IRB Approval Date of below included protocol and statistical analysis Plan: 2/13/2023

Publication date of primary results: March 18,2023

> Vidmar AP, Salvy SJ, Wee CP, Pretlow R, Fox DS, Yee JK, Garell C, Glasner S, Mittelman SD. An addiction-based digital weight loss intervention: A multi-centre randomized controlled trial. Pediatr Obes. 2023 Mar;18(3):e12990. doi: 10.1111/ijpo.12990. Epub 2022 Dec 9. PMID: 36484235; PMCID: PMC9905275.

NCT03500835

An Addiction-Based Mobile Health Weight Loss Intervention With Coaching

Find attached the study protocol and statistical analysis plan of the completed study. Primary outcome results have been published in pediatric obesity.

Sincerely,

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Background and Significance:

One in five adolescents in the U.S. is obese[3]. It has been theorized that overeating may have addictive qualities[4, 5], and there is a growing body of literature which demonstrates that craving for drugs and drive for food share similar hypothalamic pathways as seen on functional MRI (fMRI) studies[1, 2]. A recent study by Tompkins et al. reported the prevalence of adolescents meeting the criteria for food addiction as 30.7%, well above the 15%–19% range observed in adults seeking obesity treatment[6]. Interestingly, few weight management interventions have tested therapeutic techniques founded in addiction medicine principles to date[7].

The general consensus is that clinical interventions for adolescent obesity require intensive management with multidisciplinary teams, frequent visits, and many contact hours [3]. These programs often address nutritional, physical activity, and behavioral topics and only a handful of behaviors (e.g., selfmonitoring of weight, consistent physical activity, regular eating patterns). However, the high prevalence of pediatric, as well as adult, obesity precludes this as a practical strategy to combat obesity[8]. Advances in mobile health technologies (mHealth) offer an opportunity to monitor various behaviors, such as food consumption, and to deliver interventions in the adolescent's natural environment[9-12].Thus, mHealth platforms may be a cost saving alternative to an in-clinic intervention for pediatric weight management[9, 13].

Pretlow et al. reported an intervention which applied conventional addiction intervention methods to obesity in adolescents and was embodied as an iPhone® app[7]. To date, this addiction based mHealth program has been tested in two pilot studies. The first was performed in a self-selected cohort of 47 obese young people between 12-21 years of age and demonstrated that a food withdrawal approach was feasible to implement in a community based population without undue risk to participants and was useful in promoting weight loss[7, 14]. The results from this pilot study demonstrated a 7% decrease in the percent over the 50th percentile of BMI upon completion of the intervention[7].

The second pilot study was conducted in otherwise healthy adolescents referred to a tertiary care weight management clinic. A total of 50 adolescents were recruited; 18 youth self-selected to participate in the app intervention, the 32 youth that declined to participate functioned as contemporary controls who received intensive weight management intervention via a multi-disciplinary in-clinic intervention. Mean age of participants was 14.4 years (range, 12.3-17.9). The female to male ratio, racial/ethnic distribution and zBMI at baseline were comparable between groups; app participants had a significant decrease in zBMI at 3 and 6 months, compared to control. There was a statistically significant difference in zBMI between the app and control upon completion of the intervention (p=0.03). App participants had higher retention (100% vs. 37%) and lower total cost per patient ($760.00 vs. $1,428.00) than the control. An addiction medicine-based mHealth intervention, embodied as a smartphone app with telephone coaching, targeted for adolescents, reduced zBMI better than in-clinic controls and appears to be a cost-effective, timely and labor-saving method for adolescent weight management.

Although these results are encouraging, they arise from relatively small, time limited studies, which lacked a 'routine care' group and incorporated potential biases in selecting the control population. In addition, the effect of coaching on weight loss in adolescents, independent of the app intervention itself, was unable to be elucidated. There is a growing body of literature to suggest that incentivized coaching alone may be an effective technique for weight loss in this population[15, 16]. Health coaching is a personalized approach that is being widely used to improve health behaviors in patients with obesity. In adolescents, health coaching is a promising strategy that promotes healthy behaviors, goal setting and increased self-efficacy[17, 18]. Although data from randomized clinical trials in adolescents are limited a health coaching behavior modification program alone may be an effective, low-cost, personalized and flexible program that can be implemented through clinical settings.

The present study builds upon the momentum, resources, and research infrastructure of our pilot work to test the larger-scale and sustained impact of an addiction-based weight loss mHealth intervention with personalized coaching. Specifically, the proposed multi-site randomized controlled trial (RCT) tests will test the efficacy of an interactive addiction model based mobile health (mHealth) weight-loss intervention with personalized phone-coaching (AppCoach) compared to 1) interactive addiction model based mHealth weightloss intervention alone (App) or 2) Multidisciplinary in-clinic weight management program (Clinic).

The RCT will include youth regardless of their underlying co-morbidities because the targeted behaviors and weight management strategies are relevant and beneficial for all overweight and obese adolescents. Not only does this delivery modality remove many barriers (e.g., transportation, missed school days) that impact access and attrition in conventional, outpatient obesity interventions, but it strategically addresses underlying addictive eating behaviors to better support habit-formation in youth in their day-to-day environment. Assessment of the intervention's effect on zBMI, $\%BMI_{p95}$, fasting metabolic parameters, addictive eating habits, executive function, and motivation for change will be obtained at enrollment, 3, 6, 12 and 18 months (1 year post intervention follow up). Another key aim of the study is to conduct a real-life economic analysis (costs, cost-savings and non-monetary benefits) of delivering the app with personalized phone- coaching compared to multidisciplinary weight-management. We will further explore whether primary and secondary outcomes differ by race and whether race moderates the relationship between initial intervention efficacy and prolonged weight maintenance.

This study is both clinically and theoretically innovative as the notion of overeating as an addictive process in adolescents is still controversial. To our knowledge, this study is the first RCT to explore the efficacy of a weight-loss intervention premised on addiction principles delivered via mobile health. This study will contribute to the development of effective mobile health weight management interventions for use in adolescents with obesity. This extended intervention and follow-up (i.e., six months of intervention + one year of follow-up), will provide important information about the maintenance of this intervention. Second, it will aim to evaluate the use of mobile health interventions for adolescent obesity with coaching compared to mHealth intervention alone. Given the dearth of intervention options for obese children, the high likelihood that obese children will grow into obese adults, and our lack of understanding as to how best to personalize obesity interventions to optimize outcomes, this intervention may shift the approach of management of youth with obesity.

Research Design Methods:

Study Design:

Multi-center, randomized, controlled, trial of an addiction based mobile health (mHealth) weight loss intervention plus personalized coaching (AppCoach) compared to receive 1) interactive addiction model based mHealth weight-loss intervention alone (App) and 2) Multidisciplinary in-clinic weight management program (Clinic).

Recruitment and Eligibility:

Study procedures will be approved by the Children's Hospital Los Angeles (CHLA), the Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, UCLA, and Cedars Sinai Institutional Review Boards.

Recruitment Strategy:

1. *Clinical Referral:* Potential participants will be recruited for the intervention arms from newly referred patients of 4 interdisciplinary weight management clinics (CHLA, Los Angeles Biomedical Research Institute at Harbor-UCLA (LA Biomed), UCLA, and Cedars Sinai). Patients will also be referred from AltaMed (at CHLA).

2. *Targeted Mailing*: Potential participants will be recruited via targeted or direct mailing. Direct mailing provides the opportunity to target specific family demographics and zip codes, and thus, to target large populations of specific age brackets, as well as specific ethnic, racial and socioeconomic strata. In the proposed study, we will send 20,000 letters to families with children ages 14-18 across 40 neighborhoods in LA County. If we notice that some neighborhoods yield fewer calls, additional letters will be sent to ensure that our sample is evenly distributed across the randomly selected neighborhoods. Interested individuals will contact the CHLA study team if they wish to learn more about the study or participate.
    a. infogroup.com
3. *CHLA Emergency Department*: ED staff will be provided with recruitment flyers to distribute to eligible, interested youth. In addition, the CRCs will be available to come to CHLA and approach eligible youth after receiving approval to meet the family from the treating provider. CRC will screen potential ED patients via KIDs and contact parents of the kids that meet our criteria.
4. *Community Recruitment*: The flyers will also be posted on community boards across the 40 LA county neighborhoods. Interested individuals will contact the CHLA study team if they wish to learn more about the study or participate.
    a. See Flyer: “Calling all teenagers”

Sampling strategy:

LA County neighborhoods (n=272) will be stratified based on socioeconomic status, race and ethnicity. Based on this classification, 40 neighborhoods will be randomly selected. Based on LA County data and recent work with young adolescents in LA, we anticipate the following racial and ethnic distribution: 67% Hispanic, 17% white, 7% Asian, 2% black and 7% mixed or of a different race.

