STUDY PROTOCOL AND STATISTICAL ANALYSIS PLAN

Official title: Feasibility and effectiveness of real-time, remote continuous glucose monitoring in adolescents with poorly controlled type 1 diabetes

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Study Title

Feasibility and effectiveness of real-time, remote continuous glucose monitoring in adolescents with poorly controlled type 1 diabetes

Background

Achieving optimal glycemic control in patients with Type 1 diabetes mellitus (T1D) is a challenge, especially in the adolescent population; the T1D exchange registry revealed that the mean hemoglobin A1c was 9.3% between ages 15-18, higher than the ADA target of <7.5%.[1] Poor glycemic control increases risk for acute diabetes complications including diabetic ketoacidosis (DKA) and increases risk for long-term complications including nephropathy, neuropathy, retinopathy, and macrovascular disease.[2]

The demands on the adolescent for self-care are arduous: the American Diabetes Association (ADA) recommended standards of care for youth (children and adolescents) with type 1 diabetes include frequent blood glucose checks (up to 6-10 times daily) and an intensive insulin regimen (either via basal insulin and multiple daily injections of prandial insulin or via continuous subcutaneous insulin infusion).[3]

Barriers to glycemic control in patients with T1D include premature transition in responsibility for managing diabetes from parents to teens, risk taking behaviors among adolescents, lack of feeling of peer normalcy, fatigue from diabetes care, and varying insulin requirements owing to physiological pubertal changes requiring frequent dose changes.[4]

Continuous glucose monitors (CGM) measure interstitial fluid glucose readings on a real-time continuous basis. Previous studies have shown the clinical benefit of CGM in reducing hemoglobin A1C (HbA1c) with regular use of the device among patients with diabetes requiring insulin. Two devices are currently approved by the Food and Drug Association (FDA) to be used for insulin dosing. The Dexcom G6 CGM does not require scheduled calibration and has the added features of customizing alarms for hyperglycemia and hypoglycemia, which could help facilitate appropriate changes in insulin therapy. This technology also allows real-time blood glucose values to be transmitted remotely to other devices.[5]

Many parents of patients with type 1 diabetes are not appropriately involved in their care, as both neglectful and intrusive supervision can lead to poor diabetes control.[6] This raises the question of a potential role for clinicians in supervising and guiding diabetes management directly to patients with uncontrolled diabetes. To our knowledge, there are no published studies describing direct monitoring and oversight of CGM by medical professionals in an outpatient setting. A recent retrospective analysis of 15,000 children aged 2-18 years who used Dexcom CGM revealed that 94.8% had the “share” function enabled, which allows primary caregivers to follow glucose readings[7]. We plan to assess the efficacy, safety, utility and acceptability of 3 months of CGM use in adolescents with poorly controlled T1D under free-living conditions, with our clinic staff directly following blood glucose levels in real-time, and communicating reciprocally with patients and parents regarding actionable abnormalities in blood glucose levels.

Study Protocol

Study Hypothesis

A three-month real-time, remote continuous glucose monitoring period with two-way text messaging between healthcare providers, patients, and parents improves hemoglobin A1c in adolescents with poorly controlled type 1 diabetes.

Overview of methodology

We plan to conduct an open-label, single-center, single-arm three-period study. We aim to recruit 25 adolescents aged 13-18 years with poorly controlled T1D as evidenced by Hemoglobin A1c ≥ 12% or a 30% annual risk of developing DKA in the following year according to a predictive model developed at our institution. At a threshold value of probability of admission ≥ 0.3 (95% specificity) our model can identify a high-risk subset of approximately 8% of the patients who collectively have a 40% probability of admission in the 12 months following assessment.[8] We will obtain a written informed consent from guardians and assent from study participants before any study-related activities. We will obtain each patient's demographic information, time since diagnosis, previous hospital admissions. Patient Health Questionnaire (PHQ-9A)[9] and a point-of-care hemoglobin A1c as standard of care. We will administer a quality of life questionnaire (assessed by the Pediatric Quality Life Inventory for teens 13-18, PedsQL4.0)[10], a self-efficacy and self-management questionnaire (assessed by The Self-Efficacy for Diabetes Self-Management measure (SEDM)[10]), and a questionnaire to assess parent-child collaboration in diabetes care (assessed by the Collaborative Parent Involvement Scale [12]).

