MyPlan - Planned Eating Feasibility Pilot

STUDY PROTOCOL

Complete Title:	Individualized Planned Eating Patterns to Improve Glycemic Control in Adolescents with Type 1 Diabetes: A Pilot Clinical Trial
Short Title:	"MyPlan" – Pilot Planned Eating Trial for Adolescents with Type 1 Diabetes
Sponsor:	NIH/NIDDK
Protocol Date:	July 27, 2022

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Protocol Version: 4
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I confirm that I have read this protocol and understand it.

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List of Modifications

12-2021

Terminology change from "Structured Eating" to "Planned Eating"

3-2022

Definition of "recent HbA1c" clarified to any measurement within 9 months of screening for eligibility

Inclusion of non UNC and CCHMC participants (i.e., participants who attend clinics outside UNC or CCHMC hospital system if participant agrees for study to be in contact with participant's usual diabetes care provider)

Inclusion of personal continuous glucose monitoring data

4-2022

Adjustment of endline CGM wear-time to occur during active intervention period between 22-24 weeks instead of 24-26 weeks.

Adjustment of last in-person visit to occur between 24-25 weeks (maximum 26 weeks).

7-2022

Adjustment of HbA1c inclusion criteria to 7.5 – 11.0% from 8.0 – 11.0%

Option of virtual endline or baseline visit

CONTENTS

List of Abbreviations:

AE – Adverse Event
DSMB – Data Safety and Monitoring Board
MI – Motivational Interviewing
PSST – Problem Solving Skills Training
SAE – Serious Adverse Event
SMBG – Self Monitored Blood Glucose
T1D – Type 1 Diabetes
TIR – Time in Range

Protocol Synopsis

Study Title	Individualized Planned Eating Patterns to Improve Glycemic Control in Adolescents with Type 1 Diabetes: A Pilot Clinical Trial
Funder	NIH/NIDDK R21DK125033 – 01A1
Clinical Phase	Feasibility Trial
Study Rationale	Emphasis of the last two decades on flexible patterns of dietary intake for youth with type 1 diabetes (T1D) has clearly not corresponded with adequate glycemic control, despite increased use of insulin pumps and continuous glucose monitoring (CGM) in that time period. Some major T1D clinical practice guidelines explicitly recommend use of planned eating patterns. Additionally, consensus in some pediatric diabetes clinics with excellent glycemic control suggests that planned eating is a key element in successful diabetes management. Remarkably, there are no clinical trial data on the effectiveness of this strategy for glycemic control, nor data on the acceptability of and adherence to this strategy among youth with T1D.
Study Objectives	• To a) assess acceptability of and adherence to a 6-month individualized planned eating strategy ("MyPlan") among 40-50 youth with T1D and sub-optimal glycemic levels b) compare glycemic control at baseline and 6-months of the intervention ○ This information is required to inform and develop a fully powered trial designed to test the impact of behavioral strategies on diabetes outcomes in T1D youth receiving ongoing care in clinical settings

Test Article(s)	• Individualized planned eating plan with the following five behavioral targets ("MyPlan goals"):
	  ○ 3-4 meals and 0-2 snacks consumed;
	  ○ Meals/snacks consumed >2 hours and <4 hours apart
	  ○ Carbohydrate (CHO) distributed across waking hours (meals >15% daily CHO, with ~10-15% of daily CHO at snacks and ~20-30% at meals)
	  ○ No snack consumed after dinner;
	  ○ Snack/meal consumed 1-2 hours of waking.
	• If relevant, snacks will be recommended based on the participants' usual food intake, age, sex, activity and growth
	• Participant and family-specific eating schedules and routines will be incorporated into each individualized planned eating plan.
	• Behavioral counseling strategies will identify barriers to adherence and acceptability and address them through targeted education, problem solving and goal setting skills training.

Study Design	This is a pilot single arm clinical trial to assess whether planned eating is an acceptable and effective dietary strategy to be included in future fully powered trials aimed at optimizing diabetes outcomes in T1D youth. This pilot study will be conducted at two clinical sites (University of Cincinnati, and University of North Carolina at Chapel Hill), coordinated from the University of North Carolina at Chapel Hill. Approximately 33 teen/guardian dyads will be enrolled at University of Cincinnati and 17 at UNC for a total of 50 enrolled participant/guardian dyads (with 40 or more expected completers).

	A total study participation time of 6-months allows for evaluation of the acceptability of and adherence to the eating strategy and its influence on glycemic levels (comparing percent time within the glycemic range 70-180 mg/dL during 2-week wear time at baseline and 6 months). Following the baseline data collection and a 2-week run-in period, all participant dyads will be counseled to follow an individualized planned eating plan developed based on caloric needs, usual physical activity level, food preferences, previous intake and participant/family eating schedules. Counseling will take the form of weekly telehealth visits during the first 2 months followed by bi-weekly telehealth visits during the remaining 4 months. The underlying behavioral strategy for the intervention derives from the FLEX intervention, the DASH-4-Teens intervention, and Social Cognitive Theory in that motivation and self-efficacy enhancement, problem-solving skills training (PSST) and goal-setting training, and targeted education will be integrated with instruction on individualized eating plans. Barriers for adherence to the eating plan will be discussed and action steps for overcoming barriers will be set using principles of motivational interviewing (MI), PSST, and family-based strategies (FSB). The goal-setting will be focused on making incremental progress towards meeting the MyPlan eating behavior targets/goals that pose the greatest challenges to youth achievement of all five targets/goals that comprise the "MyPlan" way of eating. Adjustment to the plan (within general guidelines) at months 3 will incorporate both indicators (i.e. weight status, MyFitnessPal logs) as well as acceptability of the eating strategy to the participant and caregiver/parent.
Subject Population Key Criteria for Inclusion and Exclusion	Inclusion Criteria mimic the criteria planned for the future fully powered trial: 1. Individuals ages 12-17 years old 2. History of type 1 diabetes of at least one year *3.* A measurement of HbA1C 7.5-11% over the preceding 9 months (*Note: HbA1c at the time of the baseline visit will not preclude participation)* 4. Guardian willing to also participate 5. English as preferred language Exclusion Criteria mimic the criteria planned for the future fully powered trial: 1. Individuals with other metabolic disorders, unstable thyroid disease, diagnosed eating disorder, prohibitively strict dietary restrictions, or those with other serious condition that renders participation inappropriate. 2. Females who are pregnant, breast feeding, planning to become pregnant during the study period or delivered a baby in the last 12 months 3. Unwillingness to follow a personalized eating plan for 6 months or complete MyFitnessPal logs at least 3 days/week throughout the study
Number of Subjects	40-50 subjects (33 enrolled at University of Cincinnati and 17 at University of North Carolina at Chapel Hill)
Study Duration	Each subject's participation will last approximately 6 months Study data collection is expected to end by October 2021
Study Phases	1. Screening and Pre-Intervention Data Collection: Screening for eligibility, recruiting and obtaining consent; Collection of basic demographic, health, diabetes knowledge, eating and physical activity pattern information via

	questionnaires at baseline visit. HbA1c, height, and weight measurements at baseline visit. 2. Run-in (2 weeks): Set-up mobile device and text reminders for mobile data collection; Collection of daily logs and two 24-hour recalls to inform eating plan designed by RD; 2-week CGM wear. 3. Intervention (22 weeks): Study intervention 4. Post-Trial Data Collection: Completion of eating plan acceptability Assessment, questionnaires, 2-week CGM wear, HbA1c, height, weight measurements.
Safety Evaluations	Participants will be asked about hypoglycemic events at each study visit and support session with the RD (by phone or in-person). Participants will be instructed to contact the study endocrinologist and/or RD to report any cases of severe hypoglycemia. The RDs will communicate with the study endocrinologist to ensure that any needed insulin adjustments are made throughout the study period. Participants will be encouraged to monitor their weight at home throughout the study period. Weight and height will also be collected at baseline, 3 months, and 6 months to monitor any changes and ensure healthy maintenance of weight and growth.
Statistical and Analytic Plan	Adherence outcome: • Planned eating adherence (primary measures): Weekday and weekend adherence to five eating behavior targets/goals that define the MyPlan strategy will be calculated continuously and categorically. Additional measures will include adherence consistency, defined as the extent to which youth performance on the adherence metrics differs between the dietary recall days, as well as proportion of completed telehealth visits/phone calls, and diet-self-monitoring days (exploratory measures). Acceptability outcome: • Categorical and continuous 5-item measure of acceptability (primary measures) • Additional measures include qualitative information, which will be analyzed for themes (exploratory measures). Glycemic outcomes: • Percent time in the glycemic range 70-180mg/dL comparing CGM wear time at baseline and 6 months (primary measure) • HbA1c (secondary measure)
Data and Safety Monitoring Plan	Data quality and safety monitoring will occur within the research team (data quality committee). There will be an internal DSMB committee composed of Baiming Zou, PhD (Study Design and Statistical Analysis), Abby Pears, PhD (Nutrition) and Ingrid Libman, MD, PhD, MPH (Pediatric Endocrinology), in addition to our internal research team members (Elizabeth Mayer-Davis, PhD RD; Sarah Couch PhD RD; Amy Shah, MD; and study manager Angelica Cristello Sarteau, MSPH). The committee will monitor participant accrual and retention, progress, completeness of standardized measures, and attendance at intervention sessions, as well as occurrence of hypoglycemia or other adverse events. All aspects of data collection and data storage will be carefully monitored to ensure rapid detection of errors, inconsistencies or other problems. Distributions of key variables will be monitored for data quality and safety. AE and SAE, as defined by NIH, will be reported to the local site investigator and corresponding IRBs. AE/SAEs will be reviewed monthly.

