NCT04088097

Cognitive Behavioral Therapy for Adolescent Binge Eating and Loss of Control Eating

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HRP-503B – BIOMEDICAL RESEARCH PROTOCOL
(2017-1)

Protocol Title: Development and Initial Efficacy Testing of a Cognitive-Behavioral Intervention to Treat Adolescent Binge Eating

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SECTION I: RESEARCH PLAN

1. **Statement of Purpose:** State the scientific aim(s) of the study, or the hypotheses to be tested.

   The overall aim of the study is:

   1. To develop a cognitive-behavioral therapy (CBT) that treats adolescent binge/loss-of-control (LOC) eating and test whether this new CBT for adolescent binge/LOC eating is superior to an active control group.

   Hypothesis 1: Adolescents randomized to CBT will have a greater reduction in binge/LOC eating (episode frequency) than adolescents in the active control group.

   Hypothesis 2: Adolescents randomized to CBT will have a greater reduction in weight (BMI z-score using measured height and weight) than adolescents in the active control group.

2. **Probable Duration of Project:** State the expected duration of the project, including all follow-up and data analysis activities.

   Development and evaluation of the treatment is expected to occur over 6 years (including follow-up and data analysis).

3. **Background:** Describe the background information that led to the plan for this project. Provide references to support the expectation of obtaining useful scientific data.

   Binge eating and obesity often co-occur in adulthood (1) and during adolescence (2-5), and both carry public health costs (6). Binge-eating disorder (BED) is the most common formal eating disorder among adolescents (7). Adolescent binge eating is associated with concurrent body image concerns, depression and externalizing behaviors, and prospective depression, substance use and self-harm (8, 9). Binge eating is highly associated with obesity and obesity-related health problems (7, 9-11). Among adolescents with overweight/obesity, 31% have loss-of-control eating episodes (LOC; feeling loss of control while eating any amount of food) (12); 22% have full binge-eating episodes (feeling loss of control while eating an unambiguously large amount of food) (2). Youth with binge eating and those with LOC have similar psychopathology and both groups show more psychopathology than youth with overeating alone (13). LOC also has more predictive significance in obesity development than overeating alone (10, 14). Adolescent obesity is associated with more frequent medical visits (15), increased cardiovascular risk factors (16), diabetes (17), asthma (15), depression, anxiety and behavior problems (18) during adolescence, and adult obesity (19). Thus, adolescents who binge eat are vulnerable—because of their weight and eating behaviors—to health problems and psychosocial impairment.

   Because binge/LOC eating in adolescence is both a precursor to adult obesity and a distinct source of health problems and psychosocial impairment, treating LOC during adolescence (14) could reduce immediate and long-term health consequences. Cognitive-behavioral therapy (CBT) has a strong evidence base for adult BED (20-25). However, there are no well-established treatments for adolescent binge/LOC eating (26) with one exception (27). Hilbert et al (27) applied adult CBT to adolescents aged 12-20 years, and showed a superiority of CBT compared to waitlist. They did not report any differences by age. Adolescents have unique social, cognitive and emotional needs because of their developmental stage; these unique needs require unique treatment approaches (28). Specifically, adolescents might not have the cognitive or emotional capacity to identify

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problems that are readily-apparent to parents, which suggests a need for collaboration, education, and multiple-informant assessment. Moreover, the clinician's work with the adolescent is only part of treatment (28). The family context—parental mental health, home life and stressors, and the home food environment—influence adolescents through parenting practices related to food and parent modeling of health behaviors. This suggests a need to engage support to facilitate improvements in adolescent outcomes (29).

Despite the need for tailored treatments, adolescent treatments are understudied (26, 28). Early evidence suggests that interpersonal psychotherapy might have promise for youth LOC; however, effects are modest and superiority over active control groups (e.g., health education) is unclear (30-34). Notably, interpersonal therapy has been tested in children (not adolescents) with LOC (30-32). A cognitive-behavioral adaptation for adolescents with recurrent binge eating (with or without purging) had a small sample and used a delayed-treatment control (35); treatment focused on eating but not weight, was minimally tailored to adolescence, and minimized parental support despite evidence that parental involvement improves weight outcomes (29, 36).

Because of the evidence for CBT for adult BED (20-22), developing CBT for adolescent binge/LOC eating is a critical clinical research task. Adolescence is characterized by rapid development physically, psychosocially, and cognitively. The chief task of adolescence is to develop autonomy across life domains, including establishing health habits that will endure into adulthood (37). Adolescents strive for independence yet remain under the authority of their parents who still purchase and prepare most meals, who still seek to guide adolescents' psychosocial development, and who are gatekeepers to health services (38). Parents' attempts to help can, at times, be misguided and paradoxically exacerbate eating/weight problems, for example, when focusing on or criticizing weight (39-45). Thus, helping adolescents navigate their increasing autonomy and negotiate parental support is key in adolescent therapy for binge/LOC eating. Other target areas for tailored intervention include eliciting appropriate peer support, coping with weight-related bullying (46), identifying and challenging maladaptive eating/weight thought patterns in the context of peer and parent messages (47, 48).

