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TABLE OF CONTENTS

Table of Contents iii
Abbreviations and Definitions of Terms v
Abstract vi
Protocol Synopsis vii
Table 1: Schedule of Study Procedures x

1 BACKGROUND INFORMATION AND RATIONALE 1

1.1 INTRODUCTION 1
1.2 DESCRIPTION OF THE INTERVENTION 1
1.3 RELEVANT LITERATURE AND DATA 1
1.4 COMPLIANCE STATEMENT 3

2 STUDY OBJECTIVES 3

2.1 PRIMARY OBJECTIVE (OR AIM) 3
2.2 SECONDARY OBJECTIVES (OR AIM) 3

3 INVESTIGATIONAL PLAN 4

3.1 GENERAL SCHEMA OF STUDY DESIGN 4
3.1.1 Family Partner Program Input *4*
3.1.2 Screening Period *4*
3.1.3 Baseline Period *4*
3.1.4 Intervention Period *4*
3.1.5 Follow-up Period *5*
3.2 ALLOCATION TO TREATMENT GROUPS AND BLINDING 5
3.3 STUDY DURATION, ENROLLMENT AND NUMBER OF SITES 5
3.3.1 Duration of Subject Study Participation *5*
3.3.2 Total Number of Study Sites/Total Number of Subjects Projected *5*
3.4 STUDY POPULATION 5
3.4.1 Inclusion Criteria for Children *5*
3.4.2 Exclusion Criteria for Children *6*
3.4.3 Inclusion Criteria for Parents/Legal Guardians *6*

4 STUDY PROCEDURES 7

4.1 SCREENING PERIOD 7
4.2 BASELINE PERIOD 7
4.3 INTERVENTION PERIOD 7
4.4 FOLLOW-UP PERIOD 8
4.5 SUBJECT COMPLETION/WITHDRAWAL 8

5 STUDY EVALUATIONS AND MEASUREMENTS 9

5.1 SCREENING AND MONITORING EVALUATIONS AND MEASUREMENTS 9
5.1.1 Screening Questionnaire *9*
5.1.2 Medical Record Review *9*
5.1.3 Child Questionnaire *9*
5.1.4 Parent Questionnaire *9*
5.1.5 DXA Scan *9*
5.1.6 Anthropometry *10*
5.1.7 Continuous Glucose Monitoring *10*
5.1.8 Sleep and Physical Activity Tracker *10*
5.1.9 24-hour Dietary Recalls *10*
5.1.10 Penn Usual Diet Survey *10*
5.1.11 Urine Samples *10*
5.2 EFFICACY EVALUATIONS 11

5.2.1 Diet Quality Outcomes (Aim 1) ... *11*
5.2.2 Urinary Metabolite Outcomes (Aim 2) ... *11*
5.3 SAFETY EVALUATION ... 11

6 STATISTICAL CONSIDERATIONS ... 12

6.1 PRIMARY ENDPOINT ... 12
6.2 SECONDARY ENDPOINTS ... 12
6.3 STATISTICAL METHODS ... 12
6.3.1 Baseline Data ... *12*
6.3.2 Efficacy Analysis ... *12*
6.4 SAMPLE SIZE AND POWER ... 13

7 STUDY INTERVENTION ... 13

7.1 DESCRIPTION ... 13

8 SAFETY MANAGEMENT ... 14

8.1 CLINICAL ADVERSE EVENTS ... 14
8.2 ADVERSE EVENT REPORTING ... 14

9 STUDY ADMINISTRATION ... 14

9.1 TREATMENT ASSIGNMENT METHODS ... 14
9.1.1 Randomization ... *14*
9.1.2 Blinding ... *14*
9.2 DATA COLLECTION AND MANAGEMENT ... 14
9.3 CONFIDENTIALITY ... 15
9.4 REGULATORY AND ETHICAL CONSIDERATIONS ... 15
9.4.1 Data and Safety Monitoring Plan ... *15*
9.4.2 Risk Assessment ... *15*
9.4.3 Potential Benefits of Trial Participation ... *16*
9.4.4 Risk-Benefit Assessment ... *16*
9.5 RECRUITMENT STRATEGY ... 16
9.6 INFORMED CONSENT/ASSENT AND HIPAA AUTHORIZATION ... 17
9.6.1 Screening ... *17*
9.6.2 Main Study ... *17*
9.6.3 Individuals with Limited English Proficiency ... *17*
9.7 PAYMENT TO SUBJECTS/FAMILIES ... 18
9.7.1 Payments to children for time, effort and inconvenience (i.e. compensation) ... *18*
9.7.2 Payments to parents for time, effort, and inconvenience ... *18*

10 PUBLICATION ... 19

11 REFERENCES ... 19

Appendix ... 24
Appendix A: List of Exclusionary Medications ... 24

ABBREVIATIONS AND DEFINITIONS OF TERMS

AE	Adverse event
BMI	Body Mass Index
CGM	Continous Glucose Monitor
CHOP	Children's Hospital of Philadelphia
CHPS	Center for Human Phenomic Science
DXA	Dual Energy X-ray Absorptiometry
HEI	Healthy Eating Index
K	Potassium
MOST	Multiphase Optimization Strategy
Na	Sodium
NDSR	Nutrient Data System for Research
NMR	Nuclear Magnetic Resonance
RCT	Randomized Controlled Trial

ABSTRACT

Context: (Background)

Improving diet quality is an essential component for the treatment of adolescent obesity. Pediatric providers are recommended to incorporate nutrition recommendations as part of adolescent obesity treatment, but time and knowledge are barriers. Digital-based interventions have been shown to improve fruit and vegetable intake in adolescents. However, we do not know if a digital-based diet quality intervention is feasible or effective for adolescents with overweight or obesity.

Objectives: (primary and important secondary objectives)

The overarching objective of this pilot study is to demonstrate if a digital-based diet quality intervention for adolescents with overweight or obesity is feasible and if there is preliminary effectiveness that diet quality and meal timing traits improves as assessed by 24-hr dietary recalls, a novel urine biomarker, and continuous glucose monitoring (CGM).

Study Design:

A two-arm pilot randomized controlled trial (RCT) falling under the preparation phase of the Multiphase Optimization Strategy (MOST) framework.

