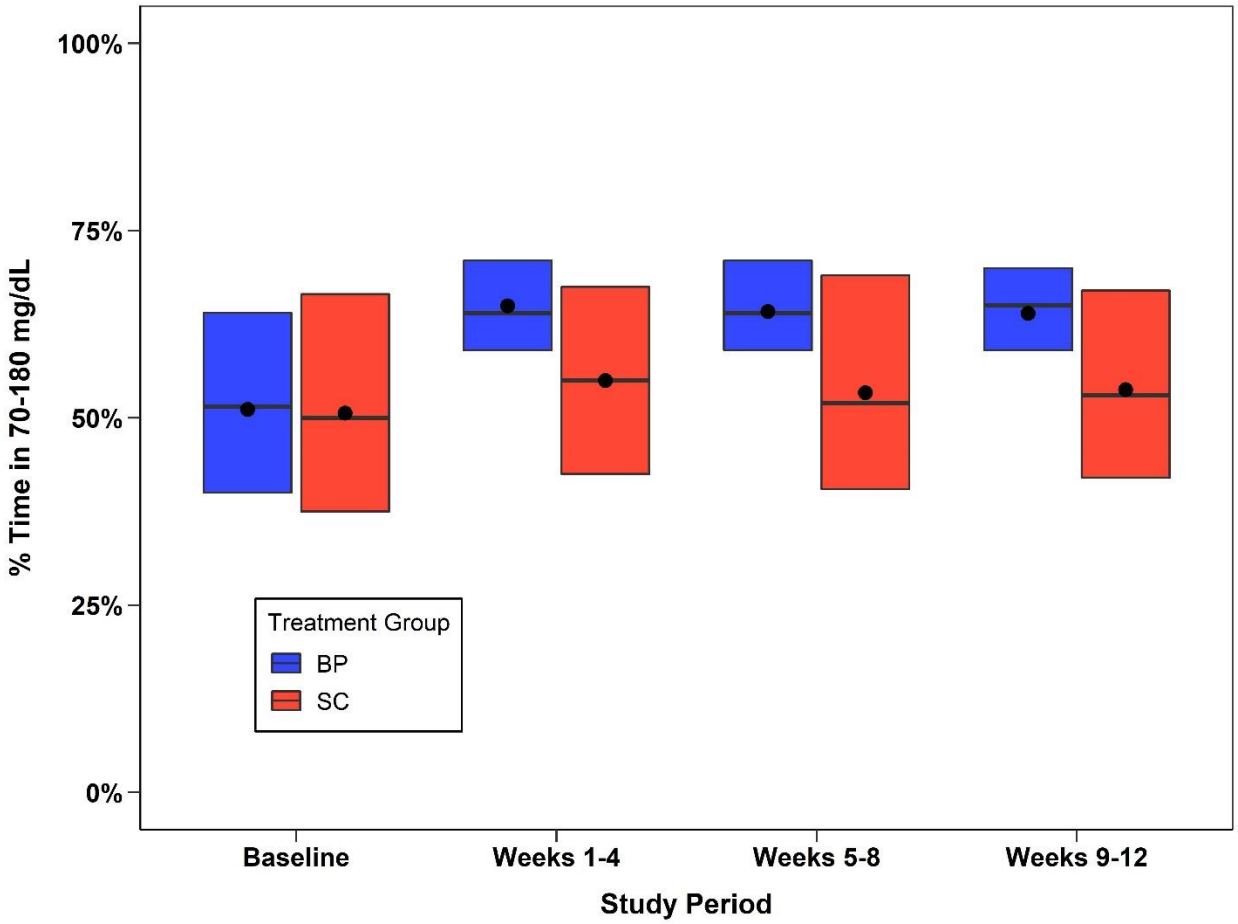

Figure S17. Boxplots of Time 70-180 mg/dL by 4-week Interval. Box plots of percentage of time with glucose 70-180 mg/dL mg/dL measured by CGM in the BP and SC groups during 4-week intervals are shown. Those randomized to the BP group are represented by blue boxes and those randomized to the SC group are represented by red boxes. Black dots indicate the mean values, horizontal bars in the boxes indicate the medians, and the bottom and top of each box represent the 25th and 75th percentiles, respectively.

