Title: Time Limited Eating in Adolescents (Time LEAd): a Pilot Study

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PI: Alaina Vidmar, MD

Center for Diabetes, Endocrinology, and Metabolism

Children's Hospital Los Angeles

Los Angeles, CA 90027

Overview of Study Design from Study Protocol:

The aim of this study will be to compare cardiometabolic effects of TLE (8-h eating period/16-h of daily fasting) versus a prolonged eating period (12+h eating period) in a randomized pilot study with careful control of continuous adherence to prescribed eating window. This study was a prospective, randomized controlled pilot study in 50 adolescents (ages 14–18) with obesity (BMI% ≥ 95th percentile) recruited from clinical programs at Children's Hospital Los Angeles (CHLA). Patients will be randomized to one of three treatment groups for a 12-week intervention: Group 1): Control - Low sugar and carbohydrate educational intervention (LSC, < 5% of total daily calories from sugar/day; < 90 g carbohydrate (CHO)/day) + blinded CGM (used to monitor adherence and glycemic outcomes without real time feedback). Group 2): LSC + TLE (16-h fast/8-h feed for 5 days per week) + blinded CGM.

Table 3: Study Procedures and Measures			
Weeks	**0**	**4**	**12**
Consent Completed	x		
Medical history	x		
Demographic Data	x		
CGM Education and equipment	x		
CGM (sensor change every 14 d, 12 w wear time)	x	x	x
Randomized	x		
Primary Outcomes			
Glycemic Control			
Percent Time in Range	x	x	x
Hemoglobin A1c	x		x
Secondary Outcomes			
Nutrient Data System Recall: 24-hour dietary recall	x		x
International Physical Activity Questionnaire	x	x	x
Pittsburg Sleep Quality Index and Chronotype Questionnaire	x	x	x
Monitoring for Adverse Events			
Dutch Eating Behavior Questionnaire	x	x	x
Binge Eating Disorder Screen	x	x	x

The implementation steps of the proposed study were as follows: **(1)** The staff introduced the study to all eligible participants either in person or virtually and consented interested families for the study; **(2)** All participants and their families completed a baseline study survey in REDcap; **(3)** All participants were trained to wear a blinded CGM using manufacturer educational materials under the supervision of research staff. Participants be changed the CGM sensor every 14 days for the duration of the study. During each study visit, the CGM reader was connected to the site database to create an individual participant report. All equipment required for the duration of the study was distributed to the participants at consent. Participants received enough sensors to wear the CGM daily for the entire study period. **(4)** All participants and their families received standard nutritional counseling and were randomized to one of three meal-timing schedules followed for 12 weeks: (1) Control or (2) TLE blinded CGM use, and (3) TLE real-time CGM use. During the eating window, participants were not required to count calories or monitor their food intake. Participants chose and paid for their own food during the intervention. All participants recorded their eating window daily and submitted it to the study staff via REDcap. All participants received standard recommendations for physical activity, screen, and sleep time as per the American Academy of Pediatrics age-appropriate recommendations at the first visit; **(5)** The study staff conducted study assessments with participants at week 0, 4, and 12; **(6)** The study staff performed weekly phone encounters with the participants to assess barriers to adherence and eating practices. If a barrier is identified the study staff created a solution plan to promote adherence and retention. The study staff recorded any medication changes or health issues that have occurred in the last 7 days. The PI reviewed CGM downloads collected at each study visit to ensure no treatment escalation is required; **(7)** To further inform future trials and scalability we collected continuously recruitment, consent, and retention rates, and barriers to engagement; **(8)** Adverse events were monitored. If at any time, the study staff noticed any unhealthy compensatory behaviors the PI was notified, and a treatment plan was created to ensure that the participant receive the appropriate screening, work-up, and diagnosis from their primary care provider and are withdrawn from the study if appropriate. **(9)** The PI and research team meet bi-weekly to monitor all study procedures and oversee data management and analysis.