1. Executive Summary

Average HbA1c among youth in the US in 2016 was 8.8%, considerably above the standard clinical target of < 7.5%, and had worsened significantly since 2011. The emphasis of the last two decades on flexible patterns of dietary intake for youth with T1D has clearly not corresponded with adequate glycemic control, despite increased use of insulin pumps and continuous glucose monitoring (CGM) in that time period. There are major gaps in knowledge about what interventions might achieve improved glycemic control, and what approach to patterns of dietary intake might be beneficial. Some T1D clinical practice guidelines explicitly recommend use of planned eating patterns. Additionally, consensus in some pediatric diabetes clinics with excellent glycemic control suggests that planned eating is a key element in successful diabetes management. Remarkably, there are no clinical trial data on the effectiveness of this strategy for glycemic control, nor data on the acceptability of and adherence to this strategy among youth with T1D. **Thus, our overarching goal is to rigorously test the effectiveness of individualized, planned eating patterns to improve glycemic levels so as to inform T1D clinical practice guidelines.** We have completed several preliminary studies that support the likely acceptability and effectiveness of an individualized structured eating plan intervention we called "MyPlan", that includes collaborative development of the individualized planned eating plan to spread intake of carbohydrate and calories over the day**. Here we propose a pilot single arm 6-month clinical trial to inform a future, fully powered pragmatic trial that tests the addition of individualized structured eating plans to ongoing diabetes care in clinical settings.** Our Specific Aims are: **Aim 1.** Assess acceptability and adherence (primary outcomes) to a 6-month individualized planned eating intervention ("MyPlan") among 40-50 youth with T1D. We will recruit adolescents, age 12-17 years, with T1D of at least 1-year duration and with HbA1c between 7.5 % and 11% (total n=50 recruited to ensure n=40 active participants across two clinical sites) to participate in a 6-month MyPlan intervention, which will guide participants in setting behavioral goals in relation to five tenets that comprise a structured eating pattern. **Aim 2.** Compare glycemic control among adolescents with T1D at baseline and at the end of the 6-month MyPlan intervention. Measures of glycemic control will include % time in range (TIR) based on continuous glucose monitoring (primary outcome) and HbA1c (secondary outcome).

2. Background and Significance

Intensive glucose control among people with type 1 diabetes (T1D) has been demonstrated to confer health benefits over 30 years later.[1-3] However, higher mean HbA1c in youth with T1D compared to adults (over 9% in 17-year-olds that remains elevated above 8% until a mean age of 30 years) indicates that despite significant advances in technology and therapeutics, obstacles remain in reducing youth HbA1c to the recommended levels that minimize diabetes-related complications.[4] Given that suboptimal T1D management behaviors and the negative effects of elevated HbA1c in youth carry into adulthood, there is a compelling need to develop a program of behavioral strategies that optimize management of the risk factors that lead to poor health outcomes in this population.

Clinical consensus in some pediatric diabetes clinics with excellent glycemic control (HbA1c < 7.5%) suggests that a planned way of eating -- characterized by daily consistency in the timing and distribution of meals, snacks, and carbohydrates —is a key element in successful diabetes management. For example, at the John Hunter Children's Hospital pediatric endocrinology clinic in Newcastle Australia where counseling on planned eating has been a standard part of diabetes management for several years, among their approximately 400 adolescent patients with T1D, recent estimate of average HbA1c is 7.1%. Although there are no clinical trial data on this topic, current international consensus guidelines and the research literature suggest the potential benefit of this strategy. Current recommendations regarding nutritional management in children and adolescents with type 1 diabetes caution that "optimal" nutrition therapy varies based on the individual and thus should be developed through an interdisciplinary clinical team to account for the individual child's unique growth, physical activity habits, cultural, ethnic, family traditions, psychosocial, and behavioral needs. Although emphasizing the importance of matching insulin dose to carbohydrate intake and providing guidelines for appropriate ranges of daily macronutrient intakes (carbohydrates: 50–55% of energy, fat: <35% of energy (saturated fat <10%), and protein 15–20%) is cited in the most recent International Society for Pediatric and Adolescent Diabetes (ISPAD) consensus guidelines, these guidelines stop short of prescribing daily consistency in the timing and distribution of meals, snacks, and carbohydrates. However, some suggestive statements of the potential benefit of planned eating practices are included: "implementation of an individualized meal plan with appropriate insulin adjustments can improve glycemic control" and "regularity in meal times and eating routines are…important for glycemic outcomes"[5].

Although no clinical trials to-date have purposefully evaluated whether planned eating as a behavioral strategy improves diabetes outcomes in T1D youth, studies have illustrated negative associations between irregular dietary intake (e.g., skipping meals/eating frequency, day-to-day variability in macronutrient composition of intake) and T1D diabetes management and outcomes. An American study of 144 adolescents with T1D showed 56% admitted to missing meals and snacks[6]. Highlighting the potentially problematic nature of such habits for diabetes management, the Norwegian Childhood Diabetes and Quality Project found that skipping meals was associated with

higher odds of sub-optimal HbA1c (>7.5%), LDL cholesterol levels (OR: 4.0, CI: 2.0-8.2; p <0.001), and being overweight (OR: 2.8, CI: 1.1-7.2; p = 0.03) among 655 children and adolescents with T1D (mean 11.4 yrs, mean duration of diabetes 3.8 years)[7]. Another study from the Norwegian Childhood Diabetes and Quality project, which examined 550 adolescents and children 2-19 years of age (mean age 11.3, diabetes duration 3.8 years) further demonstrated that even when intensive insulin treatment with insulin pumps and multiple injections were used, not skipping meals and having breakfast and supper regularly (defined as six times per week) was significantly associated with improved HbA1c[8]. Additional examination by Øverby et al. of the associations between high eating frequency and glycemic control found that two snacking events a day increased odds of suboptimal HbA1c (OR: 1.8, CI: 1.1–3.1; p=0.03)[7]. This finding was reinforced by a recent analysis of 821 T1D youth in the SEARCH for Diabetes in Youth study, where eating frequency (≤3, 4-5, or 6-10 times/day) measured at baseline and follow-up visits was significantly related to HbA1c and serum lipid levels measured repeatedly over 5 years. Increased eating frequency was associated with larger increases in HbA1c among youth with T1D. For example, for those who ate ≤3 times per day at the outset and ate 6-10 times per day 5 years later, longitudinal models predicted greater absolute increases in HbA1c (2.77%)[9]. Despite the paucity of published studies examining day-to-day variation in the timing or composition of dietary intake among the T1D population, Wolever et al. reported day-to-day variation of carbohydrate (p=0.0097), but not fat or protein, to be positively related to HbA1c in T1D youth, which remained significant when adjusted for age, sex, duration of diabetes and BMI[10].

Insights from pediatric clinics, consensus guidelines, and the literature thus suggest that day-to-day irregularity in meal/snack times and distribution of carbohydrates may be a target of intervention to improve T1D management and outcomes in youth. A potentially beneficial behavioral strategy insufficiently explored to-date, planned eating in T1D youth would benefit from rigorous testing through a fully powered clinical trial. **Our overarching goal is thus to establish the role of individualized planned eating as part of effective diabetes self-management strategies for youth with T1D to improve glycemic levels.** We have already conducted a small feasibility pilot across two centers in the US that indicates interest and willingness of patients and parents to engage in an individualized planned eating behavioral intervention we call “MyPlan.” MyPlan included the collaborative development of pattern of eating occasions and carbohydrate distribution individualized to youth and parent lifestyle constraints and preferences. MyPlan demonstrated initial adherence to and acceptability of this approach over a one-month period.

We propose a feasibility study of longer duration to assess acceptability and adherence, and to estimate impact on glycemic control of a 6-month individualized planned eating behavioral intervention. The present R21 will enable the design of a rigorous randomized clinical trial to include planned eating as part of a comprehensive approach to improve outcomes that will inform clinical practice and medical nutrition therapy guidelines.

3. Study Objectives

Our objective is to build on our initial pilot study (UNC-CH IRB 18-2767) with a 6-month feasibility study of longer duration to assess the adherence to and acceptability of the MyPlan eating strategy in youth with type 1 diabetes (T1D), as well as to estimate impact on glycemic levels between baseline and 6 months. This project will inform the design of a future pragmatic randomized clinical trial of behavioral strategies to improve diabetes self-management in youth with T1D. Our specific aims are:

Aim 1. Assess acceptability and adherence to a 6-month individualized planned eating strategy ("MyPlan") among 40 youth with T1D. We will recruit adolescents, age 12-17 years, with T1D of at least 1-year duration and with HbA1c 7.5 % and 11%. Coordinated at the University of North Carolina at Chapel Hill (UNC), we will recruit 17 participants at UNC and 33 participants at Cincinnati Children's Hospital Medical Center diabetes clinic (total n=50 recruited to ensure approximately n=40 completers) to participate in a 26 week MyPlan intervention, which will guide participants in setting behavioral goals in relation to five behavioral targets that comprise a eating behavior pattern ("MyPlan") developed based on clinical expertise and international consensus guidelines: 1) 3-4 meals and 1-2 optional snacks; 2) spacing eating occasions throughout the day; 3) spacing carbohydrates across the day; 4) no post-dinner snacking; and 5) eating within a short period of waking.

- **To assess acceptability** we will use a previously developed five-item questionnaire for diet acceptability (all participants) as well as a post-study qualitative evaluation (sub-sample of participants):
    - Satisfaction, perceived ability to stay on the plan, enjoyment of the plan, ease of staying on the plan, how the participant feels on the plan and ability to manage blood sugar on the plan.
    - Perceived pros and cons of the plan, and other acceptability related themes that emerge from answers to questionnaire free response items and qualitative evaluation questions
- **To assess adherence** we will use 24-hour dietary recalls and MyFitnessPal logs to calculate:
    - Weekday and weekend adherence (categorically and continuously specified) to five behavioral targets that define the MyPlan pattern will be calculated
    - Consistency will be defined as the extent to which youth performance on the adherence metrics differs between the dietary recall/log days.