Patient Subjects:

Inclusion criteria include:

1. Age 14-18 years
2. Able to read English
3. Body mass index [BMI] ≥85th percentile for age and gender

Exclusion criteria include:

1. Concurrent participation in an alternative weight loss intervention
2. Uncontrolled, self-reported Blood pressure ≥ 99th percentile for age, gender, and height
3. Uncontrolled, self-reported known psychiatric illness and/or developmental delay 4. Participants Inability to read English

Parent Criteria:

1. Have an eligible child who meets the eligibility requirements listed above
2. Minimum age of 18 years old
3. Speaks English and/or Spanish

Pre-Screening:

Clinic Recruitment:

Newly referred patients to the interdisciplinary clinics will be pre-screened for eligibility prior to their first clinic visit by a study team member. The patients who meet eligibility criteria will be contacted via phone by a study team member. During the call, we will briefly introduce the study aims, intervention, and different groups. We will request the youth and family to consider participation and will thoroughly discuss the study at the consent

(baseline) visit. The study team member will obtain the eligible participants' email address and send them a recruitment flyer via email if interest is expressed.

AltaMed referral/recruitment:
Patients that meet age and/or BMI criteria, will be provided with study recruitment material and/or the patient will be referred to the study team by AltaMed providers/staff. The study team will acquire patients name, age, BMI (if available) and contact information.

Initial Visit (all participants):

1. Study team member will meet in person/virtually with eligible participants and provide details about the study procedures, obtain written/electronic permission from one parent/legal guardian and assent from minor participants or consent from participants 18 years of age and answer any questions the participants and their parent/legal guardian may have.

a. Upon obtaining consent from one parent or guardian and assent from each youth to participate in the study, participants will be randomized to one of 3 intervention arms **(AppCoach vs. App vs. Clinic).** If participant is consented via mail, the randomization will occur during the second part of visit 1. The participant will have the option of curbside pickup or mailing of study supplies. If consenting via mail, the study team will mail supplies to participant after receiving signed consent back. If consenting electronically via REDCap or DocuSign, study team will mail study supplies day of consent if possible.

2. All consenting participants will complete a battery of surveys (Refer to Measurements section). a. Youth:

i. Yale Food Addiction Scale[19] ii. The Center for Epidemiologic Studies Depression scale[20]
iii. The Perceived Stress Scale[21]
iv. Behavior Rating Inventory of Executive function[22] v. Binge Eating Disorder Screener[21] vi. Physical Activity Questionnaire vii. Satisfaction Survey
viii. Food Craving Questionnaire
ix. The Adolescent Self-Regulatory Inventory (ASRI)[23] x. Short form health survey form (SF-12) xi. EQ5-D
xii. Stages of Change Questionnaire in Weight Management (S-Weight)

b. Parents:

i. Demographic Screen
ii. Health Encounters
iii. Parent Satisfaction Survey

Outcomes:

	0	**3**	**6**	**12**	**18**
Study Visit Window of Completion		**+/- 2 weeks**	**+/- 2 weeks**	**+/- 4 weeks**	**+/- 4 weeks**
Covariates:					
Demographic Information	x				
Youth's Perceived Stress Score	x	x	x	x	x
Family Member's BMI	x				x

Primary Outcomes:									
BMI Status Change- %BMIp95	Height, Weight, zBMI,	x		x		x		x	x
Secondary Outcomes:									
Adherence-		x		x		x		x	x
Satisfaction- Satisfaction Survey		x		x		x		x	x
Fasting Lab Tests-		x			x				x
Cost Analysis- Encounters*	Health Care	x	x		x		x		x
Mediators:									
Addictive eating qualities- YFAS and FCQ		x	x		x		x		x
Self-Regulation- ASRI		x	x		x		x		x
Executive Function- BRIEF 2		x	x		x		x		x

*An official Health Care Encounters questionnaire will be completed by the parents at in-person/WebEx study visits at 0, 3 ,6,12, and 18 months post consent. Additionally, all participants will receive a call monthly from a study team member during the study period. In these calls weight outcomes, barriers and any interim health encounters (physician visits, diagnosis, medication prescribed etc.) occurred in the previous 4 weeks will be assessed.

3. All consenting participants:

    a. AppCoach and AppAlone arms will receive:
        i. Loaned iPhone (app is iOS compatible only) if the participant does not already have one
        ii. Wireless Bluetooth body weight scale
        iii. Digital food scale
        iv. Measuring tape (if participating virtually)
    b. In Clinic arm will receive:
        i. Digital body weight scale
        ii. Measuring tape (if participating virtually)
    c. Participants in the AppCoach and App arms who require an iPhone will be loaned an iPhone and accessories (including protective case), with an AT&T service plan for the 6-month intervention of the study that includes: unlimited texting, unlimited plan, unlimited voice calls to and from other cell telephones, 700 voice call minutes for calls to and from landlines, unlimited night and weekend calls to and from landlines, International calls or texts including Canada are NOT allowed and not covered. iPhones will be returned at the completion of the intervention (visit 3: 6-month follow-up visit/mail equipment back to study team).
    d. One parent will complete the above-mentioned questions and have their height, weight and BMI measured/self-reported at consent and at 18-month follow up (end of study).

3. AppCoach and AppOnly Participants:

   a. Each participant will be registered with their email address via a computer and then login with the app.
   b. Participants will weigh-in on a scale in a private area and enter weight data into their iPhones. Participants will weigh themselves and their food daily. This information will be automatically synced (entered) into the app. However, if the wireless scales are not used, they will need to enter the information manually into the app.
   c. A study team member will go through each section of the App and have participants enter data.
   d. Follow-up: participants will schedule in-person/WebEx study visits at 3, 6, 12 and 18 months. Participants will also have the option of conducting visits virtually via WebEx and/or receiving survey links via email directly from REDCap.
   e. AppCoach participants will also schedule weekly 15-minute phone meetings with a coach in addition to follow up study visits in-person/WebEx visits at 3, 6, 12 and 18 months.
4. In Clinic Participants:
   a. Each participant will attend a multi-disciplinary in-clinic or WebEx intervention consisting of 6 sessions (120 minutes +/- 30 minutes); one session per month for 6 months.
   b. They will meet with several members of the provider team throughout the intervention: physical therapist, psychiatrist, Registered Dietitian, health educator, physician and research team.
   c. Participants will be weighed or provide a self-reported weight at every session and follow up visits
   d. Participants will have the option of weighing themselves daily.
   e. Follow-up: participants will attend in person/WebEx follow-up visits at months: 3, 6, 12, and 18
   f. Participants will be provided a KNF newsletter for sessions 1-6. The newsletters summarize what was discussed during the session they attended. They will also be provided with a height and weight measurement tool. The newsletter and tool will be emailed or texted.
5. Research Blood Draws (all arms):
   a. Fasting lab results at enrollment are needed to determine baseline values. Participants that were referred to a weight management clinic at any of the participating sites may have had these labs drawn as part of their routine care. These results will be abstracted from the medical record if they are within 8 weeks of consent date. However, a research blood draw will be done at enrollment if these labs were not done as part of the participant's routine care. If the consent visit takes place virtually/by mail, the participant will be expected to travel to CHLA for a baseline research blood draw.
   b. All arms will have a follow up research blood draw at months 6 and 18.
   c. Each research blood draw will collect approximately 5 mL (1 teaspoon) of blood via venipuncture that will be used for the following testing: HbA1c, Total Chol, LDL, HDL, TG, AST/ALT, Glucose and insulin.
6. All participants

*Visit 1: if consenting via mail, these procedures will be completed at the 2nd session as visit 1 will be split in 2
** Each participant will have the opportunity to earn up to $200 in gift cards for participation in this study: up to $50 for participation in the intervention at 3 and 6 months and $50 for going to the last 2 study visits (at 12 and 18 months). The amount of payment will be based upon how much of the intervention the participant completes.
***Visit 2 and 3 must occur within a 4-week period (+/- 2 weeks from the 3- or 6-month date) and Visits 4 and 5 must occur within an 8-week period (+/- 4 weeks from the 12- or 18-month date).