Participants: We recruited 50 adolescents (age 14-18 years at enrollment, all gender expressions), with obesity. Inclusion criteria are: **(1)** age 14-18 years; **(2)** Tanner stage III and above; **(3)** obesity; **(4)** hemoglobin A1c $\leq$ 5.7%; **(5)** participant must be willing and able to adhere to the assessments, visit schedules, and eating/fasting periods; and **(6)** baseline eating window greater than 10 hours. To limit confounding factors, individuals will be considered ineligible to participate if they meet any of the following exclusion criteria: **(1)** diagnosis of Prader-Willi Syndrome, brain tumor or hypothalamic obesity; **(2)** serious intellectual disability; **(3)** previous diagnosis or subthreshold symptoms of an eating disorder (anorexia nervosa, bulimia nervosa, binge-eating disorder); **(4)** parent/guardian-reported physical, mental of other inability to participate in the assessments; **(5)** previous

bariatric surgery; **(6)** current use of an anti-obesity or other diabetes medication (e.g., phentermine, topiramate, orlistat, glucagon-like-peptide-1 agonist, naltrexone, buproprion, SGLT-2 Inhibitor, or insulin); or **(7)** current participation in other interventional weight loss studies. A random block stratified randomization scheme was used. Participants were randomized 1:1 via stratified, blocked randomization to ensure the groups were balanced in terms of number of participants and distribution of potential confounding variables including sex and age.

Retention strategies. To foster treatment adherence, participants received weekly calls from the study staff for the duration of the trial. Counseling was conducted by trained research staff. The sessions served three purposes: (1) foster adherence, retention, and accountability; (2) troubleshoot intervention barriers; and (3) monitor safety endpoints. To support participants, the staff will use behavioral techniques, such as stimulus control, goal setting, behavioral contracting, and motivational interviewing. In order to reduce participant burden, if at all possible study procedures will be scheduled to coincide with participants' scheduled clinical visits.

Intervention Arms:
Components Common to All Study Arms. All participants received two hours of standard nutrition counseling recommended for adolescents living with obesity. No specific caloric restriction was recommended. All participants maintained their usual lifestyle, including physical activity and sleep patterns. Physical activity and sleep recommendations consistent with the American Academy of Pediatrics guidelines for adolescents will be encouraged but not formally prescribed.

Time Limited Eating. The TLE intervention arm involved instructing participants to consume their usual kind and amount of food and beverages (all calories) within a pre-specified 8-hour period, fasting for the remaining 16-hours. They will be free to divide their food and beverage intake into as many meals or snacks as desired during the 8-hour period. We conducted a cross sectional analysis of a cohort of 100 adolescents with obesity and found that most total calories, carbohydrates, and added sugars were consumed between 11 AM and 8 PM.[136] In addition, in our feasibility trials, most adolescents selected an afternoon/evening eating window for both week days and weekend days, consistent with their shifting sleep/wake cycle and timing of social engagements.[14] Therefore, to align with the normal developmental eating patterns seen in adolescents, we assigned an afternoon/evening TLE approach (consumption of all calories between 12:00 and 20:00 [plus or minus 1 hour] seven days per week). Participants allowed to consume non-caloric beverages (water, tea, coffee) during the fasting period. No energy restriction was required.

Control. Participants assigned to the control arm will be instructed to consume food over a 12-hour or more eating window. They were free to divide their food and beverage intake into as many meals or snacks as desired during the 12-hour period. No energy restriction was required.

Adherence Monitoring and Intervention Fidelity: To ensure differentiation between the intervention arms all participants recorded the time they start, and finish eating each day and provide their eating logs to the study staff weekly. Each week, study staff will determine the daily eating window for each participant by reviewing the time interval between the first and last caloric intake of the day. These self-reported time windows will be verified by examining the pattern of glucose excursions using the 24-h CGM data. If a participant adheres to meal timing protocol $\leq$ 4 days/week, a follow-up call or videoconference will be scheduled to address challenges, give participants additional encouragement, support, and create a specific plan to promote adherence.

Continuous Glucose Monitor. All participants will be trained to wear a blinded continuous glucose monitor sensor using manufacturer educational materials under the supervision of research staff. Participants will be asked to wear the CGM for the duration of the study. During each study visit, the CGM reader will be connected to the site database to create an individual participant report. Participants will be provided enough sensors to replace the sensor every 14 days. The participants and guardians will be educated on how to use the CGM and receive 1:1 coaching on how to change the sensor, which will be completed either independently or under study team guidance. At each weekly phone meeting, study staff will monitor any challenges related to CGM wear, including participant discomfort, skin adherence, and other issues.