Aim 2. Compare glycemic control among adolescents with T1D at baseline and at the end of the 6 month MyPlan intervention.

- **To assess glycemic control we will use** % time in range (TIR) and HbA1c.

The primary glycemic control outcome will be pre-post within-person change in % TIR measured by CGM. With 80% power, we will be able to detect an approximate change in TIR of 6.8%, equivalent to a change in HbA1c of about

0.52%.[24] We will collect HbA1c as a secondary outcome measure. We will conduct exploratory analyses to determine if change in glycemic control differs according to degree of adherence to planned eating and other clinical and demographic factors. As part of the planned post-hoc qualitative evaluation of the MyPlan project with a sub-sample of participants and their parents, we will assess self-reported/subjective effectiveness and more deeply explore potential reasons underlying why MyPlan may have improved or failed to improve participants' glycemic management to identify intervention levers for future studies.

4. Site Descriptions

The two clinical sites include 1) University of Cincinnati in Ohio) and 2) University of North Carolina Medical System. All clinical sites are well-established academic medical centers with vast experience in diabetes translational research. UNC-CH will oversee coordination of the pilot trial. The study investigators across UNC-CH and University of Cincinnati have over a decade of collaborative experiences in research among youth with T1D, and comprise the core team for the future trial for which these pilot data are being collected.

5. Selection & Recruitment of Subjects

Exclusion criteria: The following individuals will be excluded from study participation. Individuals with other metabolic disorders, unstable thyroid disease, diagnosed eating disorder, prohibitive strict dietary restrictions, or those with other serious condition that renders participation inappropriate. Females who are currently pregnant will be excluded.

Inclusion criteria: Male and female individuals ages 12-17 years old with a diagnosis of type 1 diabetes of greater than one year, and a HbA1c measurement between 7.5-11% in the preceding 9 months. A parent (or legal guardian) will also be included for each participant.

Recruitment will use a combination of in-person and remote strategies:

Introductory Recruitment Step "Initial Contact":
Medical records will be used to identify adolescents who potentially meet the eligibility criteria for this study. A mix of active and passive recruitment strategies will be used to establish initial contact with potential participants:

- We will work with NC TraCS to establish recruitment through MyChart.
- Potential participants identified in Epic will be sent a brief e-mail overviewing the study with a link and QR code which will lead to a Qualtrics interest form where the parent participant can fill out their contact information in order to be contacted by study personnel for further information about the study.
- Research4Me will connect potential participants to the Qualtrics interest form.
- Facebook posts in T1D specific groups will identify potential participants.
- Providers (i.e., endocrinologists, nurses, dieticians) at each site will alert patients about the study during routine care visits, asking parents whether they would be willing to be contacted by the study coordinator to be presented information about the study. Providers will either share the parent's contact information with the study recruitment staff, or share the Qualtrics form QR code, which will lead the participant to a short eligibility questionnaire where their parent can fill out their contact information in order to be contacted by study personnel for further information about the study.
- Recruitment personnel will scan Epic for upcoming visits and send an Epic message to the provider to remind him/her to mention the study to the participant during the visit. Providers will either share the parent's contact information with the study recruitment staff, or share the Qualtrics form QR code, which will lead the participant to a short eligibility questionnaire where their parent can fill out their contact information in order to be contacted by study personnel for further information about the study.
- Recruitment materials will also be prominently displayed in the diabetes clinic waiting area and exam rooms at both sites. The materials will have a QR code that will lead the participant to a short eligibility questionnaire where the parent can fill out their contact information in order to be contacted by study personnel for further information about the study.

- Recruitment personnel may also utilize in-person recruitment of eligible participants during usual care visits by screening Epic for upcoming appointments and intercepting the participant before or after the care appointment. If in-person, the personnel will introduce the study to the parent and obtain contact information to discuss the study further at a later date. In some cases when the parent and participant have additional time to discuss the study, personnel may be able to proceed to covering the content in "Recruitment Step 1".

Recruitment Step 1 "First Meaningful Interaction":
Once the parent agrees to be contacted at a later date and shares his/her contact information, study personnel will call the parent and adolescent to explain the study in detail. Both parent and adolescent must be present for this interaction. After this call, study personnel will send the parent and adolescent a study information sheet and the schedule of encounters, and set up another call once the parent and adolescent think they will have had a chance to review the information.

Recruitment Step 2 "Commitment Interaction": Both parent and adolescent must be present for this interaction. During this second call, study personnel will address any questions or concerns that may have arisen while parent and participant reviewed the material. If the parent and adolescent agree, the study personnel will then schedule up a time and date for in-person consent/assent and the baseline measurement visit. The consent/assent forms will be e-mailed to the participant in advance of the baseline measurement visit.

Strategies to Optimize Recruitment and Retention: Study staff at Ohio, and University of North Carolina at Chapel Hill sites will be responsible for local recruitment activities. As described above recruitment will use a combination of passive, active, remote and clinic-based strategies.

The two step-recruitment process is a pre-emptive retention strategy because it ensures parents and adolescents have an in-depth understanding of study expectations and helps them reflect on barriers to participation before signing on to the study. Further, staff will remotely monitor participation (i.e., adherence to MyFitnessPal logs) on a weekly basis to actively and pre-emptively troubleshoot engagement issues. Additionally, we will incorporate successful retention strategies from previous research in this study population (e.g., offering flexible visit options, incentives [up to $200] based on questionnaire/measurement completion and intervention participation, reminder texts/e-mails, cards and phone calls, easy parking instructions). Using similar strategies in the 18-month FLEX trial, our retention was 93%.[91] We expect the same success for MyPlan because it has approximately identical inclusion criteria as FLEX, is significantly shorter in length, and only requires two in-person measurements visits (counseling sessions and questionnaires will be completed online) –all of which make the study lower burden and more convenient for participants than the FLEX study. We also anticipate that the point-based incentive system that rewards participants We will recruit 50 youth-guardian dyads (33 at CCHMC, 17 at UNC). We

conservatively plan for 80% retention, resulting in at least 40 completers (26 at CCHMC, 14 at UNC).

Participant Recruitment: Ohio: The recruitment goal for Ohio is 33 participant/guardian dyads. Participants will be recruited from the Cincinnati Children's Hospital and Medical Center pediatric endocrinology clinic, located on the campus adjacent to University of Cincinnati. Clinics outside of Cincinnati Children's Hospital and Medical Center may also be sources of potential participants, who will either be identified through Facebook groups or MyPlan staff networks.

Participant Recruitment: University of North Carolina: The recruitment goal for University of North Carolina at Chapel Hill is 17 participant/guardian dyads. Participants will be recruited from the University of North Carolina medical system. Clinics outside of University of North Carolina medical system may also be sources of potential participants, who will either be identified through Facebook groups or MyPlan staff networks.

6. Consent, Assent, Withdrawals

Participant guardians and participants will have the opportunity to provide informed consent and assent, respectively, following the recruitment processes detailed above. For guardians and participants who agree to participate and schedule a baseline visit, at the time of the visit, study staff will review the full study consent in detail before standardized data collection begins. Guardians and participants will be given as much time as needed to review the consent and assent forms and ask any questions prior to signing it. They will be informed that participation in the study is voluntary and that they are free to withdraw their consent and discontinue participation in this research study at any time by contacting the primary investigators or study staff.

Following assent, participants may be involuntarily withdrawn from the study per the investigator's discretion if they develop a serious condition that would render participation unwise, including clinical diagnoses of serious physical or psychiatric conditions. The study physicians (Shah, Jain) will review this information and make a determination about withdrawal from the study. Females who become pregnant will also be withdrawn from study participation.

If a participant chooses to withdraw or is withdrawn from the study, they will be asked the reason for withdrawal, which will be recorded in a withdrawal form in REDcap by study staff.

8. Standardized Measurements

Measurement	**2-week run-in** **Baseline Data Collection** **Visit 1** *Insert CGM*	**Week 3** **Baseline Data Collection*** **First Session**	**Week 4-10** **7 Weekly Sessions**	**Week 12-22** **6 Bi-weekly Sessions**	**Week 22** *Insert CGM*	**Week 24** **Last Session** *take-off CGM*	**Week 26** **Endline Data Collection** **Visit 2** *return CGM*
Adherence							
Mobile Phone MyFitnessPal Logs	**X**	**X**	**X**	**X**	**X**	**X**	
24-Hour Diet and Physical Activity Recalls	**X**				**X**		
Acceptability							
MyPlan Acceptability Assessment (Parent, Participant)				**X**			**X**
MyPlan Adjustment Form			**X**	**X**	**X**	**X**	
MyPlan post-hoc qualitative evaluation							**X**
Psychosocial and Behavioral Factors							
Baseline Lifestyle Questionnaire	**X**						
Diabetes Self-Management Support	**X**						**X**
Food Frequency Questionnaire	**X**						**X**
Diabetes Eating Problem Survey	**X**						**X**
Hypoglycemia Fear Survey	**X**						**X**
Knowledge Survey	**X**						**X**
Self-Efficacy Survey*		**X***					**X**
Motivation*		**X***					**X**
Problem Solving Skills*		**X***					**X**
Glycemic Control							
Continuous glucose monitoring	**X**				**X**		**X**
HbA1c *(Note: value does not have to be 7.5-11% at time of baseline visit)*	**X**						**X**

Hypoglycemia Reporting Questionnaire	X	X	X	X	X	X	X
MyPlan post-hoc qualitative evaluation							X
Anthropometrics							
Height Weight	X			X[1]			X
Demographics and Health History	X						X
Process Measures SMART Goals set, Goals Achieved/Points received, Behavioral strategies delivered, Fidelity checklist, Behavior Change Techniques	X	X	X	X	X	X	
MyPlan post-hoc qualitative evaluation							X

* baseline assessed at Week 4 (1 week after being introduced to eating plan)

1. self-report weight at midpoint to ensure no significant loss (Week 14)

8a. Primary Outcomes

Time in range
We will compare participants' average TIR during the blinded CGM wear time at baseline (0-2 week run-in period before the active intervention period) when participants will be following their usual diet to their TIR at 22-24 weeks of the active intervention period. TIR can capture the impact of short term behavior change and allows for blood glucose fluctuations to be compared between days and weeks instead of months.[97] Because 24-hour dietary recalls will be administered during the time the CGM is worn at 0-2 and 22-24 weeks, in exploratory analyses we can examine the difference in participants' alignment to the prescribed eating behavior pattern at 22-24 vs. 0-2 weeks alongside the difference in TIR at 22-24 vs. 0-2 weeks using the matched two days of 24-hour recall and CGM data pre vs. post intervention.