Setting/Participants:

This is a single site study. Adolescents (N=14, aged 14-17 years) at risk for diet quality that is low or in need of improvement (Healthy Eating Index (HEI) < 80) and with a history of having overweight or obesity (body mass index (BMI) between the 85th and 99th percentile on at least two occasions six months apart in the medical record in the last five years) will be invited to participate. Clinical measurements will be acquired at the Children's Hospital of Philadelphia (CHOP). Diet, urine, blood glucose, physical activity, and sleep data collection will take place in the home setting.

Study Interventions and Measures:

We will randomize adolescents and their parents to receive a) usual care or b) a nutrition intervention with personal goals, meal timing, nutrition skills, and home food environment intervention components. The content for each component will be delivered through text messaging. Three 24-hr dietary recalls and the first morning urine void on two separate occasions will be collected at baseline and follow-up. HEI-2020 scores will be calculated and change in HEI-2020 will be the primary outcome. The urine Na:K will be quantified and change in Na:K will be the secondary outcome.

PROTOCOL SYNOPSIS

Study Title	Digital Intervention to Improve Diet Quality in Adolescents with Overweight or Obesity
Funder	National Center for Advancing Translational Sciences, National Institutes of Health (Grant #: UL1TR001878) Metabolism, Nutrition, and Development Research Affinity Group Pilot Program
Study Rationale	Adolescent obesity is highly prevalent (22%) and is linked to multiple chronic diseases in adulthood with high financial consequences. Diet improvement is a key strategy that is part of adolescent obesity treatment. Pediatric providers should incorporate nutrition recommendations at annual well-visits, especially for patients with overweight or obesity, but face several barriers (e.g., lack of knowledge, training, and time). A solution to this problem is to develop digital-based dietary interventions with standardized delivery of effective dietary guidance to overcome knowledge and training deficits. Further, the guidance can be delivered using text messaging to reach families in their home/community setting, to amplify any nutrition care received at in-person visits.
Study Objective(s)	**Primary** • The overarching goal of this pilot and feasibility RCT is to demonstrate if a mobile health nutrition intervention can improve diet quality and meal timing traits as assessed by gold-standard 24-hr dietary recalls, a novel nutrition biomarker, and CGM. • Aim 1: Determine if a digital nutrition intervention improves HEI-2020 scores. • Aim 2: Determine if a digital nutrition intervention improves Na:K ratio.
Study Design	A two-arm pilot randomized controlled trial (RCT) falling under the preparation phase of the Multiphase Optimization Strategy (MOST) framework.
Subject Population key criteria for Inclusion and Exclusion:	**Inclusion Criteria** 1. Aged 14-17 years old. 2. At risk for diet quality that is poor or needs improvement (HEI score < 80) determined by participants baseline 24-hour diet recall data. 3. Body mass index between the 85th and 99th percentile for age and sex on at least two occasions at least six months apart in the medical record in the last five years.

	4. Have access to a phone capable of receiving text messages. **Exclusion Criteria** 1. History of an eating disorder diagnosis (e.g., anorexia nervosa, bulimia nervosa, binge eating disorder, avoidant restrictive food intake disorder). 2. History of a condition that may alter dietary intake (e.g., diabetes, Celiac's disease, phenylketonuria, cystic fibrosis). 3. Regularly taking medications that may result in weight loss, appetite stimulation or suppression, and/or fluctuations in fluid status. 4. Currently being followed by a registered dietitian. 5. Pregnant or lactating females. 6. Have a parent, guardian, or family member that works for the Division of Gastroenterology, Hepatology, and Nutrition at CHOP.
Number Of Subjects	14
Study Duration	Up to 8 weeks
Study Periods **Screening** **Baseline** **Intervention** **Follow-Up**	1. Online Screening Questionnaire 2. 1 to 2-Week Baseline Period (consent, surveys, anthropometric measures, DXA scan, CGM, sleep and physical activity tracker, 24hr dietary recalls, urine samples) 3. 4-Week Control or Intervention Period (CGM, sleep and physical activity tracker, interview with dietitian) 4. 1-Week Follow-Up Period (CGM, sleep tracker and physical activity, 24hr dietary recalls, urine samples, closing interview)
Efficacy Evaluations	For aim 1, the primary outcome will be change in overall HEI-2020 score. HEI-2020 scores will be derived from dietary data collected through three 24-hour dietary recalls at baseline and follow-up and processed using Nutrient Data System for Research software. For aim 2, the primary outcome will be change in urinary sodium (Na) to potassium (K) ratio. Participants will collect their urine from their first morning voids at baseline and follow-up. The urine will be sent to CHOP for biobanking and proton nuclear magnetic resonance (NMR) will be used to measure Na and K. This provides an objective measure of high Na (e.g., processed foods) and K (e.g., fruits and vegetables) in the diet.
Statistical And Analytic Plan	Linear mixed effect models will test if HEI-2020 and Na:K change over time and if the changes differ by experimental arms by

	including time (0=baseline and 1=follow-up), study arm (0=control & 1=intervention) and a time-by-arm interaction as fixed effects.
DATA AND SAFETY MONITORING PLAN	Data and safety monitoring will occur continuously throughout the study period. The PI will meet weekly with research staff to monitor enrollment data, demographics, participant status, protocol deviations, adverse events, frequency of sysmptoms or concerns reported, and out-of-range values. These data will also be reported at monthly meetings with the co-investigators.

TABLE 1: SCHEDULE OF STUDY PROCEDURES

Study Period	**Screening**	**Baseline Period**		**Intervention Period**		**Follow-up Period**
Where	**Home**	**CHOP**	**Home**	**Home**		**Home**
Days in Period	**NA**	**0**	**9-13**	**28**		**7**
				Control	**Intervention**	
HIPAA Authorization	X					
Screening Survey	X					
Informed Consent/Assent		X				
Child and Parent Questionnaires		X				X
Anthropometry and DXA[a]		X				
Continous Glucose Monitor			X	X	X	X
Sleep Tracker			X	X	X	X
Physical Activity Tracker			X	X	X	X
Dietary Recall			X			X
Urine Samples			X			X
Randomization			X[b]			
Dietitian Interview					X	X
Intervention Component Text Messages					X	
Exit Survey						X

Note: Screening, baseline and follow-up phase procedures will be the same for both the control and intervention arms.

[a] If participants are female, a urine pregnancy test will be completed prior to the DXA scan.

[b] Randomization will occur on the last day of the baseline period.