Measurements: The study team will conduct all assessments at week 0, 4, and 12. All data was collected and stored in REDCap.

Statistical Analysis Plan:

Primary Outcome—Feasibility

Compliance with the recommended eating windows was collected from adolescents during the weekly phone calls with the study team. Adolescents were asked to record the time they started and finished eating daily, the number of days they adhered to their prescribed eating schedule, and barriers to adherence. Adolescents were instructed to wear their CGM daily for the duration of the study and to report deviation from the protocol during the phone calls.

Secondary Outcome

Anthropometrics. All participants received a wireless Bluetooth scale upon consent. Participants' height and weight were collected by the participant and parent/guardian at home with the research coordinator monitoring the measurement collection via a HIPAA compliant virtual platform. Height was measured using a portable wall height indicator tape ruler, accurate to 0.5 cm (Posh Rulers, Quick Medical, Issaquah, WA). Weight was measured on a self-calibrating Etekcity Digital Body Weight Scale, accurate to 0.2 kg (Etekcity, San Diego, CA). Adolescents wore minimal clothing during the height and weight measurements. BMI was calculated as kilograms per meter squared excess percent of the 95th percentile (%BMIp95) was determined utilizing the CDC growth charts.

Continuous Glucose Monitoring

CGM data were downloaded weekly by the study team. CGM data were evaluated continuously over the study period. This data was utilized to compute the following measures: mean, maximum, and minimum glucose levels; standard deviation of glucose; mean amplitude of glycemic excursion; and overall percent of total time spent in euglycemic range (percent time in range = 70–180 mg/dL). All CGM data were housed in Clarity (Dexcom and Dexcom CLARITY are registered trademarks of Dexcom, Inc., San Diego, CA, USA) and the study team had weekly access to assess all glycemic excursions that occurred during the self-reported fasting periods [50–53]. For those in the TLE + real-time

Statistical Analysis

The study was a pilot trial, thus we opted for a convenient sample size of 50 participants to estimate parameters for a larger, fully powered trial. Analyses were based on the intention to treat (ITT) population using the last observation carried forward. The ITT population was defined as at least two visits (baseline and 1 month). The study was designed as a three-group intervention analysis; however, given that very few adolescents in the TLE+ real-time CGM feedback group looked at their real-time data, we completed a post hoc analysis combining both TLE groups compared to control for all analyses performed. Baseline characteristics (age, sex, race, BMI status, household income) were summarized descriptively across arms for the ITT population using mean and standard deviation (SD) or median and interquartile range as appropriate for the distribution of continuous variables. Categorical variables are described as a frequency and percentage. Continuous variables that are skewed were analyzed in log scale. The differences in demographics, anthropometrics baseline, and eating window distributions among intervention groups were examined using analysis of variance (ANOVA) and Fisher's Exact test. Adherence was operationalized as the number of days adolescents complied with their prescribed eating window, number of days they wore their CGM, and number of weekly phone calls and scheduled research visits they attended, and satisfaction scores were summarized using mean, standard deviation (SD), minimum, and maximum score between TLE and control. The TLE effect on mean change of %BMIp95 between week 0 and week 12 was assessed by using ANOVA. Then, a mixed-effects generalized linear model based on a Gaussian or Gamma distribution as appropriate was used to further assess the TLE effect on change in weight outcome from week 0 to week 12. The mixed-effects generalized linear model based on a Gaussian or Gamma distribution was used as appropriate for the distribution of continuous outcome variables. Whereas a mixed-effects logistic regression model was used for binary clinical outcome variables. In addition, a mixed effects Tobit regression model was used to evaluate the TLE effect on the change in quality- of-life assessment, where the scores are reported in percentages, with no data below 0 or above 100. Then, the non-additive effects of TLE were also examined; specifically, whether the change on clinical outcomes during the study period varied by intervention groups by including the interaction term in the mixed-effect models. In addition, sensitivity analysis was performed to examine whether the weight change observed in the data was influenced by one adolescent who achieved a weight loss of greater than 15% from baseline weight. All results are described in beta estimate, β, percent change, and odds ratio with its associated 95% confidence interval and p-value. The statistical

significance level was set at 0.05 with two-sided throughout the analyses. All statistical computations were done in Stata/SE 17.0 (StataCorp, College Station, TX, USA).

