Statistical Analysis Plan F3Z-MC-IOQV (Version 3)

An Objective Assessment of Mealtime Bolus Insulin Behavior and Associated Factors

NCT03368807

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Statistical Analysis Plan

Protocol: F3Z-MC-IOQV(a)

An Objective Assessment of Mealtime Bolus Insulin Behavior and Associated Factors

Clinical Investigation Using the Reusable Insulin Injection Pen (LY8888AT)

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1. ABBREVIATIONS

AE(s):	Adverse Event(s)
ALBSS:	Adult Low Blood Sugar Survey
APS:	Avoidant Problem Solving
BFI:	Big Five Inventory
CRF:	Case Report Forms
CGM:	Continuous Glucose Monitoring
CSR:	Clinical Study Report
EPS:	Effective Problem Solving
HCS:	Hypoglycemic Confidence Scale
HPSS:	Health Problem Solving Scale
IPS:	Impulsive/Careless Problem Solving
MBD:	Missed Bolus Doses
MSBD:	Missed and Suboptimal Bolus Dose
NMO:	Negative Motivation/Orientation
NTR:	Negative Transfer/Learning
PRISM:	Pictorial Representation of Illness and Self Measure
PRO:	Patient-Reported Outcomes
PMO:	Positive Motivation/Orientation
PTR:	Positive Transfer/Learning
SAE:	Serious Adverse Event
SAP:	Statistical Analysis Plan
SD:	Standard Deviation
T1D:	Type 1 Diabetes
T2D:	Type 2 Diabetes

2. INTRODUCTION

This statistical analysis plan (SAP) details the analyses planned for the data collected during the study F3Z-MC-IOQV(a), an exploratory study sponsored by Eli Lilly and Company, including the definition of analysis populations, derivation of variables, convention of analysis scope, and statistical methodology for evaluation of efficacy and safety of the use of continuous glucose monitoring (CGM) and the insulin injection pen in subjects with type 1 diabetes (T1D) or type 2 diabetes (T2D). Any deviations from this SAP during the actual data analysis will be documented in a statistical analysis change request and when necessary described in the Clinical Study Report (CSR).

3. OBJECTIVES AND ENDPOINTS

3.1 Efficacy Objectives / Endpoints

Objectives	Endpoint(s)
Primary	
• To objectively estimate the average number of days per month with a missed bolus dose in subjects with type 1 or type 2 diabetes with blinded CGM	• The average number of days per month with a missed bolus dose
Secondary	
• To estimate the average number of days per month with a missed bolus dose in subjects with type 1 or type 2 diabetes with unblinded CGM	• The average number of days per month with a missed bolus dose
• To estimate the percent time-in-range in subjects with type 1 or type 2 diabetes with o Blinded CGM o Unblinded CGM	• Percent time-in-range (glucose >70 and ≤180 mg/dL)
• To estimate the percent of missed bolus doses in subjects with type 1 or type 2 diabetes with o Blinded CGM o Unblinded CGM	• Percent of missed bolus doses
• To estimate the average number of missed bolus doses per day in subjects with type 1 or type 2 diabetes with o Blinded CGM o Unblinded CGM	• Average number of missed bolus doses per day
• To estimate the Missed and Suboptimal Bolus Dose (MSBD) in subjects with type 1 or type 2 diabetes with o Blinded CGM o Unblinded CGM	• The average number of MSBD events per month

Exploratory	
• To assess the association between MSBD rate and CGM alert settings	• Correlation between MSBD rate and CGM alert settings
• To evaluate characteristics associated with short-term glycemic control in subjects with type 1 or type 2 diabetes	• Outcome for each PRO instrument*
• To estimate the average number of days per month with a missed bolus dose in subjects with type 1 diabetes with o Blinded CGM o Unblinded CGM	• The average number of days per month with a missed bolus dose
• To estimate the average number of days per month with a missed bolus dose in subjects with type 2 diabetes with o Blinded CGM o Unblinded CGM	• The average number of days per month with a missed bolus dose

Abbreviations: CGM = continuous glucose monitoring; PRO = patient-reported outcomes.
* if available for use

3.2 Safety Endpoints

The safety endpoints include:

- Adverse events,
- Local laboratory test for HbA1c.

4. STUDY DESIGN

This is a 12-week, multi-center, single-arm, outpatient, exploratory study with 2 study periods in subjects with T1D or T2D, respectively, using an investigational reusable insulin injection pen and a commercially available CGM device. Subjects participating in the study will follow an appropriate prescribed bolus insulin regimen suitable for their disease state using insulin lispro 100 units/mL injected via the reusable insulin injection pen. During the study, subjects will have their glucose monitored via a commercially available CGM device, which will be blinded during Study Period 1 and unblinded during Study Period 2. The main purpose of the study is to estimate missed bolus insulin doses in subjects with T1D or T2D.

4.1 Sample Size Consideration

Approximately 68 subjects may be entered (i.e., signed informed consent) in order that 50 subjects complete the study. Subjects who are entered but not administered treatment may be replaced to ensure that enough subjects may complete the study. Assuming a screen fail rate

of 15%, the expected number of subjects to be screened is 80. Up to 15 subjects may be enrolled at each investigator site.

A sample size of 50 completers (approximately 25 subjects with T1D and 25 subjects with T2D) is considered sufficient for this exploratory study.