The first phase of the study will be a surveillance phase in which a blinded Dexcom G6 will be used to obtain baseline values including time in range, percent highs, and percent lows, and percent CGM use. We will use this phase as a run-in period to reduce the chance of noncompliance with the study.

Participants who wore the device at least 60% of the time will then proceed to the second phase of the study which aims to provide a nonblinded CGM for patient use with professional real-time monitoring. If the CGM is worn less than 60% of the time, the participant may be withdrawn from the study at the discretion of the study investigator. Participants will be encouraged to use CGM data for insulin dosing and to monitor their own blood glucose levels. Additionally, participants will share their CGM data with our clinic and with their legal guardians, utilizing the real-time share/follow Dexcom function. Clinical personnel, who could be either endocrinology fellows, endocrinology nurse practitioners or certified diabetes educators, will provide direct supervision and will communicate routinely with participants and guardians using secure text messaging (see Procedure section for more details). Remote monitoring will occur on 7 days per week between 8:00 AM and 8:00 PM. Clinical personnel will have real-time access to patient blood glucose data and will make management recommendations based on the diabetes management plan, will review insulin trends every week, will provide motivational texts to participants, and will respond to any diabetes-related concerns raised by participants. Participants

will receive $10 gift card for every study follow-up visit completed, with a total compensation of $30 per participant.

The third study phase will provide unblinded CGM to patients without real-time monitoring. Participants and their families `will still have the ability to communicate with our clinic through routine clinically available means, mainly through the electronic patient portal and/or calling the urgent line. This study phase will be exploratory to assess whether any improvement in diabetes control after real-time monitoring continue to exist after real-time monitoring is withdrawn.

Inclusion criteria

- Age between 13-18
- Diagnosis of type 1 diabetes for at least six months.
- Both sexes and all ethnicities included.
- Subject and at least one parent able to communicate in English.
- Poorly controlled T1D as evidenced by a $\geq$30% annual risk of developing DKA in the following year OR Hemoglobin A1c $\geq$ 12%
- Treated with subcutaneous insulin, either with a basal/bolus insulin regimen or a continuous subcutaneous insulin infusion (CSII) device.
- Willing to wear CGM and utilize the share function to clinician and guardian, with measuring blood glucose checks as required by the CGM.
- Owning a smartphone compatible with Dexcom G6 software to allow the use of share/follow features with internet access capabilities
- Willing to participate in secure text messaging with study personnel.
- Female participants must have a negative pregnancy test.

Exclusion criteria

- Type 2 diabetes, secondary diabetes or CF related diabetes.
- Other severe chronic disease (e.g., cancer) which in the judgment of the investigator is likely to significantly affect glycemic control.
- Patients cannot be taking systemic corticosteroids at enrollment because of adverse effects on glycemic control, but we will not disqualify subjects who require such therapy during the study. Inhaled or topical corticosteroids are permissible.
- Patients with uncontrolled hypothyroidism (TSH >20) or uncontrolled hyperthyroidism will be excluded from the study. Patients with out of range values may be retested after medication dose adjustment.

