Protocol Title: Optimizing Glycemic Control in Metabolic Surgery with Continuous Glucose Monitoring

PI Name: Yun Shen

Sub-Investigator's Name(s): Peter T. Katzmarzyk, Gang Hu, Zubaidah Nor Hanipah, Phillip Schauer

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IRB Review History
None

Objectives
Aim 1: To identify the glycemic patterns by using CGM in severely obese patients with T2D receiving bariatric surgeries before and after the procedures. *Hypothesis: CGM will reveal distinct glycemic patterns in obese patients with T2D undergoing metabolic surgery, with significant improvements in mean glucose control but not glycemic variability compared to baseline measures.*

Aim 2: To investigate if the metrics that are derived from CGM data before and after the surgery can predict post bariatric hypoglycemia. *Hypothesis: Metrics derived from CGM data, such as time in range, glycemic variability, and mean glucose levels, can reliably predict the likelihood of* post bariatric hypoglycemia*, with specific thresholds or patterns serving as robust predictors of long-term glycemic control.*

Aim 3: To investigate the effect of CGM use on the prevention of post bariatric hypoglycemia, as well as the influence of dietary content, formulation, and patterns on glycemic responses. *Hypothesis: Dietary content, formulation, and patterns significantly influence glycemic responses in obese patients with T2D, with higher fiber and protein intake, balanced macronutrient formulation, and consistent meal patterns associated with improved glycemic control and reduced risk of post bariatric hypoglycemia as measured by CGM after the surgeries.*

Background
Diabetes is a major global health concern due to its increasing prevalence, associated complications, the burden, and places on individuals, healthcare systems, and societies at large. According to the IDF Diabetes Atlas 2021, about 10.5% of the adults worldwide had diabetes, with T2D accounting for about 90% of these cases. Diabetes poses a significant health challenge in US, with approximately 38.4 million—11.6% of the US adults—diagnosed with the condition. Each year, an estimated 1.2 million adults receive a diabetes diagnosis in the US. Obesity is listed as the most important risk factor associated with diabetes. More than 42% of US are classified as obese and 9.4% have severe obesity. About 30% of patients with T2D have severe obesity. The combination of severe obesity and T2D significantly increases the risk of CVD, non-alcoholic fatty liver disease, and other comorbidities, which contribute to higher mortality rates. To tackle this heavy burden, there's a need for coordinated efforts that encompass prevention, early diagnosis, effective treatment, and patient education. The management of T2D and obesity faces several persistent challenges, including achieving sustainable weight loss

and maintaining long-term diabetes remission. While lifestyle interventions and pharmacotherapy often lead to initial improvements, weight regain remains a significant issue, undermining long-term success. Similarly, diabetes remission achieved through these methods is frequently temporary, with many patients experiencing a relapse in glycemic control over time. In this context, metabolic surgery, including procedures such as Roux-en-Y gastric bypass (RYGB) and vertical sleeve gastrectomy (VSG), has emerged as one of the most effective interventions for significant weight loss and long-term diabetes remission, particularly in individuals with severe obesity and T2D. Its metabolic benefits extend beyond weight reduction, directly improving insulin sensitivity and glycemic control. Therefore, integrating metabolic surgery into treatment guidelines and expanding access to eligible patients are critical steps toward addressing the limitations of conventional approaches. While metabolic surgery has been shown to be more effective than intensive medical management for diabetes, its outcomes are often assessed using HbA1c, which has several limitations. HbA1c reflects average blood glucose levels but fails to capture glucose variability or detect hypoglycemia effectively. Additionally, it responds slowly to interventions, making it less suitable for tracking short-term changes post-surgery. These limitations have led to growing interest in CGM as a more precise tool for assessing glucose patterns after metabolic surgery. However, available data on CGM outcomes in this context remain limited, highlighting the need for further research. CGM holds significant potential for improving the assessment and management of obese patients with T2D undergoing metabolic surgery. Unlike traditional measures such as HbA1c, CGM provides real-time, continuous data on glucose levels, offering a detailed picture of glucose variability, postprandial spikes, and hypoglycemic events. This granular insight enables better tracking of short-term metabolic changes immediately after surgery and facilitates early detection of glycemic patterns that may be influenced by the changes in GI tract and dietary patterns after surgery. In the long term, CGM can monitor sustained glycemic control and identify signs of diabetes recurrence, contributing to personalized post-surgical care plans. In addition, post-bariatric hypoglycemia (PBH) is an increasingly recognized complication that can arise following metabolic and bariatric procedures. CGM will enable a better understanding of hypoglycemia unawareness, where patients fail to perceive symptoms despite critically low glucose levels. CGM may have the potential to revolutionize the management of PBH. Despite its promise, research on CGM among patients receiving metabolic surgery remains limited. Several studies have demonstrated the advantages of CGM in identifying post-bariatric hypoglycemia (Table 1). However, limitations of prior studies include their cross-sectional or retrospective design, small sample sizes, a lack of pre-surgery CGM data, and a short GDM monitoring period (most <10 days) with only one GDM measurement taken after surgery. As a result, there is a growing need for more robust studies, such as RCTs, to validate the effectiveness of this approach and optimize its integration into clinical practice.