4.2 Study Scheduled Activities

	Study Period 1 Blinded CGM			Study Period 2 Unblinded CGM			
Procedure Weeks from Enrollment	**Screening/ Enrollment V1 0W**	**V2 3W**	**V3 6W**	**V4 9W**	**End of Study V5 12W**	**Early D/C**	**Notes**
Visit Window	N/A	3D	3D	3D	3D	N/A	Allowable deviation +/- days or weeks from scheduled visit.
Office or home visit	X	X	X	X	X	X	
Informed consent	X						
Inclusion and exclusion criteria	X						
Demography	X						
Height and weight	X						
Medical history	X						
Current medical conditions	X						Including baseline diabetes disease characteristics
Prescribed insulin regimen	X						Currently prescribed basal and bolus insulin regimen
Concomitant medication review	X	X	X	X	X	X	
Enrollment	X						
HbA1c blood draw [a]	X		X		X	X	
Pen dispensing	X						Record pen identification for dispensed pens
Pen training and start pen	X						
Confirm pen operation		X	X	X	X		
Pen collection/return					X	X	
CGM and glucose meter training	X						
CGM and pen data download		X	X	X	X	X	
Adjust CGM alert settings				X			
Hypoglycemic Confidence Scale	X		X		X	X	

	Study Period 1 Blinded CGM			**Study Period 2 Unblinded CGM**			
Adult Low Blood Sugar Survey	X		X		X	X	
The Big Five Inventory	X						
Health Problem Solving Scale	X		X		X	X	
Pictorial Representation of Illness and Self Measure	X		X		X	X	
General Life Stress Scale	X		X		X	X	
AE and SAE review		X	X	X	X	X	
Product complaint review		X	X	X	X	X	

Abbreviations: AE = adverse event; CGM = continuous glucose monitoring; D = days; D/C = discontinuation; HbA1c = glycated hemoglobin; N/A = not applicable; SAE = serious adverse event; V = visit; W = week.

[a] HbA1c testing will be performed by local laboratories.

5. ANALYSIS POPULATIONS (ANALYSIS SETS)

5.1 Entered Analysis Set

The entered analysis set comprises all subjects who signed informed consent.

5.2 Evaluable Analysis Set

The evaluable analysis set comprises all entered subjects with ≥ 2-week use of unblinded CGM. All efficacy analyses will be performed on this analysis set.

5.3 Safety Analysis Set

The safety analysis set comprises all entered subjects with any CGM or pen usage. All safety analyses will be performed on this analysis set.

6. TREATMENT DESCRIPTIONS

Unless otherwise indicated, on the summary tables, the study periods will be identified by Period 1 (Blinded CGM) and Period 2 (Unblinded CGM) respectively, side by side in the presentation.

7. STATISTICAL ANALYSIS METHODS AND ISSUES

7.1 Statistical Methods

Given the exploratory nature of the study, the analyses will be primarily descriptive, using descriptive statistics, namely sample size (n), mean, standard deviation (SD), minimum, median, and maximum for continuous variables; frequency and percentage for categorical variables. Some data will also be presented graphically using scatter plots, for instance.

7.2 Baseline Definition

The baseline is the result collected at the screening/enrollment visit.

7.3 Interim Analysis

No interim analysis is planned in this study.

7.4 Missing Data

Missing data will not be imputed except of the missing AE data which are specified in section 9.1.

8. DEMOGRAPHICS, BASELINE CHARACTERISTICS AND STUDY SUMMARY

All demographic and baseline characteristics summaries are to be performed on the entered and evaluable analysis sets, unless stated otherwise.

8.1 Subject Disposition

The number and percentage of subjects who were screened, signed informed consent, completed, and discontinued, including discontinuation period, will be summarized. The number and percentage of subjects who discontinued will also be summarized for each reason for discontinuation. The summary will be made overall and by study site.

8.2 Demographics and Baseline Characteristics

The demographics (age, gender, ethnicity, and race) and baseline body weight and height, as well as the number of subjects in each of the categorized baseline variables, including HbA1c ($\leq 9.0\%$ vs. $> 9.0\%$), and duration of diabetes ($\leq$ median vs. $>$ median), will be summarized using descriptive statistics. Additionally, the age will be grouped into the following categories and summarized: less than 65 yrs, 65 to 84 yrs, and greater than 84 yrs.

The duration of diabetes will be calculated in months using the following formula rounding to one decimal place.

CCI [redacted]

8.3 Medical History

The medical history will be coded by MedDRA 20.1. The summary will be made by MedDRA SOC and Preferred Terms.

8.4 Diabetes Diagnosis

The Type of diabetes, duration of diabetes, and pre-enrollment bolus insulin analog collected at screening will be summarized by descriptive statistics.

8.5 Big Five Inventory (BFI)

The BFI is a 44-item inventory that measures an individual on the Big Five Factors (dimensions) of personality, Extraversion versus introversion (8 items), Agreeableness versus antagonism (9 items), Conscientiousness versus lack of direction (9 items), Neuroticism versus emotional stability (8 items), and Openness versus closedness to experience (10 items). The evaluation uses a Likert scale of (1) disagree strongly, (2) disagree a little, (3) neither agree nor disagree, (4) agree a little, and (5) agree strongly.

The results on the Likert scale in the five categories will be summarized by descriptive statistics using frequency and percentage.

8.6 Treatment Compliance

The total number of measures from the CGM device and pen per subject during the analysis periods (refer to the definition 3 in section 10.1) will be summarized for the evaluable analysis set. Note that among the several records captured for each injection in the Pen data, observations not more than 30 minutes apart will be considered one injection (refer to the definition 2 in section 10.1).

9. ANALYSIS OF SAFETY ENDPOINTS

All safety summaries are to be performed on the safety analysis set by period, unless stated otherwise.

9.1 Adverse Events

The adverse events will be coded by the Medical Dictionary for Drug Regulatory Activities (MedDRA) version 20.1.