The 24-hour dietary recalls will be obtained by trained staff certified from the NIH/NIDDK-funded UNC Nutrition Obesity Research Center (P30DK056350; MPI Mayer-Davis) using the Nutrient Data System for Research software and the multiple pass interviewing method.[98,99] It is possible that the eating behavior pattern participants follow during the intervention will affect glycemic control differently during the day and night. For instance, not eating after dinner (i.e. no bedtime snack) may reduce hyperglycemia and improve TIR overnight. As such we will also examine differences in pre- and post-intervention TIR by day and night using time cut points established by international diabetes research consensus guidelines.[100]

More detail about the unadjusted and adjusted outcome models that will be analyzed can be found in the Statistical Considerations section.

Eating behavior pattern adherence
Alignment of participant behavior to the prescribed eating behavior pattern will be objectively assessed via two unannounced 24-hour dietary recalls (1 weekday, 1 weekend per week) collected during the 0-2 week and 22-24 week CGM wear time of the MyPlan study. Adherence metrics (weekday and weekend) will include proportion of participants who followed each eating behavior target, proportion of participants who met 0-5 eating behavior targets, and average number of targets met

In exploratory analyses, participant logs and 24-hr recalls will also enable identification of which snacks/meals are most often missed, which snacks/meals deviate the most from time or carbohydrate distribution targets as specified in the planned eating plan, as well as which aspects of regular eating pose the biggest challenges to adherence. These metrics will help with targeting counseling and focusing goal-setting, as well as areas to focus the design of future trials.

Eating behavior pattern acceptability
Although acceptability of the individualized planned eating plan will be ascertained every week after the plan is introduced, acceptability will be reviewed formally at 3 months, and again at the conclusion of the intervention period. Participants and their parent/guardians will fill out an acceptability assessment that we have used in previous studies.[101] [17] We will calculate separate composite acceptability scores (5 highly acceptable, 20 highly unacceptable, >10 unacceptable) from ordinal responses to statements from an 5-item instrument designed to capture ease of eating pattern

adoption, satisfaction, food enjoyment, sustainability, and ease of blood sugar management. As part of the post-hoc qualitative evaluation of the intervention, we will conduct short semi-structured qualitative exit interviews with teenager and parent participants and project staff to ascertain barriers and facilitators to following the eating strategy, likes and dislikes, recommendations for modifications, likelihood of recommending the strategy to others, and the eating behavior target participants found most difficult to follow, alongside other feedback related to intervention design, materials, and implementation.

8b. Secondary Outcomes

HbA1c
At baseline and 26 weeks, HbA1c will be measured using point-of-care testing.

Comparing HbA1c collected at the end of the intervention to the value collected at baseline provides insight into glycemic effects of the eating behavior pattern that are complementary to the insights produced by the blinded CGM: Hba1c collected at baseline will generate understanding of 'usual' youth glycemic control up to three months before starting the intervention; HbA1c collected at 26 weeks will generate understanding of glycemic control between the midpoint and end of the intervention, thus providing information about glycemic control during up to half of the time that participants are following the eating behavior pattern.

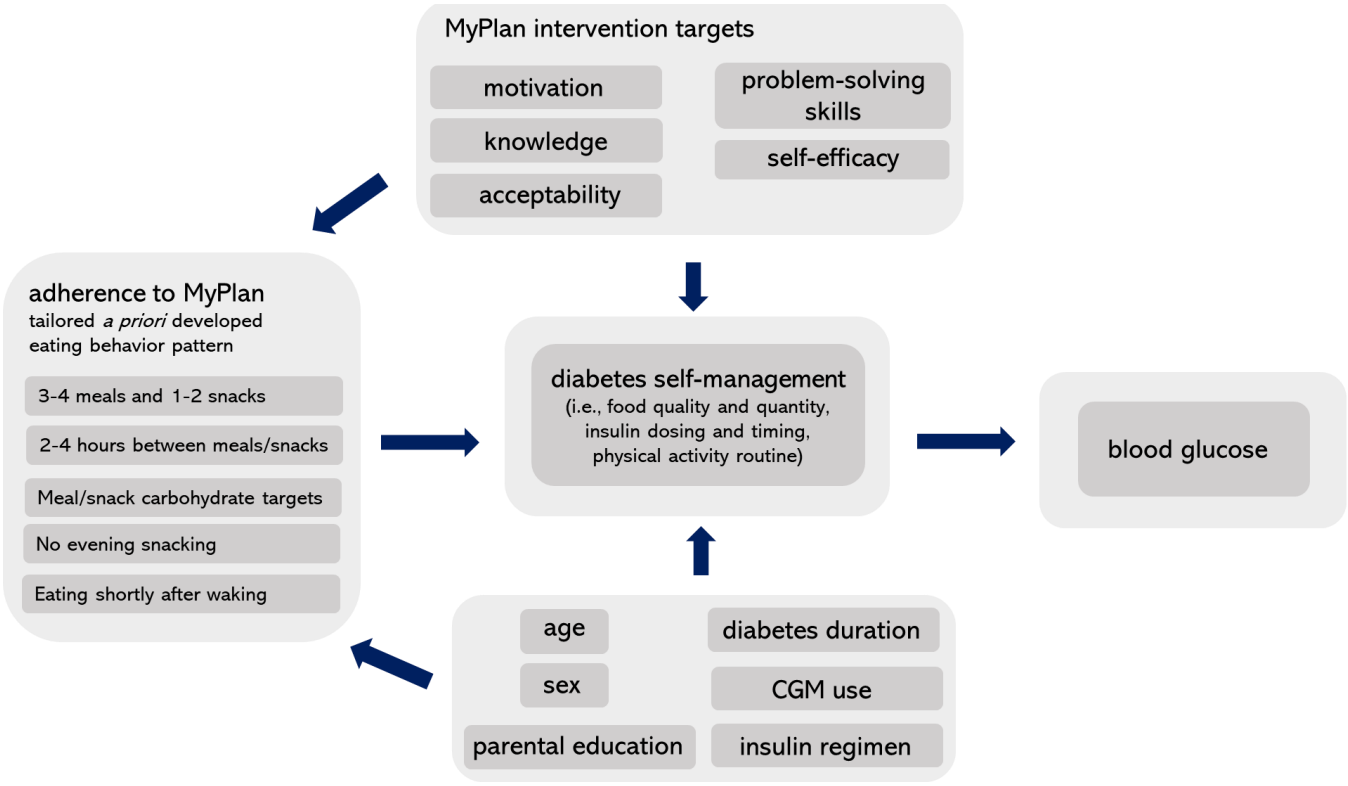
The HbA1c values will also be less affected by the potential bias of participants engaging in extra conscientious diabetes self-management behaviors during the two weeks at baseline and endline when they are wearing the study CGM, which could alter behavior even though blinded to participants. Because 2 weeks of CGM wear time can be used to estimate HbA1c with high accuracy, in exploratory analyses the CGM and HbA1c values can be compared to assess the extent to which the data produced by the blinded CGM (and transitively, the diabetes behaviors during this period) are representative of the individual's 'usual' behavior.[100]

8c. Other Measurements:

Potential confounders and effect modifiers

The DAG below highlights the key variables that we will consider in our exploratory multiple linear regression outcome models (**Figure 1**).

Figure 1. MyPlan R21 directed acyclic graph - adherence to individualized a priori developed eating behavior pattern and glycemic management



To address the possibility that the observed effect of the eating behavior pattern on TIR may be obscured by a differential number of CGM wear hours, we will calculate and report this metric in order to describe the extent to which wear time varies across our study sample and may bias our assessments of eating behavior pattern effects on glycemic control. We acknowledge that unplanned physical activity can alter usual eating habits and also affect glycemia in unpredictable ways, which may confound the effect of the eating strategy on TIR. On the days during which 24-hour dietary and physical activity recalls are conducted, data collectors will additionally probe for any unplanned physical activity as defined by consensus guidelines (>20 minutes of activity that resulted in sweating or heavy breathing).[102] Insulin timing will also be collected as part of 24-hour dietary recalls in order to understand the extent to which dosing inaccuracy may contribute to the glycemic data collected via blinded CGM at 0-2 weeks and 22-24 weeks of the study. At baseline of the trial, a medical chart review will provide information on diabetes duration, age, sex, race, ethnicity, height, weight, insurance type, diabetes self-care regimen (self-monitoring frequency, insulin dose, insulin regimen, usual use of CGM), and highest level of parental education. This data will help us understand the generalizability of our results to other populations with T1D and will also be incorporated in more fully adjusted exploratory outcome assessment models.