CHILDREN'S HOSPITAL LOS ANGELES
INFORMED CONSENT/PARENTAL PERMISSION/ASSENT TO PARTICIPATE IN A RESEARCH STUDY

Subject's Name:	_____	**Birth Date:**	_____
CHLA MRN#	_____		

A person who takes part in a research study is called a research subject or research participant. If you are reading this consent form as a parent/legal guardian, "you" also refers to "your child" (the research participant) and/or the research participant, as applicable.

KEY INFORMATION
You are being asked to participate in a research study. This section describes the key information that we believe most people need to decide whether to take part in this research. Later sections of this document will provide the details of the research.

What should I know about this research?
- Taking part in this research is voluntary. Whether you take part is up to you.
- If you don't want to take part, it won't be held against you.
- You can take part now and later drop out, and it won't be held against you.
- If you don't understand, ask the research team questions.
- Ask all the questions you want before you decide.

How long will I be in this research?
Participation will last up to 16 weeks.

Why is this research being done?
This research is being done to find the effectiveness of a diet plan (Time Limited Eating or TLE) in adolescents with obesity.

What happens to me if I agree to take part in this research?
Study procedures for this research are:
- You will be randomized into 1 of 3 groups.
    - Group 1: Non-TLE (Non Time Limited Eating) - 12-hour or more eating window without mealtime restrictions
    - Group 2: TLE (Time Limited Eating) – 8-hour eating window 7 days per week + blinded continuous glucose monitor data
    - Group 3: TLE (Time Limited Eating) – 8-hour eating window 7 days per week+ real-time continuous glucose monitor data

- You will attend 5 visits at CHLA and have follow-up phone calls.
- You will be trained and wear a continuous glucose monitor every day for 12 weeks.
- You will have weight and height measured, research blood draws.
- You will be asked to completing surveys.

Could being in the research hurt me?
The most important risks or discomforts that you may expect from taking part in the research are:

- Feeling uncomfortable answering some of the questions.
- Mild discomfort (pain), bruising and swelling where the needle is placed in your arm, and dizziness or fainting from blood draws.
- Headache or dizziness after not eating for prolonged periods if you're in the time limited eating group.
- Mild discomfort (pain), bruising or irritation at the insertion site from wearing a continuous glucose monitor.

Please see the POSSIBLE RISKS AND DISCOMFORTS section below for a complete list of expected risks.

Will being in this research benefit me?
The most important benefits that you may expect from taking part in this research are:

- Learning new skills for healthy eating and weight management.
- Improving glycemic control.
- Delaying disease progression.

What other choices do I have besides taking part in this research?
Instead of being in this study, your choices may include:

- Get routine care or treatment for your condition.
- Join another clinical research study.

INTRODUCTION
You are invited to join a research study led by Dr. Alaina Vidmar, MD from the Endocrinology Department at Children's Hospital Los Angeles (CHLA). The study is paid for by the Pediatric Endocrine Society.

You are invited to join this study because you have obesity. Participation in this study is voluntary. Please read the information below and ask questions about anything you do not understand before deciding whether to be in the study.

PURPOSE OF THE STUDY
This research is being done to find the effectiveness of a diet plan (Time Limited Eating or TLE) in adolescents with obesity.

NUMBER OF PARTICIPANTS
Up to 50 adolescents and 50family members will be invited to join the study at CHLA.

LENGTH OF PARTICIPATION
Participation in this research will last 16 weeks with up to 5 in-person study visits at CHLA.