All adverse events (AE) occurred post screening will be presented in the summary tables.

Summary tables will include the number and percentage of subjects reporting adverse events. The number of serious adverse events may be summarized in the appropriate summary table(s). Summary tables will also be presented for the frequency of adverse events by the MedDRA system organ class and preferred term. Multiple events in the same system organ class for a subject are only counted once in the statistics of that system organ

class. Summary tables will also be presented for the frequency of adverse events by MedDRA system organ class and preferred term and severity of adverse events, and relationship of adverse events to insulin, pen, or CGM respectively. In these summaries, the most extreme outcome (highest severity) will be used for those subjects who experience the same adverse event (per preferred term) on more than one occasion. A listing of adverse events that lead to discontinuation from the study will also be provided.

Missing values will be treated as missing except for causality and severity of an AE, at which occurrence a "worst case" approach will be taken in the analysis. Thus, if causality is missing the AE will be regarded as related to insulin, pen, and CGM, and if the severity is missing the severity of the AE will be regarded as severe. If the seriousness is missing, all efforts should be made prior to database lock to make sure that this information is available.

9.2 Concomitant Medications

The concomitant mediations will be coded by WHO ATC classification, and summarized by descriptive statistics for the safety analysis set disregard of the periods.

9.3 Bolus Insulin Regimen and Dose Change

The data collected in the CRF Bolus Insulin Regimen at screening and CRF Bolus Insulin Dose Change at post screening visits will be summarized. The focus will be on the dose change (Yes or No). The detail of the bolus insulin regimen will be presented in the data listing(s).

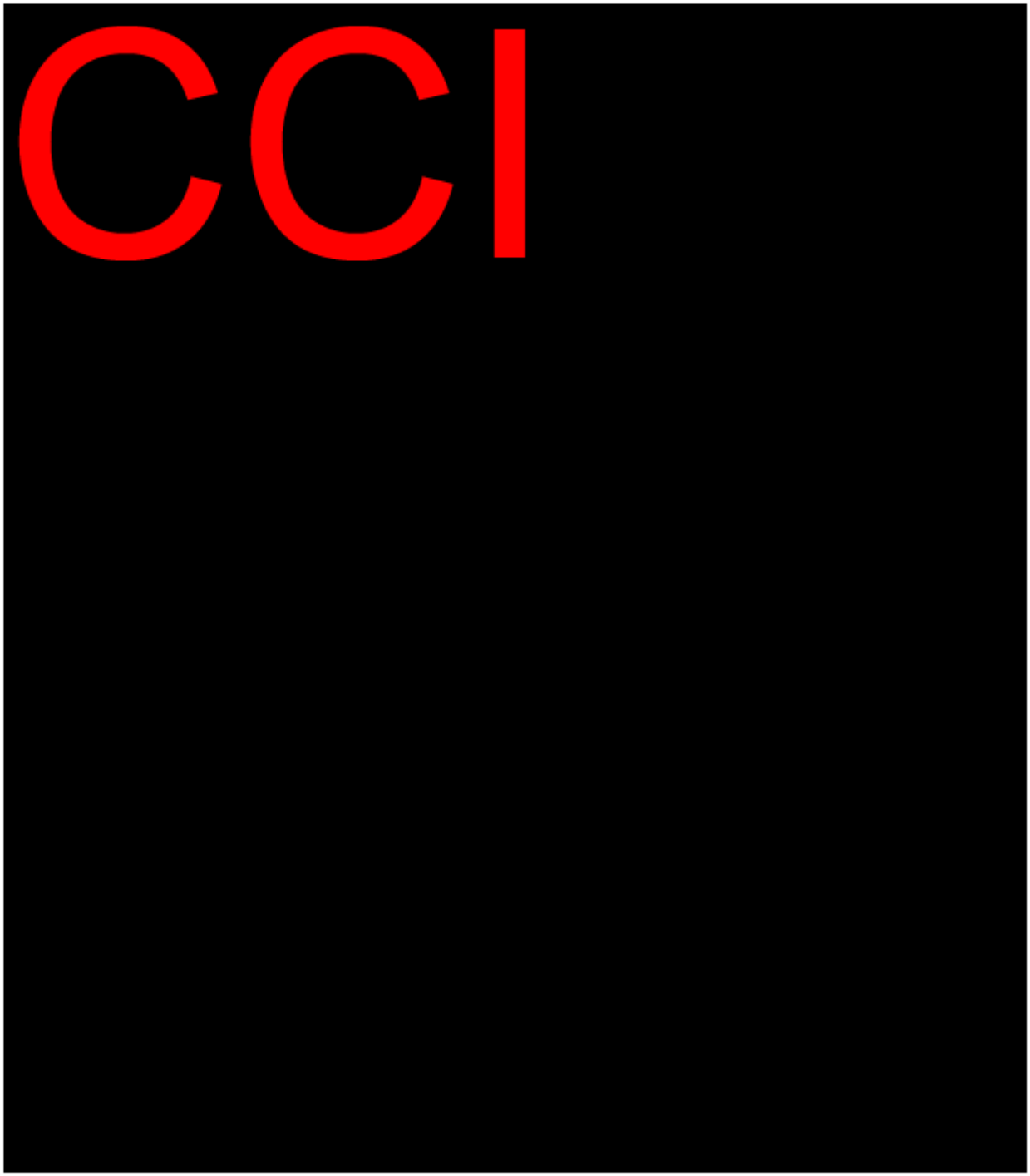
10. ANALYSIS OF EFFICACY ENDPOINTS

All efficacy summaries are to be performed on the evaluable analysis set by period. The GCM and Pen data collected for Weeks 3-6 (Visits 2 and 3) for Study Period 1 (blinded CGM) and Weeks 9-12 (Visits 4 and 5) for Study Period 2 (unblinded CGM) will be used in these calculations. The inclusion of the data will be based on the dates, disregard of the times even available, of the visits, which means that the GCM and Pen data will be included for the Study Period 1 if they are in the range from the date of the Visit 2 to the date of the Visit 3, inclusive, and included for the Study Period 2 if they are in the range

from the date of the Visit 4 to the date of Visit 5, inclusive. If a subject discontinues the study, the date of Early Termination will be used instead.