1 BACKGROUND INFORMATION AND RATIONALE

1.1 Introduction

Adolescent obesity is highly prevalent (22%)[1-5] and is linked to multiple chronic diseases in adulthood[6] with high financial consequences.[7] Diet improvement is a key strategy that can help to treat adolescent obesity.[8-10] Pediatric providers should incorporate nutrition recommendations at annual well-visits but face several barriers (e.g., lack of knowledge, training, and time).[11, 12] A solution to this problem is to develop digital-based dietary interventions with standardized delivery of effective dietary guidance to overcome knowledge and training deficits. Further, the guidance can be delivered using text messaging to reach families in their home/community setting, to amplify any nutrition care received at in-person visits. This study will pilot a digital-based diet intervention for adolescents with overweight or obesity for intended future use in the pediatric healthcare setting.

1.2 Description of the Intervention

A MOST framework *preparation phase*, pilot RCT will address the study aims. First, participants will be screened using data from their medical record and an online questionnaire. Eligible participants will be invited to the Center for Human Phenomic Science (CHPS) for baseline study measures. Participants will then be randomized to the control arm or intervention arm (1:1 ratio) using a random number assignment. The control arm will not receive any intervention materials. The intervention arm includes four components: personalized goal, meal timing, nutrition skills, and engagement strategies. The intervention period will be four weeks, followed by a one week follow-up. Though this may introduce bias, blinding of study personnel will not be used due to their role in the personalized goal component. It is not possible to blind participants to the intervention content.

1.3 Relevant Literature and Data

Healthy Eating Index (HEI)

The Healthy Eating Index (HEI) is derived from dietary intake data (e.g., 24-hour dietary recalls) and provides a measure of diet quality. The index ranges from 0 to 100, with a greater score indicating greater adherence to the Dietary Guidelines for Americans (DGA).[13] Higher intake of nine adequacy (total fruits, whole fruits, total vegetables, greens and beans, whole grains, dairy, total protein foods, seafood and plant proteins, and fatty acids) and lower intake of four moderation (refined grains, sodium, added sugars, and saturated fats) components contributes to a higher HEI-2020 score. Our data show that among adolescents in the Philadelphia region, the average HEI score was 45±13, indicating diet quality was low. Moreover, none of the adolescents had "good" diet quality (i.e., HEI score >79).[14] This aligns with other data at the national level,[13] and confirms the need for diet quality improvement interventions. This study also found that there are many paths to having a low diet quality, indicating that personalized interventions to improve diet quality are needed.[14]

Multiphase Opitmization Strategy Framework

Late evening energy intake due to misalignment with circadian rhythms may contribute to obesity.[15-18] Our data show that among adolescents, many had a late evening energy intake dietary profile, which was nominally associated with higher fat mass.[19]

In person interventions that targeted nutrition education,[20] cooking skills,[21] and limiting obesogenic foods within the home[22] showed improved diet quality. There is emerging evidence that digital health strategies can improve fruit and vegetable intake in adolescents,[23, 24] but few focused on adolescents with overweight or obesity or used a personalized digital communication strategy.[25-28]

MOST is an engineer inspired framework to develop multi-component interventions[29-33] and includes three phases: *preparation, optimization*, and *evaluation*.[34, 35] This study will use the MOST framework as a guide for developing the proposed digital diet quality intervention for pediatric healthcare. This project falls within the *preparation phase*; it will specifically test the candidate intervention components in a pilot RCT, where the intervention arm includes personalized goals, meal timing, and nutrition skills components.

Objective Assessment of Diet, Chrononutrition, and Body Composition

Weighed food records, 24-hour dietary recalls, and food frequency questionnaires provide valid assessments of dietary intake in youth.[36] Urinary metabolite analyses could supplement these measures and offer objective insight into diet quality changes in intervention studies.[37-40] This approach is currently being applied to assist with dietary quality screening in adults at the University of Pennsylvania by Dr. Gary Wu. Of promise, the Na:K can indicate the degree to which an adolescent consumes a high sodium, low fruit and vegetable diet.[41]

The field of chrononutrition is relatively new and elucidates the association between meal timing patterns, circadian rhythms, and metabolic health (e.g., obesity).[42] Chrononutrition was the focus of a recent workshop by the National Heart, Lung, and Blood Institute of the National Institutes of Health (NIH) as this aligns with the NIH Common Fund's Nutrition for Precision Health Research Plan.[43] Late evening energy intake due to misalignment with circadian rhythms may contribute to obesity.[15-18] A major knowledge gap relates to how to assess timing of energy intake in both observational and interventional studies. Although three-day 24-hr dietary recalls are the standard for assessing dietary intake (i.e., intake of macro- and micronutrients), a limitation of this method is that it requires respondents to recall over the last 24 hours the types, amounts, and preparation methods of all foods and beverages consumed as well as the times of each eating occasion.[36] CGM has been used to monitor adherence to time limited eating (TLE) interventions in adolescents with obesity, where participants are advised to eat within a prescribed window and as such, glucose spikes can be expected within that window.[44, 45] However, CGM has not been used to estimate meal timing patterns in observational and/or less restrictive meal timing interventions and has potential to be a useful addition to 24-hr dietary recalls limited by recall bias.

Additionally, total carbohydrates are the primary macronutrient impacting postprandial glycemic responses, but several other diet components (e.g., type of carbohydrate, protein and

fat content, nutrient sequence within an eating occasion) also play an important role.[46] With regards to timing of macronutrient intake, eating a greater proportion of calories and macronutrients earlier in the day has been shown to improve weight, glycemic control, and hunger regulation.[46] Further, within a meal, the timing of macronutrient consumption regulates postprandial glycemic response.[47, 48]

With regards to body composition, skinfolds, air displacement plesmythography (ADP), dual energy x-ray absorptiometry (DXA), and ultrasound provide reliable estimates of percent body fat, fat mass, and fat free mass in youth with overweight or obesity.[49] Randomized controlled trials altering the intake of certain components of the HEI (e.g., dairy, added sugars) have improved estimates of body composition in children and adolescents over time.[50] However, interventions examining the impact altering the individual and cumulative intake of other components of the HEI (e.g., fruits, vegetables, sodium) has on body composition are limited.

1.4 Compliance Statement

This study will be conducted in full accordance with all applicable CHOP Research Policies and Procedures and all applicable Federal and state laws and regulations including 45 CFR 46. All episodes of noncompliance will be documented.

