PROTOCOL TITLE: HCT Cash-Only INcentive to promote mealtime insulin DOSE Engagement (HCT COIN2DOSE)

PRINCIPAL INVESTIGATORS:

Sarah Tsai, MD, FRCPC, CPI
Pediatric Endocrinologist
Division of Endocrinology
Assistant Direct of Clinical research
Children's Mercy Kansas City
Email: sltsai@cmh.edu
Phone: 816-960-8952

Ryan McDonough, DO, FAAP
Pediatric Endocrinologist
Division of Endocrinology & Diabetes
Co-Medical Director, Children's Diabetes Center
Children's Mercy Hospital Kansas City
Email: rjmcdonough@cmh.edu
Phone: 816-960-8974

Mark Clements, MD, PhD
Endocrinologist
Pediatric Clinical Research Unit
The Children's Mercy Hospital
Email: maclements@cmh.edu
Phone: 816-983-6982

VERSION NUMBER/DATE:

Protocol Version: 5.08
Protocol Date: 26DEC2023

REVISION HISTORY

Revision #	Version Date	Summary of Changes	Consent Change?
2	June 2, 2021	Revision of protocol to exclude the AIM2DOSE intervention and add LOAN2DOSE. Protocol Title Change.	YES
3	September 22, 2021	Update to the number of participants enrolled Update to pg. 13 Study timelines	Yes
4	January 26, 2022	Changed the word 'Dexcom' to 'CGM' on pages 10,11, 13, & 15	Yes
5	May 12, 2022	Update the use of a recruitment flyer and use of POC a1c if research a1c not received	No
5	Feb 23, 2023	Updated bolus scoring protocol, the dinner window is changed to end at 2200 H.	No
6	April 5, 2023	Updated the use of email to invite potential subjects to participate.	No
7	July 19, 2023	Remove that parents can participate in study focus group even if their child does not participate (page 12). Parents may participate in focus group if their child is enrolled in the study. Removed study AIM 4 (page 6). 1 sentence added to clarify insulin delivery system deliver tracking (page 13). Remove artificial intelligence aspect of focus group consent.	yes
8	Dec 26, 2023	Correct conflicting information in Section 25.0 about Telephone Consent process. Update policy reference from 10.05 to "IRB Permission/Assent/Consent Policy" in Section 25.0 and 26.0.	No

Table of Contents

1.0 Study Summary

Study Title	HCT Cash-Only INcentive to promote mealtime insulin DOSE Engagement (HCT COIN2DOSE): a pilot trial
Study Design	Pilot randomized controlled trial
Primary Objective	To determine the impact of HCTCOIN2DOSE and LOAN2DOSE compared to control on the trajectory of glycemic control and treatment engagement among adolescences age 12-17 years who are at risk for a near-term rise in A1C.
Secondary Objective(s)	To determine both the feasibility and usability of HCTCOIN2DOSE and LOAN2DOSE intervention compared to control in adolescents age 12-17 years who are at risk for a significant near-term rise in A1C.
Research Intervention(s)/ Investigational Agent(s)	HCT COIN2DOSE: Utilization of immediate financial incentives to promote mealtime insulin dose delivery, with weekly bonuses for sustained meal dosing behavior LOAN2DOSE: Utilization of loss aversion approach to promote mealtime insulin dose delivery. Participants will start with a virtual bank balance and will have money deducted from the balance when mealtime insulin doses are missed. Additional amounts will be deducted when sustained meal dosing goals are not met.
IND/IDE #	NA
Study Population	Individuals identified by artificial intelligence who are predicted to experience a rise in A1C of greater than or equal to 0.3% in the next 70-110 days using a validated predictive algorithm created via advanced machine learning (random forest) and natural language processing. Individuals must have had the diagnosis of T1D for 6 months and be 12-17.99 years old. Parents of children who meet inclusion criteria may choose to participate in the focus group
Sample Size	A minimum of 36 and a maximum of 72 youth randomized in a 1:1:1 ratio to either the treatment or usual care (control). Participants and their parents may choose to participate in the focus group. Parents may enroll in the focus group if their child is enrolled in the study. Our aim will be to enroll 5 to 30 parents.
Study Duration for Individual Participants	26 weeks (11-13 weeks intervention and 11-13 weeks observation Participants and/or their parents may choose to participate in a focus group at the end of the study (week 26).

Study Specific Abbreviations/ Definitions	T1D = Type 1 diabetes COIN2DOSE = Behavioral Economic Incentives to promote insulin Dose Engagement in Adolescents with Type 1 Diabetes LOAN2DOSE = Behavioral Economic concept that uses an economic loss aversion approach to promote insulin dose engagement in adolescents with Type 1 Diabetes CGM = continuous glucose monitoring AI = artificial intelligence SOC = Standard Care Diabetes Clinic Visit Twilio= cloud-based communication platform that enables clinic staff to send secure SMS text messages to participants

2.0 Objectives

2.1 Primary Objectives

The *long-term goal* is to develop effective ways to improve glycemic control in youth with T1D. To that end, we propose to specifically evaluate the effectiveness, feasibility, and usability of two new interventions in diabetes care: an economic incentive (COIN2DOSE) and an approach that uses an economic loss aversion (LOAN2DOSE) to promote patient engagement with mealtime insulin dosing behavior. If initially efficacious, our results will serve as the basis for an R01 submission(s) to conduct a fully powered efficacy trial of COIN2DOSE and LOAN2DOSE. This study is significant as omission of mealtime boluses is one of the common reasons for suboptimal diabetes control in youth. This project is highly innovative because it will: 1) target youth who are predicted by artificial intelligence to experience a worsening in glycemic control, 2) use an economic incentive intervention to improve mealtime insulin dosing behavior and 3) use an economic loss aversion to improve mealtime insulin dosing behavior.

2.2 Hypotheses

Aim 1: To determine the impact of COIN2DOSE and LOAN2DOSE as compared to control on the trajectory of glycemic control and treatment engagement among adolescents age 12-17 years who are at risk for a near-term rise in A1C.

Hypothesis 1: Use of COIN2DOSE will result in a lower rise in A1C compared to the controls.

Hypothesis 2: Use of COIN2DOSE will improve engagement as measured by mealtime insulin BOLUS score compared to controls.

Hypothesis 3: Use of COIN2DOSEwill yield sustained improvements in A1C trajectory for 12 weeks after the intervention.

Hypothesis 4: Use of COIN2DOSEwill yield sustained improvements in BOLUS score for 12 weeks after the intervention.

Hypothesis 5: Use of LOAN2DOSE will result in a lower rise in A1C compared to the controls.

Hypothesis 6: Use of LOAN2DOSE will improve engagement as measured by mealtime insulin BOLUS score compared to controls.
Hypothesis 7: Use of LOAN2DOSEwill yield sustained improvements in A1C trajectory for 12 weeks after the intervention.
Hypothesis 8: Use of LOAN2DOSEwill yield sustained improvements in BOLUS score for 12 weeks after the intervention.

Aim 2: To determine the feasibility of COIN2DOSE and LOAN2DOSE interventions in adolescents age 12-17 years who are at risk for a significant near-term rise in A1C.

Hypothesis 9: The COIN2DOSE intervention will be feasible as determined by 1) ≥75% of participants in the intervention group will complete all study procedures for the duration of the intervention and post-intervention study periods, 2) ≥75% of parents will endorse the feasibility of providing an equivalent economic incentive plan, and 3) no decrease in quality of life at visit 2 compared to baseline (visit 1).
Hypothesis 10: The LOAN2DOSE intervention will be feasible as determined by 1) ≥75% of participants in the intervention group will complete all study procedures for the duration of the intervention and post-intervention study periods, 2) ≥75% of parents will endorse the feasibility of providing an equivalent economic loss aversion plan, and 3) no decrease in quality of life at visit 2 compared to baseline (visit 1).

Aim 3: To determine user satisfaction with the COIN2DOSE and LOAN2DOSE intervention in adolescents age 12-17 years who are at risk for a significant near-term rise in A1C.