10.1 Missed Bolus Doses (MBD)

Missed bolus doses will be identified by using the CGM and Pen data.

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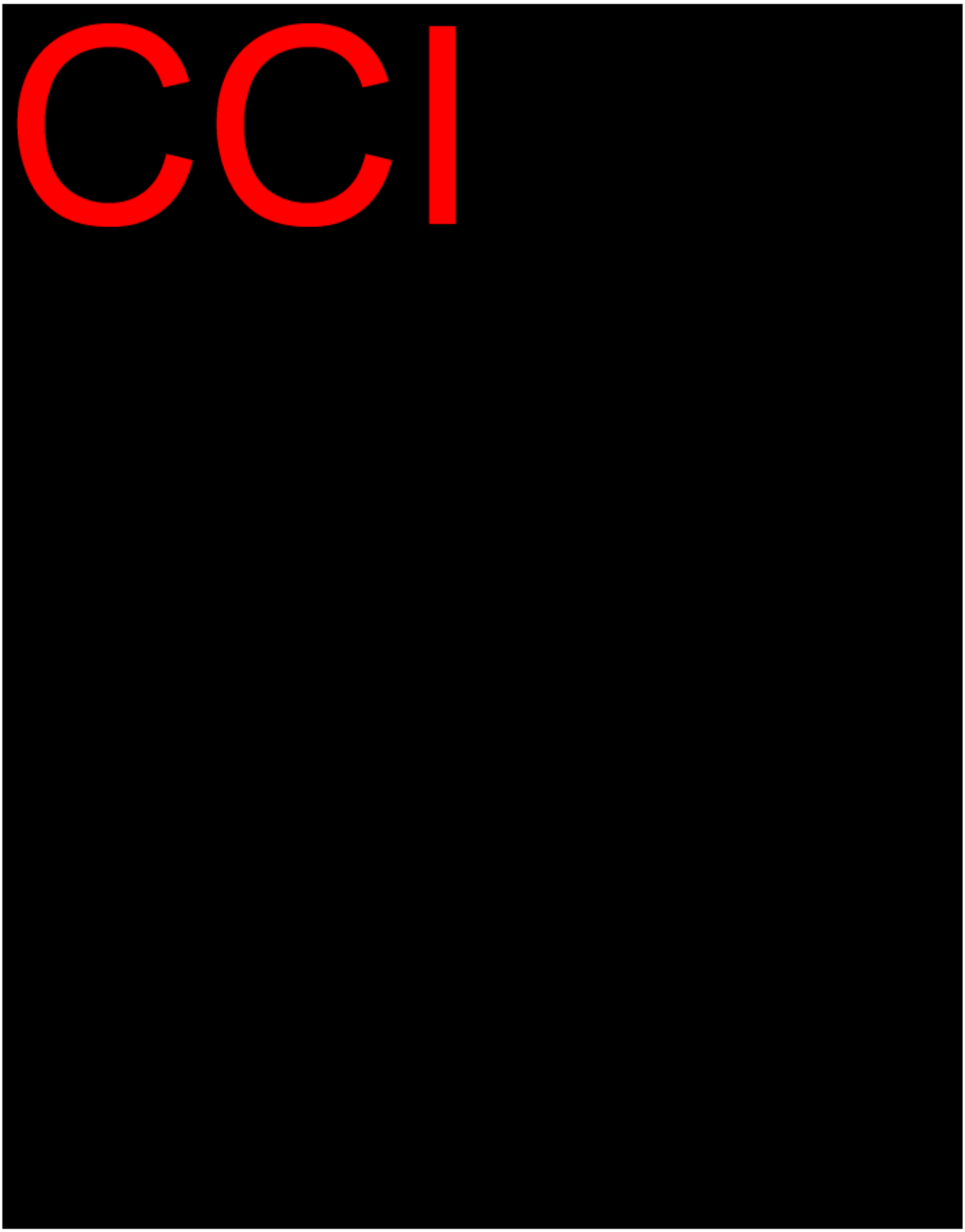
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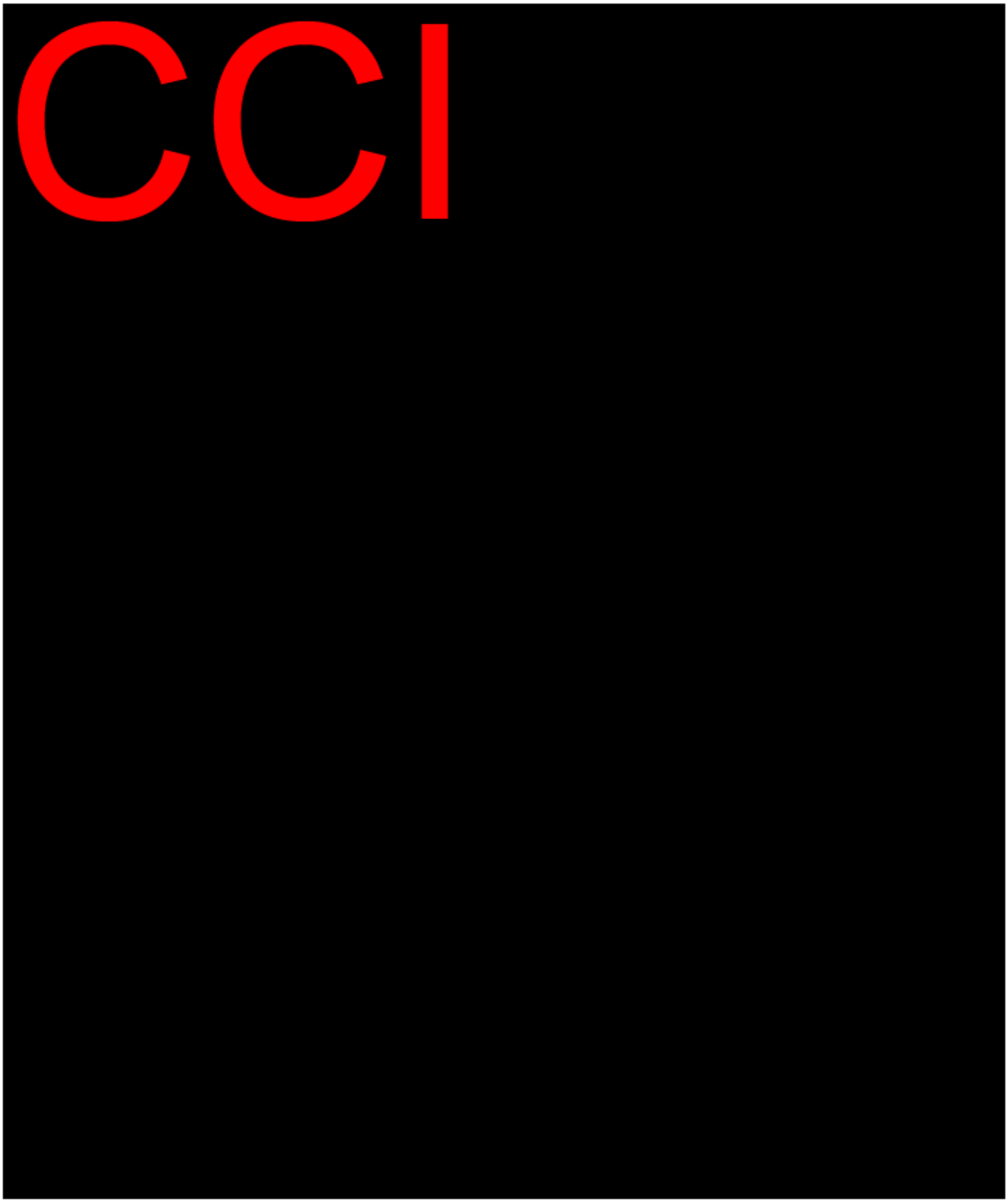
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10.2 Percent Time-in-Range of Glucose