PROCEDURES
If you volunteer to be in this study, we will ask you to do the following things:

You will be randomized into 1 of 3 groups below. A computer program will randomly (like flipping a coin) assign you to one of the following groups after 1 week of wearing a continuous glucose monitor (CGM):

- Group 1: Non-TLE (Non Time Limited Eating) - 12-hour or more eating window without mealtime restrictions
- Group 2: TLE (Time Limited Eating) – 8-hour eating window 7 days per week + blinded continuous glucose monitor data
- Group 3: TLE (Time Limited Eating) – 8-hour eating window 7 days per week+ real-time continuous glucose monitor data

During the research study you will be asked to do the following things (each of these items is specific for the research study and not considered standard of care for your condition):

- **Follow the dietary guidelines provided to you by the study team:**
  - **TLE (Group 2 only):** only eat during an 8-hour window i.e. 11 AM – 7 PM 7 days per week.
- **Continuous glucose monitor (all groups):** You will wear a continuous glucose monitor called the Dexcom G6 Mobile CGM system every day to monitor your blood sugar level. The study team will create a Dexcom research account on your behalf using a research email. The study team will review your blood sugar levels with you over the phone each week. We will provide you with the device to use for 12 weeks. You will be trained on the use of this device. The Dexcom app will be downloaded to your or family member's personal smart phone. If you, your parent, legal guardian family member does not own a Dexcom compatible smart phone, you will use the Dexcom receiver. Please see appendix B for information about this device.
- **Phone Follow Up (both groups):** A member of the research team will call you once a week to discuss any barriers you may be experiencing. These conversations will be audio-recorded for educational purposes and should last approximately 15-30 minutes. A code name of your choice will be used during these conversations.
- **Follow-up plan (both groups):** At the end of the intervention, your participation in this study will be complete.

In addition to the above, the following research procedures will be done to all subjects in both groups through the end of the study:

- **Weight and height checks:** At every visit, we will weigh you and measure your height. This will be done in a private area.
- **Surveys:** You will complete several surveys at every visit. These surveys collect information such as your eating behaviors, how well you cope with stress, and satisfaction with the intervention. Each survey will take approximately 5-10 minutes to complete. You also have the option of completing the surveys virtually via WebEx or over the phone.
- **Dietary Recall:** You will complete a dietary recall of all the food and beverages you consumed over 2 days (48 hours) prior to the day of the visit. This will take approximately 45 minutes to complete and will occur at Visit 2 and 5. The dietary recalls will take place at your in-person visits or virtually via WebEx or over the phone. **Daily Eating Log:** You will complete eating logs every day. These logs will collect the time you started eating and the time you stopped eating each day for 16 weeks. A member of the research team will record your logs once a week.
- **Medical record review:** If you are a patient at CHLA, as part of your regular care, you may have blood work done every year to evaluate for your health. We will review your medical record and collect the results of your blood work if they occurred in the last 8 weeks from the consent date.
- **Research blood draws (fasting blood tests are considered standard of care at baseline for anyone entering into a weight management program):** Approximately 9 mL (2 teaspoon) of blood will be collected by sticking a needle in a vein of your arm for each blood draw. You will have to fast (not eat anything for at least 6 hours) before each blood draw. Blood draws will occur at visit 1 and 5.
- **Research images (during Onboarding [visit 1] and at day 84 [Visit 5]):**

- DEXA scan: this will take a picture of your entire body and will take 30 minutes to obtain the image.

FOR YOUR PARENT/GUARDIAN OR OTHER FAMILY MEMBER

Your participation is optional if your child is over the age of 18 years.

- **Surveys**: Your family member will be asked to complete several surveys. These surveys will collect information such as age, job, health insurance, and ethnicity. Each survey will take about 5-10 minutes to complete. Your parent/legal guardian or family member will spend approximately 1 hour completing surveys. They will have the option to complete at in person visits or virtually via WebEx or over the phone.
- **Weight and Height**: Your family members' height and weight will be measured.

Your family member will need to travel to CHLA with you for your in-person study visits and/or to complete in person study procedures.

RESULTS OF TESTS PERFORMED FOR THE STUDY

The results of the following research tests and research information will be shared with you and your doctor upon request:

- **Lab Testing**: hemoglobin A1c, glucose level, liver function tests (AST&ALT), insulin, lipid panel, c-reactive protein (CRP), c-peptide, Insulin-Like Growth Factor (IGF-1).
- **Research image studies** – DEXA scans
- Weight trends over the study period

Any abnormal lab test results from this study will be sent to your doctor as they may be important to your safety.