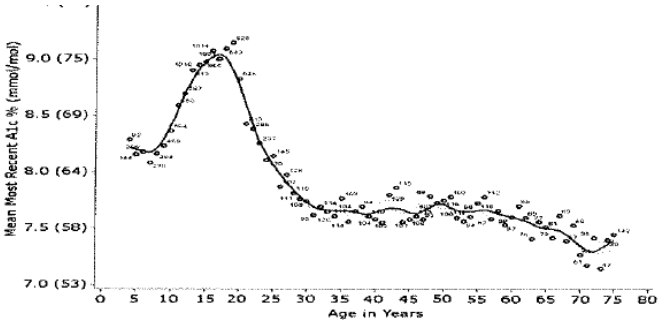
Hypothesis 11: COIN2DOSE will be usable as determined by using the Diabetes Treatment Satisfaction Questionnaire (change version).
Hypothesis 12: LOAN2DOSE will be usable as determined by using the Diabetes Treatment Satisfaction Questionnaire (change version).

3.0 Background

3.1 Background

Individuals with T1D can have a tremendous impact on their own health outcomes if they follow their T1D treatment regimen (2) (3) (4). Unfortunately, many adolescents do not adhere to their treatment and experience increased risk for both immediate medical emergencies, long-term T1D-related complications, and mortality (3) (5). Diabetic ketoacidosis (DKA) occurs at a rate of 4.81/100 patient-years in individuals with established T1D and at a rate of 15.83/100 patient years in youth with an A1C >9% (6). Adolescents who have poorly controlled T1D are much more likely to develop DKA (3)

(7). While health care professionals can offer guidance and recommendations, it is clear that traditional clinical interactions are not sufficient to promote optimal self-care and adherence for many adolescents (8) with the majority not reaching A1C targets (3). In fact, adolescents with T1D exhibit significant deterioration in glycemic control (aka rising A1C) from age 8 to 18 (9), as shown below.



Adapted from Miller et al 2015 – This figure shows mean A1C by age in years based on 16 057 participants in the Type 1 Diabetes Exchange Clinic Registry.

A number of behavioral interventions have demonstrated utility in improving adherence behaviors in youth with T1D[13-19]. Improved adherence behaviors are associated with better glycemic control and short and long-term health outcomes (3). On the other hand, lack of adherence can have serious consequences both acutely (DKA or severe hypoglycemic events) and long-term (retinopathy, neuropathy, nephropathy, and cardiovascular disease) (3). Missed mealtime boluses can have devastating metabolic consequences (16).

Adolescence is a particularly challenging time for individuals with T1D, with average A1C values that are 5% higher than during other periods of childhood and 14% higher than adults (22) (2). Glycemic control worsens from early childhood through age 16-18 (23). It is critically important to develop interventions to prevent deterioration in glycemic control. High glycemic variability is also associated with increased risk of long-term diabetes complications, such as microalbuminuria (24). Lack of adherence to diabetes treatment plans is one of the main causes of sub-optimal glycemic control (3) (25) (7). A significant part of this non-adherence is omission of insulin for ingested carbohydrates at snacks and meals, both by missing boluses entirely and by inaccurate carbohydrate counting (26) (16) (27) (28) (29). Studies have shown significant underestimation of carbohydrate content in meals of up to 20% (26). Furthermore, greater than 33% of adolescents fail to give insulin for >15% of their meals and snacks (16). Adolescents, on average, miss boluses for meals two times per week (28). In one study, youth who omitted insulin at least one time per week had an A1C of 8.8-9.5%, while those who consistently took meal-time insulin had a significantly lower A1C of 7.8-8.0% (28) (30). This is of great significance as poor glycemic control increases risk of both acute and chronic diabetes related complications (31). Meal bolus alarms on insulin pumps, which alarm at a preset time, lead to transient, modest changes in dosing behavior (32). “Lost focus” has been identified as a significant reason for missed meal-time boluses in adolescents (33). Exactly how to effectively maximize engagement with mealtime insulin dosing behavior among adolescents with T1D represents a critical gap in knowledge.

3.2 Rationale

There is an urgent need for a sustainable method that improves patient engagement with delivering mealtime insulin boluses. Improved engagement with mealtime boluses will lead to better glycemic control and will ultimately help reduce the risk of acute and chronic diabetes related complications.

Recent evidence suggests that financial incentives can successfully increase adherence to blood glucose monitoring among adolescents and young adults with type 1 diabetes with moderate to large treatment effect size. Specifically, one study of 10 adolescents evaluated a financial incentive program that delivered $0.10 per fingerstick blood glucose test, with bonus incentives for ≥4 tests per day and a maximum achievable incentive of $251.40 over 12 weeks. The authors found that SMBG increased from 1.8 ± 1.0 to 4.9 ± 1.0 tests per day ($P < 0.001$) with 90% completing four or more tests per day; that mean A1C fell from 9.3 ± 0.9% to 8.4 ± 1.5% ($P = 0.05$); and that adolescents and parents reported high satisfaction with procedures. In another study, 90 adolescents and young adults demonstrated that a $60 monthly incentive opportunity significantly increased adherence to glucose monitoring goals in the 90-day incentive period (50.0% vs 18.9%; adjusted difference, 27.2%; 95% CI, 9.5% to 45.0%; $P = .003$). The effect was not sustained during the post-interventional 90-day observation period (15.3% vs 8.7%; adjusted difference, 3.9%; 95% CI, -2.0% to 9.9%; $P = .20$), and A1C did not improve. The evidence to date suggests that it is feasible to increase adherence behaviors among adolescents and young adults with type 1 diabetes. It is unclear whether targeting blood glucose monitoring behaviors is always associated with an improvement in A1C. Whether financial incentives produce a sustained improvement in adherence is also an open question. These methods have not been applied to mealtime insulin dosing behaviors, so whether financial incentives improve adherence to mealtime insulin dosing among adolescents and young adults is also unknown.

There is a strong rationale for targeting adherence to mealtime insulin dosing for improvement. Prior observational research suggests a 1.5% decrease in A1C levels for every one-bolus increase in daily mealtime doses, supporting our premise that increasing mealtime insulin use might help youth who are at risk of increasing A1C(1).

The objective of the present study is to obtain pilot feasibility data to 1) determine whether COIN2DOSE and/or LOAN2DOSE show a preliminary trend for improvement in the outcomes of interest, 2) perform power calculations that will inform the design of a definitive trial(s) and 3) establish feasibility of the interventions and study procedures to inform the design of a definitive trial(s).

4.0 Study Endpoints

<u>Outcome Measures</u>
Primary outcome:

1) Change in A1C ($\Delta A1C_{90\text{-day}}$) from baseline visit (visit 1) to 90-day visit (visit 2).

Secondary outcomes:

1) Change in A1C ($\Delta A1C_{180\text{-day}}$) from baseline visit (visit 1) to 180-day visit (visit 3).
2) Change in percent time in range 70-180 mg/dL (%TIR70-180) from baseline visit (visit 1) to 90-day visit (visit 2) and to 180-day visit (visit 3).
3) Change in percent time hyperglycemic (>180 mg/dL; $\%Hyper_{>180}$) from baseline visit (visit 1) to 90-day visit (visit 2) and to 180-day visit (visit 3).
4) Change in percent Time hypoglycemic (<70 mg/dL; $\%Hypo_{<70}$) from baseline visit (visit 1) to 90-day visit (visit 2) and to 180-day visit (visit 3).
5) Change in percent Time severely hypoglycemic (<54 mg/dL) ($\%Hypo_{<54}$) from baseline visit (visit 1) to 90-day visit (visit 2) and to 180-day visit (visit 3).
6) Change in mealtime insulin BOLUS score (BOLUS) from baseline visit (visit 1) to 90-day visit (visit 2) and to 180-day visit (visit 3).
7) For COIN2DOSE treatment group, proportion of participants who complete >90% of study procedures throughout the intervention and post-intervention study procedures.
8) For COIN2DOSE treatment group, proportion of parents who endorse the feasibility of providing an economic incentive equivalent to that used in the intervention.
9) For COIN2DOSE treatment group, >75% of participants will exhibit a score of >80% total possible points on Diabetes Treatment Satisfaction Questionnaire (teen version)
10) Change in trust in provider from baseline visit (visit 1) to 90-day visit (visit 2) and to 180-day visit (visit 3).
11) For LOAN2DOSE treatment group, proportion of participants who complete >90% of study procedures throughout the intervention and post-intervention study procedures.
12) For LOAN2DOSE treatment group, proportion of parents who endorse the feasibility of providing an economic incentive equivalent to that used in the intervention.
13) For LOAN2DOSE treatment group, >75% of participants will exhibit a score of >80% total possible points on Diabetes Treatment Satisfaction Questionnaire (teen version)
14) Change in perceived involvement in care from baseline visit (visit 1) to 90-day visit (visit 2) and to 180-day visit (visit 3).
15) Change in health-related empowerment from baseline visit (visit 1) to 90-day visit (visit 2) and to 180-day visit (visit 3).