Figure S18. Boxplots of Time <54 mg/dL by 4-week Interval

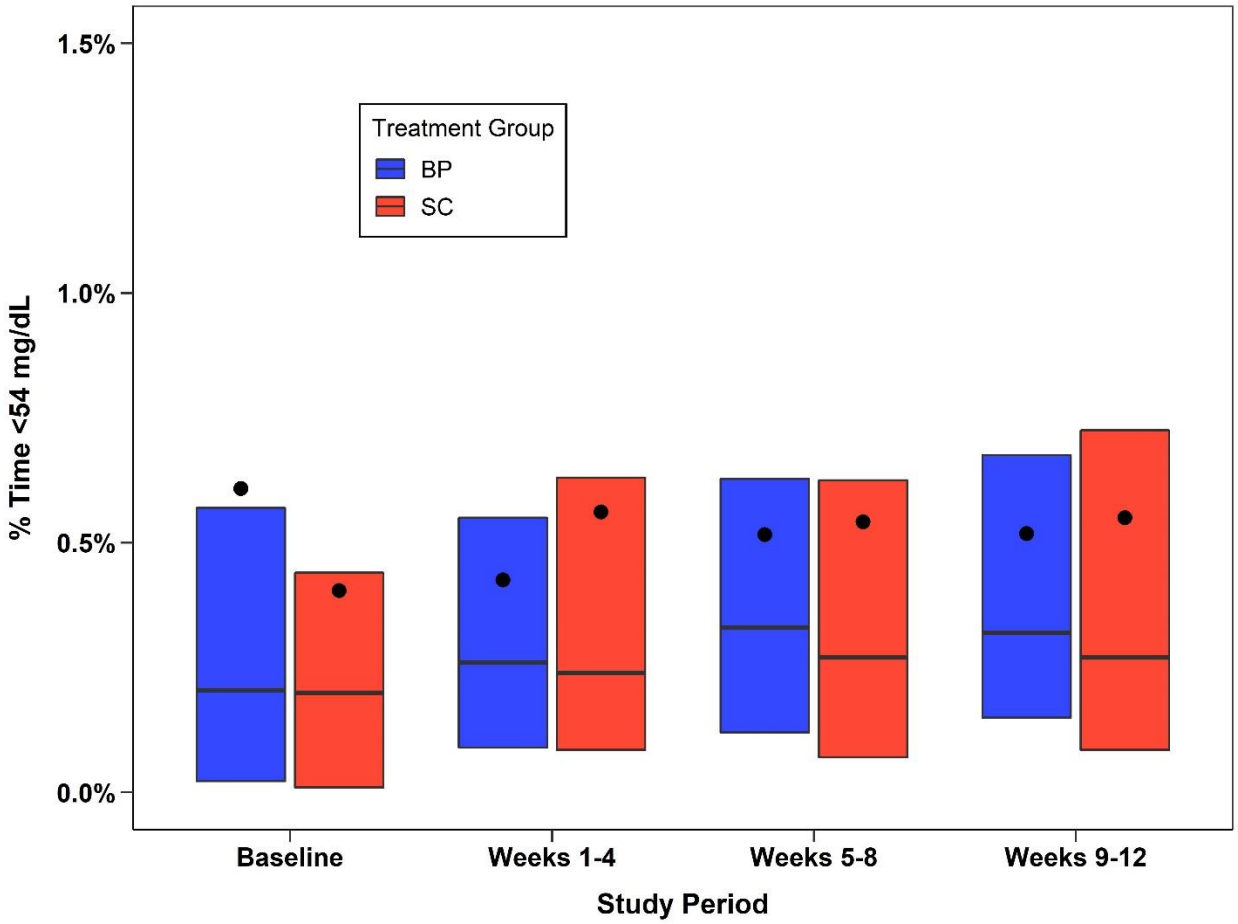

Figure S18. Boxplots of Time <54 mg/dL by 4-week Interval. Box plots of percentage of time with glucose <54 mg/dL measured by CGM in the BP and SC groups during 4-week intervals are shown. Those randomized to the BP group are represented by blue boxes and those randomized to the SC group are represented by red boxes. Black dots indicate the mean values, horizontal bars in the boxes indicate the medians, and the bottom and top of each box represent the 25th and 75th percentiles, respectively.