- Developmental delay or behavioral disorder in the patient of sufficient severity, in the judgment of the investigator, to interfere with study activities. Severe uncontrolled depression defined as PHQ-9A >15 at time of enrollment is an exclusion criterion.
- Medical or psychiatric disorder in a parent of sufficient severity, in the judgment of the investigator, to interfere with study activities.
- Pregnancy, planned pregnancy or breast feeding
- CGM adhesive allergy
- Skin condition that makes CGM placement contraindicated.
- Sickle cell disease or hemoglobinopathy
- Red blood cell transfusion within 3 months prior to study enrollment

Recruitment

Study team members or clinic providers can distribute flyers to patients who qualify to participate in this research study to aid in recruitment of participants. The patient recruitment flyer contains basic description of the study, including use of Dexcom G6, study timeline, brief descriptions of each visit, and compensation for participating in the study. Please see Appendix 1 for copy of the flyer.

Other forms of recruitment include distributing letters via mail and via Children's Health MyChart web portal to patients who may qualify for the study. Please see Appendix 2 for the template for the letters.

Study Timeline

Study procedures

Study design

This is a pilot study that will not include a control group. It will enroll 25 subjects.

Schedule of procedures

Screening, Visit 1

Screening visit. It will include review of inclusion and exclusion criteria and obtaining informed consent from legal guardians and assent from participants. The visit is expected to take around one hour. The visit can be combined with Visit 2.

Participants will be recruited from either an endocrinology inpatient floor or the outpatient clinic.

Baseline, Visit 2

The visit will include review of diabetes history including current doses, prior hospitalizations, previous complications, and detailed medical and social histories and a complete physical examination that will include measurement of height and weight. A capillary blood sample will be obtained for HbA1c determination using the Alere Afinion device. A HbA1c from within two weeks of Visit 2 may also be used. A urine pregnancy test will be performed on females capable of becoming pregnant.

Participants and guardians will be introduced to the concept of a continuous glucose monitor in general, with specific details about how to apply, use, and share the Dexcom G6 data. Mandatory alarms will be set for participants and followers for blood glucose below 70 mg/dL, blood glucoses above 250 mg/dL, "urgent low soon", "signal loss", and "no reading" alerts. Participants may set extra alarms to personalize their diabetes alerts. Participants will also be taught to log their food and insulin intake into the CGM device.

Participants will complete the PHQ-9A, PEDS-QoL4, Self-Efficacy for Diabetes Self-Management measure (SEDM) questionnaire, and Collaborative Parent Involvement Scale. A blinded CGM will be placed on the participant with the goal to obtain baseline data for 10 days. A test secure text message will be sent through TigerConnect to guardian and participant, and they will be introduced to the messaging platform used. We will determine with the participants and parents their preferred contact hours and school hours to allow texting for non-urgent matters to be done at convenient times. This visit will take up to 2 hours.

Between Visit 2 and Visit 2T, participants and clinical staff will be notified if there is signal loss from the blinded CGM. Dexcom, Inc. will provide troubleshooting of the blinded CGM if any technical issues arise. Participants will be asked to continue taking care of their diabetes as usual and will not have access to the CGM data.

Telephone or Clinic Follow-up, Visit 2B or 2T

This will be a telephone call scheduled 10 days (+ 4 days) by a clinical research staff member to review blinded CGM data for the purpose of logging CGM parameters including average glucose with standard deviation, time in range, percent highs, percent lows, and severe lows, and days with CGM data. If the CGM is worn less than 60% of the time, the participant maybe withdrawn from the study at the discretion of the study investigator. Each participant, with the help of a guardian, will insert a non-blinded sensor according to the Dexcom G6 user guide, connect the Dexcom to a compatible phone, and activate the share functions with the clinic. If the guardian is not able to set-up the Dexcom at home, the patient and guardian will be asked to come for Visit 2B within 5 days to have the non-blinded Dexcom set-up in clinic and assure that inserting the CGM is a skill that could be done independently. If the guardian or participant cannot demonstrate that they can set-up the CGM system independently, the participant will be withdrawn from the study.

Between Visit 2T and Visit 3, clinic research staff will actively monitor the participants' blood glucose levels remotely through an Apple iPad. Currently available commercial Dexcom software is able to monitor up to 10 devices on a single iPad, and we plan to have two iPads

throughout the study period. Active remote monitoring of CGM data will occur during 7 days per week between 8:00 AM and 8:00 PM.