Inclusion and Exclusion Criteria

Inclusion criteria: (1) age 20 to 60 years; (2) T2D not well controlled with medications (HbA1c >7.0%); (3) body mass index (BMI) ≥35 kg/m2; and (4) diabetes duration ≤ 10 years.

Exclusion criteria: (1) age <20 or ≥60 years; (2) confirmed type 1 diabetes; (3) pregnancy or breastfeeding; (4) history of hypersensitivity to any of the components of the subcutaneous infusions; (5) without access at home to a telephone or other factor

likely to interfere with ability to participate reliably in the study; (6) history of any medical, psychological or other condition, or use of any medications, including over-the-counter products, which, in the opinion of the investigators, would either interfere with the study or potentially cause harm to the volunteer; (7) patients on insulin therapy before surgery; and (8) patients receiving revisional surgery.

Number of Subjects
10 in CGM group and 10 in non-CGM group.

Recruitment Methods
The proposed study will include data from one new RCT. We will recruit 20 severely obese participants with T2D at Metamor Institute. Participants with obesity and diabetes who are eligible for bariatric surgery will be randomized to either CGM group or self-monitoring of blood glucose (SMBG) group before the surgery based on a 1:1 ratio. All participants live in Baton Rouge, Louisiana. The nurses in Metamor will introduce our study to the patients. If the patients are interested, the evaluation process includes verifying basic personal information, assessing health status and medical history, and evaluating specific eligibility criteria relevant to the study. The study coordinator will be discussing informed consent, ensuring participants understand the study's purpose, procedures, and any associated risks or benefits. Participants are encouraged to ask questions, ensuring clarity and comfort with the study. All collected data is documented and securely stored, respecting data privacy protocols. Eligible individuals are informed about the screening visit, while those not suitable are considered for future studies.

Study Timelines
The recruitment and baseline survey will last for 1 month when the project is funded. We will need a total of 11 months to finish the intervention program, and then need an additional 1 month to finish all clinical laboratory measurements, data cleaning, analysis and writing of the primary outcome papers. We will need 1 year of funding to carry out our study, with a possible extension to 1.5 years.

Study Endpoints
The primary outcome is the differences in coefficient of variance (CV) evaluated by CGM data between CGM group and SMBG group. The secondary outcomes are differences in HbA1c, total number of hypoglycemia events and the remission rate of diabetes.

Procedures Involved
Bariatric procedures: The RYGB procedure will involve creating a 15- to 20-ml gastric pouch, a 150-cm Roux limb, and a 50-cm biliopancreatic limb. The VSG procedure will involve reducing gastric volume by 75 to 80% using a 30-French endoscope, starting 3 cm from the pylorus and ending at the angle of His. Study participants will return for follow-up visits at 1 month, 3 months, 6 months, 12 months, and 18 months. These visits will include anthropometric measurements, lifestyle counseling, questionnaires, and blood investigations at the Metamor Institute (**Table 2**).