Study Visit Schedule for Group 3 (In-Clinic) (total visits = 9)

*Visit 1: if consenting via mail, these procedures will be completed at the 2nd session as visit 1 will be split in 2

The youth participants in this group will also earn up to $50 at 3 months (visits 4) and 6 months (visit 7) for participation in the 6-month intervention and $50 for completion of study visits 8 and 9.

The table below depicts the assessment time points and key measures.

Month	0	3	6	12	18
Covariates					
Co-Morbidities, race/ethnicity, household composition, socioeconomic status, and previous weight loss programs completed	x				
Primary Outcomes (Aim 1)					
Height, Weight, zBMI, %BMIp95	x	x	x	x	x
Secondary Outcomes / Mediators (Aims 2, 3)					
Youth Surveyed: Yale Food Addiction Scale-Children	x	x	x	x	x
CES-D	x	x	x	x	x
Perceived Stress Score	x	x	x	x	x
BRIEF 2	x				
ASRI	x	x	x	x	x
Food Craving Questionnaire	x	x	x	x	x
Binge-Eating Disorder Screener	x		x	x	x
Satisfactory Survey			x		x
Physical Activity Questionnaire	x	x	x	x	x
SF-12	x	x	x	x	x
EQ5D	x	x	x	x	x
S-Weight	x		x		
Parent Surveyed:					
Demographic (Including Fast Food Consumption)	x				x
Height, Weight BMI	x	x	x	x	x
Health Encounters	x	x	x	x	x
Satisfactory Survey			x		x
Fasting Lab Tests: HbA1c, Total Chol, LDL, HDL, TG, AST/ALT, Glucose, Insulin	x		x		x

Post Study Follow-up Options:

1. After completion of the 6-month interventions participants will be offered the following choices for continued care:
    a. Participants in groups 1 and 2 will have access to use the mobile app without coaching upon completion of the 6-month intervention. However, a participant owned iPhone is required in order to use the mobile app. Group 3 will have access to use the mobile app without coaching upon

completion of the study (post 18 month). Participants will have to own an iPhone in order to use the mobile app as it is an IOS App only.

2. All participants will receive a call from a study team member monthly for the 18-month study period.
    a. They will discuss weight trends since the intervention completion and any interim health encounters (ED visits, hospitalizations, PMD visits, changes to medical history).
    b. They will also discuss if any interim weight management strategies have been utilized or started.

3. All Participants will have an in person/virtual follow up 12 months and 18 months post consent (baseline) where a repeat weigh in and survey completion will occur. All participants will also have a fasting research blood draw at 6 and 18 months.

Enrollment and Retention:

Up to 404 adolescents (plus 1 parent/youth enrolled) will be recruited for the intervention arms and randomized 1:1:1 via stratified block randomization into one of the following groups: AppCoach, App or Clinic. Demographic information will be collected from all participants. During the intervention period the participants will not attend an inter-disciplinary in-clinic weight management intervention or any other medically supervised weight loss programs. If the participants have underlying comorbidities, they will continue to follow with routine subspecialty providers for standard of care of each underlying condition. Each participant's primary care provider, regardless of the method in which they were recruited (including those recruited from the greater LA county) upon request from participant, will receive a letter from the PI explaining that the individual will be participating in the research intervention during the allotted study period. Parental involvement is not required for those participants randomized to the AppCoach or App group; these participants will complete the intervention independently with the assistance of the coach (if applicable). Parental involvement is required for those participants randomized into the In-Clinic group. Upon completion of the intervention, if the participant was initially referred to a weight management clinic by their primary care provider, they will be offered continued enrollment in the inter-disciplinary weight management clinic for which they were initially referred. In order to further remove barriers to participation, all families who do not have a car will be offered free ridesharing transportation (UBER or Lyft) to- and from CHLA. Additionally, parking validation will be offered for families to park onsite at CHLA for research and/or intervention visits. To increase retention, participants are contacted once per month to maintain engagement. Research staff will provide families with dates of their scheduled assessments/visits. Participants are also given reminder phone calls the day before their assessment/visit.

Trial sites:

A participating trial site must fulfill the following eligibility criteria:

1) Have an independent weight management clinic that cares for adolescents.
2) The principal investigator and all the clinical research coordinators/staff at the site have been trained on, and understand, the study protocol.
3) The site is within mobile phone range on the other hand, a trial site will be ineligible if it satisfies one or more of the following conditions:

1) The principal investigator withdraws consent for participating in the study.
2) The steering committee of the present trial judges the site to be inappropriate to recruit participants.

Initial trial sites include: CHLA, Los Angeles Biomedical Research Institute at Harbor-UCLA (LA Biomed), UCLA, and Cedars Sinai.

Site Training:

Each on-site CRC will receive 8 hours of training prior to recruitment start date.

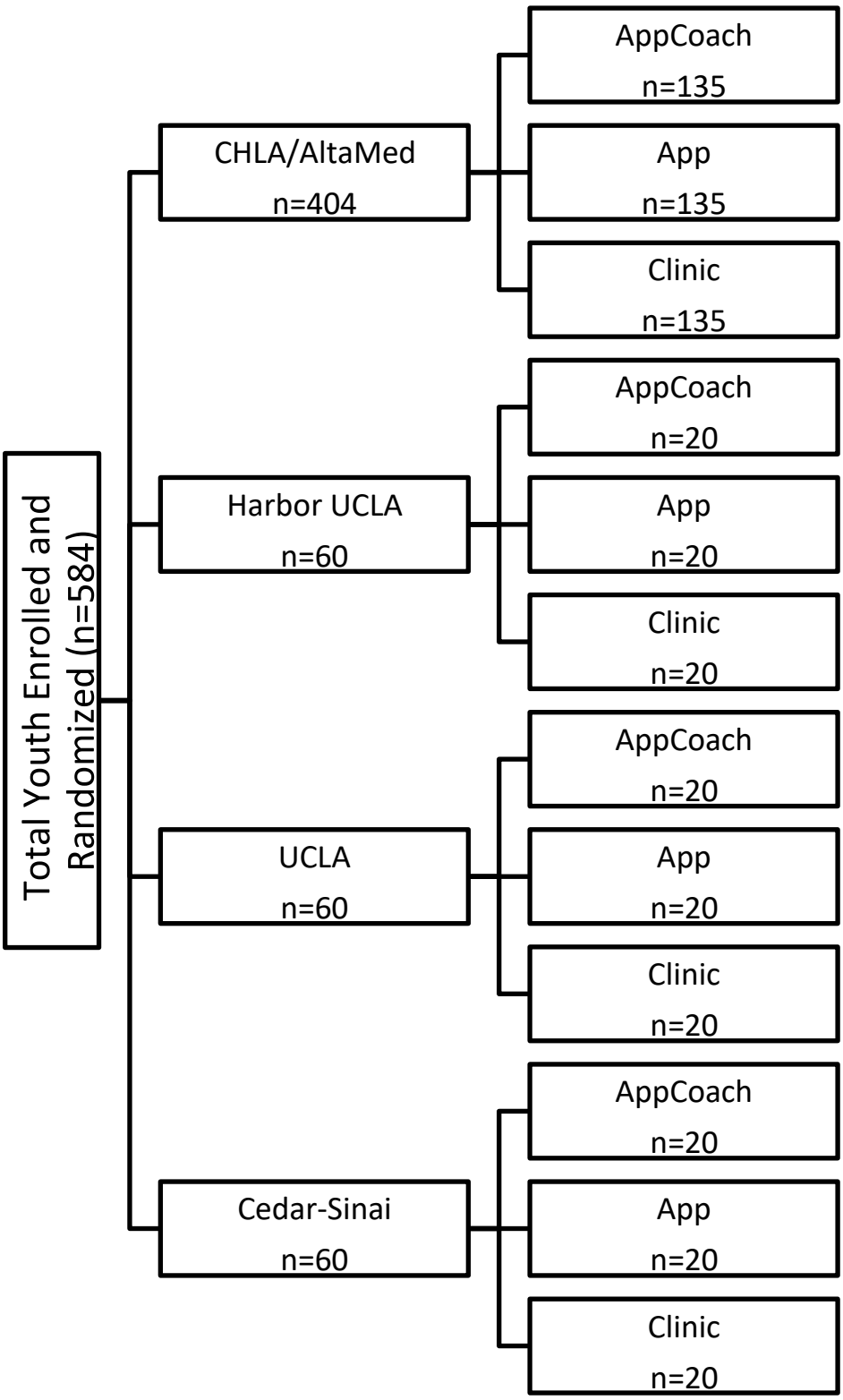
Study Design:
404 reflect the 190 youth and 190 parent/guardians plus the 12 youth and 12 parent/guardian subjects that will be enrolled for the pilot study at CHLA.