Outcome Measures

Hemoglobin A1C will be measured via a fingerstick capillary blood collection and analyzed on the Tosoh G8 HPLC. This approach is validated ant traceable to DCCT standards.

CGM-derived glycemic metrics. Participants will have the Dexcom G6 Pro (blinded CGM) inserted 1 week after enrollment and at visit 1, and at visit 2. Participants will wear the CGM for 10 days following each insertion. We will consider >120 hours (>50% of total possible capture) of CGM data to be analyzable, otherwise data will be considered missing. Percent time in range (70-180), percent time >180, percent time >250, percent time <70, and percent time <54 mg/dL will be collected.

Participants who already have their own CGM will wear and use it as usual. They will not require a blinded Dexcom.

For patient-reported outcomes, questionnaires may be completed on iPad for in-person visit or via email or text via Twilio for remote visits. If completing by email or text, a link to REDCap will be sent to participant.

Quality of Life will be assessed using the MIND Youth Questionnaire (My-Q), which is a valid measure of quality of life for teenagers with diabetes (49).

Acceptability will be assessed based on treatment satisfaction scores using the Diabetes treatment Satisfaction Questionnaire, DTSQ-Teen, which has been validated for use in youth with T1D (50).

Trust in provider: Will be measured as a change score (visit 2-visit 1; visit 3-visit 1) with 10-items from the validated Wake Forest Physician Trust Scale (58).

Perceived Involvement in Care: Will be measured as a change score (visit 2-visit 1; visit 3-visit 1) with 13-items from the Perceived Involvement in Care Scale (59).

Health-related empowerment: Will be measured as a change score (visit 2-visit 1; visit 3-visit 1) with 8-items from the Health-related empowerment scale (60).

Covariate Measures

Demographics: Age, sex, race, duration of diabetes.

Depression will be measured as a covariate using the validated PHQ-A (which is the Patient Health Questionnaire, PHQ-9, adapted for adolescents) (51). *Note: no notification of medical personnel is necessary if adolescents endorse depressive symptoms because a) the survey does not ask about current suicidal ideation, and b) adolescents in the Children's Mercy Diabetes Center are monitored for depression symptoms at every clinical encounter, with clinical encounters occurring every 3-4 months typically.*

5.0 Study Intervention

To identify an at-risk population for more intensive intervention opportunities, the Children's Mercy Diabetes Center now routinely uses a validated prediction model based on advanced machine learning (random forest method) and natural language processing to identify individuals who are predicted experience a rise in A1C in the next 90 days. The model analyzes all patients who presented for a diabetes visit in the prior week. To accomplish this task, the complete health record for the CMH Diabetes Center registry is analyzed. We will select patients from this cohort for recruitment into the present study.

COIN2DOSE intervention: From one-week post-randomization to the 12-week study visit, youth randomized to this treatment arm will receive personalized feedback via monetary incentives for dosing insulin at mealtimes. We will define mealtimes based on hour of the day and the presence of a carbohydrate entry associated with the insulin bolus. According to the methodology for calculating BOLUS(1) breakfast will be 0600-1000, lunch will be 1100-1500, and dinner will be 1600-2200. Thus, we will reimburse youth up to $0.50 per mealtime with at least one meal-associated (carbohydrate-associated) insulin bolus completed (maximum $1.50/day). We will offer the opportunity for youth to earn a bonus reimbursement of up to $5.00/week for weeks during which they achieve at least 5 days of 3 mealtime insulin boluses. Finally, we will pay youth up to $2.00 per week for sharing their insulin use data at least two times per week with the study team during the three-month treatment phase (maximum $24.00). Therefore, maximum total incentive available is $210.

LOAN2DOSE intervention: From one-week post-randomization to the 12-week study visit, youth randomized to this treatment arm will receive personalized feedback via monetary deductions from a virtual bank of $210 for missed doses of insulin at mealtimes. Participants will receive a weekly email or text message using Twilio to communicate their current virtual bank balance. We will define mealtimes based on hour of the day and the presence of a carbohydrate entry associated with the insulin bolus. According to the methodology for calculating BOLUS (1) breakfast will be 0600-1000, lunch will be 1100-1500, and dinner will be 1600-2200. Thus, we will deduct $0.50 per mealtime with at least one meal-associated (carbohydrate-associated) insulin bolus missed (maximum -$1.50/day). Youth can also lose an additional amount of up to $5.00/week for weeks during which they don't achieve at least 5 days of 3 mealtime insulin boluses. Finally, we will deduct the virtual account up to $2.00 per week for failing to share their insulin use data at least two times per week with the study team during the three-month treatment phase (maximum deduction of $24.00). Therefore, maximum total deductions is $210.

6.0 Procedures Involved

Study Design

The study is an unblinded, 3-arm, randomized, controlled trial. After successful screening and consent, individuals will wear a blinded Dexcom G6 Pro CGM inserted 1 week after consent. Families who have previously used a CGM device

will be allowed to insert the G6 Pro during a remote visit. At the baseline visit (visit 1; day 1), participants will be randomized to the COIN2DOSE, LOAN2DOSE, or control treatment arms and will be trained on the procedures appropriate to their treatment arm. Participants will also complete baseline measures by questionnaire. Participants will complete procedures specific to their treatment arm weekly. Visit 2 will occur after 12 weeks (90 days). Participants will stop any treatment interventions after this visit. A1C and questionnaire measures will be completed, and participants will again wear the Dexcom G6 Pro CGM for 10 days (the device will be returned by mail post-visit). Participants will receive no treatment intervention from week 13 to week 24. Visit 3 will occur after week 24. Again, A1C and questionnaire measures will be completed and participants will wear the Dexcom G6 Pro CGM for 10 days.
Participants who have their own CGM will wear it as usual and will not require a blinded Dexcom.

All study participants will also have the option to participate in a focus group discussion (FGD) regarding study participation.

Parents of children who meet inclusion criteria and participate in the study may also elect to participate in a focus group.

Study Visits
Study visits may occur in-person or remotely (i.e., from home). Procedures will be adapted to accommodate both scenarios.

7.0 Data and Specimen Banking

Data Collection
Demographic data: Demographic data will be collected from the participant via an electronic data collection form in REDCap which shall serve as the source. Demographic data will be verified with review of electronic medical record data. For remote visits, a web URL linking to the REDCap survey will be shared with participants.

A1C data: Participants will use a capillary A1C kit to collect a fingerstick A1C sample. An educational document and video (YouTube https://youtu.be/e9loR3N4Rho) have been created to educate approved study staff and participants on collection of the sample. The A1C is analyzed in a CMH lab by automated high performance liquid chromatography (reference range 4.0-6.0%, Tosoh 2.2, Tosoh Corporation, San Francisco, CA), which is a measurement method reliable to DCCT standards. The CMH A1C mail-in kit has excellent reliability to fresh samples (r=0.98). Samples will be delivered to the Broadway lab by approved study staff for in-person study visits; samples will be mailed to the Broadway lab by participants completing remote visits from home. Sample tubes will be pre-labeled by study staff with the participant's study ID. If insufficient sample for analysis is collected at any time point, participants may be asked to repeat the sample collection to rescue data collection.

If participant does not return A1C mail-in-kit, point-of-care A1C or serum A1C may be used instead if available.

CGM data: Participants will use the Dexcom G6 Pro in blinded mode for data collection purposes only. If insufficient data for analysis are collected at any time point, participants may be asked to replace the CGM device to rescue data collection. No treatment decisions will be based on G6 Pro data. Dexcom G6 Pro data will be uploaded from the Dexcom receiver to Dexcom Clarity using the participant's personal, CMH-connected Dexcom Clarity account; data will then be collected as a .csv file for analysis. Files will be aggregated into a study database using MS Excel or equivalent software. Participants with their own CGM will use it as usual. They will be asked to share their CGM information with the study team per the usual procedure for diabetes clinic visits.

Insulin delivery data: Participants will use their personal, prescribed insulin delivery device throughout the study. Insulin delivery devices will be uploaded to Children's Mercy-approved software compatible with the specific device. Data will be uploaded to the participant's personal, CMH-connected account in the relevant upload system. Data will then be collected as a .csv file for analysis. Files will be aggregated into a study database using MS Excel or equivalent software. Insulin delivery systems and/or any date of system change will be noted at enrollment and on REDCap questionnaires.