The percent time-in-range of glucose (> 70 and ≤ 180 mg/dL) will be calculated based on CGM data collected in the study period and summarized for each period by descriptive statistics.

10.3 Missed and Suboptimal Bolus Dose (MSBD)

The suboptimal bolus doses will be identified by using the CGM and Pen data.


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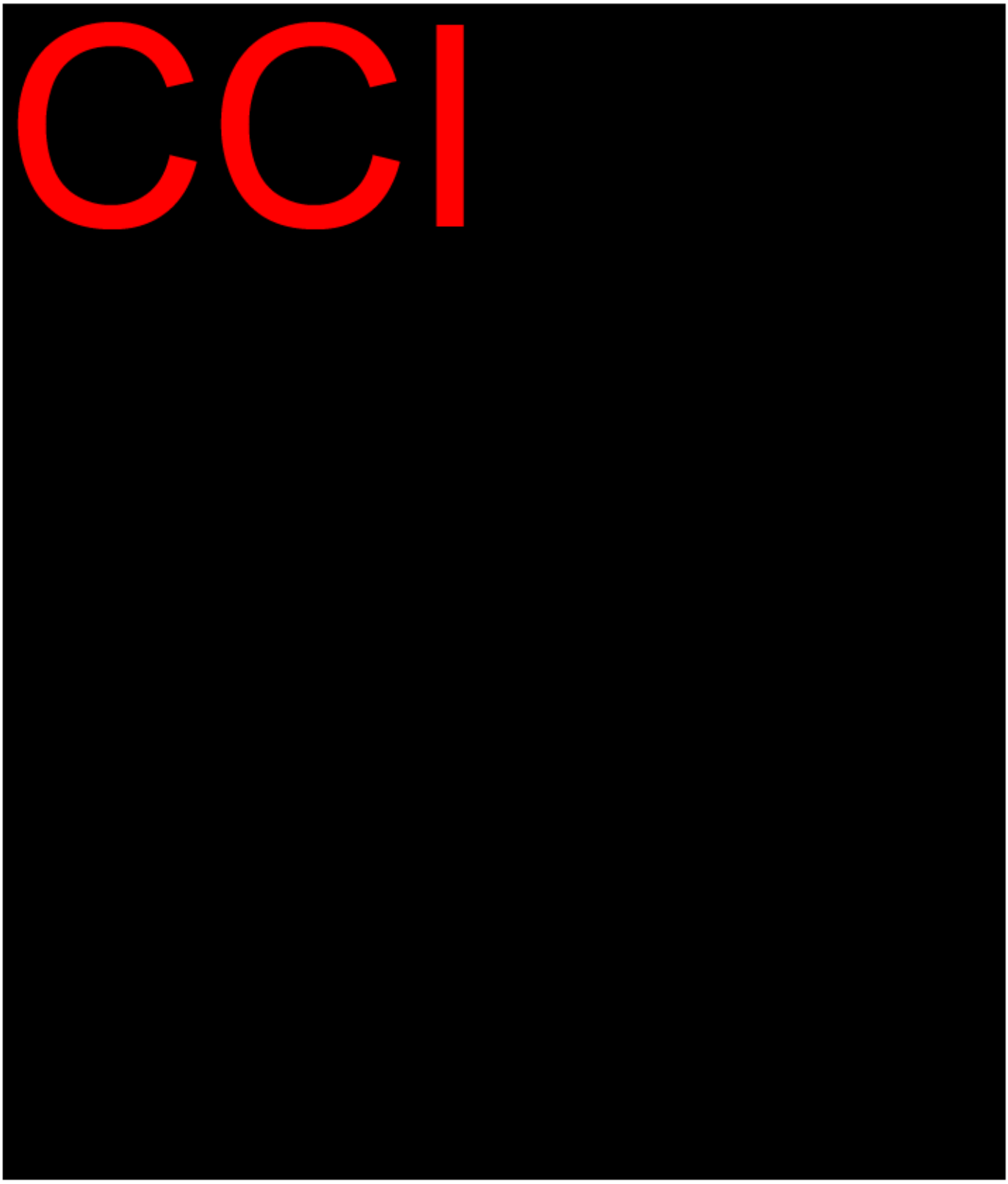
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10.4 Glycated Hemoglobin (HbA1c) Results