The goal of the secure text messaging is to provide supervision and feedback to the adolescents that is supportive and collaborative, with the ultimate goals of increasing self-efficacy and improving diabetic self-management skills. The intention is not to make the texting platform cumbersome and to allow the participants freedom in making lifestyle choices that will not interfere with their diabetes control. Only reactive texts and coaching texts will be sent during the school hours.

Participants will still be able to use normal clinic communication methods through the electronic patient portal and diabetes telephone emergency line as usual. Participants will be free to optimize their treatment independently as previously educated about trend management. We will provide a letter for school indicating that the participants are a part of a study and they have to carry their cell phones with them and respond to text messaging from us.

We will utilize texting interventions as described in the Novel Interventions in Children's Healthcare (NICH) program[13] which was a recent study that implemented texting interventions for participants with uncontrolled diabetes. Texts will be sent in the following categories:

- Reminding: this will include texts to request or prompt the participant or the parent for a reminder or an immediate diabetes related actions. The following situations are **immediate situations** that require immediate mandatory reminder text from the research staff:
    - If blood glucose level is above 300 mg/dL for more than 2 hours, the research staff will send a text to remind about action regarding insulin. One possible example text is as follows: "I have seen that you have constant highs ↑↑↑ since last night. Did you get your Lantus last night? Please check ketones and let me know so we can help dose your insulin (syringe emoji)". Insulin dosing recommendations will be provided according to clinic established protocols for managing hyperglycemia with or without ketones.
    - If blood glucose is below 70 mg/dL for more than 10 minutes with double arrows down, a text will be sent to treat a low. One possible example text will be as follows: "your CGM is reading that you're 63. Time for some carb snack to treat that low (cookie Emoji)"
    - If there is no CGM data for 4 hours, a text will be sent. An example text is as follows: "Is your Dexcom working? I cannot see any numbers from my end".

  If a reactive text has not been responded to within 30 minutes, the research staff will attempt to call guardian or contact school to get the issue resolved.
  In addition to the reactive texts, reminders can also include messages to remind of regular diabetes tasks, such as "It's Lantus time. Don't forget it please (smiley emoji)". Log reminders will also be sent "It will be easier for us "and you" if you enter how much insulin you have received. Can you please enter your insulin doses in Dexcom (target emoji)?"

  Research staff will coordinate a "trend review time" every 7 days (+/- 3 days) to walk through glucose trends and insulin adjustments necessary. Example texts will include

"time for some trend review… seems that you've been having high blood sugars after your breakfast literally every day. I think you're currently dividing your carbs by 12 for breakfast. I suggest that we change that to 1:10 to give you more insulin…".

Reminder texts will also be sent to remind participants and guardians about upcoming research Visit appointments.

- Reinforcing. Texts will provide encouragement and reinforcement for adherence to diabetes related tasks. Examples will include texts stating "(screenshot image from the participant's glucose trend), followed by "awesome control! Keep it up!".
- Coaching. Texts in this category will include response to participants and guardians' complaints and questions. They could include management of participant or guardian questions about abnormal blood glucoses or ketone management interventions. Clinic protocols to manage sick days will be utilized.

All Tigertext communication will be stored electronically in a secure shared file. It will be used to retrospectively calculate time invested by clinical staff, and analyze percentage of texting category used.

First Follow-up, Visit 3

This visit will be scheduled 11-12 weeks (+/- 5 days) after Visit 2B or visit 2T. Adverse events, insulin doses and concomitant medications will be reviewed by study staff. Height and weight will be measured, and a physical exam will be performed. A capillary blood sample will be obtained for HbA1c determination. CGM reports will be analyzed. Participants will complete the PHQ-9A, PEDS-QoL4, Collaborative Parent Involvement Scale, and SEDM.