We are aiming to recruit a total of 292 youth total with 1 parent/legal guardian per youth (total of 584 including the parent/guardian in the subject accrual number + 12 pilot youth + 12 pilot parent/guardian).

We plan to enroll 584 participants (youth & parent/guardian) into each intervention arm as follows:

CHLA/AltaMed = 404 (Pilot: 12 youth + 12 parent/guardians; Open enrollment: 190 youth & 190 parent/guardians)
UCLA = 60 (30 youth & 30 parent/guardians)
Harbor UCLA = 60 (30 youth & 30 parent/guardians)
Cedars Sinai = 60 (30 youth & 30 parent/guardians)

Pilot Group: We plan to initially recruit 12 patients from the CHLA EMPOWER clinic. The patients will be randomized to the three intervention arms and will complete a 2-month trial to assess intervention fidelity of the curriculum and identify any potential difficulties. The pilot subjects are reflected in the information above. .



Assessments:

Anthropometric Data

Height and weight will be assessed at in-person visits by study team member or or self-reported if visit is conducted virtually via WebEx. Height will be measured using a Quick Medical stadiometer, accurate to 0.1 cm (Quick Medical, Issaquah, WA). Weight will be measured on a self-calibrating Mobile Stand Digital Scale,

accurate to 0.1 kg. Participants will wear minimal clothing during the height and weight measurements. BMI will be calculated as kilograms per square meter and BMI Z-score (zBMI) and percent over the 95th percentile (%BMI_{p95}) will be determined utilizing the CDC growth charts.

Physical Activity

To evaluate the effect of the intervention arms on amount of physical activity performed by the youth, each youth will complete the physical activity questionnaire and recall their activity level over the last 7 days at each study visit.

Measurements (~ 1.5 hour to complete)

1. **Yale Food Addiction Scale (YFAS-c, 25 questions, ~7 minutes)**: The YFAS-c is a validated measure of addictive-like eating behavior based on the Diagnostic and Statistical Manual of Mental Disorder V diagnostic criteria for substance dependence[19, 25, 26]. Intervention participants will complete the YFAS-c at consent and at 3, 6, 12 and 18 months.
2. **The Center for Epidemiologic Studies Depression scale (10 questions, ~5 minutes)**: The CES-D is a short self-report measure used to measure depressive symptoms in the general population[20]. The scale demonstrates strong internal consistency (Cronbach's $\alpha > 0.85$), moderate test-retest reliability (>0.50), and moderate validity ($r > 0.50$)[20]. This will be completed at all in person / WebEx study visits 0,3,6,12, and 18.
3. **The Perceived Stress Scale (14 questions, 10 minutes):** The PSS measures subjective perceptions of distress in one's own life situations. Based on Lazarus' transactional model of stress and coping, the PSS assesses how well a person feels they can cope with stressors, rather than measuring the nature of the stressors themselves. The measure has demonstrated strong reliability ($r > 0.80$) and validity in social and health science studies[21]. This will be completed at all in person/ WebEx study visits 0,3,6,12, and 18.
4. **Health Encounters (6 questions, 5 minutes):** This brief questionnaire will assess how often the participant has utilize health services in the preceding time period. An official Health Care Encounters questionnaire will be completed by the parents at in-person/WebEx study visits at 0,3 ,6,12, and 18 months post consent. Additionally, all participants will receive a call from a study team member monthly during the study period. In these calls the study team member will assess weight outcomes, barriers and ask if any interim health encounters (physician visits, diagnosis, medication prescribed etc.) have occurred in the previous 4 weeks). 5. **Intervention Satisfaction Survey (12 questions, ~6 minutes):** Both the study participant and a family member will complete an intervention satisfaction survey to be completed at the 6 and 18 month follow up visits to assess the level of satisfaction with the intervention period and the satisfaction with the coaching. a. Participant Satisfaction
    b. Coach Satisfaction
    c. Parent Satisfaction
6. **Demographic Questionnaire (15 questions, 6 minutes)**:
    a. Age of consenting parent/guardian
    b. Ethnicity
    c. Highest education obtained of consenting parent/guardian
    d. Household Composition
    e. Parent employment status
    f. <u>Fast Food Consumptions Question:</u> How often did you eat outside the house in the last 7 days
        1. Guardians will be asked to report how often in the past 7 days the participant ate a meal or a snack from a fast-food restaurant. Response options range from "none" to "5 or more times. This procedure is similar to measures used in other studies of fast-food consumption. Guardians will also be asked to report the location (e.g., McDonald close to school) and the social context in which eating occur (e.g., with school friends).
7. **The Adolescent Self-Regulatory Inventory (ASRI, 36 questions, ~15 minutes)[23]:** This is a 36 item measure that evaluates the degree to which adolescents are able to activate, monitor, maintain, inhibit, and

adapt their emotions, thoughts, attention, and behavior. This will be completed at all in person/ WebEx study visits 0,3,6,12, and 18.

8. **Behavior Rating Inventory of Executive function 2 (55 questions, 15 minutes)**[22]: The Behavior Rating Inventory of Executive Function (BRIEF2) provides theoretically and empirically derived clinical scales that measure aspects of executive function. The clinical scales form broad indices of behavior and cognition and an overall score, the global executive composite (GEC)[22]. This will be completed at baseline only.

9. **Food Cravings Questionnaire (FCQ, 15 questions, ~5 minutes)**[24]: Scores on the FCQ-T have been found to be positively associated with eating pathology, body mass index (BMI), low dieting success and increases in state food craving during cognitive tasks involving appealing food stimuli. This will be completed at all in person/ WebEx study visits 0,3,6,12, and 18.

10. **Binge Eating Disorder Screener (BEDS-7, 7 questions, 4 minutes):** This questionnaire is utilized to screen for binge eating disorders. This will be completed at in person/ WebEx study visits 0,6,12, and 18.

11. **Physical Activity Score (PAQ, 12 questions, 4 minutes):** This instrument was developed to assess general levels of physical activity for adolescents 14-19 years of age.[27] This will be completed at all in person/ WebEx study visits 0,3,6,12, and 18.

12. **SF-12 Health Survey (12 questions, 3 minutes):** The SF-12 is a practical, reliable and valid measure of physical and mental health. It is particularly useful in large population health surveys or for applications that combine a generic and disease-specific health survey. This will be completed at all in person/ WebEx study visits 0,3,6,12, and 18.

13. **EQ5D (15 questions, 4 minutes):** EQ-5D is a standardized instrument for measuring generic health status. It has been widely used in population health surveys, clinical studies, and economic evaluation and in routine outcome measurement in the delivery of operational healthcare. This will be completed at all in person/WebEx study visits 0,3,6,12, and 18.

14. **S-Weight (5 item questionnaire, 3 minutes):** S-Weight is a tool used to determine the individual's stage of change. This allows the research team to assess and monitor motivation and readiness for change to determine if baseline levels promote success in the intervention.

Adherence and Retention

Data relating to participant interaction with the app and the coach and attendance with scheduled research visits will be tracked remotely and stored on HIPAA-compliant central servers. Data will be reported on three key components specific to the underlying addiction model implemented in the intervention: (1) ‘‘problem foods’’ withdrawal; (2) snacking elimination; and (3) food amount reductions at meals[12]. We will also use strategies (implemented with participants in the intervention arms) that we have found effective for retention: (1) providing incentive for participation and adherence; (2) ensuring frequent contacts with all participants to maintain engagement and foster open communication; (3) sending email and text reminders about face-to-face/WebEx visits; (4) seeking contact information of relatives or friends to be able to reach participants; and (5) Study participants will be invited to participate in two optional audio recorded focus groups to: 1) collect information on their experience with the study and 2) their understanding of displacement theory and their input on the development of a new app based intervention that targets the displacement theory. The focus group sessions will last 60 minutes each. As we are recording the sessions, if a patient’s real name is accidentally used, it will be erased from the transcript and if possible, from the audio-recording. Participants will have the option of participating in both or just one of the focus groups in no particular order so long as they have completed their 6-month follow up visit or none. This will help us identify adherence outcomes.