The HbA1c results (%) at each scheduled visit will be summarized by descriptive statistics.

10.5 Hypoglycemic Confidence Scale (HCS)

This evaluation uses the Likert scale with ratings of not confident at all, a little confident, moderately confident, and very confident to rate a subject's response to 9 items during the evaluation (8 items for subjects without a partner and 9 for subjects with a partner). Each item will receive a score from 1 to 4 based on the subject's response. HCS score is calculated as the sum of the item scores divided by the number of items completed.

The results on the Likert scale in the four categories will be summarized by descriptive statistics using frequency and percentage. The HCS score and the change from baseline will be summarized respectively.

The change from baseline to end of the period in HCS score vs. the percent time-in-range of glucose in the period will be graphically presented by a scatterplot.

10.6 Adult Low Blood Sugar Survey (ALBSS)

This is an evaluation of the fear of hypoglycemia derived from the widely used and validated ALBSS. This evaluation uses the Likert scale of 0 ("never") to 4 ("almost always") to rate 11 items (Behavior domain with 5 items; Worry domain with 6 items). The behaviour domain score is the sum of the 5 item scores, and the worry domain score is the sum of the 6 item scores. The total score is the sum of the two domain scores (i.e. the sum of the 11 item scores).

The results on the Likert scale in the five categories will be summarized by descriptive statistics using frequency and percentage. The domain and the total scores and the change from baseline will be summarized respectively.

The change from baseline to end of the period in ALBSS total score vs. the percent time-in-range of glucose in the period will be graphically presented by a scatterplot.

10.7 Health Problem Solving Scale (HPSS)

The HPSS scale is a set of 50 items that the subject rates using a 5-point Likert scale ranging from "not at all true of me" (0 points) to "extremely true of me" (4 points). Seven subscale scores are calculated by summing scores for each item in the respective subscale. The HPSS total score is derived using the formula:

which sums the subscale averages, with reverse scoring of the negative subscales.

The seven HPSS subscale scores are:

Effective Problem Solving (EPS) = sum of scores of items 7, 9, 13, 20, 21, 24, 28, 44, and 49;

Impulsive/Careless Problem Solving (IPS) = sum of scores of items 8, 12, 27, 30, 38, 39, 41, and 42;

Avoidant Problem Solving (APS) = sum of scores of items 4, 25, 31, 33, 43, 46, and 48;

Positive Transfer/Learning (PTR) = sum of scores of items 5, 16, 19, 45, and 50;

Negative Transfer/Learning (NTR) = sum of scores of items 2, 3, 10, 14, 17, 23, 26, 29, 35, 37, and 40;

Positive Motivation/Orientation (PMO) = sum of scores of items 1, 6, 18, 32, and 36;

Negative Motivation/Orientation (NMO) = sum of scores of items 11, 15, 22, 34, and 47.

The results on the Likert scale in the five categories will be summarized by descriptive statistics using frequency and percentage. The HPSS subscale scores and the total score and the change from baseline will be summarized respectively.

The change from baseline to end of the period in HPSS total score vs. the percent time-in-range of glucose in the period will be graphically presented by a scatterplot.

10.8 Pictorial Representation of Illness and Self Measure (PRISM)

The data collected on the CRF PRISM Revised II will be summarized by descriptive statistics, including Self Illness Separation (mm) and the Illness Perception Measure (small, medium, and large) for the subject's diabetes today and the goal.

The change from baseline in self illness separation will be summarized by descriptive statistics as well. The shift from baseline in illness perception measure will be generated.

The change from baseline to end of the period in self illness separation vs. the percent time-in-range of glucose in the period will be graphically presented by a scatterplot.

10.9 General Life Stress Scale (GLSS)

The GLSS assesses the degree of stress an individual is currently experiencing in 6 general areas of life (work/household chores, friends/social activity, family, money/financial, housing/neighbourhood, and health), with five response options ranging from "not at all stressful" (score = 0) to "extremely stressful" (score = 4). The total score is the sum of the 6 individual scores.

The results of the 6 general areas of life in the five categories will be summarized by descriptive statistics using frequency and percentage. The GLSS total score and the change from baseline will be summarized respectively.