The investigators will perform the study in accordance with this protocol, will obtain consent and assent, and will report unanticipated problems involving risks to subjects or others in accordance with CHOP IRB Policies and Procedures and all federal requirements. Collection, recording, and reporting of data will be accurate and will ensure the privacy, health, and welfare of research subjects during and after the study.

2 STUDY OBJECTIVES

The overarching goal of this pilot and feasibility RCT is to demonstrate if a mobile health nutrition intervention can improve diet quality and meal timing traits as assessed by gold-standard 24-hr dietary recalls, a novel nutrition biomarker, and CGM. Our central hypothesis is that we will demonstrate feasibility of a mobile health nutrition intervention to improve diet quality.

2.1 Primary Objective (or Aim)

Determine if a digital nutrition intervention improves HEI-2020 scores.

Determine if a digital nutrition intervention improves Na:K.

2.2 Secondary Objectives (or Aim)

Determine if a digital nutrition intervention improves meal timing traits.

3 INVESTIGATIONAL PLAN

3.1 General Schema of Study Design

This single site trial will randomize 14 child-parent dyads to either receive or not receive intervention materials. Before beginning the 4-week intervention period, 3-day 24-hour dietary recalls will be collected to measure baseline diet quality. After the intervention period, 3-day 24-hour dietary recalls will be repeated to measure changes in diet quality from baseline. Clinical measurements (e.g., DXA) will be obtained at baseline. Glycemic profiles, sleep, and physical activity will be obtained during the baseline, intervention, and follow-up phases.

3.1.1 Family Partner Program Input

The Family Partners Program at CHOP will invite adults of youth to the monthly Family Advisory Council meeting. Attending adults will provide general feedback on study related questions. The family consultants will complete the online Family and Youth Research Education (FYREworks) program, which is designed to help researchers, children, and families work together to answer questions about children's health.

3.1.2 Screening Period

A parent/guardian will complete an online screening questionnaire to determine eligibility. Prior to completing the screening questionnaire, the parent/guardian will read the HIPAA authorization form and will provide their authorization by means of an electronic signature. The parent/guardian will then be directed to complete the eligibility screening questions online. Once eligibility has been confirmed, a study team member will contact the parent/guardian to verify eligibility and schedule a time to attend the in-person baseline study visit.

3.1.3 Baseline Period

Participants who pass the screening period will be invited to CHOP for an in-person study visit. Prior to any research procedures, the parent/guardian and child will complete the informed consent/assent process. At this visit, the parent/guardian and child will complete questionnaires. In addition, the child will complete clinical assessments (anthropometry and DXA scan). Research staff will provide participants with a CGM (DG6 Model, Dexcom, San Diego, CA) and sleep/physical activity tracker (Flex2, Fitbit, San Francisco, CA) at the end of their baseline visit to wear for up to seven weeks. Three 24-hour dietary recalls and two urine samples will be collected at home in the week immediately following the baseline visit to CHOP. Baseline HEI-2020 score will be calculated from the baseline 24-hour dietary recalls; participants with a baseline HEI-2020 score > 80 will not be eligible to participate in the remainder of the study. Otherwise, participants will be randomized to the control arm or intervention arm (1:1 ratio) using a random number assignment upon completion of the baseline phase procedures.

3.1.4 Intervention Period

The control arm will not receive any intervention materials. The trial duration will be four weeks. The intervention arm includes five components: personalized goal, meal timing,

nutrition skills, home food environment, and engagement strategies. The specific number, design and content of the text messages for each component will be prepared and vetted by the investigators and by adolescents and parents through CHOP's Family Partners Program prior to study launch. The text messages will be sent through the REDCap Twilio integration. Participants will continue to wear the CGM and sleep/physical activity tracker for the duration of the intervention phase.

3.1.5 Follow-up Period

Upon completing the four week intervention period, participants will be contacted to complete three additional 24-hour dietary recalls and two urine samples. Participants will continue to wear the CGM and sleep tracker for the duration of the follow-up phase (up to 7 days) and the parent/guardian and child will complete questionnaires, including an exit survey to assess intervention acceptability.

3.2 Allocation to Treatment Groups and Blinding

Participants will be randomized to the control arm or intervention arm (1:1 ratio) using a random number assignment. It is not possible to blind participants to the intervention content.

3.3 Study Duration, Enrollment and Number of Sites

3.3.1 Duration of Subject Study Participation

The study duration per subject will be up to 8 weeks. This includes 1 day in screening, up to 13 days in the baseline phase, 28 days in the intervention phase and 7 days in the follow-up phase.

3.3.2 Total Number of Study Sites/Total Number of Subjects Projected

The study will be conducted at one investigative site in the United States.

Recruitment will stop when 14 evaluable subjects are enrolled. It is expected that approximately 210 subjects will be enrolled to produce 14 evaluable subjects.

3.4 Study Population

3.4.1 Inclusion Criteria for Children

1) Males or females age 14 to 17 years.
2) At risk for diet quality that is poor or needs improvement (HEI score < 80) determined by participants' baseline 24-hour diet recall data.
3) History of having overweight or obesity (having a BMI between the 85th and 99th percentile on at least two occasions at least six months apart in the medical record in the last five years).
4) Have access to a phone capable of receiving text messages.
5) Speak, read and write in English.

6) All females must have a negative urine pregnancy test.

7) Parental/guardian permission (informed consent) and if appropriate, child assent.

3.4.2 Exclusion Criteria for Children

1) A history of an eating disorder diagnosis (e.g., anorexia nervosa, bulimia nervosa, binge eating disorder, avoidant restrictive food intake disorder).

2) A history of a condition that may alter dietary intake (e.g., diabetes, Celiac's disease, phenylketonureia, cystic fibrosis)

3) Regularly taking prescribed medications that may result in weight loss, appetite stimulation, appetite suppression and/or fluctuations in fluid status (Appendix A).

4) Currently being followed by a registered dietitian.
5) Pregnant or lactating females.

6) Have a parent/guardian or a family member that works for the Division of Gastroenterology, Hepatology, and Nutrition at CHOP.

3.4.3 Inclusion Criteria for Parents/Legal Guardians

1) Be the parent/guardian of an eligible participant enrolled in the main study.

2) Be at least 18 years of age.

3) Speak, read and write in English.

4) Are compliant with study schedules and procedures.