A developmentally-appropriate CBT needs to be developed and tested because of unique adolescent needs such as complex parent-teen relations (29, 36, 49), peer influences on eating and weight (50), and executive function deficits and growth (51, 52). To do this, the current study will make use of rigorous treatment development methodology and test the new treatment in a pilot study comparing CBT for adolescent binge/LOC eating to an active control group.

4. Research Plan: Summarize the study design and research procedures using non-technical language that can be readily understood by someone outside the discipline. Be sure to distinguish between standard of care vs. research procedures when applicable, and include any flowcharts of visits specifying their individual times and lengths. Describe the setting in which the research will take place.

There are two phases of this protocol, based on the Stage Model of Behavioral Therapies Research (53-55). First is the **treatment-development phase**, in which materials are developed. This involves focus interviews with target patients and administering treatment to an open series of pilot patients to refine the treatment manual. Second is the **initial efficacy pilot testing**. This involves an RCT comparing the treatment developed in the first phase to a control condition.

Thus, focus interviews will be completed first and can be concurrent to or followed by the open series. Participants who complete the focus interview will have the option of transitioning to the open series to receive treatment. Alternatively, participants can be recruited directly for the open

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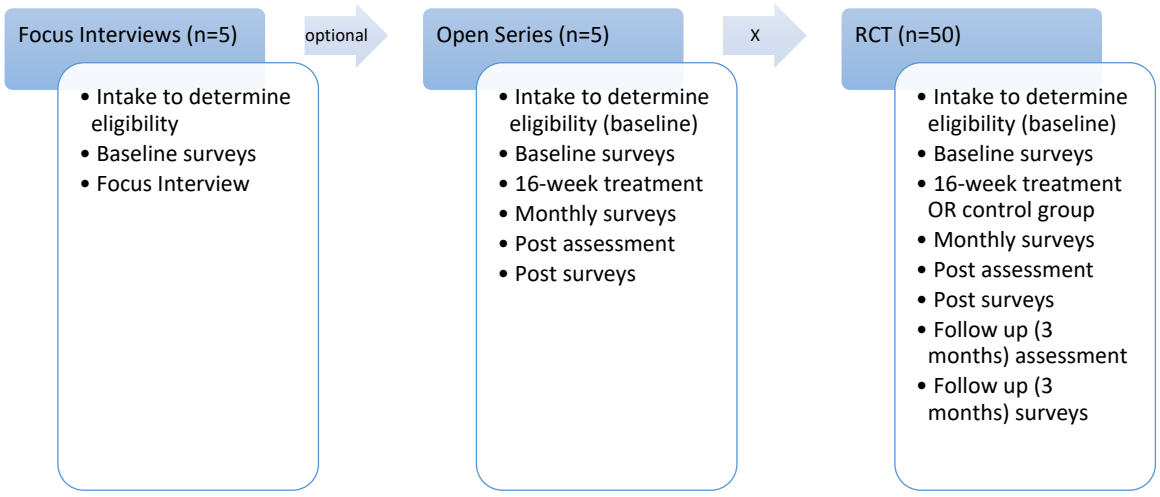
series after focus interviews are complete. When the treatment has been developed and the RCT begins, no further participants will be recruited for the first phase (focus interviews or open series).



Treatment-Development Phase. CBT for adolescent binge/LOC eating will be developed by modifying existing evidence-based treatments for adults with obesity and BED (Grilo et al., 23, 56). A working version of the clinician manual will be written specifying session format, detailed session-by-session content (unique, essential, recommended, proscribed treatment elements), primary and secondary treatment goals, and treatment materials.

"Focus interviews" will be conducted with adolescents and their parents based on the method described by Shea et al (57). Briefly, participants will be given a copy of "Overcoming Binge Eating," a book that describes cognitive-behavioral therapy for binge eating in a self-help format, and then will be interviewed by a research clinician about the aspects of the treatment that they believe would work well for adolescents and the aspects of the treatment that they believe need to be adapted. Focus interviews will be recorded and transcribed. Participants who complete the focus interviews will have the option of participating in the "open series" of patients (see below) but will not be eligible for the RCT.

Treatment (see "adolescent treatment," below) will be conducted with an open series of patients (N=5) to elaborate and refine the manual. Patients enrolled in the treatment-development phase will all receive active treatment. Patients and their parents will be asked to provide feedback about the new adolescent CBT in semi-structured interviews. Open-ended questions will explore preferences, acceptability of session content, and perceived benefits and costs to treatment parameters. Feedback from patients will refine protocols.

Initial Efficacy Testing. CBT for adolescent binge/LOC eating will be piloted with N=50 adolescents (randomly assigned to CBT n=25, or control n=25). Research clinicians with doctoral training in psychology will administer CBT and control conditions under the supervision of the PI. To demonstrate treatment acceptability (sessions attended; retention; patient/clinician ratings), feasibility, and efficacy, parents *and* adolescents will complete assessments (baseline, Month 1,

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Month 2, Month 3, post, 3 month follow-up) for CBT and control conditions.