Questionnaire data: All questionnaire data will be collected directly from participants via electronic (REDCap).

Focus group discussions: Focus group discussions (FGD) will optional and stratified by intervention arm. As the ideal size for FGDs are 6-8 participants, it is possible that we will conduct two FGDs per arm if there is enough interest among participants. Thus, we anticipate conducting 3-6 FGDs. FGDs will be approximately 90 minutes in duration, conducted by a trained moderator using a semi-structured guide. Both youth and their parents will be invited to participate in the focus groups.

FGDs will be conducted virtually on Microsoft Teams according to Standard Operating Procedures currently in pilot testing with the CMH Formative Research Team. De-identified data will be transcribed using Teams software and uploaded into Dedoose software for analysis.

Data and Specimen Banking

8.0 Genetic Analysis Information

N/A

9.0 Sharing of Results with Subjects

Results will not be shared with subjects.

10.0 Study Timelines

Table 1. Schedule of events

visit #	Visit 1	CGM placement	Intervention	Visit 2	Maintenance	Visit 3
		1 week post enrollment	1-12 week post CGM placement	3 months (+/-14 days)	12 weeks post visit 2	6 months (+/-14 days)
Consent	x					
Randomization	x					
CGM (10-day)		x*		x*		x*
A1C	x			x		x
Demographic	x			x		x
PHQ9	x			x		x
DTSQteen	x			x		x
MyQ	x			x		x
Wake Forest Physician Trust Scale	x			x		x
Perceived Involvement in Care Scale	x			x		x
Health-related empowerment scale.	x			x		x
Concerns about AI	x			x		x
Pump/pen** download	x		x	x	x	x
Focus Group Participation - Youth						x
Focus Group Participation - Parents						x

*CGM will be returned by pre-paid, registered delivery service with tracking.
** Control: pump/pen upload will occur monthly; COIN2DOSE and LOAN2DOSE pump/pen upload will occur twice weekly.

Participant activities:

Participants enroll in COIN2DOSE	Participants randomized and fill out questionnaires Setting: at regularly scheduled standard of care (SOC) visit, in-person or virtual visit utilizing a CMH IRB approved remote platform.
1 week post enrollment	All groups will have Dexcom sensor inserted and will be worn x 10 days. Setting: in-person at the PCRU or virtual meeting.** Dexcom sensor may be mailed to participants. If mailed, the 1-week visit may take place via virtual visit utilizing a CMH IRB approved remote platform. Participants with their own CGM will wear it as usual.
3 months post enrollment	Participants fill out questionnaires + have blinded Dexcom sensor inserted during SOC visit or virtual visit. Participants will wear Dexcom x 10 days. Setting: SOC visit, in-person or virtual visit utilizing a CMH IRB approved remote platform.
6 months post enrollment	Participants fill out questionnaires and wear Dexcom x 10 days. Dexcom inserted during SOC visit or virtual visit utilizing a CMH IRB approved remote platform. Setting: clinic or remote visit utilizing a CMH IRB approved remote platform. Finally, participants return CGM by mail. (Not applicable to participants with their own CGM.) Focus group discussions are conducted. Both youth and parents will be invited to participate.

**Participants may choose to have in-person Dexcom insertion instruction at the PCRU or online via virtual instruction. If participant is Dexcom naive, they may insert Dexcom for the first time via online instruction, as it is a relatively simple procedure. If a participant is uncomfortable inserting the Dexcom for the for the first time virtually, they will have the option to do this with in-person instruction at the PCRU.

The link that patients will be sent for learning to use Dexcom is:
https://www.dexcom.com/training-videos

Participants with their own CGM will not be anticipated to require training; however, this will be offered if needed.

11.0 Inclusion and Exclusion Criteria

Individuals who have been predicted via an artificial intelligence-intelligence based model to experience a rise in A1C in the near future (90 days) will be approached for recruitment. 36 participants will be recruited from the Children's Mercy Diabetes Center (any clinic or hospital location). Based on preliminary data review of our clinic population, there were at least 81 individuals who met inclusion criteria who were seen in clinic in the month of May 2019 alone. Patients will be randomized to, COIN2DOSE, LOAN2DOSE, or control group using a 1:1:1 randomization scheme.

Inclusion Criteria:
1) Aged 12-17.99 years
2) The youth must have been diagnosed with T1D for at least 6 months
3) The youth must have attended at least 2 routine T1D standard of care visits in the past 12 months

4) The youth must be using an insulin delivery device capable of recording, storing, and downloading insulin bolus behaviors (insulin pump or smart Bluetooth insulin pen that can be uploaded to standard clinic upload software).
5) The youth must have a current A1C >7.2% and/or be predicted to have a rise in A1C in of 0.3% or higher the next 90 days.
6) Not pregnant or planning to become pregnant by self-report.

Exclusion Criteria:
1) Participants with any type of diabetes mellitus other than T1D
2) Participant has any disease-causing anemia or affecting red blood cell physiology (which would impact A1C)
3) Participant has a physical disability, which in the opinion of the investigator would interfere with individual's ability to feed themselves or use one's hands to facilitate eating
4) Participants with no internet access or ability to upload device(s) to data aggregation software that is accessible to study team.

For Focus Groups:

Any parent or legal guardian whose child is participating in the study is invited to participate in a focus group discussion.

12.0 Vulnerable Populations

This study will include children. Parent/LAR permission will be sought before a child may be enrolled. Written assent of children 7 and older will be obtained per CMH policy; all children in this study will be above the age of assent and therefore required to assent for participation.

If a child subject reaches the age of majority (18 years old) during the study, he or she will be asked to consent to further participation using an Adult Addendum.

Parents or legal guardians of youth who are eligible to participate in this study will be eligible to participate in a focus group. It is possible that a parent or legal guardian will be pregnant at the time of focus group participation.

We will not enroll other vulnerable populations, i.e. prisoners, neonates, and/or adults lacking capacity.

Children's Mercy Kansas City employees or children of employees will not be recruited.

13.0 Local Number of Subjects

Target sample size is 36 adolescents. The maximum number of subjects enrolled will be 72.

Parents or legal guardians of youth eligible for inclusion in the study may choose to participate in a focus group. We may enroll up to 30 parents or legal guardians.

14.0 Screening and Recruitment Methods

Patients will be prescreened to see if they meet enrollment criteria by a member of the research team. Patients who appear to meet criteria may be contacted by telephone, email or approached during a standard of care visit by a study team member and informed about this study. Patients and their parent/legal guardian will be given information about the study and they will determine if they wish to participate. Recruitment will also take place via telephone utilizing an IRB-approved telephone script.

Flyers will be used as a means of advertising the study to help with recruitment. IRB approved flyers will be used to advertise via email invitation and at all CMH locations. Recruitment will then be in person or via phone call. A copy of the flyer is attached to the submission.

Parents/legal guardians of children who meet enrollment criteria and are approached for the study will be invited to participate in a focus group at the end of the study. Recruitment for the parent/legal guardian focus group participation will occur at the same time and using the same method for recruiting the pediatric patient (i.e. by telephone or in person).

Prescreening may involve either a review of clinic schedules or a report generated by IT that will involve a review of the electronic medical record (EMR) system to generate a list of potentially eligible participants.

A HIPAA waiver is requested for the purpose of generating a pre-screening list of qualified candidates for research recruitment as described above. Information collected to track recruitment will be included in the pre-screening log for determining and tracking eligibility and tracking clinic visits where participants may be approached about the study. PHI on non-participants will be kept until completion of enrollment. Upon the completion of enrollment, the study team will also request a de-identified, aggregate report containing demographic information on individuals who declined enrollment. This information will be used to compare recruited individuals to non-recruited individuals in dissemination work products (e.g., manuscripts, presentations) so that any biases in sampling the eligible population can be reported.

15.0 Reimbursement, Payment and Tangible Property provided to subjects

Participants in all groups will be compensated a total of $120 for their time and participation. They will receive $40 for study visit attendance and questionnaire completion. The 40 participants will each participate in 3 visits. It is possible that we may need to enroll additional participants if subjects withdraw, therefore additional funds for stipends for 4 additional subjects have been added.

Participants in the COIN2DOSE arm may earn up to an additional $210 as incentive for completing mealtime insulin doses; the incentive payment is the intervention in this case. The total compensation for this group would be $330.