If due to participant or family scheduling conflicts, the participant is unable to complete a clinic visit for Visit 3, then they can participate in a telemedicine visit. Participants will be requested to measure height and weight at home. A physical exam will be performed as fully able within the telemedicine platform. HbA1c will be obtained with other standard of care labs. CGM report analysis will not be affected by the telemedicine visit. Surveys for PHQ-9A, PEDS-QoL4, Collaborative Parent Involvement Scale, and SEDM will be sent via MyChart to the participant's parent to be completed by the participant. Parents will send images of the completed surveys to the research team via MyChart.

We will discuss the next phase of the study during that visit. We will emphasize that the research staff will not monitor CGM data remotely, that research staff will not be real-time followers of their CGM data, and they will not be able to use TigerText to communicate with our clinic anymore. They will be encouraged to continue the activated alarms to allow for self-control.

We will discuss that CGMs will continue to be made available to participants and guardians for diabetes care. Participants and guardians will still be able to communicate with our clinic through previously available means, mainly through the electronic participant portal and/or calling the urgent line, and they could ask the clinic staff to review past CGM readings to give clinical advice.

Second Follow-up, Visit 4/EOSV

This visit will be scheduled 11-12 weeks (+/- 5 days) after Visit 3. Adverse events, insulin doses and concomitant medications will be reviewed by study staff. Height and weight will be measured, and a physical exam will be performed. A capillary blood sample will be obtained for HbA1c. Participants will complete the PHQ-9A and PEDS-QoL4 surveys, Collaborative Parent Involvement Scale, and SEDM.

If due to participant or family scheduling conflicts, the participant is unable to complete a clinic visit for Visit 4, then they can participate in a telemedicine visit. Participants will be requested to measure height and weight at home. A physical exam will be performed as fully able within the telemedicine platform. HbA1c will be obtained with other standard of care labs. CGM report analysis will not be affected by the telemedicine visit. Surveys for PHQ-9A, PEDS-QoL4, Collaborative Parent Involvement Scale, and SEDM will be sent via MyChart to the participant's parent to be completed by the participant. Parents will send images of the completed surveys to the research team via MyChart.

This is the final study visit.

Evaluations

Medical History

- Age
- Gender
- Race/ethnicity
- Date of diagnosis of type 1 diabetes
- Hospitalizations and emergency department visits, particularly for diabetic ketoacidosis or hyperglycemia/ketosis/vomiting, or for severe hypoglycemia
- Surgeries
- Growth records for both height and weight
- Current doses of insulin
- Meal plan
- Other chronic medical conditions, particularly hypothyroidism or celiac disease
- Concomitant medications

Social history

- Family structure—one or two parent household, parents married or divorced, custody arrangements if divorced, genders and ages of siblings

- School details: name, grade, extracurricular activities, sports, schedule, school nurse information, and information about student insulin dosing during school hours if it is done through school nurse or independently by student.
- Primary language spoken at home, patient and parents' ability to converse in English if not primary

Laboratory data

- Present and past HbA1c

New clinical data will be obtained in this study. Please refer to the Table of Assessments for a list of these data.

Height and weight

Participant's heights will be measured with a properly calibrated stadiometer at times specified in the study timeline. Heights will be measured three times in immediate succession (with subjects instructed to bend and stretch between measurements) and the average used. Weight will be measured with the subject lightly clothed and without shoes. If the research visit must be performed via telemedicine visit, the participants will measure their height and weight using a measuring tape and weight scale available at their home.

Physical Examination

Physical examinations, including general appearance, head, eyes, ears, nose and throat, chest, cardiac, abdomen, extremities and neurologic and injection site examinations will be conducted at times specified in the study timeline. Any clinically significant abnormality in physical findings noted during the study should be reported as an adverse event. Any clinically significant abnormalities persisting at the end of the study will be followed by the investigator until resolution or until reaching a clinically stable endpoint. If the research visit must be performed via telemedicine visit, the physical examination will be performed as able within the telemedicine platform. This includes visual appearance of general appearance, head, eyes, nose, mouth, chest, extremities, and injection sites. Vital signs will not be able to be measured during a telemedicine visit.