CGM group: Participants assigned to the CGM group will receive the Libre 2+ systems (Abbott Diabetes Care, Alameda, CA) upon randomization. This will include comprehensive training provided by a qualified healthcare professional. The training will

cover detailed instructions on sensor placement, how to download and use the associated smartphone application, and guidance on interpreting the glucose data effectively. To ensure continuous and accurate monitoring, the CGM sensor will be routinely replaced every 14 days following randomization. Additionally, in the event of sensor detachment or loss, immediate replacement will be arranged to maintain uninterrupted glucose tracking. Regular sessions are conducted to analyze glucose trends, refine management strategies, and provide additional support or education on device usage.

SMBG group: Participants assigned to the SMBG group in the study will receive detailed instructions on monitoring and documenting their blood glucose levels at critical times: fasting, before meals, 2 hours after meals, and at bedtime, as well as whenever a participant encounters symptomatic hypoglycemia. For this purpose, each participant will be provided with a FreeStyle Optium Neo glucometer and test strips (Abbott Diabetes Care, Alameda, CA). Participants will also be shown how to interpret these readings to understand their glycemic control. Each participant will be informed of the specific glucose targets they should aim for, based on the glucose targets recommended by the ADA guidelines. Participants in this group will be provided with a masked CGM sensor at randomization and 2 weeks before the end of the trial to collect data. However, they will receive biweekly guidance by telephone on any necessary adjustments to their management plan based on their recorded data. In this group, participants will be equipped with the Abbott FreeStyle Libre Pro (masked) for data collection before, 1 month after the surgery and at the end of the study.

Physical activity assessment: All participants will be counseled to maintain their physical activity level as is recommended by American Diabetes Association either through phone call or in-person visits. We will utilize a global physical activity questionnaire to collect physical activity data at baseline and follow-up visits.

Nutrition counseling: All participants will be provided with a tailored nutrition plan collaboratively created by the participant and a registered dietitian nutritionist (RDN) with expertise in post-surgical management at Metamor Institute. This personalized food plan aims to support metabolic health and achieve glycemic control. Research dietitians will play a pivotal role in overseeing the dietary aspects of various study protocols. The preparation and serving of research-specific diets will be expertly handled by research specialists and a dedicated food service worker. To ensure adherence to dietary protocols, meal monitors will be assigned to accompany participants during mealtimes, providing supervision and support to ensure compliance with the research dietary guidelines. This structured approach will ensure that every aspect of dietary management in research studies is attended.

Medication counseling: A tailored approach to medication management will be provided by the clinicians at Metamor. Personalized adjustments to pharmacologic therapy, as well as instructions on dietary supplementations will be included. The clinician team will also reassess the needs of antihypertensives and statins. In case participants encounter severe postoperative gastrointestinal symptoms, including dumping syndrome and delayed gastric emptying, the clinician team will prescribe targeted medication strategies.

Data and Specimen Banking

All study-related data, including clinical, biochemical, and CGM-derived glycemic metrics, will be securely stored and maintained at PBRC. The data will be de-identified and encrypted to ensure participant's confidentiality and compliance with **HIPAA** and **IRB** guidelines. Data collected will include demographic and clinical information such as age, sex, BMI, comorbidities, and medication use, as well as CGM-derived glycemic variability metrics, laboratory values like HbA1c, fasting glucose, lipid panels, and inflammatory markers, dietary intake records from food frequency questionnaires and 24-hour recalls, and physical activity assessments from Fitbit tracking and self-reports. All data will be stored on **PBRC's NORC repository**, accessible only to authorized study personnel, and retained for a period of **seven (7) years** post-study completion in accordance with regulatory and funding agency requirements. Any sharing of data with external collaborators will require a **data use agreement** approved by the PBRC Office of Research. De-identified data may be used for secondary analyses, validation of predictive models, and future research on metabolic surgery and glycemic control, with explicit participant consent obtained for potential future use.