Participants in the LOAN2DOSE arm will begin the study with a virtual bank balance of $210 and will keep this amount if mealtime boluses and data sharing are completed as study activities are scheduled. They will also receive $40 for study visit attendance and questionnaire completion. The total compensation for this group could be $330.

Youth who are enrolled in the study and who elect to participate in a focus group discussion will receive an additional $35 for doing this.

Parents/legal guardians who participate will also receive $35 for participating.

16.0 Withdrawal of Subjects

Participants may withdraw from the study at any time and this will not affect their medical care. No additional study related data will be collected on participants after withdrawal from the study, but previously collected information will be retained. All participants who enroll into the study will be included in the primary analysis, with the exception of those who are withdrawn from the study for not meeting eligibility criteria.

17.0 Risks to Subjects

The overall risks of participation in this project are no more than minimal. Because the research requires the collection of personally identifying data, there is a risk breach of confidentiality. Participants will be requested to disclose information about their diabetes adherence, blood glucose values, regimen knowledge, and psychological and behavioral functioning. Disclosing this information may potentially lead to emotional discomfort. If a participant reports any concerning symptoms regarding his or her emotional stature, the participants and his/her parent/guardian will be provided with information on how to get help. If a participant has a positive screen on the PHQ-A (depression), social work will be notified and will see the participant during the study visit. Social work will assess the patient and develop a plan of action in conjunction with the attending physician based on the clinical situation. Participants may also feel inconvenienced by the time required to participate in the study. Participants may

experience some discomfort with Dexcom insertion, which is similar to insulin pump site insertions. Participants will be instructed on proper care of the Dexcom site.

In the virtual focus group discussions, there is minor risk of unauthorized disclosure of confidential information, which would be made known to participants and will be minimized by the research team's efforts to ensure confidentiality (see section 20.0). Every effort will be made to keep data de-identified, including having participants use pseudonyms for the discussion and being reminded not to respond in a way that might include personal identifying information. Risks are greatly reduced by using secure files, storing data on secure computers, de-identification of data. Subjects and/or their parents/legal guardians may choose not to participate in the focus groups. There may be a risk that some of the questions make participants feel uncomfortable. Participants may skip a question or stop the study at any time.

18.0 Potential Benefits to Subjects

Participants could benefit by responding to the financial incentives (COIN2DOSE or LOAN2DOSE) and improve their mealtime dosing behaviors. With improved insulin dosing behaviors, the participants may improve their overall glycemic control. It is possible that participants will not derive any benefit from participation.

Parents/legal guardians who choose to participate in the focus group may or may not gain useful information to help their child improve diabetes care. It is possible that parents/legal guardians will not derive any benefit from participation.

19.0 Investigator Assessment of Risk/Benefits Ratio: (IRB makes the final determination)

Select as applicable:	**Pediatric Risk Category:**	
x	Category 1	Research not involving greater than minimal risk (45 CFR §46.404 and 21 CFR §50.51)
	Category 2	Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects. (45 CFR §46.405 and 21 CFR §50.52)
	Category 3	Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition. (45 CFR §46.406 and 21 CFR §50.53)
	Category 4	Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children. (45 CFR §46.407 and 21 CFR §50.54)
Select if applicable:	**Adult Risk Category:**	
x	Not Greater than Minimal Risk	
	Greater than Minimal Risk	

20.0 Data Management and Confidentiality

20.1 Statistical Analysis Plan

Database construction and management will involve acquisition of data from each source (see above), imported into Microsoft Excel or an equivalent database program. All analysis will be completed using Stata/SE 15.1 (StataCorp. 2017. Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC), SPSS version 20, SAS version 9.4, other statistical programs as needed. Univariate analysis will be performed on all dependent and independent variables. Analysis includes determining whether the variables have non-normal distributions or outliers. Determinations then will be made as to whether the data transformations are needed. For example, if variance heteroscedasticity, exists, data will be analyzed using log-transformed or other transformations based upon Box-Cox approximations to normal distributions. Measures of other central dependency and dispersion will be evaluated. Primary analyses will be modified intention to treat analysis. All individuals who are randomized will be included in the analysis. A secondary per-protocol analysis may also be performed. Multivariable regression models will be examined to estimate the effects of study variables on the primary outcome – predicted trajectory of glycemic control base on A1C over 90 days – for this sample of T1D patients' data collected at three time points: baseline, 3 months, and 6 months. If the independent variables are highly correlated, we will explore General Linear Models (GLM) or other models. It is possible that Generalized Estimating

Equations (GEE) will be explored for their appropriateness in a larger study and/or for comparisons with the GLM results. Demographic and clinical variables will be entered into models following the independent variable: treatment group assignment. Since time effects may be important in the analyses due to treatments, censoring of data, time sequences, or other reasons, time of observation (i.e. visit 1[day 0], visit 2 [day 90], or visit 3 [day 180]) will also be explicitly accounted for in the regression models. All models will account for the clustering effect of participants having more than one clinic visit during the study timeframe. Additional variables will be collected as listed above. Statistical significance will be $p<0.5$ (one-sided).

20.2 Power analysis

To evaluate the primary outcome: glycemic control (measures as predicted trajectory of A1C over 90 days), a multivariable regression model will be developed that accounts for seven independent variables: two primary – adherence and quality of life – and an additional five covariates: participant age, sex, insurance status, intervention/control group status, and time (52). Using an F-test and significant level (alpha) of 0.025, a sample of 20 T1D patients per treatment arm would achieve 74% power to detect an effect size of 0.35 (53). Findings from this pilot study will be used as estimates in planning future studies including recruitment of enough patients to achieve a power of greater than or equal to 80% to evaluate glycemic control (54).

20.3 Data security

Study information will be collected electronically and stored on a secure division drive on the CMH network domain or on Microsoft OneDrive or equivalent; access will be restricted to research team members. All the questionnaires listed above will be collected in REDCap if possible.

Paper data collection forms will be stored in the Endocrine Research Coordinator secure office where only research staff have access. Research records containing PHI will be transported when necessary and will be transported in hospital approved PHI lockboxes per CMH policy. A Certificate of Confidentiality has not been issued for this study.

Data will be stored per the Record Retention and Management Policy and the Record Retention Schedule.

Approved study staff will have access to research records. Lab & study staff will have access to samples.

The PI is ultimately responsible for receipt or transmission of the data or specimens. Families will mail in the A1C kit which will only contain the Subject ID. When the sample arrives in the lab, research staff is contacted so that the sample can be matched to the MRN so that the sample can be resulted as a "research result" in the electronic health record.

Virtual focus groups will be conducted on a CMH Microsoft Teams channel. Parents/legal guardians and/or participating youth may be in the focus groups. Participants will be instructed to not include any identifying information in their responses. After participants are instructed to change their screenname to a pseudonym, the meeting will be recorded and transcribed directly into the Teams folder, accessible only to the research team. Files will be scrutinized to ensure there is no PHI, censored if necessary, and uploaded directly into Dedoose for coding.

21.0 Provisions to Monitor the Data to Ensure the Safety of Subjects

N/A

The proposed project is a new intervention, therefore we will recruit a Data Safety and Monitoring Board (DSMB) to oversee and monitor the treatment implementation and data collection. We proposed members of the DSMB will include an endocrinologist, a biostatistician, and a certified diabetes educator. Members of the DSMB will be employees of CMH but will not be involved in this study in any way. As part of the DSMB oversight, we propose to meet by every 6 month during the conduct of the study. For each of the meetings, the PIs (Dr. Tsai and Dr. McDonough) and biostatistician (Mr. David Williams) will jointly prepare a summary of the following topics: performance monitoring (a report of subject recruitment/retention, protocol adherence, and quality of data collection procedures), safety monitoring (a review of safety of the participants, including confidentiality and any adverse events or side effects related to the study procedures).

22.0 Provisions to Protect the Privacy Interests of Subjects

Participation in this research study is voluntary. Participants and their parents/legal guardians will be notified of the voluntary status of the research at the onset of the study enrollment and content in process. Any participant or parent who declines to participate will not incur any penalty or loss of benefits to which they are already entitled. No change to the patient's medical care will occur as a result of the participation, or nonparticipation in the study.

Prior to enrollment, participants and their parents/legal guardians will have all risks and benefits clearly explained to them. After explanation for study and consent, subjects and their parents/legal guardians will be offered an opportunity to discuss participation in private, without a study team member present, in order to avoid any potential feelings of bias or coercion. They will be given time to ask questions. They may come back to participate at a later date if they would like to take the study materials home for review prior to agreeing to participate in this study.