Anthropomorphic measurements

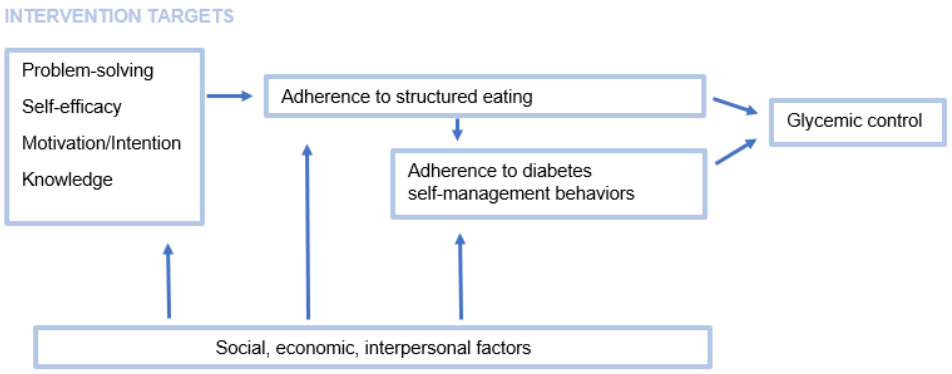
The planned eating plans are not anticipated to significantly change weight status because the timing and distribution of participants' usual dietary intake throughout the

day are the target of study, not the magnitude or quality of intake. Nevertheless, to monitor healthy weight and growth throughout the study period, weight and height will be measured at baseline and at the end of the study utilizing standardized methods described in the SEARCH for Diabetes in Youth study protocol (available online, www.searchfordiabetes.org). Participants will also be encouraged to self-monitor their weight and communicate any changes to the RD. They will use their home scale to self-report weight at baseline, midpoint, and end of the study.

Psychosocial and behavior change measurements

A conceptual framework **(Figure 2)** underpins the design of the structured behavior change counseling module, which is based on the Social Cognitive Theory and the Transtheoretical Model.[92,93] The underlying premise is that improving knowledge (i.e., targeted education), motivation (i.e., creating a motivational framework for change), and skills (i.e., decisional balancing, problem solving skills) will reduce perceived barriers to adherence, improve diabetes self-management, and subsequently glycemic control.[92-94] Our previous testing in the FLEX study of a structured counseling module with the same core elements improved scores for motivation (p=0.01), problem solving (p=0.02), and diabetes self-management profile (p=0.01) among adolescents with T1D over an 18-month period.[91] We are thus confident that the structured counseling module we plan to use will support youth in our study adopt and maintain their adherence to the eating behavior pattern over a significantly shorter six month period than the FLEX trial. We will assess problem-solving skills, self-efficacy, motivation, knowledge, and adherence self-management behaviors at the beginning and end of the study, so that we can monitor change in these intervention targets throughout the study and conduct exploratory structural equation modeling to test the conceptual model underpinning intervention design. We will assess problem-solving skills, self-efficacy, and motivation using validated instruments that were adapted to ask questions about these constructs as pertains to the personalized eating plan because the intervention is designed specifically to target motivation, self-efficacy, and problem-solving skills in relation to plan adherence. We will use the validated Nutrition Knowledge Questionnaire (NQS) and Diabetes Self-Management Profile Survey to assess knowledge and overall diabetes self-management adherence, respectively.

Figure 2. MyPlan Study Conceptual Framework



To capture perceptions of food and body weight, as well as disordered eating behavior that may pose challenges for planned eating plan adherence, the validated Diabetes Eating Problem Survey[17] will be administered to participants at baseline and at the end of the study. It is also possible that personalized eating plan may positively or negatively impact disordered eating behavior. Results from this survey, including change in survey scores throughout the study, will facilitate identification of barriers to planned eating

plans and help inform the counseling strategies and individualized eating plans given to participants.

Hypoglycemia
Severe and non-severe hypoglycemia will be defined according to recent consensus guidelines (54-70mg/dl; <54 mg/dl; requiring external assistance for recovery)[11]. To ensure continued safety of participants and the compatibility of the planned eating plan with the participant's lifestyle, the participants will be systematically queried regarding occurrence of serious hypoglycemia, at the end of the study, and during each meeting and support call with the RD using the hypoglycemia reporting instrument that queries instances of hypoglycemia that occurred since the last session. Fear of hypoglycemia and behaviors used to manage this fear will also be assessed at baseline and the end of the study through a questionnaire in order to ascertain whether this fear is impacted at all by the predictability of the planned eating intervention that the participant is being asked to follow. In the case of any event of serious hypoglycemia in between structured meetings and calls, participants will be instructed to contact their study physician either directly, or through the RD, to determine any needed adjustments to the planned eating plan or insulin dosing.

Eating and Physical Activity Pattern
In order to assess participants' baseline eating and physical activity patterns and inform the design of the individualized planned eating plan, a questionnaire will also be administered to participants during the pre-trial data collection that queries frequency and timing of meals, snacks, insulin administration, and physical activity on week days and weekends. The questionnaire will also collect how frequency and timing of participants' weekday or weekend meals, snacks, and physical activity vary from day-to-day. Participants will be asked whether they take insulin each time they eat a snack or meal, and will be asked to report any common variability in this practice. They will also be queried about hypoglycemic events. Additionally, participants will be asked about carbohydrate counting for insulin dosing and any other dietary intake planning method they or their caregivers/parents use, if applicable. The questionnaire will also assess participant waking and sleeping times and the extent to which these times vary throughout the week.

In addition to providing information about baseline eating pattern, two 24-hour dietary recalls will be collected at baseline and at 6 months to assess change in dietary behavior and adherence to the planned eating plan. Recalls will be obtained by telephone by trained and certified interviewers from the UNC NIH/NIDDK Nutrition Obesity Research Center (NORC) staff (P30DK056350; MPI Mayer-Davis) under the direction of Dr. Mayer-Davis (Diet Assessment Core Director), using the Nutrient Data System for Research (NDSR) software and the multiple pass interviewing method.[12,13]

The *Previous Day Physical Activity Recall (PDPAR)* will also be administered to help ascertain baseline physical activity pattern and contextualize glycemic levels observed in the trial. The validated[14,15] *Previous Day Physical Activity Recall (PDPAR)* will be

under the direction of the UNC NORC, to be administered concurrent with the 24-hr dietary recalls, as we have done previously.[16] The PDPAR divides the day into half-hour time blocks and queries the dominant activity and the approximate intensity of that activity for that period, categorized as ‘‘light,’’ ‘‘medium,’’ ‘‘hard,’’ or ‘‘very hard.’’

To assist participants and families in planning meals and snacks that align with participants' individualized planned eating plans, participants will be given a subscription to MyFitnessPal Premium, which will also conveniently serve as the platform through which mobile phone logs are collected. Any changes to the personalized eating plan made throughout the study will be captured in Qualtrics.

Because it is possible that planful eating may also affect types of foods consumed, we will also administer a food frequency questionnaire at baseline and end of the study to capture dietary quality throughout the study.

MyFitnessPal logs
Eating pattern and physical activity will be monitored via participant mobile phone logs collected through MyFitnessPal.

In addition to the 24-hour dietary recalls, the logs collected during the first two weeks will be used to understand participants' preferred foods and timing of snacks and meals. This information will inform the design of the individualized planned eating plan. This information will also be used to inform the design of a sample menu of meals and snacks that will be introduced to and adjusted with the participant on the first week of the active intervention (week 3). Participants will therefore be instructed to follow their usual eating and physical activity habits during this run-in week, and RDs will emphasize that honesty in logging usual habits will optimize the RD's ability to design a planned eating plan that fits into the participant's lifestyle and is sustainable. Once the planned eating plan has been designed and delivered to the participant in the first week of the active intervention (week 3), subsequent logs collected throughout the intervention period will facilitate discussions about challenges with adherence, focus problem solving and goal setting, and inform needed adjustments to the planned eating plan. As discussed in a subsequent section, adherence to logging will be used to allocate points/incentive money to participants throughout the study.

Other Health Information
At the Pre-Trial Data Collection Visit, we will conduct a medical chart review to collect basic demographics, including birth date, sex, ethnicity, and race. Medical chart review will also enable ascertainment of date of diabetes diagnosis, diabetes care (i.e. insulin regimen), and other relevant health history.

9. Trial Procedures and Components

The schedule of intervention sessions, measurements, and questionnaires is depicted in **Figure 3** below.

Figure 3. MyPlan Study Schedule of Intervention Sessions, Measurements, Questionnaires

Participant Timeline	In-Person Visits	Remote Video Sessions with Dietician	Remote Food and Exercise Measurements	Remote Questionnaires
Week 1	HbA1c, Height, Weight *Insert CGM*	1 session	MyFitnessPal logs 1 weekday 1 weekend 24-hour recall	Most Questionnaires
Week 3-10	*Mail back CGM (Week 3)*	8 sessions *(every week)*	MyFitnessPal logs	Eating Plan Questionnaires *(Week 3)*
Week 12-24	*Receive CGM (Week 21)* *Insert CGM (Week 22)*	7 sessions *(every other week)*	MyFitnessPal logs 1 weekday 1 weekend 24-hour recall *(Week 22)*	Acceptability Questionnaire *(Week 14)*
Week 26	HbA1c, Height, Weight *Return CGM*			All Questionnaires

In-person visits

Participants and their parents/guardians will attend two in-person measurement visits at baseline and end (26 weeks) of the intervention. HbA1c, height, and weight will be collected at these time points. Although participants will be sent questionnaires electronically ahead of the measurement visit, participants will finish any outstanding questionnaires in person to ensure data completeness. At the baseline visit, after consent/assent is completed, the participants will be given the blinded CGM, and explained how to insert it independently. They will insert it at the Baseline session with the study dietician. Participants will be provided a pre-paid envelope to send back the CGM after 2 weeks of wear time. Participants will receive another CGM in the mail at 22 weeks, which they will insert independently to avoid the burden of another in-person visit. They will receive virtual insertion assistance from the study dietician at the 22 week session. They will return the CGM at the 26 week in-person visit. Two 24-hour dietary and physical activity recalls will be collected during the 2 week CGM wear time at both time points.