Although the primary focus of this study is glycemic variability using CGM, biological specimens such as fasting blood samples for HbA1c, glucose, lipid profiles, and inflammatory markers will also be collected. Additional blood draws for exploratory biomarkers, including insulin sensitivity and gut microbiome metabolites, may be performed if additional funding is secured. Blood samples will be stored at **-80°C** in the **PBRC biorepository** under secure and monitored conditions, with each sample assigned a coded identifier to ensure anonymity and compliance with IRB regulations. Access to these specimens will be limited to authorized researchers and will require approval from the study's principal investigator and IRB.

Power analysis.

Given the small sample size and the exploration nature of this pilot study, a formal power analysis is not necessary.

Data and Specimen Management

Aim 1: To monitor and compare the glycemic patterns, assess the number and duration of percentage time within or outside the target range of glucose levels 70-180 mg/dL, we will quantify the metric derived from the CGM device. We will also analyze the association between CGM-derived metrics and dietary patterns. Several key metrics will be explored to assess glycemic control and documented as was recommended by the International Consensus on Use of Continuous Glucose Monitoring:

- Mean glucose levels
- Percentage of time in level 2 hypoglycemic range (<54 mg/dL [3.0 mmol/L])
- Percentage of time in level 1 hypoglycemic range (<54–70 mg/dL [3.0-3.9 mmol/L])
- Percentage of time in target range 70-180 mg/dL (3.9-10.0 mmol/L)
- Percentage of time in hyperglycemic range (>180 mg/dL [10.0 mmol/L])
- Glycemic variability, reported as CV and standard deviation (SD)
- Glycemic management index (GMI or the estimated A1c)
- Data for glucose metrics above reported in three time blocks (sleep, wake, 24 h) with the default times for the sleep (12:00 A.M.–6:00 A.M.) and wake (6:00 A.M.–12:00 A.M.) often written as midnight to 6:00 A.M. and 6:00 A.M. to midnight, respectively.
- Data sufficiency (the length of data)
- Area under the curve
- Low blood glucose index (LBGI) and high blood glucose index (HBGI).

The comparisons between the baseline and end-of-trial values for each metric will be performed using paired t-tests. We will make substantial efforts to minimize missing data, and potential missing values will be imputed using the Predictive Mean Matching method. Due to the pilot nature of the study, adjustments for multiple testing will not be performed. The results from this analysis are intended to provide preliminary data for identifying the most appropriate metrics for use in a future full-scale study.

Aim 2: To identify independent predictors of diabetes remission, a multivariable logistic regression model will be developed. The dependent variables will be diabetes remission status (remission vs. no remission), and the independent variables will include key CGM-derived metrics (e.g., TIR, glycemic variability, GMI) alongside clinical covariates (e.g., pre-operative HbA1c, BMI, and diabetes duration). The model will be adjusted for potential confounders, if feasible, and the final selection of predictors will be based on statistical significance and clinical relevance. In addition, to comprehensively utilize CGM data, patients will also be classified into different groups using the multilevel clustering method developed by Tao et al. Specifically, all patients will be assigned to distinct clusters based on their CGM profiles, and then these clusters will be treated as independent variables to assess whether specific CGM profile patterns are associated with diabetes remission. To assess model performance, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) will be computed, along with the area under the Receiver Operating Characteristic (ROC) curve. Model assumptions, such as linearity and multicollinearity, will be checked.