Subjects that do not meet all of the enrollment criteria may not be enrolled. Any violations of these criteria must be reported in accordance with CHOP IRB Policies and Procedures.

4 STUDY PROCEDURES

4.1 Screening Period

- Parent/guardian HIPAA Authorization and completion of online screening questionnaire (parent/guardian on behalf of child).
- If found to be eligible, the parent/guardian and their child will be invited to CHOP for a study visit.

4.2 Baseline Period

Informed assent/consent: Trained staff will complete the informed consent form process prior to any study measurement and will document that they followed all elements of the consent process. Parent/guardians will provide consent and the children will provide their assent.

Child questionnaire: The questionnaires will capture participant contact information, demographics, home information, eating behavior, cooking and food skills, chrononutrition, physical activity, and sleep.

Parent questionnaire: The questionnaire will capture parent contact information, demographics, pregnancy and early life information, eating behavior, cooking and food skills, and the home food environment. The child's participation will not be impacted by the parent's decision to complete the questionnaires.

Anthropometric measures (child): We will measure height, weight, and waist circumference.

DXA scan (child): We will use a DXA scanner to measure the amount of fat, lean and bone tissue in each child participant.

Continuous Glucose Monitor (child): We will use a Dexcom G6 CGM to measure blood glucose profiles.

Sleep Tracker (child): We will use a Fitbit to measure physical activity and sleep.

Diet Assessment (child): The participants will be asked to recall the foods and drinks consumed in the past 24 hours on three occasions, during the week following their in person visit. Participants will also be asked to complete a diet screener on the same days as their diet recalls.

Urine samples (child): The participants will be asked to collect their first morning void on two occasions, during the week following their in person visit on the same days as their dietary recall.

Randomization (child): Participants will be randomized to the intervention or control arm.

4.3 Intervention Period

Dietitian interview and personalized goal component (child): Participants will complete an interview with a registered dietitian (Lead Investigator: Jessica Decker) to review their baseline HEI data and establish their personalized dietary goals. This will be done virtually during the intervention phase.

- Meal timing component: Participants will receive information on why eating later at night is detrimental and specific strategies on how to limit eating past 8pm in the evening. This information will be delivered by text message during the 4-week intervention period.
- Nutrition skills component: Participants will receive nutrition education text messages, using adolescent specific guidance from the Dietary Guidelines for Americans. They will also receive text messages on how to improve cooking skills to enhance their self-efficacy for meal preparation (e.g., safe meal preparation).
- Home food environment component: Participants will receive text messages on how to better select and prepare foods in the home environment (e.g., fruit and vegetable availability).
- Engagement strategies: We will design and implement text messages that recognize participant time and effort (e.g., text badges in recognition of completing the first study week).

- Continuous Glucose Monitor (child): We will use a Dexcom G6 CGM to measure blood glucose profiles.

- Sleep Tracker (child): We will use a Fitbit to measure physical activity and sleep.

4.4 Follow-up Period

Child questionnaire: The questionnaires will capture eating behavior, cooking and food skills, chrononutrition, physical activity, and sleep. An exit survey will also be collected to assess intervention acceptability.

Parent questionnaire: The questionnaire will capture parent eating behavior, cooking and food skills, and the home food environment. The child's participation will not be impacted by the parent's decision to complete the questionnaires.

Continuous Glucose Monitor (child): We will use a Dexcom G6 CGM to measure blood glucose profiles.

Sleep Tracker (child): We will use a Fitbit to measure physical activity and sleep.

24-hour dietary recalls (child): The participants will be asked to recall the foods and drinks consumed in the past 24 hours on three occasions. Participants will also be asked to complete a diet screener on the same days as their diet recalls.

Urine samples (child): The participants will be asked to collect their first morning void on two occasions.

4.5 Subject Completion/Withdrawal

Subjects may withdraw from the study at any time without prejudice to their care. They may also be discontinued from the study at the discretion of the Investigator for lack of adherence to study treatment or visit schedules. The Investigator may also withdraw subjects who violate the study plan or for administrative reasons. It will be documented whether or not each subject completes the clinical study.

5 STUDY EVALUATIONS AND MEASUREMENTS

5.1 Screening and Monitoring Evaluations and Measurements

5.1.1 Screening Questionnaire

A parent/guardian will complete an online screening form to assess for eligibility according to the inclusion and exclusion criteria in section 3.4 of this protocol. The parent/guardian will complete an online electronic screening HIPAA authorization to agree to answer the questions related to the health status of their child.

5.1.2 Medical Record Review

We will extract the following measurements from each participant's electronic medical record for screening purposes: date of birth, sex, race and ethnicity, active medications list, height, and weight.

5.1.3 Child Questionnaire

In the child questionnaire, we will capture participant contact information, demographics, home information, eating behavior, cooking and food skills, chrononutrition, physical activity, and sleep. Cooking and food skills will be assessed from questions validated by Lavelle et al[51]. Chrononutrition will be assessed from the Chrononutritio Profile Questionnaire[52]. Physical activity will be assessed by the Evaluation of Activity Surveys for Youth (EASY)[53]. Sleep will be assessed by the PROMIS Sleep Disturbance and Sleep Related Impairment survey[54]. During the follow-up period, participants will also complete an exit survey to determine intervention acceptability. Research staff will assist children with the completion of their questionnaire at the in-person visit.

5.1.4 Parent Questionnaire

In the parent questionnaire, we will capture parent contact information, demographics, pregnancy and early life information, eating behavior, cooking and food skills, and the home food environment. Cooking and food skills will be assessed from questions validated by Lavelle et al[51]. The home food environment will be assessed by the home food inventory validated by Fulkerson et al[55].

5.1.5 DXA Scan

We will use a DXA scanner to measure the amount of fat, lean and bone tissue in each participant. This method uses a very low powered X-ray beam to scan the entire body. The results are analyzed by computer, which provides an estimate of the amount and density of bones, fat mass and muscle mass. The whole body scan takes less than 5 minutes. It will take about 20 minutes to complete this procedure because staff will need time to properly position participants and calibrate the machine. In the event of movement during the scan, we will attempt to repeat a scan up to two times (a total of 3 tries). The radiation used in this machine is very minimal. This is the standard method for measuring fat mass, bone mineralization and body composition, and is considered safe for children. A urine pregnancy test will be performed for all female subjects.