For subjects that enroll in the study, they will be informed that they may withdraw at any time without penalty or loss of benefits. Any new information gathered during the course of the study that may impact the subject desire to continue in the study, will be revealed as soon as it becomes available.

All the study information will be kept confidential. Data collected as part of routine diabetes care is protected by CMH's Cerner Electronic Health Record (EHR) and associated policies from the Health Information Management Department (HIM). Data collected specifically for this study will be stored securely as described above. Participation in this study will be recorded into the EHR in accordance for CMH policy. Any of the research data collected, with the exception of personal health information (PHI), maybe shared in aggregate form in presentations and publications. At the termination of the study, the enrollment, prescreening, and master logs will be destroyed. During the course of the study, the PHI (with the exception of name and MRN) that is collected on individuals who do not wish to participate will be deleted from the prescreening log. The name and MRN will be kept until enrollment is complete so that individuals not interested in participating will not be re-approached for recruitment, and so that MIT can prepare a deidentified, aggregate report of demographic data on individuals who declined participation in the study.

Any PHI in the data collection files will be removed and/or converted to a deidentified number upon completion of the study.

Name, initials, dates of service, date of birth, medical record number, hospital account number, street address, telephone number, and email address may be accessed and/or recorded for research purposes.

HIPAA Authorization for research collection of PHI will be obtained with the permission assent/consent forms.

Focus group participants will be instructed to not include any identifying information in their responses and to use a pseudonym. They will also be instructed not to talk about the discussion outside of the virtual focus group, particularly not to reveal the participation of any other participant that they might know or recognize. They the meeting will be recorded and transcribed directly into the Teams folder, accessible only to the research team. Files will be uploaded directly into Dedoose for coding.

23.0 Compensation for Research-Related Injury – NA, Minimal Risk

N/A

24.0 Economic Burden to Subjects

Subjects will not have any additional costs associated with participation. Participants may complete study visits in the PCRU, via Microsoft Teams, or InTouch Solo (telemedicine platform used at Children's Mercy Hospital that is designed to be used in a clinical setting with a tele-facilitator). There will not be any additional costs to participants associated with study-related procedures.

If the participant damages the Dexcom, they will be asked to return the device to the study team. If a participant loses a device, a note to file will be documented in the participant binder. The participant will be given replacement devices if study budget

allows. They will not be asked to pay for a replacement device or pay for repairs. All participants will be informed that they are expected to return their devices when they have completed the study at the time of informed consent/assent.

25.0 Permission/Assent/Consent Process

Permission Assent/Consent will be obtained in the CMH Endocrine Clinic, PCRU, via telephone, or using approved Children's Mercy teleconferencing platforms.

When obtaining consent via telephone, the study team will follow CMH "IRB Permission/Assent/Consent Policy". Permission Assent/Consent will be reviewed thoroughly and participants will be given the opportunity to ask questions. Study staff will emphasize the voluntary nature of participating in research when obtaining consent. CMH Research Policies will be followed.

Assent of children 7 and older will be obtained per CMH policy. Parental/LAR permission will be obtained for all participants

Parents or legal guardians who choose to participate in the focus group discussions will also sign an informed consent.

Consent at 18 years of age, when minor subjects become adults

Participants who turn 18 while actively participating in study, will sign an Adult Addendum if they choose to continue participation. We are requesting a Waiver of Documentation of Consent for continued use of identifiable data for participants whose active participation has ended.

This protocol, and any subsequent modifications, will be reviewed and approved by the Pediatric IRB at The Children's Mercy Hospital & Clinics. Qualifying patients will be identified by review of daily clinic schedules by research team personnel. Only study personnel will give details about the study to subjects and families. The study will be explained briefly and subjects/parents/legal guardians will be asked whether they are interested in the study. All interested subjects and parents/legal guardians will have the study thoroughly explained using the consent (or permission/assent form as applicable) including risks and benefits. They will then be given copies of the consent to review without staff present so that they have time to discuss with each other. Subjects and parents/legal guardians will also be given the opportunity to ask additional questions after they have read the consent. If subjects and parent agree to participate then consent (or permission/assent form as applicable) will be signed by all required parties and a copy will be given to them. Alternatively, subjects and parents/legal guardians will be given the opportunity to take consents home for further reading, discussion, and decision making at a later date. No pressure will be placed on any subject or family to enroll. All questions will be answered and signatures will be obtained by study staff form the parent before study enrollment.

Non-English Speaking Subjects - NA

Cognitively Impaired Adults - NA

Adults Unable to Consent - NA

26.0 Process to Document Permission/Assent/Consent

In addition to the permission assent/consent document itself, the consent process will be documented in the medical record and/or research record per CMH policy.

Study personnel will follow CMH "IRB Permission/Assent/Consent Policy" to collect participant written informed consent for their own participation, and parent/caregiver permission for child participation. All of these will be documented on the study informed consent document.

27.0 Setting

The study visits will take place at Children's Mercy Kansas City diabetes clinics in the Kansas City Metro area, the PCRU, or using approved Children's Mercy teleconferencing platforms including Microsoft Teams, Polycom, InTouch, Doximity.

28.0 Resources Available

Data resources and tools:

- REDCap (Research Electronic Data Capture) – an internet-based software solution and workflow methodology for designing clinical and translational research databases that is widely used in the academic community

- Library subscriptions to online medical and research websites including Lexicomp, PubMed, Ovid, Google Scholar, and CINAHL will allow for literature review and aid in manuscript development

- Statistics applications such as SAS, SPSS and R will be utilized for data management and analysis

- Approved Children's Mercy teleconferencing platforms including Microsoft Teams, Polycom, InTouch, Doximity, or other approved platforms

Office: Drs. Tsai and McDonough will utilize office spaced allocated to them through their appointment as faculty in the Division of Pediatric Endocrinology & Diabetes. No additional space is requested as part of this grant proposal.

Pediatric Clinical Research Unit (PCRU): The PCRU, constructed in 2012 and opened in January 2013, is located on the ground floor of the Hall Inpatient Tower. Occupying approximately 4,500 ft^2, it was designed based on the primary goal of creating an ideal environment for all types of clinical research investigation. The unit includes three private patient rooms and one larger three-bed room suited ideally for overnight and multiple sibling studies. The layout of all patient rooms was specifically designed to facilitate patient and family comfort throughout the duration of their stay. The unit includes a large playroom, office space for clinical research faculty and staff members, an exam room, a small laboratory for processing, nutrition room, medication room, soiled utility room, and significant storage space for both patient care supplies and clinical research documents. Facilities are available for phlebotomy, urine collection, initial specimen processing, and temporary specimen storage prior to delivery to the research laboratory. The space is in close proximity to other institutional resources such as the cafeteria, gift shop, and new 3,000 ft^2 Inter-Faith Chapel. Recreational items such as games, crafts, TV, Nintendo, Playstation, and videos are available to entertain children during their stay. In addition, Child Life staff may assist with constructive activities for children. The unit is located one floor below the Pediatric Intensive Care Unit which affords immediate proximity to critical care medicine services should they be required in emergent situations. The unit has been constructed to meet all applicable FDA/ICH guidelines for an early phase study unit and fully meets accreditation standards by The Joint Commission.

General Computer and Network Infrastructure: All faculty and staff have desk top computers running on Windows7 or Windows10 connected to a Children's Mercy client/server LAN with word processing, spreadsheet, database, electronic mail, presentation, and graphical software. Hospital Information Services professional staff support the network, including security and regular backups.

The Windows-based network is configured with security such that a user logging onto the system has a personalized desktop displayed and access to a personal directory on a server that is backed up daily, regardless of which computer in the hospital the user is using. Resources provide full support for electronic data collection, storage, analysis, and exchange. The network is maintained by the Hospital Information Services professional staff.

In addition, CMH has two firewall protected Internet connections that allow transmission of large data and graphics files between CMH investigators and collaborators with I-2 connections. A site on the World Wide Web (http://www.childrensmercy.org) is maintained.

Electronic Medical Record (EMR): Children's Mercy uses **Cerner Millennium**, a limited access EMR protected by a closed system with a dual firewall and user sign on authorization. CMH utilizes rigorous security measures, change management procedures, system testing, and a variety of other measures to protect the security and integrity of clinical information in the EMR.