Aim 3: This is a two-arm randomized trial with a binary outcome. Descriptive statistics will be presented as means and standard deviations for continuous variables, and frequencies and percentages for categorical variables. To account for repeated measurements over time and intra-individual variability, a generalized linear mixed-effects model will be employed to test the effect of CGM intervention on the occurrence of hypoglycemia events. The dependent variable is the occurrence of at least one hypoglycemia event, and the dietary content (macronutrient percentages), dietary patterns (meal timing and frequency), and food formulations (liquid vs. solid meals) will be the covariates. In addition, all glycemic outcomes (e.g., mean glucose, TIR, glycemic variability) will also be used as dependent variables, to explore the relationship between CGM intervention with the before and after intervention changes in these CGM metrics. The model will also adjust for potential confounders, including age, sex, BMI, and type of surgery. Alternative, given the dynamic nature of post-surgical glycemic responses, generalized estimating equations (GEE) will be used to analyze longitudinal associations between dietary intake and glycemic metrics. This approach will account for the correlation between repeated measures and provide robust standard errors. An intention-to-treat analysis that includes all randomized participants, regardless of the number of assessment visits attended, will be conducted. The robustness of the inferential findings to these analytic methods will be assessed in a sensitivity analysis to investigate whether different analyses under different assumptions provide robust effectiveness inferences. These analytical plans are flexible and may be adapted as needs change and as improved scientific perspectives are advanced. We will examine adherence to diet and physical activity.

Provisions to Monitor the Data to Ensure the Safety of Subjects

PI will oversee and implement the data and safety monitoring for the trial. The members of the Advisory Committee provide an annual review throughout the trial. The adverse event form, a list of symptoms, is given at baseline, and every 6 months during the follow-up. Serious adverse events can be reported on any visit. Because of protocol-mandated contacts of participants during the study, ascertainment of adverse events is high and likely complete. Participants are asked to report to the staff any symptoms or health problems at baseline and during the study. Serious adverse events are entered onto a

form, reviewed by Dr. Philip R Schauer (one of the collaborators at Metamor institute) and reported to the IRB, LA CaTS and senior scientists of advisory committee. While there are some potential risks for the proposed study, the design makes every attempt to prevent the possibility of any adverse events. Monitoring by the experienced investigators and professionals involved in the study will minimize all potential risks.

Withdrawal of Subjects
Subjects may be withdrawn from the research without their consent under circumstances such as non-compliance with study procedures, the development of medical conditions that contraindicate continued participation, adverse events that pose health risks, or at the discretion of the principal investigator if continued participation is deemed unsafe or unfeasible. If a subject is withdrawn, an orderly termination process will be followed, including notifying the subject, documenting the reason for withdrawal, and ensuring appropriate medical follow-up if needed. When subjects choose to withdraw from the study, they may opt for complete withdrawal, in which case no further data will be collected, or partial withdrawal, allowing continued data collection through specific follow-up measures such as long-term monitoring or scheduled follow-up visits via telephone. If a participant consents to partial withdrawal, only pre-specified data, such as post-surgical glycemic trends or clinical outcomes, will be collected, ensuring that their preferences are respected while maintaining the integrity of the study's longitudinal data.

Risks to Subjects
The proposed study is minimal risk. However, the potential exists for anticipated and/or unanticipated adverse events, serious or otherwise, to occur since it is not possible to predict with certainty the absolute risk in any given individual or in advance of firsthand experience with the proposed study methods.

Potential Benefits to Subjects
Participants in this study may experience potential benefits, including improved monitoring of their glycemic patterns through CGM, which may provide them and their healthcare providers with valuable insights into glucose fluctuations that are not captured by traditional HbA1c measurements. The use of CGM may help identify periods of hypoglycemia or hyperglycemia, allowing for more personalized and timely adjustments to dietary intake and diabetes management strategies. Additionally, participants may receive dietary guidance based on their individual glucose responses, which could contribute to better glycemic control and overall metabolic health. While the probability and magnitude of these benefits may vary among individuals, those with higher glycemic variability or greater risk of post-bariatric hypoglycemia may particularly benefit from early detection and intervention. The potential benefits are expected to extend throughout the study period, with continued monitoring and follow-up assessments at multiple times. However, it is important to note that there may be no direct benefit to some participants, as the primary purpose of the study is to improve understanding of glycemic patterns after bariatric surgery rather than to provide a therapeutic intervention.

