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Title	CGM Use in Poorly Controlled Youth With Type 1 Diabetes
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## **A Introduction**

### ***A1 Study Abstract and Background***

The American Diabetes Association (ADA) recommends that continuous glucose monitoring (CGM) be considered for all children with Type 1 Diabetes (T1D).<sup>1</sup> Continuous glucose monitoring is associated with improved glycemic control; however, only 60% of children use CGM. Further, minority and low-income youth are less likely to use diabetes technology, including CGM and insulin pumps.<sup>2</sup>

Barriers to CGM use are well described; however, initiatives to improve CGM uptake in underserved and poorly controlled youth with T1D are limited.<sup>3-5</sup>

In order to increase use of this technology in this high-risk diabetes population, this study will provide complementary trial CGM at the point of care in a prospective study to determine if providing a short-term trial use of a CGM device increases subsequent uptake of personal CGM and improves glycemic control and measures of diabetes-related distress.

### ***A2 Primary Hypothesis***

We hypothesize that providing sample complementary CGM at the point of care with standardized CGM education will increase uptake of personal CGM use in pediatric patients with diabetes.

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## **B Study Objectives**

### ***B1 Primary Aim***

To determine if providing a complementary short-term trial use of CGM increases subsequent uptake of personal CGM.

### ***B2 Secondary Aim***

To determine if providing a complementary short-term trial use of CGM improves glycemic control and measures of diabetes distress and diabetes related quality of life.

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## **C Study Design**

### ***C1 Overview of Study Design***

This is a hypothesis-driven, pre-registered, prospective cohort study to determine if point of care placement of complementary CGM with standardized CGM education increases uptake of personal CGM.

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The study will consist of a baseline visit (coincident with routine clinical care) where a complementary trial CGM is placed at the point of care with standardized CGM education. CGM-related apps will be downloaded on the participant's smartphone. Follow-up phone calls will be conducted by the study team at 5-days and 10-days after CGM placement. Use of personal CGM will be recorded at the next follow-up visit (at 3-6 months), with CGM data recorded (if available) and hemoglobin A1c level (performed as part of routine clinical care) recorded. Surveys will be completed at baseline, 10-days (via email), and at follow-up (3-6months)

## ***C2 Subject Selection and Withdrawal***

### **2.a Inclusion Criteria**

- Patients with type 1 diabetes for more than 3 months
- Ages 5-21 years
- CGM naive or no CGM use in the 9 months prior to enrollment
- No minimum A1C level required for eligibility.

### **2.b Exclusion Criteria**

- CGM use in the 9 months prior to enrollment

### **2.c Subject Recruitment Plans and Consent Process**

Individual(s) responsible for approaching participant(s): Research coordinators

Where and when recruitment will take place:

Participants will be recruited, screened for eligibility, and consented in a private clinic/room to ensure privacy.

Consent process:

Participants will read through the consent form with the research coordinator, have time to review it and ask questions about the study and study procedures.

### **2.d Randomization Method and Blinding**

Not applicable

### **2.e Risks and Benefits**

This study involves no more than minimal medical risk to the participants as use of CGM is considered standard of care per the American Diabetes Association guidelines.

Risks associated with use of CGM may include hypoglycemia (low blood sugar) or hyperglycemia (high blood sugar) in cases where information provided by the CGM device is inaccurate and used to make treatment decisions or where hardware or set-up issues disable alarms and alerts. Patients will be advised to confirm with a fingerstick blood sugar if symptoms do not match CGM readings.

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Patients may also experience skin irritation or redness around the CGM device's adhesive patch. The CGM may inadvertently fall off, and if that occurs, the patient will resume checking fingerstick blood sugars as they were previously.

To minimize risk, when the diabetes nurse/CDCES places the CGM, the nurse will perform routine standardized education including setting up alerts. The CGM devices provide blood sugars every 5 minutes (that creates a continuous reading) versus the typical 4-5 fingerstick blood sugars usually checked per day. Therefore, the CGM actually minimizes risk of hypoglycemia by alerting users to impending hypoglycemia which may not have been previously detected. Participants will have been taught signs/symptoms of hypoglycemia per routine new-onset diabetes education. They will be educated to check blood sugar via fingerstick if they have any sign/symptoms of hypoglycemia and treat accordingly. If they do not understand how to use the device, they have access to Pediatric Endocrinology on-call provider and Dexcom customer service for assistance, and device may be removed early. The risk of device malfunction is extremely low.

The CGM will be applied in clinic by diabetes nursing staff. If patient reports any irritation or signs of infection at the site, the CGM will be removed early. If the CGM is removed early either accidentally or intentionally, participants will be offered a replacement CGM. They will have to resume previous blood sugar monitoring with glucometer and fingersticks, as the patient was using prior to placement of CGM.