Electronic signatures in the EMR are validated by assignment to unique individuals, and this system employs a secure, computer-generated, time-stamped audit trail. CMH maintains written policies holding study team members accountable and responsible for their actions under their electronic signature and while using the EMR while employed at CMH.

CMH patient care records can be generated and complete copies may be obtained for inspection, review, and copy by a sponsor or their designated representative, as appropriate.

Cerner Millennium complies with the Health Information Portability and Accountability Act (HIPAA) and has been certified to fulfill the HITECH Act of 2009 Meaningful Use requirements.

Children's Mercy Hospital Clinical Facilities:

Ambulatory: Ambulatory pediatric diabetes care is predominantly delivered in ambulatory buildings across the Kansas City Metro and Regional Sites. Metro sites in which diabetes care is provided include the Clinics on Broadway, Northland, East, and College Boulevard. Regional ("outreach" or "outpost") care is provided in St. Joseph, MO, Joplin, MO, Junction City, KS, Great Bend, KS, and Wichita, KS. Each of these sites may be used to recruit potential subjects for this study.

Main Clinical Laboratory: The clinical laboratory is a full service laboratory operated by the Department of Pathology which occupies 8,000 ft^2 on the second floor of the hospital and provides laboratory services to the hospital and ambulatory clinics 24 hours/day, 7 days per week. Areas of clinical service provided include routine and special chemistry, endocrinology, flow cytometry, coagulation, hematology, histology, diagnostic immunology, microbiology, transfusion services, toxicology/TDM, in vitro nuclear medicine, cytogenetics, biochemical genetics and urinalysis. The laboratory is fully accredited by CAP #19365-01 and licensed by CLIA #26DO443323. It is capable of providing clinical laboratory testing required for clinical research protocols, specifically including the Hemoglobin A1C included in this study.

Children's Research Institute:

Health Services and Outcomes Research:

The department of Health Services and Outcomes Research (HSOR) is committed to scientific discovery that enhances the delivery of evidence-based care and optimizes the outcomes that patients and parents/legal guardians value most. Distinct from traditional biomedical research that relies solely on biomedical measures of success to determine whether a health intervention is necessary and/or successful, outcomes researchers include a broader focus that includes the clinical outcomes that matter most to patients. In addition to disease outcomes, HSOR includes a focus on patients' biopsychosocial functioning, quality of life, barriers to care and experience with care which are often key to addressing chronic disease, as well as, health disparities. A multi-disciplinary effort, HSOR focuses

on discoveries that improve key aspects of the healthcare system (e.g., patient/parent-provider communication, treatment engagement, medication adherence), while reducing health disparities and inappropriate use of health care resources.

29.0 Multi-Site Research

N/A

30.0 International Research

N/A

Bibliography and References Cited

1. Association of A1C to BOLUS Scores Among Youths with Type 1 Diabetes. Clements MA, DeLurgio SA, Williams DD, Habib S, Halpin K, Patton SR. 6, 2016, Diabetes Technol Ther, Vol. 18, pp. 351-9.

2. Metabolic control as reflected by A1C in children, adolescents, and young adults with type-1 diabetes mellitus: combined longitudinal analysis including 27, 035 patients from 207 centers in Germany and Austria during the last decade. Gerstl E, Rabl W, Rosenbauer J, et al. 4, Eur J Pediatr, Vol. 167, pp. 477-453.

3. A contrast between children and adolescents with excellent and poor control: the T1D exchange clinic registry experience. Campbell M, Shatz D, Chen V., et al. 2014, Pediatr Diabetes, pp. 110-117.

4. Association between adherence and glycemic control in pediatric type 1 diabetes: a meta-analysis. Hood K, Peterson C, Rohan J, Drotar D. 6, 2009, Pediatrics, Vol. 124, pp. e1171-1179.

5. The impact of treatment non-compliance on mortality in people with type 1 diabetes. Currie C, Peyrot M, Morgan C, et al. 3, 2013, J Diabetes Complications, Vol. 27, pp. 219-223.

6. Hospital admission for diabetic ketoacidosis or severe hypoglycemia in 31 300 young patients with type 1 diabetes. Karges B, Rosenbauer J, Holterhus P, et al. 3, 2015, Eur J Endocrinol, Vol. 173, pp. 341-350.

7. Predictors of deteriorations in diabetes management and control in adolescents with type 1 diabetes. Hilliard ME, Wu YP, Rausch J, Dolan LM, Hood KK. 2013, J Adolescent Health, pp. 28-34.

8. Normalizing: Adolescent experiences living with Type 1 Diabetes. Babler E, Strickland C. 3, 2014, Diabetes Educ, Vol. 41, pp. 351-60.

9. Current state of type 1 diabetes treatment in the U.S.: updated data from the T1D Exchange clinic registry. Miller KM, Foster NC, Beck RW, Bergenstal RM, DuBose SN, DeMeglio LA, Maahs DM, Tamborlane WV, T1D Exchange Network. 6, 2015, Vol. 38, pp. 971-8.

10. A multicenter randomized control trial of motivational interviewing in teenagers with diabetes. Channon S, Huws-Thomas M, Hood K, Cannings-Johnson R, Rogers C, Gregory J. 2007, Diabetes Care, Vol. 30, pp. 1390-1395.

11. Motivational/solution-focused intervention improves A1C in adolescents with type 1 diabetes. Viner R, Taylor V, Hey S. 2003, Diabetes Med, Vol. 20, pp. 739-742.

12. A multicomponent motivational intervention to improve adherence among adolescents with poorly controlled type 1 diabetes: a pilot study. Stranger C, Ryan S, Delhey L, et al. 6, 2013, Vol. 38, pp. 629-637.

13. Stabilization of glycemic control and improved quality of life using a shared medical appointment in adolescents with type 1 diabetes in suboptimal control. Floyd B, Block J, Buckingham B, et al. 3, 2017, Pediatr Diabetes, Vol. 18, pp. 201-212.

14. Randomized Clinical Trial of Clinic-Integrated, Low-Intensity Treatment to Precent Deterioration of Disease Care in Adolescents with Type 1 Diabetes. Holmes C, Chen R, Mackey E, Grey M, Streisand R. 6, 2014, Diabetes Care, Vol. 37, pp. 1535-43.

15. Multisystemic Therapy of Adolescents with Poorly Controlled Type 1 Diabetes. Ellis D, Naar-King S, Templin T, et al. 9, 2008, Diabetes Care, Vol. 31, pp. 1746-47.

16. Missed bolus doses: devastating for metabolic control in CSII-treated adolescents with type 1 diabetes. . Olinder AL, Kernell A, Smide B. 2009, Pediatr Diabetes, pp. 142-148.

17. A mobile app for the self-management of type 1 diabetes among adolescents: a randomized controlled trial. Goyal S, Nunn CA, Rotondi M, Couperthwaite AB, Reiser S, Simone A, Katzman DK, Cafazzo JA, Palmert MR. 6, 2017, JMIR MHealth Uhealth, Vol. 5, p. e82.

18. A Mobile App for Synchronizing Glucometer Data: Impact on Adherence and Glycemic Control Among Youths with Type 1 Diabetes in Routine Care. Clements MA, Staggs VS. 3, 2017, J Diabetes Sci Tech, Vol. 11, pp. 461-467.

19. Sustained effects of a nurse coaching intervention via telehealth to improve health behavior change in diabetes. Young H, Miyamoto S, Ward D, Dharmar M, Tang-Feldman Y, Berglund L. 9, 2014, Vol. 20, pp. 828-34.

20. Participants' Experience and Engagement in Check It!: a Positive Psychology Intervention for Adolescents with Type 1 Diabetes. Bergner EM, Whittemore R, Patel NJ, Savin KL, Hamburger ER, Jaser SS. 3, 2018, Transl Issues Psychol Sci, Vol. 4, pp. 215-227.

21. Mobile health in the management of type 1 diabetes: a systematic review and meta-analysis. Wang X, Shu W, Du J, Du M, Wang P, Zue M, Zheng H, Jiang Y, Yin S, Liang D, Wang R, Hou L. 6, 2019, BMC Endocrine Disorders, Vol. 18, pp. 351-9.

22. The T1D Exchange clinic registry. Beck RW, Tamborlane WV, Bergenstal RM et al. 2012, J Clin Endocrinol Metabol, pp. 4383-4389.