POSSIBLE RISKS AND DISCOMFORTS

Surveys: You may feel uncomfortable answering some of the questions. You can choose to skip or stop answering questions at any time. Surveys that will be completed by you and your family member ask about anxiety and depression. If you report extreme anxiety, binge eating disorder, or depression, we will refer you to a healthcare provider for immediate evaluation and a referral for mental health services if appropriate. This may result in additional costs to you if you require additional procedures, tests and/or treatments as determined by your healthcare providers.

Research blood draws: Having blood taken may cause pain, swelling, bruising, redness, and/or minor bleeding at the site of the needle stick. In rare cases, an infection or small blood clot may happen.

Imaging:

Risk associated with DEXA: You will be exposed to a small amount of radiation during your DEXA scan (radiation dose of 0.001 mSv) which is equivalent to 3 hours of natural background radiation and less than a coast-to-coast round trip airline flight which is about 0.03 mSv and poses minimal risk.
Unexpected (incidental) Findings: It is possible that unexpected findings may be discovered from the research DEXA or MRI which you may find upsetting. You will be notified by the principal investigator if any unexpected findings are discovered. The principal investigator will advise you as to the nature of the findings and provide recommendations regarding appropriate follow-up with your physician. These findings may result in the need for you to have additional procedures, testing, and/or treatments as determined by your physician. This may result in additional costs to you and/or your health insurance.

Time Limited Eating: There are risks and discomforts associated with calorie restricted diet, such as hunger, anxiety, drowsiness, dizziness, headache, muscle aches, fatigue, low blood pressure and, in rare cases,

fainting. These diet interventions may also cause abnormal heart rhythms, short-term nutrient deficiency, and a weakened immune response.

Continuous Glucose Monitor: While wearing the Continuous Glucose Monitor, you are at risk for developing pain, bleeding, or burning at the insertion site. In rare cases, an infection may develop.

Psychological risks: It is possible that you may become upset thinking about some of the questions or topics in this study.

Bullying or violence: If we suspect that you are a victim of bullying or violence at home or in your neighborhood, either through completion of the questionnaires, we will implement the following procedures: 1) we will make you are aware of resources available in your community; 2) we will work with you to develop a safety plan for addressing bullying or violence; 3) we will ascertain the risk to you. If we suspect that you have been abused or witnessed domestic violence, we will make a report to child protective services. Children/adolescents who are victims of bullying or domestic violence will not be dropped from the study, unless they ask to drop out.

Suicidal Behavior: If we suspect that you are suicidal, we will follow the Substance Abuse and Mental Health Services Administration SAFE-T: Suicide Assessment Five-Step Evaluation and Triage approach to determining risk and clinical response. The five steps are Identify Risk Factors, Identify Protective Factors, Conduct Suicide Inquiry, Determine Risk Level/Intervention, and Document (which includes intervention and follow-up). Adolescents who experience psychiatric emergencies such as suicidal behavior will not be dropped from the study, unless they request to terminate their participation.

Binge Eating Behavior: If we suspect that you are developing any binge eating behaviors either assessed in the screening questionnaires or reported by you to a research staff during a weekly phone meeting, we will implement the following procedure: (1) we will make you aware of resources available in your community, (2) we will encourage you to contact your primary care physician for an evaluation and determination is psychiatric referral is warranted, (3) we will ascertain risk to you and (4) the PI will contact your primary care provider to ensure you receive the appropriate evaluation and referrals for treatment. If we suspect that you are purging or placing yourself in immediate medical danger, we will contact your parent or guardian and instruct you to go the local emergency room for evaluation.

Privacy Risks (for both youth and the parent/legal guardian/family member subjects): As this study involves the use of your identifiable, personal information, there is a chance that a loss of confidentiality may occur. The researchers have procedures in place to lessen the possibility of this happening (see the CONFIDENTIALITY section below for details).

There may be additional risks to participation in this research that we do not know about and therefore cannot describe.

POSSIBLE BENEFITS TO SUBJECTS

You may benefit from participating in this study by

- learning new skills for healthy eating and weight management.
- improving glycemic control.
- delaying disease progression.

Your parent/legal guardian/family member will not have direct benefits from participating in this study.