Counseling and online intervention sessions

A dietitian will meet with the participant via HIPAA compliant videoconference every week for the first 2 months, and bi-weekly for the last 4 months. Sessions will involve a structured behavior change counseling module focused on a) anticipating barriers to adhering to the eating behavior pattern b) developing and revising SMART goals focused on meeting the five targets that comprise the eating behavior pattern, and c) adding on new goals or increasing the challenge level of goals week to week. The structured behavior change counseling module is designed so that participants will incrementally improve behavioral alignment with the eating behavior pattern throughout

the study. The design, underpinned by the previously described conceptual framework, also considers that motivation, self-efficacy, knowledge, and baseline eating behavior will shape the rate at which participants increase the number of goals they set, how advanced the goals are (i.e., meet carbohydrate target at lunch vs. meet carbohydrate target at lunch and improve carbohydrate quality), and ultimately, how closely they adhere with the eating behavior pattern.

In addition to the content of the intervention sessions themselves, which will focus goal setting on meeting the eating behavior pattern and target psychosocial barriers to behavior change, we will use other behavior change strategies to promote adherence. Participants will log their food intake and physical activity in MyFitnessPal at least three days per week throughout the study. The benefits of self-monitoring for behavior change have been widely documented and MyFitnessPal has features (i.e., carbohydrate estimation) that facilitate choosing types and amounts of food that align with the eating behavior pattern.[95,96] Logs collected during the 2 week baseline period will reflect usual intake, which together with the 24-hour recalls collected at baseline and a questionnaire about usual eating pattern, will help the dietician understand participant preferred foods and eating schedule. This information will be incorporated into the eating behavior pattern the dietician presents to the participant and parent at the first intervention session to enhance acceptability and adherence to the pattern. The logs collected throughout the study will also enable the dietician to remotely monitor adherence to the eating behavior pattern between sessions, provide personalized feedback, help the participant troubleshoot barriers to adherence, and focus goal setting around the eating behavior targets the participants find particularly challenging.

Logs will additionally be used by dieticians to reward participants with points for achieving their goals every week. In order to maintain participant engagement with logging and meeting weekly goals, participants will earn points that translate into dollars based on the number of days they log and the number of goals they achieve throughout the course of the intervention –for a total possible incentive amount of 200 USD. Incentives are discussed in greater detail in the following section

Participant incentives

The point/incentive allocation scheme **(Table 2)** is designed to incentivize participants to complete all questionnaires/measurements, maximize the number of days they log and the number of eating behavior targets they try to meet each week, and minimize disengagement over the course of the intervention.

Table 2. MyPlan Study Point/Incentive Allocation Procedure

Intervention Activity	Point Allocation Procedure	Total Possible Points	Total Possible Incentive Amount (USD)[2]
Mobile phone logs	3 points for 3 days of logs per week 2 points per each additional day	275	137.50
Goals	1 point per each goal met[1]	116	58
Measurements/ questionnaires	3 points for completing assessments at each time point	9	4.50

1. Goals are considered met if ≥2 of required 3 log days reflect participant adherence to goal. To incentivize logging, best 3 log days will be used to ascertain goal achievement

2. A conversion of 2 points per dollar translates into a total possible incentive of 200 USD

To reduce the risk of logging fatigue, participants will be asked to log all their meals, snacks, and physical activity on a minimum of three days per week, but will receive points for each additional day they log above the minimum. This minimum of three logs per week will be required to reward the participant with points for making progress towards their goals (i.e., points for meeting the goals focused on the targets that define

the eating behavior pattern). Participants will receive points for every goal they set as long as they meet the goal on at least two of the three required days of logs. The best three days of logs will be used to assess goal attainment, so that participants are incentivized instead of penalized for logging more than the minimum, since more days of logs may reveal more days where the participant struggle to meet their goals. Participants will receive text reminders on the three minimum days they are expected to log. Study staff will monitor logs throughout the week, and the RD will reach out such to troubleshoot logging issues with participants and encourage participants to get back on track if they have not completed any logs.

To promote logging adherence, the dietician will thoroughly instruct the participant and parent/guardian how to log in MyFitnessPal, provide additional resources for navigating MyFitnessPal, and help troubleshoot barriers to logging at the beginning of the study. Dieticians will monitor logging adherence over time, so that in the case that participants begin to disengage from logging, additional strategies will be used to keep the participant engaged in self-monitoring such as simpler MyFitnessPal logs (i.e., entry of grams of carbohydrate at each meal and snack and the corresponding time), paper/pdf logs (i.e., entry of number of carbohydrate servings/exchanges per meal and the corresponding time), and having parents systematically help with logging.

To encourage the participant adherence, the RD will review the number of points the participant has earned each week as well as the total possible points that can be earned the upcoming week. The total amount of incentive earned by the participant will be disbursed upon completion of the study. In the case of study withdrawal, participants will receive an incentive amount based on the total number of points they earned up until study withdrawal.

Parent/guardian involvement in online intervention sessions

Parent/guardian will be required to attend the first three online counseling sessions in order to learn how to log in MyFitnessPal, become familiar with the eating behavior pattern, and understand the process of setting and revising SMART goals session-to-session. This information will enable the parent to support participant adherence to logging and meeting goals week-to-week, (i.e., parent/guardian can ensure meal times, cooking, and grocery shopping are supportive of participant's eating behavior pattern). The parent/guardian will also attend the midpoint online intervention session when the eating behavior pattern will be formally reviewed and revised based on participant and parent/guardian acceptability.

10. Data management

All data will be transmitted to UNC, which serves as the Coordinating Center as was done for the FLEX trial. To ensure impeccable data quality and cost efficiency for this pilot work, we will build on the secure data management system (RedCAP) already in place at UNC for our MyPlan feasibility work. All questionnaires collected at baseline, 3 months, and 6 months of the intervention will be completed by participants in RedCAP. The counseling guide that the RD uses to deliver online intervention sessions with participants will be created in Qualtrics, which ensures standardization of content delivery within and across study participants, while also enabling certain process and intermediary outcome data are captured. The eligibility questionnaire used as part of recruitment will also be created in Qualtrics.

11. Statistical Considerations

Statistical power

Power analyses are based on matched-pairs t-tests and a conservative estimate of 40 participants (alpha level of 0.05). Drawing from our previous study with a similar population to estimate the within-subject correlation, we have 80% power to detect an improvement in TIR of 10%.[94] In this previous study, the average TIR was 34.7% (SD=13.6), so this would correspond to an increase to an average of 42.5% TIR. The detectable effects are large, which is appropriate in this study that aims to assess preliminary effectiveness and acceptability to inform the design of a future fully-powered RCT of longer duration.

Outcome evaluation

Aim 1. Assess acceptability and adherence to a 6-month individualized planned eating intervention ("MyPlan") among 40 youth with T1D.

1) **Adherence:**

We will calculate and report continuous and categorical overall adherence to the eating behavior pattern and adherence specific to each of the five eating behavior targets that make up the pattern (i.e. mean number of eating behavior targets met, proportion of participants who met each type of target, proportion of individuals who met 0, 1, 2, 3, 4, or 5 targets). Further exploratory modeling will be conducted to identify the contributions that adherence to each of the five individual behavioral targets make to overall adherence scores, as well as the relative magnitude of associations between adherence to each of the five individual behavioral targets and glycemic measures.

Acceptability:

- We will calculate continuous and categorical participant and guardian acceptability of the eating behavior pattern. Additional analyses include combined composite scores, exploratory modeling of demographic, clinical, and psychosocial predictors of acceptability will be conducted to inform both recruitment and targeted counseling strategies in future trials. We will assess acceptability related themes that emerge from answers to questionnaire free response items and questions posed as part of the qualitative post-hoc analysis of the intervention.

Aim 2. Compare glycemic control among adolescents with T1D at baseline and at the end of the 6month MyPlan intervention.

2) **Effect on glycemic control:**

We will compare continuous difference in TIR under the eating behavior pattern (22-24 weeks) vs. usual diet (0-2 weeks). We hypothesize that a) $TIR_{\text{MyPlan eating behavior pattern}} > TIR_{\text{usual diet}}$

a) Matched-pairs t-tests will compare average TIR at 22-24 weeks vs. 0-2 weeks (overall and stratified by day/night)

b) Linear regression modeling will examine whether change in overall degree of adherence (comparing the two 24-hour recall days at 22-24 weeks and two 24-hour recall days during 0-2 weeks) is associated with average change in 14 day TIR at endline vs. baseline

c) Linear regression modeling will examine whether change in overall degree of adherence (comparing the two 24-hour recall days at 22-24 weeks and two 24-hour recall days at during 0-2 weeks) is associated with change in TIR using the two days of CGM data at 22-24 weeks and 0-2 weeks that are matched to the two 24-hour recalls collected at those time points.

d) Exploratory linear regression modeling will assess whether the differences in TIR observed in models (a) (b) and (c) above persist after adjustment for self-management technology use (i.e., insulin pump vs. multiple daily injections, routine personal CGM use), physical activity, and other key clinical and demographic factors (i.e., age, sex, insurance status, parental education or other measure of socioeconomic status). Before including any of these factors in the model, we will examine their distributions as well as their bivariate associations with TIR to assess the magnitude, precision, and functional form of the relationship. An *a priori* ranking of the relative importance of these factors based on theory and existing literature will also inform the sequence with which we add them to the model. Changes in magnitude and precision of beta coefficients when different combinations of the variables are included in the model will also be considered in selection of the fully adjusted model.

e) As part of the post-hoc qualitative evaluation of the MyPlan pilot intervention (detailed in a subsequent section), we will more deeply explore potential reasons underlying why the MyPlan eating behavior strategy may have improved or failed to improve participants' glycemic management to identify intervention levers for future studies. We will probe participants and staff about their perceived effectiveness of the strategy and reasons for this self-reported effectiveness via interviews and focus groups with project staff and a sub-sample of participants.