23. Metabolic control as reflected by A1C in children, adolescents and young adults with type-1 diabetes mellitus: combined longitudinal analysis including 27, 305 patients from 207 centers in Germany and Austria during the last decade. Gerstl EM, Rabl W, Rosenbauer J et al. 2008, Eur J Pediatr, pp. 447-453.

24. Hemoglobin A1C (A1C) changes over time among adolescents and young adult participants in the T1D exchange clinic registry. Clements MA, Foster NC, Maahs DM, Schatz DA, Olson BA, Tsalikian E, Lee JM, Burt-Solorzano CM, Tamborlane W, Chen V, Miller KM, Beck RW, T1D Exchange Clinic Registry. 5, 2016, Pediatr Diabetes, Vol. 17, pp. 327-36.

25. High hemoglobin A1C variability is associated with early risk of microalbuminuria in children with T1D. Raman S, Dai H, DeLurgio SA, Williams DD, Lind M, Patton SR, Spertus JA, Kosiborod M, Clements MA. 6, 2016, Pediatr Diabetes, Vol. 17, pp. 398-406.

26. Blood glucose monitoring and glycemic control in adolescents with type 1 diabetes: meter downloads versus self-report. Guilfoyle SM, Crimmins NA, Hood KK. 2011, Pediatr Diabetes, pp. 560-566.

27. Can children with type 1 diabetes and their caregivers estimate the carbohydrate content of meals and snacks? Smart CE, Ross K, Edge JA, King BR, McElduff P, Collins CE. 2010, Diabet Med, pp. 348-353.

28. Missed insulin boluses for snacks in youth with type 1 diabetes. VanderWel BW, Messer LH, Horton LA, et al. 2010, Diabetes Care, pp. 507-508.

29. Missed insulin meal boluses and elevated hemoglobin A(1c) in children receiving insulin pump therapy. Burdick J, Chase HP, Slover, RH, et al. 2004, Pediatrics, pp. E221-E224.

30. Poor adherence to integral daily tasks limits the efficacy of CSII in youth. O'Connell MA, Donath S, Cameron FJ. 2011, Pediatr Diabetes, pp. 556-559.

31. Frequently of mealtime insulin bolus as a proxy measure of adherence for children and youths with type 1 diabetes mellitus. Patton SR, Clements MA, Fridlington A, Cohoon C, Turpin AL, DeLurgio SA. 2013, Diabetes Technol Ther, pp. 124-128.

32. Lifetime benefits and costs of intensive therapy as practiced in the diabetes control and complications trial. The Diabetes Control and Complications Trial Research Group. 1996, JAMA, pp. 1409-1415.

33. The use of insulin pumps with meal bolus alarms in children with type 1 diabetes to improve glycemic control. Chase HP, Horner B, McFann K, Yetzer H, Gaston J, Banion. 2006, Diabetes Care, pp. 1012-1015.

34. Reasons for missed meal-time insulin boluses from the perspective of adolescents using insulin pumps" lost focus". Olinder AL, Nyhlin KT, Smide B. 2011, Pediatric diabetes, pp. 402-409.

39. Reflections on Incorporating a Behavioral Intervention into a Busy Pediatric Subspecialty Clinic. Tsai S, Clements M, Apodaca T. 3, 2016, J Pediatric Health Care, Vol. 31.

40. A New Paediatric Diabetes Knowledge Test - M-WIKAD Development and Factor Analysis. Tsai SL, Patton SR, DeLurgio S, Williams DD, Dileepan K, Karmazin A, Storm M, Clements MA. 1, 2019, European Endocrinology, Vol. 15, pp. 48-52.

41. Sleep and its Impact on Adherence in Adolescents with Type 1 Diabetes Mellitus. McDonough RJ, Clements MA, De Lurgio SA, Patton SR. 4, 2017, Pediatric Diabetes, Vol. 18, pp. 262-270.

42. Sleep and type 1 diabetes in children and adolescents: Proposed theoretical model and clinical implications. Monzon A, McDonough RJ, Meltzer LJ, Patton SR. 1, Pediatric Diabetes, Vol. 20, pp. 78-85.

43. Implementing clinic-wide depression screening for pediatric diabetes: An initiative to improve healthcare processes. Marker AM, Patton SR, McDonough RJ, Feingold H, Simon L, Clements MA. June 2019, Pediatric Diabetes, p. Accepted for publication.

44. Utilizing health information technology to improve recognition and management of life-threatening adrenal crisis in the pediatric emergency department: medical alert identification in the 21st century. Halpin K, Paprocki E, McDonough RJ. 5, 2019, Journal of Pediatric Endocrinology & Metabolism, Vol. 32, pp. 513-518.

45. Employing a Results-Based Algorithm to Reduce Laboratory Utilization in ACTH Stimulation Testing. McDonough RJ, Alba PM, Dileepan K, Cernich JT. 4, 2018, Journal of Pediatric Endocrinology & Metabolism, Vol. 31, pp. 429-433.

46. Research electronic data capture (REDCap) - A metadata-driven methodology and workflow process for providing translational research informatics support. Harris P, Taylor R, Thielke R, Payne J, Gonzalez N, Conde J. 2, 2009, J Biomed Inform, Vol. 42, pp. 377-381.

47. Children and Adolescents: Standards of Medical Care in Diabetes - 2018. American Diabetes Association. Suppl 1, 2018, Vol. 41, pp. S126-S136.

48. Evaluation of a fully automated high-performance liquid chromatography assay for hemoglobin A1C. Khuu M, Robinson c, Goolsby K, Hardy R, Konrad R. 1999, Arch Pathol Lab Med, Vol. 123, pp. 763-767.

49. Health Information Technology usability Evaluation Scale (Health-ITUES) for Usability Assessment of Mobile Health Technology: Validation Study. Schnall R, Cho Hwayoung, Liu Jianfang. 1, 2018, JMIR Mhealth Uhealth, Vol. 6, p. e4.

50. Asses diabetes-related quality of life of youth with type 1 diabetes in routine clinical care: the MIND Youth Questionnaire (MY-Q). deWit M, Winterdijk P, Aanstoot H-J, et al. 2012, Pediatric diabetes, Vol. 13, pp. 638-646.

51. Development of the diabetes treatment satisfaction questionnaire (DTSQ) for teenagers and parents: the DTSQ-Teen and the DTSQ-Parent. Bradley C, Loewenthal K, Woodcock A, McMillan C. 52, 2009, Diabetologica, Vol. Suppl (1). Abstract 1013.

52. The Patient Health Questionnaire for Adolescents: Validation of an instrument for the assessment of mental disorders among adolescent primary care patients. . Johnson J, Harris E, Spitzer R, Williams J. 2002, J Adoles Health, Vol. 30, pp. 196-204.

53. PASS 16 Power Analysis and Sample Size Software. [Online] 2018. ncss.com/software/pass.

54. Cohen, H. Statistical Power Analysis for the Behavioral Sciences (2nd Edition). Hillsdale, NJ : Lawrence Earlbaum, 1988.

55. Rebe-Hesketh S, Skrondal A. Multilevel and Longitudinal Modeling Using Strata, Volumes I and III (3rd Edition). College Station, TX, USA : Stata Press, 2012.

56. Frequency of SMBG correlates with A1C and acute complications in children and adolescents with type 1 diabetes. Ziegler R, Heidtman B, Hilgard D, Hofer S, Rosenbauer J, Holl RW. 1, 2010, Pediatr Diabetes, Vol. 12, pp. 11-17.

57. J, Cohen. Statistical Power Analysis for the Behavior

58. Hall, M. A., Zheng, B., Dugan, E., Camacho, F., Kidd, K. E., Mishra, A., & Balkrishnan, R. (2002). Measuring patients' trust in their primary care providers. *Medical care research and review*, *59*(3), 293-318

59. Lerman, C. E., Brody, D. S., Caputo, G. C., Smith, D. G., Lazaro, C. G., & Wolfson, H. G. (1990). Patients' perceived involvement in care scale. *Journal of General Internal Medicine*, *5*(1), 29-33.

60. Anderson, R. M., Funnell, M. M., Fitzgerald, J. T., & Marrero, D. G. (2000). The Diabetes Empowerment Scale: a measure of psychosocial self-efficacy. *Diabetes care*, *23*(6), 739-743.

61. Madsen, M., & Gregor, S. (2000, December). Measuring human-computer trust. In *11th Australasian conference on information systems* (Vol. 53, pp. 6-8).