Psychological and Quality of Life Assessment

PHQ-9A and PEDS-QoL4 are validated surveys will be used to screen for depression and to assess for quality of life, respectively.

Measure of self-efficacy and diabetes management

We will utilize the "Self-Efficacy for Diabetes Self-Management measure (SEDM)" questionnaire[10], which is a 10-item self-report scale with good reliability (Cronbach's alpha = .90). It covers the major aspects of diabetes self-management including monitoring blood

glucose levels, dosing insulin, food choices, and exercise, and performance of diabetes-related tasks when feeling overwhelmed or frustrated. Total score range for the SEDM is 1–10.

Measure of Collaborative Parent Involvement

We will utilize the Collaborative Parent Involvement Scale[11], a 12-item questionnaire with a five-point Likert scale, from almost never to always, and is targeted for adolescents. The scale aims to assess parental use of problem solving, teachable moments, diabetes, help with autonomy, and supervision of diabetes care when the adolescent is not around.

TigerConnect

TigerConnect is a secure messaging application approved by many large healthcare organizations, including Children's Medical Center Dallas, to allow for secure exchange of Protected Health Information (PHI) that is compliant with HIPAA. It allows sharing texts, emoji, images and videos.

We will utilize the TigerConnect platform to communicate with participants and guardians. A participant receives a text message alert that a new secure message was sent, with a clickable hyperlink provided to check the contents. The hyperlink opens in the phone's default browser, directs the participant or guardian to the encrypted secure chatting window, and allows direct communication with research staff. When a participant or parent replies to the window, an alert is sent to the research staff's phone and to an open webpage that has the chat open.

Estimated study duration

Study duration for participants

The duration of the study for participants from Visit 2 until Visit 4, the final study visit, is approximately 6-7 months.

End of study

The study will end with Visit 4 of the last subject.

	Screening Visit (1)	Baseline Visit (2)	Telephone/Clinic Follow-up (2T/2B)	First Follow-up visit (3)/(Potential telemedicine visit)	Second Follow-up visit (4)/ /(Potential telemedicine visit)/EOSV
Consent	X				

Inclusion/Exclusion					
Demographic Information	X				
Full physical exam		X		X (or telemedicine exam if telemedicine visit)	X (or telemedicine exam if telemedicine visit)
Vital signs		X		X (not applicable for telemedicine visit)	X (not applicable for telemedicine visit)
Height and Weight		X		X	X
Hemoglobin A1c		X		X	X
Urine pregnancy test		X			
Blinded continuous glucose monitor placement		X			
Un-blinded continuous glucose monitor placement			X		
Education about continuous glucose monitor use and placement		X	X		
Review of CGM data			X	X	X
Establishing messaging platform with patient and parent		X			
Patient Health Questionnaire (PHQ-9A)		X		X	X
Pediatric Quality Life Inventory for teens 13-18, PedsQL4.0		X		X	X
Self-Efficacy for Diabetes Self-Management measure (SEDM)" questionnaire		X		X	X
Collaborative Parent Involvement Scale		X		X	X

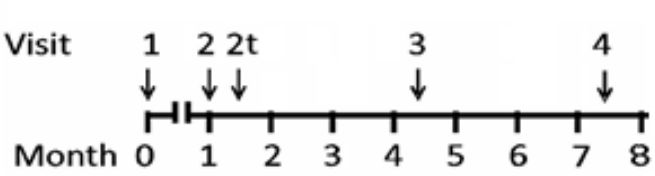

Figure 1. Timeline for study. Study visits are denoted by arrows. A timescale in months is below the timeline; there is not a specified interval between Visits 1 & 2.