Process evaluation

To identify the "active ingredients" and intermediary outcomes that may explain the observed results of the intervention and help inform future efforts to change eating behavior in the study population, we will collect a series of additional measures **(Table 3)** to enable a robust process evaluation.

Table 3. MyPlan Process and Intermediary Outcome Measures
Fidelity checklist coded with Behavior Change Technique Taxonomy (BCT)
Number of sessions attended by participants
Number of sessions attended by parents
Number of logs completed
Type of logs completed (i.e. original, simple, paper)
Number of goals met
Number of points earned
Participant perceived challenge level of goals
RD perceived challenge level of goals set

Optional counseling/educational materials used
Adjustments made to the eating behavior pattern throughout trial
Semi-structured interview questions from post-hoc qualitative evaluation (focus groups with MyPlan staff, interviews and focus groups with responder and non-responder teenagers and parents)

Intervention sessions will be coded *a priori* with Behavior Change Technique Taxonomy (BCTs) based on the activities, messaging, and counseling techniques to be delivered by the dietician, which will produce a checklist for each session.[103,104] Fidelity will be assessed by audio-recording all intervention sessions and coding the sessions for alignment with this checklist. Modeling will also explore the type and frequency of BCTs delivered that are associated with the outcomes observed. Number of points achieved by participants (i.e., number of logs made, number of goals met), characteristics of goals set by participants (i.e., type of goal areas focused on, self-perceived and dietician perceived challenge level of the goal), number and type of optional counseling/educational materials delivered, level of parental involvement, and adjustments made to the eating behavior pattern throughout the course of the study will also be reported and examined in association with study outcomes.

Post-hoc qualitative evaluation of the MyPlan pilot

A qualitative evaluation of the MyPlan pilot will also be undertaken via focus groups and interviews with MyPlan project staff who implemented the intervention, as well as a sub-sample of teenage and parent project participants who will be purposively sampled from intervention responders and non-responders (responder = participant or parent of participant who experienced an improvement in HbA1c or TIR over between baseline and endline, non-responder = participant or parent of participant who experienced no change or deterioration in HbA1c or TIR between baseline and endline). Financial and human resources available nearing project completion will guide the number of teenager and parent participants sampled, and comprise no fewer than 10% of the teenager and parent participants. The purpose of this evaluation is to complement the quantitative process and outcome data collected by the MyPlan project and inform refinement of the MyPlan intervention and its implementation to improve **efficacy** and **implementation** in future studies and real-world clinical settings. As such, qualitative questions will be selected according to each of the dimensions of the RE-AIM framework. In order to promote obtainment of unbiased perspectives from project staff and participants and minimize recall bias, this evaluation will occur within 12 months of project completion, and will be conducted by independent researchers who played no role in project implementation.

12. Potential Risks, Discomforts, Inconveniences, & Precautions:

Potential Risks

Since the majority of the data collection will occur at the CCHMC and NC TraCS with medical confidentiality safeguards in place, the potential risks to study subjects are minimal and do not exceed what occurs in a routine visit to the CCHMC and UNC Pediatric Endocrinology. Safeguards will be taken to code, encrypt and lock access to study data, thus, the risk of disclosure of medical information is low (see protection against risks for further details). All data collection instruments are benign in nature or are used in routine care assessment at the CCHMC and UNC Pediatric Endocrinology without any adverse effects or risks. No social or legal risks could be identified. The physical risks from the study do not exceed what occurs as a result of routine care at the

CCHMC and UNC Pediatric Endocrinology. This could include slight pain associated with the finger stick for accessing blood for point of care HbA1c or with sensor insertion for CGM and unanticipated impact on glycemic control as a result of dietary intervention. (e.g., potential embarrassment about answering questions related to adherence). The completion of diet recalls using MyFitnessPal © app and questionnaires could be burdensome; however, we will work with adolescents to make data collection as easy and meaningful as possible.

Adequacy of Protection against Risks

Recruitment and Informed Consent

Research staff at the clinical sites will obtain written informed consent from parents and assent from youth. The study consent and assent forms will explain the purpose of the study and measures taken to protect confidentiality (e.g., the data will not be linked with personal identifying information). Patients and their parents will be assured that participation is voluntary and that non-participation will not result in any consequences to them. In addition, they will be informed that they may withdraw from the study at any time without consequences. Finally, youth and parents are informed that the data are used exclusively for research purposes, that identifying data will not be released by the investigators to their families or to any other individual or organization, and that any identifying information will be destroyed at the end of the project. In soliciting the cooperation of each adolescent in our study, we will stress the data safeguards that will be taken to protect the confidentiality of the survey and other data. Minimizing the risk of disclosure requires careful data safeguards. Most important is the need to prevent the association of an individual's name with sensitive information. We will keep participants' names separate from their survey responses and other data and store the link between names and study identification numbers in a password-protected file that is accessible only to authorized staff at the respective clinical sites. Consent and assent will be documented via signature on electronic copy consent and assent forms. Parents and participants will be provided a copy of the consent/assent documents. Date of consent/assent will be documented in the study data management system.

Protections against Risk

All institutions associated with this study are experienced with handling sensitive and confidential data. Routine administrative, personnel, physical security, information management, and computer system or network security practices are always in place given the policies and the requirements for safeguards consistent with the management of PHI at both clinical sites. All PHI will be used or disclosed in compliance with the Health Insurance Portability and Accountability Act (HIPAA). Forms will be kept in password protected files when not in use. Subjects will be assigned identification numbers in lieu of names on data management and data analysis files. A master list of identification numbers and names will be kept separate from all data base files and will be maintained in a password protected file that is accessible only to authorized staff at the respective clinical sites. Upon completion of the study, these files will be

destroyed. No individual PHI will be used in reports or manuscripts. Data entered and stored on the microcomputer will be archived daily. The data collectors will follow a strict written protocol that describes study measures for protecting data privacy. Patients and parents always have the right to refuse to participate or to refuse to answer any individual question they might find objectionable. Raw data will be cleaned and edited prior to data entry, and again once data are entered. Databases will not contain any identifying information. We will develop a master database of the data collection for all participants.

The physical risks to adolescents in this study are the same as those that would occur as a result of routine nutrition care; however, any adverse changes in glycemic control as a result of dietary intervention will be reported to CCHMC and UNC providers and medical staff who will evaluate these cases individually. Study personnel will be trained to identify the signs and symptoms of a blood glucose level that is low or high. They will also be trained to check the blood glucose level if necessary, using a glucometer. Any youth experiencing hypo/hyperglycemia or an otherwise potentially expected symptom related to diabetes will be encouraged by study personnel to consult their diabetes care provider or to go to the emergency room immediately as needed. Local medical policies and procedures for handling adverse events in clinic will be followed. If participants experience hypoglycemia or hyperglycemia outside of study visits, they will be advised to treat these situations per their usual diabetes care plan. Participants will receive the results for study HbA1c and CGM measurements after the study. Their providers will also receive these results. Participants and their parents will be encouraged to discuss their results with their providers.

The interventionists (Registered Dietitians) and study physicians will communicate regularly (verbally and in writing per protocol) regarding glucose control so that any changes in medical management can be made in a timely fashion, as it is understood that with changes in dietary patterns, adjustments in medical management for glycemic control may be needed.

At each study visit and RD check-in call, hypoglycemia events will be reviewed with the participant. Participants will be asked to notify the study team within 48 hours of any severe hypoglycemic event (seizure, coma, or need for glucagon administration).

Psychological and social risks are expected to be minimal as previously discussed. We will briefly query use of illegal behaviors including recreational drug and alcohol use as these may impact on adherence and priorities for problem solving as relates to diabetes self management. If participants reveal information that indicates that he or she is a risk to self or others, research staff will follow local clinic site procedures, including mandated reporting. Participants will be informed, as part of the informed consent process, regarding the limitations of confidentiality.

Vulnerable Subjects

Children ages 12-17 at enrollment are included in this study as we are specifically examining the impact of structured eating on adolescents with Type 1 diabetes. We anticipate this research does not involve greater than minimal risk given that the participant will maintain usual diabetes care and suggested changes made to the participant's eating pattern will be individualized. Changes in eating will be monitored by the study registered dietitians, pediatric endocrinologists, and investigators. As described earlier, adequate provisions will be put in place to ensure both parent and child are allowed to provide consent and assent respectively.

13. Risk/Benefit Analysis

Potential Benefits of the Proposed Research to Human Subjects and Others

The proposed research may lead to potential benefits for individuals with diabetes, including improved glycemic control, and thus reduced risk of both short- and long-term complications. The risks to participants are reasonable in relation to the anticipated benefits to participants and others because: the risks are judged to be minimal and unlikely; safeguards against these risks are in place, and the potential benefits are important, both to individuals who participate in the study and to the broader population of individuals with T1D.

Importance of the Knowledge to be Gained

This study should yield new information contributing to the self-management of diabetes and the use of structured eating combined with behavioral strategies to manage glycemic variation. This knowledge may lead to better care for adolescents with diabetes. The development of a feasible and effective novel intervention for adolescents far outweighs potential risk of harm. We anticipate the risk associated with these dietary and behavioral changes does not involve greater than the risk associated with routing diabetes care, while potential for impact on improved glycemic control for youth with diabetes has potential long-term implications for current and future health of youth with diabetes.

Single IRB Plan

We plan to comply with the sIRB plan by obtaining consent from UNC's Institutional Review Board. University of Cincinnati and Cincinnati Children's Hospital and Medical Center will rely on UNC's approval with sites signing an authorization/reliance agreement that will clarify the role and responsibilities of the sIRB and the relying sites. Communication between the OH site and the UNC IRB will be facilitated by the UNC study project manager, Joan Thomas. UNC Department of Nutrition and the UNC IRB will maintain the records for the authorization/reliance agreements along with documentation of the associated communication plan.