5.1.6 Anthropometry

Trained staff in CHOP's Nutrition and Growth Lab will measure height, weight, and waist circumference. It will take approximately 5 minutes to complete these measurements.

5.1.7 Continuous Glucose Monitoring

We will use a Dexcom G6 CGM to measure blood glucose profiles. The Dexcom G6 is currently in clinical use at CHOP. These data will be collected and synced through a smartphone application and stored within Clarity software (Version 2.22.0). The data will be stored in 5-minute intervals for all four weeks of the study period. From the CGM data, on weekday and weekend days, we will calculate time of first and last meal, first and last meal mid-point, duration of overnight fast, regularity of energy consumption, and eating occasion frequency. The following measures will be calculated from the CGM data at the daily meal level and aggregated daily level: mean standard deviation, maximum, and minimum glucose measurements.

5.1.8 Sleep and Physical Activity Tracker

We will use a Fitbit to measure sleep and physical activity. These data will be accessed using the Fitbit/REDCap integration. The Fitbit Flex 2 uses a micro electro-mechanical system (MEMS) 3-axis accelerometer, which tracks motion patterns. Using proprietary algorithms, estimates of time in bed and total sleep time per day are accessible through the Fitbit application. Physical activity (active minutes and steps per day) will also be estimated from the Fitbit devices.

5.1.9 24-hour Dietary Recalls

Trained research staff will call the participants three times during each of the following study periods: baseline and follow-up. The participants will be asked to recall the foods and drinks they have consumed in the past 24 hours. This dietary intake data will be entered into a computer program to estimate total energy intake, macronutrient intake, and micronutrient intake.

5.1.10 Penn Usual Diet Survey

Participants will be asked to complete the Penn Usual Diet Survey at baseline and follow-up. These data will be compared to data collected from 24-hour dietary recalls.

5.1.11 Urine Samples

The participants will be asked to collect their first morning void on two occasions at baseline and follow-up. Participants will be provided with towelette(s) and a pre-labeled urine collection cup and provided with sex-specific instructions to collect clean-catch urine. Samples will be shipped from participants' homes to the CHOP Biorepository Center for processing, aliquoting, and biobanking. De-identified samples will be shipped to the University of Pennsylvania for sodium and potassium quantification and to Penn State University for proton NMR analysis.

5.2 Efficacy Evaluations

5.2.1 Diet Quality Outcomes (Aim 1)

For aim 1, the primary outcome will be change in overall HEI-2020 score. HEI-2020 scores will be derived from dietary data collected through three 24-hour dietary recalls at baseline and follow-up and processed using Nutrient Data System for Research software.

5.2.2 Urinary Metabolite Outcomes (Aim 2)

For aim 2, the primary outcome will be change in urinary Na:K. Participants will collect their urine from their first morning voids at baseline and follow-up. The urine will be sent to CHOP for biobanking and proton NMR will be used to measure Na and K. This provides an objective measure of high sodium (e.g., processed foods) and potassium (e.g., fruits and vegetables) in the diet.

5.3 Safety Evaluation

Subject safety will be monitored by adverse events and PI oversight.

6 STATISTICAL CONSIDERATIONS

6.1 Primary Endpoint

Aim 1: The primary outcome will be change in overall HEI-2020 score from baseline measured by 3-day 24-hour dietary recalls.

Aim 2: The primary outcome will be change in urinary Na:K from baseline measured by 2-first morning voids.

6.2 Secondary Endpoints

Secondary endpoints will include the following:

- The change in intake of adequacy components of the HEI.
- The change in intake of moderation components of the HEI.
- The change in assessment of nutrition skills.
- The change in assessment of the home food envionrment.
- The change in timing of energy intake.
- Frequency of daily glucose excursions.
- Change in postprandial glycemic responses from baseline measured by CGM.
- Agreement in meal timing measures from 24-hour dietary recalls and CGM.
- Association between total HEI and intake of adequacy and moderation components of the HEI and body composition at baseline.
- Frequency of participants rating the intervention as acceptable.

6.3 Statistical Methods

6.3.1 Baseline Data

Baseline and demographic characteristics will be summarized by standard descriptive summaries (e.g. means and standard deviations for continuous variables such as age and percentages for categorical variables such as gender).

6.3.2 Efficacy Analysis

The primary analysis will be based on an intention-to-treat approach and will include all subjects randomized at Visit 1.

For aim 1, the primary outcome will be change in overall HEI-2020 score. HEI-2020 scores will be derived from dietary data collected through three 24-hour dietary recalls at screening, baseline and follow-up and processed using Nutrient Data System for Research software. For aim 2, the primary outcome will be change in urinary Na:K. Participants will collect their urine from their first morning voids at baseline and follow-up. The urine will be sent to CHOP for biobanking and proton nuclear magnetic resonance (NMR) will be used to measure Na

and K. This provides an objective measure of high sodium (e.g., processed foods) and potassium (e.g., fruits and vegetables) in the diet. Linear mixed effect models will test if HEI-2020 and Na:K change over time and if the changes differ by experimental arms by including time (0=baseline and 1=follow-up), study arm (0=control & 1=intervention) and a time-by-arm interaction as fixed effects. Using the same linear mixed model approach, exploratory analyses will be performed to assess if cooking skills, home food environment, and timing of energy intake are more favorable in the intervention versus control arm. For aim 3, the primary outcome will be change in postprandial glycemic responses. Correlations will be performed to assess the degree of agreement in self-reported meal timing and CGM estimated meal timing. Linear mixed effect models will test if the macronutrient composition of a meal impacts postprandial glycemic responses. Linear mixed effect models will test if the intervention positively impacted meal timing traits assessed by CGM by including time (0=baseline; 1=intervention), study arm (0=control; 1=intervention) and a time-by-arm interaction as fixed effects.

6.4 Sample Size and Power

Feasibility will be determined based on recruitment and retention metrics, and acceptability of the digital intervention via a post-intervention exit survey. This is a pilot study; the data generated will inform the power calculation in a future fully powered study.

7 STUDY INTERVENTION

7.1 Description

This study will pilot a digital-based diet intervention for adolescents with overweight or obesity for intended use in the pediatric healthcare setting.

The intervention arm includes four components. The specific number, design and content of the text messages for each component will be prepared and vetted by the investigators and by adolescents and parents through CHOP's Family Partners Program prior to study launch. The text messages will be sent through the REDCap Twilio integration.