Participant withdrawal criteria

The following study withdrawal criteria will apply:

1. Participants can terminate involvement in the study at any time point without any repercussions.
2. If data on the CGM is available < 60% of the time worn, patient may be withdrawn at the discretion of the research investigator.
3. If pregnancy occurs during study period.
4. Allergic reaction to adhesive surface of CGM sensor

Primary endpoint

The primary outcome is change in Hemoglobin A1c (HbA1c) between the baseline visit (Visit 2) and three-month follow-up visit (Visit 3) after active remote monitoring and secure text messaging.

A 5% significance level will be used to declare statistical significance for the primary outcome comparison.

Exploratory endpoints

- Change in Peds PHQ-9A, PED-QOL4A, SEDM, and Collaborative Parent Involvement Scale scores.
- Time taken for a text to be read by participant and guardian.
- Time spent by medical provider per participant per day.
- The difference in A1c between clinical remote monitoring HbA1c (Visit 3) and self-monitoring utilizing CGM (Visit 4)
- The difference in A1c from baseline (Visit 2) and after the two phases of the study intervention (Visit 4).
- The following outcomes will be compared between baseline, three months and six months using repeated measures ANOVA as follows:
    - Time spent in the target glucose range from 70–180 mg/dL
    - Time spent below target glucose 70 mg/dL

- Time spent above target glucose 180 mg/dL
- Average of time the participants wore the CGM

Statistical Plan

Paired sample t-tests will be used to assess continuous variable differences between two time points. Generalized linear models will be run to identify items in medical and social histories that could predict hemoglobin A1c, the primary outcome. Point estimates will be reported with 95% CIs.

As this is a pilot exploratory study, we will implement per-protocol analysis and not an intention-to-treat analysis. Only patients who have completed the three phases of the study will be included for analysis.

Utilizing a standard deviation of HbA1c of 1.5%, a sample size of 18 participants will be required to detect a 1% change in HbA1c between the baseline measurement and 3-month measurement, assuming an alpha of 0.05 and a beta of 0.20 (80% power).

Safety endpoints

The following safety outcomes will be tabulated by treatment group:

- Number of subjects with any DKA events requiring hospitalization
- Number of subjects with any severe hypoglycemic or hyperglycemic events requiring an emergency room visit or hospitalization
- Number of episodes of moderate to large ketones managed in an outpatient basis

All adverse events will be listed for the entire study duration.

Data management

Dexcom Clarity reports will be used to obtain aggregate 90-day data regarding CGM parameters including average glucose with standard deviation, time in range, percent highs, percent lows, severe lows, and percent days with CGM data (this will be used to compare data across Visits 2T and Visit 4). Additionally, we will collect above data points retrospectively week-by-week for secondary analysis to evaluate progress over time.

Confidentiality of participant data will be observed during the study. Electronic data will be stored in secure password protected computers, and all paper records will be stored in locked researcher's offices. Anonymous data could be shared with third parties to advance diabetes treatment and for study publication purposes.

Protections Against Risk

Confidentiality

Privacy of Personal Data

The collection and processing of personal data from subjects enrolled in this study will be limited to those data that are necessary to fulfill the objectives of the study. These data will be collected and processed with adequate precautions to ensure confidentiality and compliance with applicable data privacy protection laws and regulations. Electronic data will be stored on secure servers that require password protection and maintain audit records of access, and/or on laptops with password-protected encrypted hard drives. All data sent between institutions via e-mail, file transfer protocols or physical media must be encrypted and password protected. Sponsor personnel whose responsibilities require access to personal data agree to keep the identity of study subjects confidential. Hardcopy documentation must be stored in locked file cabinets or locked offices secured with either key or badge access.

The informed consent and HIPAA permission obtained from the subject's legally acceptable representative includes explicit consent for the processing of personal data and for the investigator to allow direct access to his or her original medical records for study-related monitoring, audit, IRB review, and regulatory inspection. This consent also addresses the transfer of the data to other entities and to other countries.