14. Data Safety & Monitoring:

Data Safety and Monitoring Plan

To ensure timely completion of the study, MPIs Mayer-Davis and Couch, study endocrinologists (Shah and Jain) and program manager (Angelica Cristello Sarteau), will constitute the study Executive Committee that will meet weekly during the first six months and bi-weekly thereafter to oversee progress, participant well-being, data quality and completion, and problem-solve as needed. A 3-member DSMB will be convened to meet three times over the course of the study via video conference call. These meetings will be held prior to the start of the study, mid-way through the study, and at the end of the study. DSMB members represent expertise in endocrinology, nutrition, and study design and statistical analysis. Prior to the start of the study, the DSMB will review and approve the final study protocol and any significant changes to the protocol over the course of the study especially as related to participant burden or safety. Midway through the study, the DSMB will meet to monitor and advise on study participant accrual and retention, progress and completeness for all standardized measurement visits and attendance at intervention sessions. Data quality will be reviewed and staff training and certification will be monitored. Adverse events will be monitored. A summary of the DSMB report will be sent to both the local site IRBs and NIDDK as part of the annual progress reports.

Members of the DSMB have been identified by area of scientific expertise (all with relevant expertise applied to T1D), are non-conflicted, and have agreed to serve:

- Pediatric Endocrinology: Ingrid Libman, MD, PhD, MPH Associate Professor of Pediatrics and Epidemiology, Director, Diabetes Program, UPMC Children's Hospital of Pittsburgh
- Nutrition: Abigail Peairs, PhD, Associate Professor, Department of Rehabilitation, Exercise and Nutrition Sciences, University of Cincinnati
- Study Design and Statistical Analysis: Baiming Zou, PhD, Gillings School of Global Public Health, University of North Carolina, Chapel Hill

Data Monitoring

Questionnaires will be administered to participants. Data will also be obtained via CGM, HbA1c point of care measurement, and dietary recalls. All aspects of data collection and data storage will be carefully monitored to ensure rapid detection of errors, inconsistencies or other problems. The data collectors will follow a strict written protocol that describes study measures for protecting data privacy. They will explain to each participant that s/he has the right to refuse to participate or to refuse to answer any individual question that s/he finds objectionable, and emphasize the importance of telling the truth. All institutions associated with this application are experienced in training data collection fieldwork personnel how to handle, store, and process sensitive and confidential data. Certain routine administrative, personnel, physical security, information management, and computer system or network security practices are always in

place. These practices include building and audio-tape vault security, non-disclosure pledges, and account/keyword security on computer networks. In addition, we take multiple project-specific steps to protect subjects from the risk of a breach in confidentiality. All data will be collected using study identification numbers. Thus, no questionnaire will contain identifying information, and the list that links identification numbers to names will be kept in a password-protected file that is accessible only to authorized staff at the respective clinical sites. Only aggregate data that cannot be used to identify individuals will be included in any reports released to other agencies or for publication.

Adverse Events

The intervention will involve individuals with T1D who are 12-17 years of age. It is unlikely that participation in our studies will cause youth to experience an "adverse event." However, trained staff will be conducting the intervention sessions to address any potential issues. Any youth experiencing hypo/hyperglycemia or an otherwise potentially expected symptom related to diabetes will be encouraged to consult their diabetes care provider or to go to the emergency room immediately as needed.
For purposes of monitoring and reporting adverse events, the following NIH definitions will be used:
Adverse Event (AE): any unanticipated, untoward medical occurrence that may present itself during treatment or administration of an intervention, and which may or may not have a causal relationship with the treatment. Adverse events could arise from the study (e.g., breach of confidentiality) or could arise due to the population under study.
Serious Adverse Event (SAE): Any medical occurrence that results in death; is life-threatening; requires inpatient hospitalization or prolongation of existing hospitalizations; creates persistent or significant disability/incapacity, or a congenital anomaly/birth defect.

It is highly unlikely that participation in the dietary intervention will cause an AE or SAE. Should an AE occur, however, the research dietitian and study coordinator will immediately report any AE's connected to the implementation of the intervention to the study investigators, who will keep a log of AE's and SAE's. The log will also be used to provide information about AE's in annual progress reports to participating IRBs and NIDDK.

Our team will file a written report to the site IRBs in accordance with local IRB requirements, and to NIDDK. Outcomes for AE's will be monitored by the DSMB and outcome information will be entered into a log for inclusion in reports to participating IRBs and NIDDK as required. Anticipated events relative to the population under study or relative to the study (e.g., low or high blood glucose) will be noted as potential risks on the informed consent form. The DSMB will also monitor the occurrence of these events. Should any other problems or concerns arise with the data collection or intervention program, the PI or local clinical PI will be available to address these. In addition, resource

and referral listings for community services will also be provided on a routine basis as needed. Drs. Mayer-Davis, Couch, Jain and Shah will also work extensively with the staff at each of the clinics to ensure that if adolescents need to be referred that these situations are managed in a manner consistent with clinic preferences/ policies.

The following grading scale will be used to adjudicate AE/SAEs.

Study Relatedness:	*Action Taken:*	*Status:*
1=Definitely Unrelated	*0 = None*	*1 = Resolved*
2=Possibly Related	*1 = Counteractive Medication*	*2 = Recovered with minor sequelae*
3=Probably Related	*2 = Medical/surgical intervention*	*3 = Recovered with major sequelae*
4=Definitely Related	*3 = Hospitalization*	*4 = Condition still present and under treatment*
5=Diabetes Related; Definitely Unrelated	*4 = Other (specify under comments)*	*5 = Condition continues to worsen*
		6 = Patient died

All AEs will be reviewed by the study Data and Safety Monitoring Board to determine if an AE is related to the research project. Our team will file a written report to the site IRBs in accordance with local IRB requirements. Outcomes for AE's will be monitored by the DSMB and outcome information will be entered into a log for inclusion in reports to participating IRBs and NIDDK as required.

Anticipated events relevant to the population under study (e.g., low or high blood glucose) will be noted as potential risks on the informed consent form. The DSMB will also monitor the occurrence of these events. The study PIs will also work with the staff at each of the clinics to ensure that if participants need to be referred, these situations are managed in a manner consistent with clinic preferences/policies.

Should any other problems or concerns arise with the data collection or intervention program, the PI or local clinical PI will be available to address these.

15. Privacy & Confidentiality

In-person recruitment will occur in the diabetes clinics by study personnel. Study visits will occur in private settings or on secure videoconference platforms. Unencrypted messaging will only occur between study personnel and parents reminding them of study sessions, encouraging them to complete questionnaires or other study activities, and only if they consent. Encrypted e-mails and text messages will be sent to minors to encourage and remind them.

To minimize the risk of loss of confidentiality, all information related to study subjects will be confidential and kept in a locked cabinet or in password-protected computer files, in compliance with NIH and HIPAA requirements as detailed in NIH Notice OD-020 issued December 30, 2004.

Each participant will be assigned a unique study identification (ID) number. Participants will be identified on all study-related documents only by their study ID numbers. The roster containing the unique identifying number and direct participant identifiers will be kept in a local password-protected database on a secure network drive at the clinical sites.

Almost all data will be entered in REDcap or Qualtrics. Only in rare cases will hard copy data collection forms be used, and this data will be entered like the data collected electronically within 1 week of collection and the hard copy will be subsequently destroyed. Data will be entered onto a secure Web-based data management system. Only the study coordinator and relevant research study staff will have access to this study database. Secure access will be assured by use of individual login codes and password protection. Entered data will be stored securely and accessed in accordance with current HIPAA standards, the HCFA's Internet Security Policy, and other state and local requirements.

All data interactions for the study by all users including participants, RDs, clinical staff, research staff, and investigators, are web-based communications between the given user's web browser and the web server running the study website and/or data management software. All of these web-based communications are configured to use the standard HTTPS protocol with 128-bit encryption. This includes online forms submitted by participants as they are transferred to the servers at UNC.

For the purposes of tracking recruitment, scheduling, and reminders, basic participant information, including first and last name, Study ID, and dates and other pertinent information regarding scheduled appointments (reminder calls, etc.) will be kept in a password-protected Microsoft Access database stored securely at each clinical site.

As is the case with all behavior intervention utilizing current technology, particularly mobile phones, we will explain to participants that transmission of such information is not secure.

All aspects of data collection and data storage will be carefully monitored to ensure rapid detection of errors, inconsistencies or other problems. The data collectors will follow a strict written protocol that describes study measures for protecting data privacy, explain to each participant that s/he has the right to refuse to participate or to refuse to answer any individual question that s/he finds objectionable, and emphasize the importance of telling the truth. All institutions associated with this study are experienced in training data collection fieldwork personnel how to handle, store, and process sensitive and confidential data. Certain routine administrative, personnel, physical security, information management, and computer system or network security practices are always in place. These practices include non-disclosure pledges, and account/keyword security on computer networks.

In addition, we take multiple project-specific steps to protect subjects from the risk of a breach in confidentiality. All data will be collected using study ID numbers. Thus, no questionnaire will contain identifying information, and the roster containing the unique identifying number and direct participant identifiers will be kept in a local password-protected database on a secure network drive at the clinical sites. Finally, only aggregate data that cannot be used to identify individuals will be included in any reports released to other agencies or for publication.

16. Study Timeline

The study is planned to complete in May 2023. The timeline is as follows [see detailed table in spreadsheet]:

IRB approval: March 2021
Staff training: April/May 2021
Participant recruitment: October 2021
Intervention: December 2021 – May 2023
Analysis, Abstract and Publication preparation: January – December 2024

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