1. *Personalized Goal.* Participants will complete an interview with a registered dietitian to review their baseline HEI data. This will be done virtually during the first two weeks of the intervention period. With the guidance of the dietitian, participants will identify three SMART goals aimed towards improving their overall diet quality. If the call cannot be scheduled during this time frame, participants will receive three standard SMART goals aimed towards improving their oval diet quality through text message.
2. *Meal Timing*. Participants will receive information on why eating later at night is detrimental and specific strategies on how to limit eating past 8pm in the evening. This information will be delivered by text message during the 4-week intervention period.
3. *Nutrition Skills*. Participants will receive nutrition education text messages, using adolescent specific guidance from the Dietary Guidelines for Americans. They will also receive text messages on how to improve cooking skills to enhance their self-efficacy for meal preparation (e.g., safe meal preparation).

4. *Home Food Environment*. Participants will receive text messages on how to better select and prepare foods in the home environment (e.g., fruit and vegetable availability).
5. *Engagement Strategies*. We will design and implement text messages that recognize participant time and effort (e.g., text badges in recognition of completing the first study week).

8 SAFETY MANAGEMENT

8.1 Clinical Adverse Events

Clinical adverse events (AEs) will be monitored throughout the study.

8.2 Adverse Event Reporting

Since the study procedures are not greater than minimal risk, SAEs are not expected. If any unanticipated problems related to the research involving risks to subjects or others happen during the course of this study (including SAEs) they will be reported to the IRB in accordance with CHOP IRB SOP 408: Unanticipated Problems Involving Risks to Subjects. AEs that do not meet prompt reporting requirements will be summarized in narrative or other format and submitted to the IRB at the time of continuing review (if continuing reviews are required), or will be tracked and documented internally by the study team but not submitted to the IRB (if continuing reviews are not required).

9 STUDY ADMINISTRATION

9.1 Treatment Assignment Methods

9.1.1 Randomization

Participants will be randomized to the control arm or intervention arm (1:1 ratio) using a random number assignment.

9.1.2 Blinding

Though this may introduce bias, blinding of study personnel will not be used due to their role in the personalized goal component. It is not possible to blind participants to the intervention content.

9.2 Data Collection and Management

1. Confidentiality. Confidentiality of the data will be ensured by using password-protected files. Data will be collected and managed using password-protected Excel and REDCap databases. Excel databases will be stored on a password-protected research shared drive at CHOP that is only accessible to approved staff. Data downloaded from REDCap will be stored on a password-protected research shared drive at CHOP that is only accessible to approved staff. Analytical datasets will be stored on a password-protected research shared drive at CHOP. Unique study ID's will be used in analytical datasets.

2. Security. All data will be stored on secure, password-ptotected servers. REDCap is a secure, HIPAA-compliant application for data collection and storage that provides

logging of all project activity and data entry history for all records, as well as HIPAA-compliant security and daily backups. Data stored in Excel spreadsheets and data that are downloaded from REDCap will be stored on a password-protected CHOP, HIPAA-compliant research shared drive that is only available on the CHOP network, is backed-up daily, and supported by CHOP Research Information Services.

3. Destruction. Data will be maintined for at least six years before being destroyed.

9.3 Confidentiality

No identifiable data will be used for future studies without first obtaining IRB approval or determination of exemption. The investigator will obtain a data use agreement between the provider (the PI) of the data and any recipient researchers (including others at CHOP) before sharing a limited dataset (PHI limited to dates and zip codes).

9.4 Regulatory and Ethical Considerations

9.4.1 Data and Safety Monitoring Plan

The Data and Safety Monitoring Plan includes the following elements: study identification information; an overview of the study objectives; a confidentiality section; an adverse event section; a data quality and safety review plan section; an informed consent/assent process section; and a reporting changes in study status section. Template tables and figures will be used to report data and safety information including: enrollment data, demographics, participant status, protocol deviations, adverse events, frequency of symptoms or concerns reported, and out-of-range values.

Data and safety monitoring will occur continuously throughout the study period. The PI will meet weekly with the research staff to monitor enrollment data, demographics, participant status, protocol deviations, adverse events, frequency of symptoms or concerns reported, and out-of-range values. These data will also be reported at monthly key investigator meetings with the co-investigators.

For data security, survey data will be entered directly into the online REDCap database. The PI will periodically review data entered into REDCap. The PI will generate datasets for final analyses; and all analytical datasets and source codes will be preserved on a secure research shared drive at CHOP.

The CHOP PI will monitor and review the study progress, subject safety, and the accuracy and security of the emerging data. There are no plans for interim analyses in this study. Therefore, there are no stopping rules for this study. This decision is based on the minimal risk to participant safety of the proposed research.

9.4.2 Risk Assessment

This study involves risks that are not greater than minimal.

Questionnaire Risks: There are no physical risks associated with completing questionnaires, but participants might experience momentary embarrassment or discomfort. Participants do not have to answer any questions that make them too uncomfortable.

Identity Risks: We cannot guarantee total privacy. Participant's personal information may be given out if required by law. Name and other personal information will not be used at scientific meeting or in publications. Participants will be assigned a study number. Their name and other identifying information will be securely stored in password-protected databases that are HIPAA compliant and designed for research data management.

Anthropemetric Exam Risks: The potential risks associated with the anthropometric exam include distress and embarrassment. However, these are minimal as height, weight and limb lengths will be measured in a private room by trained personnel.

DXA Risks: The DXA scans will expose participants to a small amount of radiation. These scans are acceptable for use in infants, children, adolescents and adults. The scans will be performed at the Nutrition and Growth Lab at CHOP by highly trained staff and the need for repeated scans will be very unlikely. A maximum of two repeat scans (three in total) will be performed at a single visit to minimize radiation exposure. All female subjects will complete a pregnancy test prior to being exposed to any radiation and will be excluded if the test is positive.

CGM Risks: The risks of wearing the CGM are minimal. Bruising can occur. Mild skin irritation is common. Rarely an infection can occur at the site of CGM sensor needle placement. An allergic reaction to the tape used to hold the sensor in place is possible.

Sleep Tracker Risks: There is a potential for skin irritation.

9.4.3 Potential Benefits of Trial Participation

Our proposed research will provide essential pilot data that is needed to demonstrate feasibility of a mobile health intervention to improve diet quality in adolescents. Participants may benefit directly from our research if they respond positively to the intervention. Given the low risks associated with participation in this study, the potential benefits to knowledge outweight the risks.