Intervention Groups:

App Intervention Groups (AppCoach and App groups)

The specific details of the App intervention have been described by Pretlow et al[7]. Briefly, the intervention will be implemented through an iPhone® app, which will be securely integrated with a networkserver for real-time data access and storage[7]. Problem foods will be defined as specific foods for which participants felt they have cravings, cannot resist when immediately available, and cannot stop eating when

started. Participants will sequentially withdrawal from two self-selected problem foods at a time, with the goals of total abstinence from the food for a minimum of 10 days in a row, and craving resolution[2].

During the second phase, which will overlap with the first, participants will eliminate snacking by choosing time periods to avoid snacking (i.e. morning, afternoon, or evening). Once the participant has abstained from snacking during their chosen time interval for 10 days, the participant will then choose additional time intervals to abstain from snacking, with the overall goal of abstinence from snacking between meals. In the third stage, excessive food amounts at meals will be targeted. Participants will weigh all food items served at meals, and an algorithm in the app will gradually reduce each participant's food amounts to result in 1 pound weight loss per week. Participants will take photos of meals via the app, post weighing, to allow for external confirmation of amount reduction. In addition, participants will have access to the app home page, which includes various addiction model strategies, including: motivation, distraction ideas, displacement methods and coping skills techniques[7].

Participants in the AppCoach and App group will be asked to weigh themselves and food daily. All participations (AppCoach, App and Clinic) will receive monthly phone calls from the research team to speak with either the subject or the parent to review any barriers to adherence or technological problems that may have occurred with any of the study equipment. All phone conversations will be recorded.

Coaching (AppCoach group)

Interactions between coach and participants are of three types: face-to-face/WebEx visits, phone calls and text messages. Each participant will interact with the coach for 6 months via text messages, 5 days per week, weekly phone calls (15-minute duration) and four one-hour face-to-face visits (at 3, 6, 12 and 18 months post baseline visit). Participants will keep track of their progress through the mobile app, throughout the intervention; this log will be reviewed with the coach weekly. The face-to-face visits (1 baseline consent visit and 4 follow up visits) will be qualitative interviews (of approximately 60 minutes duration), which will occur at Visit 2 (month 3), 3 (month 6), 4 (month 12) and 5 (month 18). The semi-structured interviews will include questions designed to elicit both positive and negative impacts on weight management and identify barriers such as emotional eating, displacement behaviors, poor coping skills to life stressors and social challenges. The interviews will be broadly structured around key domains of life before the intervention, life during the intervention, and anticipated future life. Upon completion of the intervention the participants will be interviewed on their own sense of what was important about the intervention in terms of what did/didn't impact them and their thoughts on how the intervention could be improved.

Most of the participant-coach interactions take place through phone calls. Each coach will have a cell phone used solely for this study, so that participants may directly contact their coach as needed regarding any questions or concerns that the participant may have. Phone calls and text messages will be utilized for appointment reminders, scheduling weekly phone meetings, providing emotional support, following up on items discussed in a prior visit or phone call[30]. All interactions are documented in a database created for the study, including date, time, type, and duration of contact, topics discussed, and any relevant notes. The coach will utilize a motivational interviewing paradigm to interact with the participants, and an electronic system within the app database to document each encounter. All phone conversations, for those in the AppCoach group, will be audio recorded. In addition, AV will attend 1 coaching session per month for intervention fidelity assessment in real time with the coaches.

Addiction Model Based Coaching Curriculum:

The curriculum is founded on three principles of addiction medicine:1) Divide-and-conquer approach; 2) Staged withdrawal / abstinence; and 3) Behavioral addiction (BFRB intervention methods (See Manual of Procedure entitled: Addiction Model Intervention for Obesity in Young People for additional detail). Specifically, the intervention targets three features of addictive behavior: 1) Staged withdrawal from participant identified problem foods; 2) Staged withdrawal from daytime snacking between meals; and 3) Withdrawal from excessive amounts of food consumed at meals. The curriculum also addresses self-monitoring of weight and targeted

behaviors to support habit-formation of eating behaviors. Regular self- weighing and completion of the records are associated with program adherence and successful weight management.

The divide-and-conquer approach breaks down the addictive behavior and the withdrawal process into components, which are attacked one at a time in discrete, small increments. It is productive to divide intervention into problem foods, snacking, and excessive amounts at meals, and each involves treating both the sensory and motor addiction components.

1) Withdrawal from problem foods: Problem foods are specific foods for which the child or teen has cravings, seeks out or purchases, cannot resist when immediately available, and cannot stop eating when started. The child or teen identifies and lists all his/her problem foods and then abstains from each food, one-at-a-time, for nominally 10 days each, and until cravings and difficulty resisting the food have resolved (designated as "in-control" for that food). Then the child/teen progresses to the next problem food on his/her list. Two problem foods may be withdrawn from concurrently, but it is recommended that no more than two problem foods be withdrawn from at a time.
2) Withdrawal from snacking/grazing: This is accomplished by abstinence from snacking during distinct time intervals, such as morning, afternoon, evening or nighttime, nominally for 10 days each time period and until difficulty resisting snacking during that time period has resolved (designated as in-control for that time period). Then the child/teen progresses to the next time period, with the goal of zero snacking during the entire day. Snacking may be withdrawn from in more than one time period concurrently.
3) Withdrawal from excessive food amounts: This may be accomplished in two ways:
    a) Cutting in half method. Cut everything in half eaten at meals, put half back, and eat only half. Sharing with a friend or boxing up half when eating out is useful.
    b) Measuring/weighing method. Measure or weigh typical amounts of all foods frequently eaten at meals and reduce amounts in incremental, staged percentages from starting amounts. Weighing foods is much easier to implement that the cutting in half method, as it turns the quantity of food served into a number. Thus, there is no "decision" and minimal stress.
4) Behavioral addiction methods are used in parallel for each withdrawal process.

Coach Training Procedures:

The coaches delivering the curriculum will receive 60 hours of training over a 4-week period from Dr. Vidmar. The training covers: 1) the importance, rational and education about the theory of food addiction and the proposed intervention, 2) the concept of behavior change, patient centered approach and motivationalinterviewing techniques, and 3) practical advice specific to each stage of the intervention and ways to assist the youth with common barriers and triggers. The coaches will also tailor the delivery of information and the setting of goals to the participant's readiness for change. Coaching curriculum will cover active listening, nonjudgmental communications, motivational interviewing techniques, and creating self-management goals. In addition, the two coaches will be required to demonstrate mastery of coaching skills through simulated roleplays and observations of coaching sessions. Coaches will have ongoing support from the study PI (AV) via bimonthly meetings at which they may present participant cases and request guidance with specific issues and may consult with the study investigators as needed.

Once the coaches complete the training and demonstrate mastery of the skills, they will be assigned participants in the AppCoach group. The AppCoach group will be the only arm with a personalized coach. Each coach makes initial contact (via HIPAA secure video conferencing) with the participant at the time of enrollment to describe his or her role and to discuss participant identified goals.

Coaches will have undergraduate training and be highly knowledgeable about motivational interviewing clinical practice guidelines regarding strategies for obesity management in youth. Coaches will be taught to table unfamiliar clinical and counseling questions, which may arise during coaching. They will then discuss these questions with Alaina Vidmar (AV) at bi-monthly team meetings, who will provide direction about management on future calls. Coaches will record all calls, and AV and SS will review a subset of these

recordings. Coaches will receive monthly feedback regarding implementation of directive and nondirective coaching modes.

Clinic: Multi-Disciplinary In-Clinic Monthly Intervention (In-Clinic Group)

The team consists of a coordinator/health educator, physicians (MD), registered dietitian (RD), physical therapist (PT) and psychologist, who will assess participants in a clinic setting/virtually, with monthly visits with one or more providers (averaging 100 minutes at the initial visit and 80 minutes per follow up visit, ~8 contact hours per participant per 6-month intervention period). Core principals of the clinic include motivational interviewing (MI) and family-centered care. Patients and their parent/guardian are expected to attend monthly clinic visits for at least six visits (6 months). The study team member will obtain height and weight at the beginning of each visit.