POSSIBLE BENEFITS TO SOCIETY
Your participation in this study may allow us to learn more about how adolescents can lose weight and develop healthier eating habits in the future by limiting the time during the day in which they eat. Hopefully this information will help in the treatment of future patients with obesity and Type-2 Diabetes.

YOUR OPTIONS IF YOU CHOOSE NOT TO BE IN THIS STUDY
The alternative to being in this research is to get the standard of care. The standard of care is to receive care at a multi-disciplinary weight management clinic which includes meeting with several doctors to develop a weight loss program and techniques to help you lose weight and maintain your weight loss. You can also choose not to participate in this study.

COSTS TO YOU FOR BEING IN THIS STUDY
Participants and their families are not responsible for any of the costs involved in this study. The CGM will be provided to you at no cost while you take part in the study. Neither you nor your insurance company will be billed for your participation in this research. However, participants will continue to be responsible for their phone and service plans.

Parking validation will be provided on an as needed basis, upon request. All families who do not have a car will be offered ride share options (UBER or Lyft) for travel to and from CHLA for the study visits.

RESEARCH INJURY
If you think you have been hurt by taking part in this study, tell the doctor in charge of this research study as soon as possible. The research doctor's name and phone number are provided in this consent form. CHLA will offer you the care needed to treat injuries directly resulting from taking part in this research. This care will be billed to you or your insurance company. You will be responsible for deductible and co-payments, or any costs not paid by your insurer.

CONFIDENTIALITY
The telephone sessions will be audio-recorded; therefore, the audio-recordings are considered "directly identifiable" since they will contain your voice. The audio-recordings will be kept in a secure location and only the research team will have access to them. These recordings will be listened to by people on the research team.

If audio recordings of you will be used for educational purposes, your identity will be protected or disguised. The recordings will be listened to at 1.5 times speed to disguise the voices. You have the right to review the tapes if you desire.

The data collected as part of this study will be "coded." Coded means that the data collected for this study will be assigned a unique code or Study ID. Your research data will not include your name or any other identifying information about you. The code that could be linked back to your identifying information will be kept separate from your research data and specimens. Only the members of the study team will be able to see the link or the information that can identify you.

People on the research team and your doctors and nurses will know that you are in this research study. All results will be kept confidential.

You will be asked to sign a separate form authorizing access, use, creation, or disclosure of health information about you. Your private information, data and medical records will be shared with individuals and organizations that oversee this research, including:

- Government agencies, such as the Food and Drug Administration (FDA), and the Department of Health and Human Services.
- Pediatric Endocrine Society
- The CHLA Institutional Review Board (IRB) that reviewed this research, and authorized representatives of CHLA.

Because this study involves medical procedures, a copy of this consent form will be placed in your medical record. This will allow the doctors that are caring for you to obtain information about any medications and/or procedures you are receiving in the study and treat you appropriately.

We will take steps to keep your personal information private, but we cannot guarantee complete secrecy. All identifiable information about you will be replaced with a unique code or study ID. A list linking the code and your identifiable information will be kept separate from the research data. All research data and records will be stored electronically on a secure network with encryption and password protection to help prevent unauthorized access to your personal information.

We will not release information about you to others not listed above, unless required or permitted by law. For instance:

- if we learn of child or elder abuse, harm to self or others, or
- if you have certain infectious diseases; or
- you are injured and need emergency care.

The results of the research may be presented or published. We will keep your name and other identifying information confidential.

FUTURE RESEARCH USE OF DATA AND/OR SPECIMENS

The data and specimens collected as part of this study will not be used for future research, even if all identifiers are removed.

STUDY WITHDRAWAL

The researchers may end your participation in this study for a number of reasons, such as if your safety and welfare are at risk, if you do not follow instructions or if you miss scheduled visits. The researchers might also decide to stop the study at any time.

If you decide to stop being in the study, or are removed from the study, or the study is stopped, the data/specimens collected before you leave will be used but no more data will be collected.

QUESTIONS ABOUT THE STUDY

If you have questions, concerns, or complaints about the study, or think this research has hurt you or made you sick, talk to the CHLA research team:

Daytime, Monday through Friday, 8:00 A.M. through 4:30 P.M. you may call the CHLA Principal Investigator, Dr. Alaina Vidmar at 323-361-3385.