**Confidentiality:** There is the risk that psychological, emotional, financial, social, and legal risks might result if confidentiality cannot be maintained in this study. All study team members are HIPAA trained and will take every step to respect participants' privacy and protect their confidentiality throughout the study. We share the information gathered in the study only with the people who need to know this information. All information gathered during this study will be kept in a secure HIPAA compliant database, REDCap.

**Benefit:** Use of CGM may increase blood sugar monitoring, reduce hypoglycemia, and improve glycemic control.

## **2.f Early Withdrawal of Subjects**

Participants may withdraw from the study at any time by notifying the study team.

## **2.g When and How to Withdraw Subjects**

The participant may choose to withdraw from the study. It will also not impact the course of the participant's clinical care.

## **2.h Data Collection and Follow-up for Withdrawn Subjects**

Data collected from subjects will remain in the dataset, but no follow-up will be conducted on withdrawn subjects.

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# **D Study Procedures**

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## ***D1 Screening for Eligibility***

Patients being seen in the diabetes center will be pre-screened for eligibility by the research team based on the inclusion criteria. Eligibility will be confirmed with the patient's diabetes provider at the time of the clinic visit, and with the potential participant based on the inclusion criteria. The study coordinator will confirm that the participant that they have never used a CGM, or have not used CGM in the prior 9 months.

## ***D2 Schedule of Procedures***

Eligibility and Consent: If the patient is eligible and interested in the study, the research coordinator will meet with the patient and caregiver in an exam room for privacy and confidentiality. The research coordinator will explain the study and study procedures, read the informed consent form with the participant and caregiver, and allow time for questions on the study and consent form.

If the participant is less than 18 years of age, the parent will sign the consent form and the participant will sign the assent. If the participant is 18 years of age or over, the participant will sign the consent.

At the time of consent, 3 phone numbers are collected from the participant for future follow-up.

At the baseline visit, barriers to prior CGM use or sustained use will be recorded.

The certified diabetes educator (CDCES) will place the CGM and provide standardized education, including education on use of the Dexcom apps, including Dexcom G6 Dexcom Clarity, and Dexcom Follow (optional) for caregivers. The participant's Dexcom Clarity account will be connected to the clinic portal for remote viewing of data.

The nurse/CDCES will follow up with the patient by phone in 5 days (4-6 days if day 5 falls over a weekend) and again at 10 (9-11) days at the end of the CGM session. Assessment and education during these follow-up phone calls will include report of behavior changes related to blood glucose monitoring and insulin administration, and nurse/CDCES recommended dose adjustments based on observed patterns, as well as education on obtaining personal CGM. CGM data (when available) will be recorded.

At the participant's next follow-up visit at 3 months (or up until 6 months if a visit is cancelled), use of personal CGM will be recorded, in addition to Hemoglobin A1c measured at that visit, questions about behavioral changes, and CGM data, if available.

Questionnaires will be administered before and after initiation of the CGM and at their routine diabetes clinic visit 3-months later to assess changes in psychosocial outcomes of diabetes distress and hypoglycemia worry. Surveys will be administered via REDcap survey.

## ***D3 Point of Care CGM Placement and education***

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Participants will be provided with a Dexcom G6 CGM, which will be placed during the clinic visit by diabetes staff, and CGM education will be provided at the point of care by the nurse/Certified Diabetes Care and Education Specialist (CDCES). Additionally, participants will download apps on their smartphones including Dexcom G6 and Dexcom Clarity. Caregivers and family members will download Dexcom Follow (optional). Education will be provided on using all the apps. Participants' Dexcom Clarity app will be connected to the clinic's Clarity account for remote viewing of data. Participants without a compatible smartphone will be provided a loaner smartphone for the duration of the 10-day CGM use.

## ***D4 Safety and Adverse Events***

### **4.a Safety and Compliance Monitoring**

Site investigators will monitor compliance with the protocol and good clinical practice (GCP) guidelines.

### **4.b Medical Monitoring for adverse events**

Participants will be monitored for adverse events during the study visit, during their CGM wear, and during the follow-up period of up to 6 months.

### **4.c Definitions of Adverse Events**

An adverse event (AE) is defined as any untoward medical occurrence in a patient or clinical investigation subject.

### **4.d Classification of Events**

- **Relationship**

Medical judgement should be used to determine the relationship, considering all relevant factors, including pattern of reaction, temporal relationship, de-challenge or re-challenge, confounding factors such as concomitant medication, concomitant diseases and relevant history.

- **Severity**

The severity of the AE should be judged based on the following:

Mild:	Awareness of sign(s) or symptom(s) that is/are easily tolerated
Moderate:	Sufficient discomfort to cause interference with usual activity
Severe:	Incapacitating or causing inability to work or to perform usual activities

### **4.e Data Collection Procedures for Adverse Events**

All enrolled participants will be monitored for untoward incidents (e.g., "Adverse Events") occurring during the study. The Principal Investigator (and other designated individuals, if necessary) will conduct regular monitoring for safety concerns and provide general oversight for human subject safety requirements during the study visit and followup period. All adverse events that are anticipated or described in the informed consent form



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will be logged appropriately and reported to the IRB on at least an annual basis (e.g., at continuing review).