The coordinator/health educator will evaluate the patient and families overall emotional health and address anxiety, psychosocial stressors, and emotional eating. Healthy eating goals focus on hunger management, portion control, decreasing sugar-based beverage intake, increasing fruit and vegetable intake, and modifying eating behaviors. Changes in behavior for the entire family are strongly encouraged. The multi-disciplinary team utilizes treatment strategies that include MI, nutritional education, and behavioral therapies targeted at improving daily routines, emotional health, sleep quality and quantity, diet, and physical activity. Each team member documents the patient's goals identified at each visit and distributes a summary check-out document to the team and the family. Goals for healthy eating, increased physical activity, better sleep habits, emotional well-being, and family support are then followed up at subsequent monthly visits.

The Clinic Intervention will utilize the Kids N Fitness Curriculum and will address the following topics over the 6-month intervention:
Session 1: Nutrition and Food Groups
Session 2: Portion Power
Session 3: Real Foods, Fat and Fiber
Session 4: Sugar Savvy
Sessions 5: Healthy Shopping, Healthy Eating
Sessions 6: Special Occasions and Moving Forward

Those youth randomized to the in-clinic control arm will complete the intervention at CHLA or virtually via WebEx. The participant and their parent/guardian will meet with each team member for 20-30 minutes to discuss the topic of the session. The youth will participate in some mild physical activity exercises, such as stretching. Treatment fidelity strategies will be utilized for all three intervention arms to ensure the accurate and precise delivery of each arm as intended. (See Treatment Fidelity Below).

Example Follow up Phone Calls Curriculum Outline (AppCoach):

Call	
1	Introduction: --Coach introduction --Curriculum introduction --Problem Food Identification --Goal setting
2	Personal Motivation: Identify personal motivation and goals of each participant. Have participant identify in and out of home barriers to weight management success. Problem Food Withdrawal Instruct to complete personal story
3	Problem Food Withdrawal -Assess barriers to compliance

4	Problem Food Withdrawal Progress
5	Introduce Snacking Elimination. Identify period of time to start withdrawal Problem Food and Snacking Withdrawal
6	Problem Food and Snacking Withdrawal
7	Problem Food and Snacking Withdrawal
8	Problem Food and Snacking Withdrawal
9	Continue PF and Snacking Withdrawal start food amount reduction Evaluate current barriers to weight management success. Have participant identify one goal to achieve over the next 4 weeks
	Introduce food weigh AppCoach and App: Distribute App setup instructional video
10	Progress report on above. Review frequency of eating out. Review missed weighed meals
11	Review progress, compensation and points earned. Identify successes and barriers. Make goals for second half of intervention
12	Review Face to Face / WebEx Visit 2 Goal of withdrawing from all 10 PF by week 12
13	Review maintenance PF avoidance. Encourage to consider assigning additional PF as tolerated
14	Goal of eliminating snacking by week 14
15	Review maintenance of PF and snacking avoidance
16	Review daily foods weigh in. Review how many meals have been weighed. Review how to weigh accurately. Review food amounts and discuss if within target. Review food pictures to ensure honest measurement
17	Review weight loss and create goals for weight loss. Review addiction model and review for signs of withdrawal/tolerance since removal of PF and snacking
18	Identify barriers to food amount withdrawal. Create personal goals to overcome barriers.
19	Assess barriers to long term adherence. Identify in home and out of home barriers to weight loss success/maintenance
20	Review maintenance of PF and snacking avoidance
21	Review food amount withdrawals and strategies to consume smaller portions
22	Review weight loss and create goals for weight loss. Review addiction model and review for signs of withdrawal/tolerance since removal of PF and snacking
23	Review weight maintenance strategies Review print out of weighed foods
24	Review Face to Face / WebEx Visit 3

Intervention Delivery:

The proposed model of delivery makes it possible to: 1) Intervene with the adolescent and provide autonomy, 2) deliver the material over an extended period of time in a more convenient platform for the youth and families, 3) reduce many access barriers (transportation, missed days of school and work) common to conventional outpatient obesity interventions, and 4) help youth learn skills to help them overcome their addictive eating traits.

Intervention Fidelity:

AppCoach and App Groups

Intervention fidelity encompasses integrity (interventions are implemented according to established procedures) and differentiation (interventions are distinct from one another). Our formative work suggests that the following strategies and safeguards are effective in preserving integrity and differentiation: (1) Comprehensive assessment of the curriculum. (2) As described above coaches will receive extensive training to master the curriculum's psychosocial and educational curriculum (supported by scripted manuals) and they receive weekly supervision. The training, scripted manuals and supervision prevent drifting (i.e., avoid covering topics/areas not included in the curriculum). (3) Coaches will receive an initial training period and refresher courses throughout the study period. Implementation quality is further supported by scripted manuals and by weekly supervision to review progress, dosage and timing of delivery, and to provide the opportunity to resolve problems or issues encountered. (4) Coaching is delivered via phone with audio recording of each sessions. Coaches will be provided with session outlines as a material guide and following the sessions, Drs. Salvy and Vidmar will review the sessions utilizing a session checklist to ensure treatment fidelity. The recorded sessions will be monitored by Dr. Salvy periodically over the course of the study to ensure compliance with coaching instructions and prevent any drifting.

In-Clinic Arm:

A similar treatment fidelity schema will be implemented for the in-clinic intervention. The curriculum will be adapted to target youth ages 14-18. The providers implementing the intervention will complete 12 hours of training that will include mock implementation. The providers will implement the intervention and Dr. Salvy will evaluate the implementation and ensure session objective and checklists were correctly incorporated and prevent any drifting over time.

Pilot Sessions:

Twelve participants (and one of their parent/guardian) will be recruited from CHLA to complete a pilot intervention starting 2 months before the initial open recruitment commences. The youth participants will be randomized to one of the three arms and complete that intervention accordingly. The team members will continue to be monitored as they implement the intervention and barriers to execution will be evaluated. Those 12 participates will complete the full study period. If not protocol amendments are made they will be included in the final analysis, if protocol amendments are made they will be excluded.

Intervention Compensation:

Traditional payment: Payments will be provided at the end of study visits at months 3, 6, 12, and 18 as shown in the table below. Monthly payment: The participant may elect to receive compensation at monthly intervals for the first 6 months if desired. If this method is selected, the participant will provide the study team with their email address and a gift card will be emailed to them monthly based upon how much of the intervention they participate in or they can opt for the study team to email them images of the gift cards.

Each youth participant, regardless of which group they are assigned to, will receive compensation in the form of gift cards. Each youth participant has the opportunity to earn up to a total of $200 for participation in this study. The amount of payment will be based upon how much intervention adherence occurs. The amount will be rounded to the nearest ten-dollar increment, by rounding up.

Parents/guardians will not be paid for their participation in this study.

<u>For Group 1 (AppCoach) and 2 (App):</u>

The app will automatically accrue points as the participant interacts with the app components. They will receive a pre-determined amount of points each time they open the app, each time they weigh in, each time they log a problem food, etc. The participants will be able to enter the motivation section of the app as desired to evaluate

how many points they have accrued. In addition, lack of participation with the app results in loss of points which will result in decreased financial gain. This balance is also available to the participants in real time. Points will be associated with financial quantity (1 point = 5 cents) and the youth participants will earn compensation as they complete the intervention as directed.

The youth participants will be able to earn up to $50 for participation in the 3 and 6-month intervention and $50 for completion of visits 4 and 5. Payment will be provided at the end of the study visits at 3 months (visit 2), 6 months (visit 3), 12 months (visit 4), and 18 months (visit 5).

	Visit 1	**Visit 2**	**Visit 3**	**Visit 4**	**Visit 5**
Months Post consent	0	3	6	12	18
Group 1 and 2	-	Up to $50	Up to $50	$50	$50

The table below depicts point accrual for the 6-month intervention for Group 1 (AppCoach):

	#	**Points per visit**	**Total points**	**Total payment**
Face to face/ WebEx visits in which compensation is received	4 visits	200/visit	200*4 = 800	800 * 0.05 = $40
Daily weigh in (7 days/week)	168 weigh ins (24 weeks * 7 days/per week)	1.5 /weigh in	168*1.5=252	252*0.05=$12.60
Daily text messages (5 days/week)	120 text messages (5 days * 24 weeks)	4 /text	120*4=480	480*0.05=$24.00
Weekly phone calls (1 call/week)	24 calls	20/call	24*20=480	480*0.05=$24
Totals			**2012**	**$100.6**

The table below depicts point accrual for the 6-month intervention for **Group 2 (App):**

	#	**Points per visit**	**Total points**	**Total payment**
Face to face/ WebEx visits in which compensation is received	4 visits	200/visit	2004 = 800	800 * 0.05 = $40
Daily weigh in (7 days/week)	168 weigh ins (24 weeks * 7 days/per week)	1.5 /weigh in	168*1.5=252	252*0.05=$12.60

App participation (7 days/week)	168 (7 days * 24 weeks)	5.7/daily interaction	168*5.7=960	960*0.05=$48.00
Totals			**2012**	**$100.6**

For Group 3 (In Clinic)

The youth participants in this group will also earn up to $50 at 3 months (visits 4) and 6 months (visit 7) for participation in the 6-month intervention and $50 for completion of study visits 8 and 9. The amount of payment will be based upon how many visits are attended during the 6 month intervention ($16.75 per visit). Payment will be provided at the end of the study visits at 3 months (visit 4), 6 months (visit 7), 12 months (visit 8), and 18 months (visit 9).