The change from baseline to end of the period in GLSS total score vs. the percent time-in-range of glucose in the period will be graphically presented by a scatterplot.

11. LIST OF TABLES AND DATA LISTINGS

11.1 Statistical Tables

The statistical tables will be generated using SAS® version 9.4. The sample size (n) and frequency (count) will be presented by whole number. The mean, standard deviation, median, minimum, and maximum will be rounded to one decimal place. The percentage will be presented to one decimal place.

Number	Title	Population
14.1.1	Subject Disposition	Screened
14.1.2.1	Demographics and Baseline Characteristics	Entered

Number	Title	Population
14.1.2.2	Demographics and Baseline Characteristics	Evaluable
14.1.3.1	Medical History	Entered
14.1.3.2	Medical History	Evaluable
14.1.4.1	Diabetes Diagnosis	Entered
14.1.4.2	Diabetes Diagnosis	Evaluable
14.1.5.1	Big Five Inventory	Entered
14.1.5.2	Big Five Inventory	Evaluable
14.1.6	Treatment Compliance	Evaluable
14.2.1*	Missed Bolus Dose	Evaluable
14.2.2.1.1	Number of Missed Bolus Doses per Month by HbA1c	Evaluable
14.2.2.1.2	Number of Missed Bolus Doses per Month by Duration of Diabetes	Evaluable
14.2.2.2	Percent Time-in-Range of Glucose	Evaluable
14.2.2.3	Missed or Suboptimal Bolus Dose	Evaluable
14.2.2.4	Glycated Hemoglobin (HbA1c) Results	Evaluable
14.2.3.1	Hypoglycemic Confidence Scale (HCS)	Evaluable
14.2.3.2	Adult Low Blood Sugar Survey (ALBSS)	Evaluable
14.2.3.3	Health Problem Solving Scale (HPSS)	Evaluable
14.2.3.4	Pictorial Representation of Illness and Self Measure (PRISM)	Evaluable
14.2.3.5	General Life Stress Scale (GLSS)	Evaluable
14.2.3.6.1	Number of Days per Month with Missed Bolus Dose in Subjects with Type 1 Diabetes	Evaluable
14.2.3.6.2	Number of Days per Month with Missed Bolus Dose in Subjects with Type 2 Diabetes	Evaluable
14.3.1.1	Number of Subjects with Adverse Events	Safety
14.3.1.2	Number of Adverse Events	Safety
14.3.1.3	Number of Subjects with Adverse Events by MedDRA System Organ Class / Preferred Term	Safety
14.3.1.4	Number of Subjects with Adverse Events by MedDRA System Organ Class / Preferred Term and Severity	Safety
14.3.1.5	Number of Subjects with Insulin Related Adverse Events by MedDRA System Organ Class / Preferred Term	Safety
14.3.1.6	Number of Subjects with Pen Related Adverse Events by MedDRA System Organ Class / Preferred Term	Safety
14.3.1.7	Number of Subjects with CGM Related Adverse Events by MedDRA System Organ Class / Preferred Term	Safety
14.3.1.8	List of Adverse Events Leading to Withdrawal from the Study	Safety
14.3.1.9	List of Serious Adverse Events	Safety
14.3.1.10	List of Death (if there is any)	Safety

Number	Title	Population
14.3.1.11	Number of Subjects with Non-Serious Adverse Events by MedDRA System Organ Class / Preferred Term	Safety
14.3.5.1	Bolus Insulin Regimen and Dose Changes	Safety
14.3.5.2	Concomitant Medication	Safety

* include the summaries of the number of days per month with MBD, percent of missed bolus doses, and number of MBD per day.

11.2 Figures

The figures of the change from baseline for these patient-reported outcomes vs. percent time-in-range of glucose will be generated for each period.

Number	Title	Population
14.2.3.2	Scatterplot of Hypoglycemic Confidence Scale (HCS) Score vs. Percent Time-in-Range of Glucose	Evaluable
14.2.3.3	Scatterplot of Adult Low Blood Sugar Survey (ALBSS) Total Score vs. Percent Time-in-Range of Glucose	Evaluable
14.2.3.4	Scatterplot of Health Problem Solving Scale (HPSS) Total Score vs. Percent Time-in-Range of Glucose	Evaluable
14.2.3.5	Scatterplot of PRISM Self Illness Separation vs. Percent Time-in-Range of Glucose	Evaluable
14.2.3.6	Scatterplot of General Life Stress Scale (GLSS) Total Score vs. Percent Time-in-Range of Glucose	Evaluable

11.3 Data Listings

Data listings will be sorted by subject and visit.

Number	Title
16.2.1	Subject Dispositions
16.2.2	Inclusion / Exclusion Criteria Not Met
16.2.3	Subjects Excluded from the Evaluable Population
16.2.4	Demographics
16.2.4.1	Baseline Characteristics
16.2.4.2	Medical History
16.2.4.3	Diabetes Diagnosis
16.2.4.4	Big Five Inventory
16.2.5	Treatment Compliance
16.2.6.1.1	Continuous Glucose Monitoring (CGM) Results
16.2.6.1.2	Missed Bolus Doses Measurements
16.2.6.2.1	Percent Time-in-Range of Glucose
16.2.6.2.2	Glycated Hemoglobin (HbA1c) Results

Number	Title
16.2.6.2.3	Hypoglycemic Confidence Scale (HCS)
16.2.6.2.4	Adult Low Blood Sugar Survey (ALBSS)
16.2.6.2.5	Health Problem Solving Scale (HPSS)
16.2.6.2.6	Pictorial Representation of Illness and Self Measure (PRISM)
16.2.7.1	Adverse Events by CRF & MedDRA Coded Terms
16.2.7.2	Adverse Event MedDRA Coding Glossary
16.2.8	Insulin Injection Records
16.2.9	Concomitant Medication

12. TABLE SHELLS

The following table shells are provided in order to provide a framework of the statistical analysis for the study. These shells may not be reflective of every aspect of the analyses, but are intended to show the general layout of the tables that will be included in the final report.