For any telemedicine visits completed, verbal consent to perform a telemedicine visit will be obtained from the participant's parent/legal guardian/legal representative. All telemedicine visits will be completed using Children's Health telemedicine platform.

The subject's legally acceptable representative has the right to request through the investigator access to the subject's personal data and the right to request rectification of any data that are not correct or complete. Reasonable steps will be taken to respond to such a request, taking into consideration the nature of the request, the conditions of the study, and the applicable laws and regulations.

Disclosure to outside entities

All data, whether electronic or hardcopy, will be referenced to a unique patient identifier, with subjects' identifying information kept in separate secure files. The following entities will be granted access to some or all data and specimens from this study:

- The UT Southwestern Institutional Review Board (IRB).
- Dexcom, Inc.
- Representatives of other governmental and regulatory agencies.

Data and Safety Monitoring Plan

This study represents minimal incremental risk over routine care for children with type 1 diabetes. Accordingly, a separate DSMB is not indicated.

ClinicalTrials.gov

We will register the study with ClinicalTrials.gov prior to enrolling any subjects.

Adverse event reporting

No investigational drug or device will be used in these studies, and consequently adverse event reporting, *per se,* is not applicable. However, we will monitor as secondary outcomes hypoglycemia frequency, DKA admission risk, and report all study adverse events.

Budget: $37,300 (Dexcom, Inc will provide the CGM devices for the study)
Certified Diabetes Educator time - 36 hours per week × 20 weeks of study × $50 per hour = $36,000
iPad devices for monitoring CGM data – 2 devices × $350 per iPad = $700
Patient incentive gift cards – $10 × 3 visits × 25 participants) = $600
Dexcom CGM devices for 6 months – Provided by Dexcom.

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Appendix 1: Patient Recruitment Flyer

Diabetes Buddies: Remote Realtime CGM Monitoring

Do you have Type 1 Diabetes? Want more help with improving your blood sugars?

Let us tell you more about our research study where you get free Dexcom G6 continuous glucose monitors, and our team will monitor your blood sugars and help you reach your blood sugar goals!

Visit 1	Visit 2 Two weeks later	Visit 3 3 months later	Visit 4 6 months later
• Introduction to the Study • Consent • Getting started with the Dexcom G6 with a 10-day trial	• Starting daily contact with study team who monitors your blood sugars with Dexcom G6 • Setting up text messaging with study team	• This is the time for you to use what you learned in the past 3 months! • Keep using the Dexcom G6 • Study team won't be monitoring your blood sugars	• Checking HbA1c • Sharing what you learned • End of study!

All visits take place at the Children's Health Diabetes Clinic at Dallas.

For your participation, you will receive a total of $30 during the study!

If you are interested in learning more or participating in this study, please talk to your diabetes provider or send the Diabetes Clinic a MyChart message (include the name Dr. Pooja Choudhari, study team member, in the message).

Appendix 2: Patient Recruitment Letter

Dear Parents,

I am one of the Pediatric Endocrinology doctors at Children's Health. I am part of a research team that is looking into ways to help teenagers with Type 1 Diabetes improve their blood sugars.

The goal of the study is to see if live monitoring of blood sugars seen on a Dexcom G6 continuous glucose monitor can help improve blood sugars in teenagers with Type 1 Diabetes. Members of our research team use a secure text messaging app to send @fname@ and you reminders to take insulin, help with low and high blood sugars, and send encouraging messages.

We will provide you with Dexcom G6 CGMs throughout the 6.5 months study. There will be four visits to the Children's Health Endocrinology Clinic in Dallas during this study period.

If you and @fname@ are interested in learning more about this research study, please reply to this MyChart message, call our clinic and ask to speak to Dr. Pooja Choudhari about the CGM study, or talk to your diabetes provider.

Thank you,

Dr. Pooja Choudhari