The table below depicts the payment schedule for this group:

	Visit 1	**Visit 2-6**	**Visit 7**	**Visit 8**	**Visit 9**
Months Post consent	0	1-5	6	12	18
Group 3	-	Up to $50	Up to $50($16.75	$50	$50
		Administered at Visit 4 ($16.75 per visit attended)	per visit attended)		

Outcomes

The primary outcome will be change in zBMI and excess BMI percent over the 95th percentile ($\%BMI_{p95}$) compared to baseline, assessed at 3, 6, 12 and 18 months, both within the groups and compared between groups and in clinic group. For analysis over time, the $\Delta\%BMI_{p95}$ (BMI percentile – 95th percentile), which is the distance (in kg/m^2) from the 95^{th} percentile, will be utilized[31].

Secondary outcomes will include: compliance with App intervention, retention rates with scheduled phone calls and clinic visits, ASRI, BRIEF, Satisfaction survey, YFAS-c, fasting lab testing compared pre and post intervention. Collected lab studies will include: HbA1c, Lipid Panel, AST/ALT. Each of these lab tests are currently recommended for routine clinical care screening every 6-12 months in obese adolescents[3].

An estimated cost analysis will be completed to determine the cost per patient to implement the 6 month AppCoach intervention, App alone intervention and multi-disciplinary in-clinic intervention (Clinic)[32]. Cost Analysis to include: time or expenses saved compared to in-clinic (travel, missed work or school); efficiency of clinic and staffing needs, including appointment duration and physical space requirements, and health care utilization rates and costs of care[33, 34].

Analytic Plan:

Power and Sample Size Estimates:

The power analysis is prepared for comparing (1) the difference in the mean change of zBMI and %BMIp95 between baseline, 6 months, and 18 months across App+Coach, App, and Clinic, (2) the difference in zBMI and %BMIp95 mean change between App+Coach and Clinic, and (3) the difference in zBMI and %BMIp95 mean change between App+Coach and App. Review of the literature revealed that the majority of studies utilize the change in zBMI to evaluate the effectiveness of weight management interventions in adolescents. However, Freedman et al. and the CDC have proposed utilizing alternative metrics for weight change such as %BMI95 which may be more strongly associated with change in body size in adolescents. Therefore, both metrics were considered in the power calculation to further explore their use as outcome measures in youth with obesity and severe obesity.

This study will enroll 292 patients and equally allocate into 3 groups. All these calculations utilize an estimate of standard deviation of change based on the conservation of correlation of 0.5 between pre and post measurements within each group, based on Analysis of Variance (ANOVA) with two-sided Type I error of 5%. For the first study aim, the difference in the mean change of zBMI and %BMIp95 between baseline, 6 months, and 18 months across App+Coach, App, and Clinic, this study has at least 83% power to detect the effect size of 0.244 with the variance of the group means of 0.0003 for the mean change of zBMI and at least 89% power to detect the effect size of 0.263 with the variance of the group means of 2.903 for the mean change of %BMIp95. For the second study aim, the difference in zBMI and %BMIp95 mean change between App+Coach and Clinic, based on two sample t-test with two-sided Type I error of 5%, this study has 88% to detect an effect size of 0.580 corresponds to the mean difference of pre and post change in zBMI at least 0.040 standard deviation between the two groups and a 92% power to detect an effect size of 0.625 corresponds to the mean difference of pre and post change in %BMIp95 at least 4.08 percent between the two groups. For the third study aim, the difference in zBMI and %BMIp95 mean change between App+Coach and App, based on two sample t-test with two-sided Type I error of 5%, this study has 71% power to detect an effect size of 0.464 corresponds to the mean difference of pre and post change in zBMI at least 0.032 standard deviation between the two groups and a 68% power to detect an effect size of 0.452 corresponds to the mean difference of pre and post change in %BMIp95 at least 2.80 percent between the two comparison groups. Assuming 20% dropout rate, this study will achieve the desired study power of 80% for study aim 1 and 2. (nQuery + nTerim 4.0 and Stata/SE 15.1).

Statistical Analysis

Statistical analysis: All statistical analyses were conducted in accordance with the planned study protocol.19 We estimated that 180 participants (60 in each group) would provide 89% power (α = 0.05, 2 sided), to detect an effect size of 0.29 which corresponds to a difference of 4.0% %BMIp95 between the three groups. Analyses followed principles of intention-to-treat (ITT) and were performed in nQuery + nTerim 4.0 and Stata/SE 17 (StataCorp, College Station, TX). A two-sided significance level of 0.05 was utilized throughout the analyses. Our analysis approach is based under the assumption that data are missing at random, therefore, imputation using last observation was carried forward, and multiple imputation based on logistic regression model (for BEDS-7 scores only) were utilized to account for missing data. Results from the ITT analysis using imputation were compared as per protocol analysis with completed data. For all outcomes a per-protocol analysis was conducted for: full-program (completed full 24-week intervention period), pre-COVID (completed 24-week intervention prior to 3/15/2020), and during COVID (completed 24-week intervention after 3/16/2020). In addition, to account for impacts of the intervention dosage received on each primary outcome measure we conducted an analysis of participants who were adherent to at least 80% of the prescribed intervention modalities versus those who were nonadherence. Participants' demographic characteristics and baseline anthropometric measurements were reported as appropriately, mean and standard deviation or median and interquartile range for continuous variables, and frequency and percentages for categorical variables. The change in %BMI95 between week 24 and baseline was assessed using analysis of variance (ANOVA) for all participants via ITT, per-protocol, PreCOVID and during COVID. First, the %BMIp95 was analysed in log scale mixed-effects linear regression model to assess the association between change in %BMIp95 and demographic characteristics (sex, ethnicity,

obesity related co-morbidities), CED-SC, PSS, BRIEF-2, YFAS-c, and BEDS-7 scores univariately and adjusting for recruitment site as a covariate. Then, a multivariable mixedeffects linear regression model was utilized to examine the effect of the possible factors on change in %BMIp95 accounting for recruitment site, demographic and other measured characteristics. The results are expressed in percent change with its associated 95th% confidence interval and p-value.

Data management and quality assurance

Principles underlying our approach to quality control includes: (1) standardization of measurements; (2) use of clear and specific protocols for all study activities including training for data collection and processing; (3) validation and verification of data management procedures by using of software capable of checking for out-of-range values and other sources of outliers; (4) implementation of a data cleaning protocol; and (5) periodic meetings and progress reports to provide specific, well-documented feedback to the investigators concerning potential difficulties as well as sufficient follow-up to ensure that problems are resolved in a timely fashion. Confidentiality will be strictly maintained during all data management. Children's Hospital of Los Angeles Biostatistics Core, Saban Research Institute, will follow aforementioned schemes to collect and manage with maintaining consistent quality and security of the study observations.

Data Collection Management Plan AppCoach:

The iPhone app will be securely integrated with a network server for real-time data access and storage. All participant app data will be periodically backed up to a secure server to preserve data in the event the participant loses or damages his/her iPhone. Artificial intelligence in the app will supplement coach functions. The investigators will have ongoing access to this data in order to monitor proper use of the app and participant weight loss. The developer of the app will have access to coded data including weight trends, app usage, problem foods identified, aversion techniques identified and food weights measured by the wireless scale and uploaded to the app. The app will utilize a code name chosen by the participant for guided prompts and all secure app messages to and from the mentor. No medical advice will be given. Investigators will provide support and prompt participant to enter data as necessary. All phone conversations will be recorded. Phone meetings will be documented by the coach via a secure electronic form system incorporated in the app database.