Vulnerable Populations
No vulnerable population will be involved in.

Multi-Site Research

Not applicable

Sharing of Results with Subjects
Study results and individual subject results will be shared with participants if deemed clinically relevant or upon request. Individual continuous glucose monitoring (CGM) data, including glycemic patterns, variability, and hypoglycemia episodes, may be provided to participants and, if applicable, their primary care physicians to aid in diabetes management and post-surgical follow-up. Any significant findings related to glycemic fluctuations or metabolic health that could impact clinical care will be communicated directly to the participant through scheduled follow-up visits or secure electronic reports. However, aggregated study findings will only be shared after data analysis is complete, and participants will not receive individualized interpretations of investigational metrics unless such information is determined to have direct clinical relevance. The method of sharing results will be tailored to each participant's preference, including in-person discussions during follow-up visits or electronically via a secure patient portal. If incidental findings arise that may have medical significance, participants will be informed appropriately and referred for further clinical evaluation if necessary.

Setting
The research will be conducted at PBRC and Metamor institute where metabolic surgery patients receive preoperative and postoperative care. Research procedures, including participant screening, informed consent, baseline assessments, and follow-up visits, will be performed at Pennington's outpatient clinic. CGM device placement and data collection will take place at these sites, while dietary assessments and follow-up consultations may be conducted remotely through telemedicine or phone interviews. If any research activities extend beyond Pennington and its affiliates, site-specific regulations and customs affecting the research will be carefully considered, including compliance with local institutional policies and ethical guidelines.

Resources Available
About 2500 obese patients at Metamor were treated in 2023 including about 470 operations for severe obesity (190 RYGB and 280 VSG). Of them, about 50% patients were diagnosed as T2D. The nurses in Metamor will introduce our study to the patients. If the patients are interested, the evaluation process includes verifying basic personal information, assessing health status and medical history, and evaluating specific eligibility criteria relevant to the study.

Prior Approvals
Not applicable

Compensation
Participants will receive $100 as compensation for their time and participation in the study. Payments will be provided at specific milestones, including after the completion of baseline assessments, CGM data collection periods, and follow-up visits. The total compensation amount will be determined based on the duration and complexity of participation, ensuring fair reimbursement for their commitment. Payments will be disbursed incrementally rather than as a lump sum to encourage study completion and adherence to scheduled visits. Compensation will be provided either through direct

payment, gift cards, or another approved method, and participants will be informed of the payment structure during the informed consent process.

Confidentiality
All data and specimens will be securely stored at PBRC in restricted-access facilities. De-identified electronic data will be stored on password-protected, encrypted servers, while physical documents, if any, will be kept in locked filing cabinets within a secured research office. Biological specimens, including blood samples, will be stored at -80°C in the PBRC Biorepository, with strict monitoring to ensure sample integrity. Data and specimens will be retained for seven (7) years after study completion, following institutional policies and regulatory requirements.

Access to data and specimens will be limited to authorized study personnel, including the principal investigator, co-investigators, and designated research staff who have received training in data security and confidentiality. The principal investigator will be responsible for overseeing data management, while designated research personnel will handle the receipt and transmission of data and specimens according to institutional guidelines. Data and specimens will be transported within the institution using secure, labeled containers, and all electronic transmissions will be conducted via encrypted channels to prevent unauthorized access.