9.4.4 Risk-Benefit Assessment

Potential risks to the participants are minimal and the intervention has potential to benefit the dietary patterns of adolescents.

9.5 Recruitment Strategy

Recruitment will be achieved through the CHOP Primary Care Network in collaboration with CHOP's Recruitment Enhancement Core, Pediatric Research Consortium, and Community Relations Team. Participants aged 14-17y with a history of having a BMI between the 85th and 99th percentile on at least two occasions at least six months apart in the medical record in the last five years will be identified in the electronic health record. They will be contacted and invited to participate by email or mailed letters. Additionally, study

information will be posted on the CHOP Research Discovery page and in This Week at CHOP newsletters. Finally, tearpads will be posted in select CHOP primary care sites.

We request a waiver of consent/assent/HIPAA authorization to query the electronic health record to identify patients diagnosed with BMIs from the 85th to 99th percentile, aged 14-17y, not taking medications that may result in weight loss, and not diagnosed with any behavioral or psychiatric disorders.

9.6 Informed Consent/Assent and HIPAA Authorization

9.6.1 Screening

A stand-alone online HIPAA Authorization form will be used to acquire parent/guardian consent prior to completing the online screening questionnaire (we request a waiver of assent for this step in our study as the child may not always be with their parent/guardian when completing the screening questionnaire). Parents will have the option to either save it to their computer or print it out.

9.6.2 Main Study

We will acquire e-consent from the parents and written e-assent from the children. We will send a copy of the informed consent/assent form for families to review prior to their study visit. The parent and their eligible child will meet with a trained research coordinator prior to the baseline visit (via video call) or at the baseline visit in a private room, to review the electronic consent/ assent documents. If the consent meeting takes place via video call, Microsoft Teams, a HIPAA compliant application, will be used. Participants will be informed that they do not have to sign the e-consent form and that participation in the study is completely voluntary. The families will have as much time as they need to consider their participation. The parent will consent and the child will assent before any measurements are taken. If they decide not to enroll into the study, there will be no penalties and their care at CHOP will not be affected.

A combined consent-HIPAA authorization form will be used and delivered using an electronic approach via a secure REDCap portal. The parent and child participants will fill out the consent form on a tablet computer, in which they will be asked to enter their name, provide a valid signature, and the date to indicate their consent. The staff member acquiring consent will also provide their name, valid signature and date. A copy of the completed electronic consent form will be emailed to the family, with the instruction to either save or print a copy of this form. The staff member acquiring consent will complete an elements of consent checklist to help ensure the correct procedure was used.

9.6.3 Individuals with Limited English Proficiency

Questionnaires are only available and validated in English. Therefore, individuals with limited English proficiency are excluded from this study.

9.7 Payment to Subjects/Families

9.7.1 Payments to children for time, effort and inconvenience (i.e. compensation)

Each child will be paid $60 for completing the baseline phase procedures, $50 for completing intervention phase procedures, and $40 for completing the follow-up phase procedures. ClinCard will be used for payments. Please reference Table 1 for a complete breakfdown of the compensation structure.

9.7.2 Payments to parents for time, effort, and inconvenience

Each parent will receive a $20 payment to compensate for travel to the baseline visit and for completing questionnaires. ClinCard will be used for payments. Please reference Table 1 for a complete breakfdown of the compensation structure.

Table 1. Child and parent compensation by study period and procedure.

Procedure	**Compensation**
Baseline Period	
Child: Anthropometric measures	$10
Child: DXA scan	$10
Child: Questionnaires	$5
Child: Continuous Glucose Monitor (Synced & worn ≥5 days)	$5
Child: Sleep Tracker (Synced & worn ≥5 days)	$5
Child: Diet Assessment ($5/day of recall)	$15
Child: Urine Samples ($5/sample)	$10
Parent: Travel & Questionnaires	$20
	Child Total: $60
	Parent Total: $20
Intervention Period	
Child: Continuous Glucose Monitor (Synced & worn ≥25 days)	$25
Child: Sleep Tracker (Synced & worn ≥25 days)	$25
	Child Total: $50
Follow-up Period	

Child: Continuous Glucose Monitor (Synced & worn ≥5 days)	$5
Child: Sleep Tracker (Synced & worn ≥5 days)	$5
Child: Diet Assessment ($5/day of recall)	$15
Child: Urine Samples ($5/sample)	$10
Child: Questionnaires	$5
Child Total:	$40

Note: Children that ineligible after completing the diet assessment during the baseline period will not be compensated beyond the baseline period.

10 PUBLICATION

The results from this study will be published in peer-reviewed medical journals. No individually identifiable personal health information will be published.

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APPENDIX

APPENDIX A: LIST OF EXCLUSIONARY MEDICATIONS

Medications Resulting in Weight Loss

1. Orlistat
2. Phentermine
3. GLP-1 Receptor Agonists (e.g., exenatide, liraglutide, dulaglutide, semaglutide)
4. Metformin

Medications Resulting in Appetite Stimulation

1. Amitriptyline
2. Cyprophetadine
3. Dronabinol
4. Fluoxymesterone
5. Ginger powder
6. Megesterol
7. Melatonin
8. Metoclopramide
9. Mirtazapine
10. Ondansetron
11. Benzodiazepines
12. Clemastine
13. Cyproheptadine HCl
14. Dronabional
15. Glucocorticouds
16. Insulin
17. Lithium
18. Megestrol acetate
19. Oral contraceptives
20. Phenothiazines
21. Tricyclic antidepressants

Medications Resulting in Appetite Suppression

1. Aluminum hydroxide
2. Amphetamines
3. Cisplatin
4. Cholestyramine
5. Dactinomycin
6. Digoxin
7. Ethambutol
8. Furosemide
9. Griseofulvin
10. Hydralazine
11. Hydroxychloroquine
12. Hydroxyurea
13. Itraconazole
14. Lamivudine
15. Methenamine
16. Methylcellulos
17. Mineral oil
18. Nitrofurantoin
19. Penicillamine
20. Sibutramine
21. Spironolactone
22. Sulfasalazine
23. Thiazide diuretics
24. Topiramate

Medications Resulting in Fluctuations in Fluid Status

1. Diuretics (e.g., bumetanide, torsemide, hydrochlorothiazide, metolazone)
2. Potassium Supplements