Evenings, nights, weekends or holidays you may call the hospital number, (323) 660-2450 and ask for the Endocrinology Service doctor on-call.

ClinicalTrials.gov is a Web site that provides information about federally and privately supported clinical trials. A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

This research is being overseen by the CHLA Institutional Review Board ("IRB"). An IRB is a group of people who perform ethical review of research studies. You may talk to them at (323) 361-2265, or hspp@chla.usc.edu if:

- You have questions, concerns, or complaints that are not being answered by the research team.
- You are not getting answers from the research team.
- You cannot reach the research team.
- You want to talk to someone else about the research.
- You have questions about your rights as a research subject.

FINANCIAL INTEREST OF THE INVESTIGATOR

If your doctor is an investigator for this study, he/she is interested in both your healthcare and the conduct of this research. You are not under any obligation to participate in a research study conducted by your doctor.

RIGHTS OF RESEARCH SUBJECTS

You can agree to take part in this study and stop your participation in the study anytime. You should not sign this form if you have any questions that have not been answered or if you are unclear about any information in this form.

Your participation in the study is entirely voluntary. If you choose not to take part in the study or decide to stop your participation in this study at any time, there will be no penalty or loss of benefits to which you are otherwise entitled. If you wish to leave the study after agreeing to participate, you should let the Principal Investigator know. You are not under any obligation to participate in a research study conducted by your doctor.

You will be told about any new information found during the course of the study that may affect your health, welfare, or choice to stay in the research. If this happens, you might be asked to sign a new consent form.

- You have a right to have all of your questions answered before deciding whether to take part.
- Your decision will not affect the medical care you receive from CHLA.
- If you decide not to take part, you can still receive medical care from CHLA.
- You will be given a copy of this signed and dated consent form and the "Experimental Subject's Bill of Rights" to keep.
- You will be asked to sign a separate CHLA HIPAA Research Authorization form authorizing the access, use, creation, and/or disclosure of your health information.

SIGNATURE OF RESEARCH SUBJECT

(*For adults who are capable of providing consent; children ages 14 to 17 years old who are capable of providing assent*)

Your signature below indicates:

- You have read this document and understand its meaning;
- You have had a chance to ask questions and have had these questions answered to your satisfaction;
- You consent/assent to your participation in this research study; and
- You will be given a signed copy of this form.

_____

Print Name of Subject

_____ _____

Signature of Subject Date

SIGNATURE OF RESEARCH SUBJECT (PARENT/LEGAL GUARDIAN/FAMILY MEMBER)

Your signature(s) below indicates:

- You have read this document and understand its meaning;
- You have had a chance to ask questions and have had these questions answered to your satisfaction;
- You agree to your participation in this research study; and
- You will be given a signed copy of this form.

_____

Print Name(s) of Subject

_____ _____

Signature of Subject Date

SIGNATURE OF PARENT(S)/LEGAL GUARDIAN(S)

(*For all subjects under the age of 18*)

Your signature(s) below indicates:

- You have read this document and understand its meaning;
- You have had a chance to ask questions and have had these questions answered to your satisfaction;
- You agree to your child's participation in this research study; and
- You will be given a signed copy of this form.

_____ _____

Print Name(s) of Parent(s)/Legal Guardian(s)

_____ _____

Signature of Parent/Legal Guardian Date

_____ _____

Signature of Parent/Legal Guardian Date

SIGNATURE OF INDIVIDUAL OBTAINING CONSENT

I have explained the research to the subject and/or the subject's parent(s)/legal guardian(s) and have answered all of their questions. I believe that they understand all of the information described in this document and freely give consent/permission/assent to participate.

_____

Print Name of Individual Obtaining Consent

_____ _____

Signature of Individual Obtaining Consent Date

SIGNATURE OF WITNESS (if applicable)

Your signature below indicates:

- You were present for the entire consent conference.
- The information in the consent document and any other written information was accurately explained to the subject and/or the subject's parent(s)
- The subject and/or the subject's parent(s)/legal guardian(s) had an opportunity to ask questions and those questions were answered; and
- The subject and/or the subject's parent(s)/legal guardian(s) voluntarily signed the consent/permission/assent form in your presence.

_____

Print Name of Witness

_____ _____

Signature of Witness Date