Provisions to Protect the Privacy Interests of Subjects
To protect the privacy interests of participants, all study interactions, data collection, and discussions will take place in private clinical research rooms at PBRC, ensuring confidentiality and minimizing unintended disclosure of personal health information. Participants will be informed about the study procedures in detail, and all research staff will be trained to conduct interviews and assessments in a respectful and non-intrusive manner. During data collection, only necessary personal and health-related information will be obtained, and participants will have the option to decline any questions or procedures that they find uncomfortable without affecting their participation in the study. To make participants feel at ease, the research team will clearly explain the purpose of each assessment, provide ample opportunity for questions, and allow flexibility in scheduling visits. All interviews and assessments will be conducted by trained personnel who will use neutral and non-judgmental language to avoid making participants feel pressured or scrutinized. For potentially sensitive topics, such as dietary habits and glycemic control, discussions will be approached with empathy and discretion to respect personal boundaries and reduce feelings of intrusiveness. Access to participant information will be strictly limited to authorized study personnel, including the principal investigator, co-investigators, and trained research staff. The research team will obtain participant information only through direct interactions, informed consent forms, and approved electronic medical records (EMR) access, as permitted by the study protocol and institutional review board (IRB) guidelines. Any access to external medical records or third-party data sources will require explicit participant consent, ensuring that privacy rights are upheld throughout the research process.

Compensation for Research-Related Injury
If the research involves more than minimal risk to participants, compensation for research-related injury will be available as per institutional and regulatory guidelines. In

the event of an injury directly resulting from participation in the study, medical treatment will be provided, but financial compensation beyond necessary medical care may not be guaranteed. Participants will be informed that they may seek medical care for any adverse events, and costs may be covered by their health insurance or other applicable sources.

Economic Burden to Subjects

Participants will not be responsible for any direct costs associated with study procedures, including continuous glucose monitoring (CGM devices), laboratory tests, or follow-up visits conducted as part of the research. However, they may incur indirect costs, such as transportation expenses for in-person visits or potential lost wages if study appointments require time away from work. While efforts will be made to minimize these burdens, participants will be informed during the consent process that any additional medical care outside the scope of the study, such as routine clinical visits or treatments unrelated to the research, will be their financial responsibility.

Consent Process

In this study, informed consent will be obtained from all participants prior to their enrollment. The consent process will take place in a private clinical research room at Pennington Biomedical Research Center, ensuring that participants have the opportunity to ask questions and make an informed decision without external pressure. Prospective participants will be provided with a detailed explanation of the study, including its purpose, procedures, risks, and benefits. They will be given a waiting period of at least 24 hours between receiving the study information and signing the consent form to allow sufficient time for consideration. Ongoing consent will be ensured by regularly informing participants of any new findings or protocol changes that may affect their willingness to continue participation.

This study does not involve minors, so parental permission and child assent procedures do not apply. For cognitively impaired adults, a screening process will be conducted to assess their ability to provide consent. If an individual is determined to be incapable of making an informed decision, permission will be obtained from a legally authorized representative in the following priority: durable power of attorney for healthcare, court-appointed guardian, spouse, or adult child. For research conducted outside of the state, applicable laws will be reviewed to determine who is authorized to consent on behalf of a participant. If assent is required, it will be obtained from all participants capable of providing it, and documentation will follow IRB guidelines. In cases where assent cannot be obtained due to cognitive impairment, an explanation will be provided, and alternative procedures will be followed to ensure ethical participation. The IRB permits documentation of assent on the primary consent form, and separate assent documents will not be required unless specifically mandated.

Drugs or Devices

This study involves the use of CGM devices, which will be stored, handled, and administered in accordance with institutional guidelines and manufacturer specifications to ensure their proper use. All CGM devices will be securely stored in a controlled-access research facility at Pennington Biomedical Research Center, where only authorized investigators and trained research staff will have access. Devices will be distributed exclusively to enrolled study participants and will be assigned based on unique study

identification numbers to maintain accurate tracking. Trained research personnel will provide participants with detailed instructions on device use, application, and data collection procedures to ensure proper adherence. CGM data will be collected according to the study protocol, and any malfunctions or deviations will be reported to the research team immediately. Only authorized investigators and trained study personnel will be permitted to oversee the use of CGM devices, ensuring they are utilized solely for study purposes. Compliance with storage and handling procedures will be monitored regularly, and any issues will be documented and addressed in accordance with regulatory requirements.