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Table 14.1.1 - Disposition of Subjects

		Study Sites				
		xxx	xxx	xxx	xxx	Overall
Screened		xx	xx	xx	xx	xx
Signed Informed Consent		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Completed	N	xx	xx	xx	xx	xx
	YES	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	NO	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Discontinuation in	Period 1 (Blinded CGM)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Period 2 (Unblinded CGM)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Primary Reason for Discontinuation	N	x	x	x	x	x
	Adverse Event	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	Protocol Violation	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	Withdrawal by Subject	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	Physician Decision	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	Sponsor Decision	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	Lack of Efficacy	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	Lost to Follow-Up	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	Other	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)

Program: 14.1.1.xxxx.sas

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Table 14.2.1 - Missed Bolus Dose (Evaluable Population)

		Insulin Injection	
		Period 1 (Blinded CGM)	Period 2 (Unblinded CGM)
Parameter	Statistics	N = xx	N = xx
Number of Days per Month with MBD	N	xx	xx
	Mean	xx.x	xx.x
	SD	xx.x	xx.x
	Median	xx.x	xx.x
	Minimum	xx.x	xx.x
	Maximum	xx.x	xx.x
Percent of Missed Bolus Doses	N	xx	xx
	Mean	xx.x	xx.x
	SD	xx.x	xx.x
	Median	xx.x	xx.x
	Minimum	xx.x	xx.x
	Maximum	xx.x	xx.x
Number of Missed Bolus Doses per Day	N	xx	xx
	Mean	xx.x	xx.x
	SD	xx.x	xx.x
	Median	xx.x	xx.x
	Minimum	xx.x	xx.x
	Maximum	xx.x	xx.x

Program: 14.2.1.xxxx.sas

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Table 14.3.1.1 - Number of Subjects with Adverse Events (Safety Population)

	Insulin Injection	
	Period 1 (Blinded CGM) N = xx	Period 2 (Unblinded CGM) N = xx
With At Least One Adverse Event	xx (xx.x%)	xx (xx.x%)
With At Least One Mild or Moderate Adverse Event	xx (xx.x%)	xx (xx.x%)
With At Least One Severe Adverse Event	xx (xx.x%)	xx (xx.x%)
With At Least One Serious Adverse Event	xx (xx.x%)	xx (xx.x%)
With At Least One Insulin Related Adverse Event	xx (xx.x%)	xx (xx.x%)
With At Least One Pen Related Adverse Event	xx (xx.x%)	xx (xx.x%)
With At Least One CGM Related Adverse Event	xx (xx.x%)	xx (xx.x%)

Program: 14.3.1.1.xxxx.sas

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Table 14.3.1.2 - Number of Adverse Events (Safety Population)

	Insulin Injection	
	Period 1 (Blinded CGM) N = xx	Period 2 (Unblinded CGM) N = xx
Total Number of Adverse Events	xx	xx
Mild or Moderate Adverse Events	xx	xx
Severe Adverse Events	xx	xx
Serious Adverse Events	xx	xx
Adverse Events Related to Insulin	xx	xx
Adverse Events Related to Pen	xx	xx
Adverse Events Related to CGM	xx	xx

Program: 14.3.1.2.xxxx.sas

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Table 14.3.1.3 - Number of Subjects with Adverse Events by MedDRA System Organ Class / Preferred Term
(Safety Population)

	Insulin Injection	
	Period 1 (Blinded CGM)	Period 2 (Unblinded CGM)
SYSTEM ORGAN CLASS / PREFERRED TERM	N = xx	N = xx
Subjects with at least one adverse event	xx (xx.x%)	xx (xx.x%)
System Organ Class #1	xx (xx.x%)	xx (xx.x%)
Preferred Term #1	x (xx.x%)	x (xx.x%)
Preferred Term #2	x (xx.x%)	x (xx.x%)
Preferred Term #3	x (xx.x%)	x (xx.x%)
etc.		
System Organ Class #2	xx (xx.x%)	xx (xx.x%)
Preferred Term #1	x (xx.x%)	x (xx.x%)
Preferred Term #2	x (xx.x%)	x (xx.x%)
Preferred Term #3	x (xx.x%)	x (xx.x%)
etc.		

Multiple events in the same preferred term or system organ class for a subject are only counted once in the statistics of that preferred term or system organ class.

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Table 14.3.1.4 - Number of Subjects with Adverse Events by MedDRA System Organ Class / Preferred Term and Severity
(Safety Population)

Period 1 (Blinded CGM) N = xx

SYSTEM ORGAN CLASS / PREFERRED TERM	MILD	MODERATE	SEVERE	TOTAL
Subjects with at least one adverse event	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
System Organ Class #1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred Term #1	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Preferred Term #2	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Preferred Term #3	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
etc.				
System Organ Class #2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred Term #1	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Preferred Term #2	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Preferred Term #3	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
etc.				

System Organ Classes are presented alphabetically. Preferred Terms are sorted within System Organ Class in descending frequency of the overall events.

When there are multiple events with the same preferred term in a system organ class for a subject, the most severe event is counted. Multiple events in the same system organ class for a subject are counted only once in the statistics of that system organ class. The percentage represents the incidence of an event by the system organ class or the preferred term as a percentage of the total number of subjects in the period.

Program: 14.3.1.4.xxxx.sas