#### **4.f Reporting Procedures**

Any Unanticipated Problems or unexpected “Serious Adverse Events” related to the study intervention or in the follow-up period, will be reported to the IRB promptly. Unplanned and non-emergent deviations from the IRB approved protocol will be logged and reported to the IRB annually at continuing review; all planned deviations will be submitted as a Change in Research to the IRB for approval and prior to implementation. All other event reporting requirements will be followed and all necessary parties will be notified of events/problems encountered in the study and/or changes in research, in accordance with all applicable regulations and guidelines.

#### **4.g Adverse Event Reporting Period**

Any Unanticipated Problems or unexpected “Serious Adverse Events” related to the study intervention and/or test article and affecting the risk/benefit profile of the study, will be reported to the IRB promptly, and, in all cases, within 10 business days of discovery.

#### **4.h Post-study Adverse Event**

Not applicable

### **E. Statistical Plan**

#### ***E1. Sample Size Determination and Power***

The following *a priori* sample size calculation is based on improvements in TIR data and assumes 80% power and a 2-tailed type 1 error of 0.05. In order to detect a 10% improvement of TIR from the first 5-days compared to the second 5 days of CGM wear, assuming a TIR SD of 15%, a 2-sided alpha level of 0.05 and 80% power, 20 participants are required. To allow for participant attrition, 30 participants are planned for recruitment.

#### ***E2. Interim Monitoring and Early Stopping***

Interim monitoring will be performed by the study team. No early stopping rules planned for this study.

#### ***E3. Analysis Plan***

Primary outcome variable.

The primary outcome is the *proportion* of participants who obtain a personal CGM and are using it at follow-up.

Secondary outcome variables.

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The secondary outcome is change in glycemic control, as measured by the TIR for the first 5 days (days 1-5) of CGM wear compared to the 2<sup>nd</sup> 5 days (days 6-10) of CGM wear, and in the long term as measured by A1C between baseline and follow-up.

Change in patient-reported outcomes through surveys assessing quality of life and diabetes-distress will be compared between baseline and followup after trial CGM use.

#### ***E4. Statistical Methods***

Statistical analyses will be performed using SAS version 9.4 Copyright © 2020 SAS Institute Inc., Cary, NC, USA.

Categorical variables will be described using frequencies and percentages. The Shapiro-Wilks test will be used to assess the normality distribution of continuous variables. Normally distributed variables will be described by mean and standard deviation. Non-normally distributed variables will be described by median and interquartile range. Paired *t* tests will be used to assess differences in normally distributed continuous measures between baseline and follow up, while Wilcoxon signed rank tests will be used for non-normally distributed measures.

Two sample *t* tests will be used to assess differences between groups in survey responses.

The values  $p < 0.05$  will be considered statistically significant.

#### ***E5. Missing Outcome Data***

Dataset will be assessed for missing-ness and noted in results. Statistical tests will be performed to compare groups with and without missing data, to assess for data missing at random.

### **F. Data Handling and Record Keeping**

#### ***F1. Confidentiality and Security***

All data for this study will be recorded, stored and analyzed in a password-protected file on a HIPAA-compliant and secure drive through Johns Hopkins Medicine, called the SAFE (Secure Analytic Framework Environment) Desktop. This secure environment is provided by JHM and includes productivity software and statistical software. Storing the Data on the SAFE Desktop complies with federal and institutional requirements to protect patient data. Using SAFE reduces the risk of copying data to an unencrypted desktop or device because the SAFE provides the tools to securely analyze and share PHI/PII all within the SAFE environment. Only authorized persons will have access to SAFE Desktop, login and passwords will not be shared and databases will not be left unattended to further minimize risk of loss of confidentiality.

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## ***F2. Records Retention***

Informed consent documents will be securely stored in a locked file cabinet within a locked office. Informed consents will also be scanned into the participant's electronic medical record. Data will be stored for up to 7 years.

## **G. Study Administration**

### ***G1. Organization and Participating Centers***

Johns Hopkins Pediatric Diabetes Center  
Mount Washington Pediatric Hospital Diabetes Center

### ***G2. Funding Source***

Funding for this study is provided by the Johns Hopkins Children's Center Innovation Award (PI: Wolf) and an investigator initiated research grant from Dexcom, Inc (PI: Wolf)

### ***G3. Subject Stipends or Payments***

Participants will receive a \$10.00 gift card, and a parking pass at the baseline study visit and a \$10.00 gift card at the completed follow-up visit.

## **E References**

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