Coaching:

Trained clinical research coordinators will conduct semi-structured, in-person/WebEx interviews with each participant and all present family members using coaching session outlines developed by the research team. Interviews will begin with open-ended questions to prevent biased answers. Open-ended questions will include current health concerns and desired elements of health coaching to address these concerns during the intervention period. Parent/Guardian of all subjects will receive monthly calls to allow for technical difficulties to be remedied and to assist with improved adherence and retention. All interviews will be audio recorded verbatim for period evaluation of intervention fidelity. The weekly telephone call documentation will be reviewed monthly as well to ensure validity and identify discussion topics, themes and barriers.

All survey responses that are completed will be stored in a REDCap database.

Feasibility:

CHLA: The EMPOWER Clinic at CHLA cares for obese patients one half-day each week, seeing approximately 8 patients per week. Approximately 25% of these participants are 14-18 years of age, and ~70% of these should be eligible based on inclusion/exclusion criteria, yielding ~1-2 eligible participants per week. We expect to recruit 292 participants over a 36-month period.

Randomization and Blinding:

Blocked randomization will be utilized, to ensure the groups are balanced in terms of number of subjects and the distribution of potential confounding variables. Blocked randomization will be used to ensure the number of eligible subjects assigned to each group is equally distributed. Block size will be blinded from the primary investigator performing the study.

Potential Risks/Adverse Events and Procedures Used to Minimize the Risks

For purposes of monitoring and reporting adverse events, the following definitions will be used:

Adverse event (AE): any 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 because of the population under study (e.g., a mother reports extensive use of drugs).

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. Such an event could include suicidal ideation or attempted drug overdose or withdrawal, etc.

Adverse events monitoring: Each participant will be evaluated for any adverse events. All events will be graded by their attribution (unrelated to protocol; or possibly, probably, or definitely related to protocol). Any event reported to the Principal Investigator or to designated research associates by the participants or their parents. Events will be carefully documented in a report submitted to the IRBs. The report will include a description of the event; when and how it was reported; any official charts, records, or documentation to corroborate the event or the reporting of the event; and an action plan to prevent future occurrences. All adverse events will be graded as mild, moderate, or severe. Any severe and/or unanticipated adverse event will be immediately reported to the IRBs (within 48 hours of occurrence or recognition). All adverse events will be summarized annually and submitted to the IRBs. Any action resulting in a temporary or permanent suspension of this study (e.g., IRB actions) will be reported to the funding source.

Physical risks: Symptoms of fasting blood draw usually are not serious and generally resolve within a few minutes without treatment, by simply lying down and resting.

Psychological risks: It is possible that a participant may become upset thinking about some of the questions or topics in this study. Trained research staff will be conducting the assessment sessions to address any potential incident. All participants will be informed that they are free to refuse to answer any particular questions or questionnaires. They will also be informed that they can withdraw from the study at any time without penalty. Staff will immediately report any AEs connected to the data collection to Dr. Vidmar who will keep a log of AEs and SAEs. Dr. Vidmar will file a written report within 24 hours of being notified to the IRB, whether the event relates to the project or not. As part of this process, members of the IRB committee review the event and determine whether the event is directly related to project procedures so that it can be determined whether procedures need to be modified to avoid a similar AE in the future. Whether the event is related to the project, we will keep a log to provide information about all AEs in annual progress reports to the IRB. Dr. Vidmar will monitor outcomes for AEs, and outcome information will be entered into a log for inclusion in reports to the IRB and NIH.

Social risks: There are no added social risks from participating in this study.

Legal/other risks: There are no legal risks added from participating in this study.

Bullying or violence: If we suspect that participants are victims of bullying or violence at home or in their neighborhood, either through completion of the questionnaires or through adolescents' report to research staff, we will implement the following procedures: (1) we will make adolescents aware of resources available to them in their communities; (2) we will work with the youths to develop a safety plan for addressing bullying or violence; (3) we will ascertain risk to the adolescent. If we suspect that an adolescent has been abused or witnessed domestic violence, we will make a report to child protective services. Children/adolescents who are victims of bullying or domestic violence will not be dropped from the study, unless they ask to drop out. Suicidal Behavior. If we suspect that participants are suicidal, we will follow the Substance Abuse and Mental Health Services Administration SAFE-T: Suicide Assessment Five-Step Evaluation and Triage approach to

determining risk and clinical response. The five steps are Identify Risk Factors, Identify Protective Factors, Conduct Suicide Inquiry, Determine Risk Level/Intervention, and Document (which includes intervention and follow-up). As per Practice Guidelines, we will estimate suicide risk as Low, Moderate, or High. All potentially suicidal students will be provided an emergency plan with numbers to call, including local hospital emergency rooms, suicide hotlines, and research and school staff contacts. Each plan will be individually tailored to the needs and resources of the adolescent. Family members will be incorporated into the plan. We will be available to parents to work with them as to how to proceed if their child present with suicidal behavior. Adolescents who experience psychiatric emergencies such as suicidal behavior will not be dropped from the study, unless they request to terminate their participation.

Protection Against Risk:

Safety reviews: The Principal Investigator (Dr. Vidmar) and the IRB will review this protocol on a continuing basis for subject safety and include results of the review in the annual progress reports submitted to the funding source. The annual reports will include a list of adverse events and address: 1) whether adverse event rates are consistent with pre-study assumptions; 2) reasons for dropouts from the study; 3) whether all participants met entry criteria; and 4) whether continuation of the study is justified on the basis that additional data are needed to accomplish the stated aims of the study.

Monitoring plan: The study's data safety and monitoring plan will entail several components, overseen by the Principal Investigator (Dr. Vidmar):

1.All Children's Hospital of Los Angeles IRB policies and continuous reporting requirements will be followed in conducting the proposed study. Any actions taken by the IRB as part of its continuing review will be immediately reported to the funding source.

2. The PIs will implement and monitor procedures to ensure that the participants provide informed consent, that parents provide consent and permission and that all data remains confidential. This will also include a rigorous data management protocol to optimize data entry, accuracy/checking, and retrieval. Data will be stored in password-protected files accessible only to the investigators and staff under their supervision. In the database, only an ID code number will identify subjects. A list linking names and other identifiers with their ID codes will be stored in a separate file with a separate password. All original paper surveys will be stored in locked file cabinets. The PI will review all data collection forms for completeness and accuracy of the data and for protocol compliance. In the case of a breach of confidentiality or other adverse event, the Principal Investigator will report the event to the IRB, and appropriate procedural changes will be implemented to prevent future breaches or adverse events.
3. Internal committee. The Principal Investigator (Dr. Vidmar) and the Co-Investigators will meet quarterly to assess participant recruitment, accrual, and retention; data quality and timeliness; participant risk versus benefit; and the development of external conditions that could potentially affect the study. Significant problems or adverse events will be reported immediately to the CHLA IRB (if relevant).
4. As part of their training for the study, all study personnel who will interact with subjects will receive instruction in the completion of an adverse event reporting form. In response to any adverse event, these forms will be completed promptly and returned to the corresponding study team supervisor, who in turn will report the information to the Principal Investigator.

Potential benefits of the proposed research to human subjects and others: This study will help researchers and professionals understand how mobile health interventions help adolescents with weight management. Thus, the benefits of this project to the individual and society greatly outweigh the risks.

Importance of the knowledge to be gained: The proposed study tests whether mHealth interventions founded in addictive theory may be a cost effective and beneficial weight loss intervention for youth with obesity. This is important to bridge the gaps in our understanding of how to best treat obesity in this population. Our goal is to refine our understanding of mHealth interventions and the use of evaluating obesity through an addictive paradigm.

Risk-to-benefit ratio. The risks to the participants are minimal and procedures are in place to reduce the risk and minimize the impact of adverse events. Therefore, the potential gains of this study, which include informing policies and interventions addressing disease prevention and health promotion in adolescents, outweigh the risk of conducting this research.

ClinicalTrials.gov Requirements: **ClinicalTrials.gov Identifier: NCT03500835**

The project will be registered in ClinicalTrials.gov no later than 21 days after the first subject is enrolled. Reporting of summary results information (including adverse events) will be reported no later than 1 year after the completion date. The ClinicalTrials.gov registry number (also known as NCT number), brief lay public title, and a certification that all required submissions to ClinicalTrials.gov were completed will be provided in progress reports. The PI (Dr. Vidmar) will assume responsibility for these aspects of the trial.

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