Format and Content of Treatment. The 16-session treatment (4 months; weekly sessions) will be delivered by research clinicians with doctoral training in psychology, supervised by the PI. Participants will be audio-recorded if they consent to this procedure. Audio recordings will be for the purpose of evaluating treatment fidelity, as well as part of monitoring research-clinicians in the delivery of the treatment as specified in the protocol.

Adolescent Treatment. Adolescent therapy (see table) will have five stages and will occur during both the treatment-development and RCT phases of the study: 1) Orienting to treatment and establishing a therapeutic foundation; 2) Specific behavioral strategies and their implementation; 3) Coping skills training and implementation; 4) Integrated executive function skills; and 5) Relapse prevention planning to maintain health behaviors. As in general adolescent therapy (58), parents will have some involvement in therapy but the focus will be on adolescents. Parents will attend sessions monthly, during which they will learn about binge/LOC eating, collaborate to enhance adolescent awareness, identify parent and family factors that could inhibit change, and help the adolescent establish behavioral strategies that maximize improvement. Adolescents will teach parents what they have learned to increase self-efficacy and positive communication. Other developmentally-tailored content includes using tangible therapeutic tools, setting communication strategies and boundaries with parents, eliciting peer support and parent health-behavior support, and focus on both short- and long-term health goals. Executive function techniques will be taught as skills to reduce impulsivity, increase behavioral inhibition, improve planning, and promote long-term benefits in the context of health decision making, as has been done in anorexia nervosa treatment research (59-61). Executive function skills are expected to enhance therapeutic gains from behavioral and coping strategies.

Active Control. The control condition (see table) will address eating behaviors and nutrition, thereby having face validity and broad clinical appeal. The active control will be 4 months with mailed publicly-available information (weekly to match CBT; e.g., USDA healthy recipes, list of local recreation areas and activities) and monthly assessments (parent and adolescent attendance will be matched to CBT).

TABLE 1: CBT for adolescent binge/LOC eating and control conditions

<table>
<tr><th>Week</th><th>CBT for Adolescents</th><th>Control Condition</th></tr>
<tr><td>1</td><td>Orient to treatment: Establish collaborative therapeutic relationship with adolescent and parent cooperation; Educate adolescent and parent about binge/LOC eating</td><td>Orient to treatment: Establish collaborative relationship with adolescent and parent; Explain program format</td></tr>
<tr><td>2</td><td>Therapeutic foundation: Collaborative formulation with adolescent using moveable cards; Demonstrate importance of self-monitoring (mood, food), including format; Practice private, regular self-weighing; Establish adolescent-parent-clinician communication boundaries</td><td>Nutrition foundation: Information about food labels; MyPlate and food groups; Different types of fats; Benefits of eating fruits and vegetables</td></tr>
<tr><td>3</td><td>Specific behavioral strategies: Review self-monitoring to identify eating patterns and external influences; Minimize restriction and snacking outside of meals to establish a regular eating pattern</td><td rowspan="2">Healthy lifestyle: Information about serving sizes and portion sizes; List of local recreational areas for physical activity</td></tr>
<tr><td>4</td><td>Work with parents to create healthy, regular meals; Engage parents in behavioral reinforcement to enhance motivation</td></tr>
<tr><td>5</td><td rowspan="3">Coping skills: Review progress to enhance motivation; Practice emotional regulation and distress tolerance skills; Problem-solve using alternative behaviors; Elicit support from peers; Query weight-related bullying</td><td rowspan="3">Food groups: Information about carbs and fiber; Healthy proteins; Calcium and water; Using MyPlate to make meals at home and eat away from home</td></tr>
<tr><td>6</td></tr>
<tr><td>7</td></tr>
<tr><td>8</td><td>Identify parent and family factors that inhibit (promote) change</td><td></td></tr>
<tr><td>9</td><td>Executive function techniques: Teach executive function skills</td><td>Nutrition extras: Information about food</td></tr>
</table>

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10	(planning, behavioral inhibition) and practice applying to eating/weight; Identify and challenge maladaptive eating/weight cognitions	safety when cooking; Added sugars, sodium, herbs/spices; Food marketing
11		
12	Relapse prevention planning: Establish communication and behavioral strategies with parents to maximize improvement; Set collaborative goals with parent to solicit health behavior support	
13	Prepare to end treatment: Create monument of progress; Review skills learned to prepare education for parents; Set long-term health goals and plans to maintain progress throughout development; Prepare adolescent to identify lapses as opportunity to cope and maintain progress	Problematic eating: Information about snacks and comfort foods; Vitamins and long-term health
14		Prepare to end program: Summaries of materials learned; Quizzes on nutrition information
15		
16	Treatment summary by adolescent for parent; Treatment completion celebration	Summarize new knowledge; Treatment completion celebration

Yale Teen Power Advisory Board. Adolescents who have an interest in eating disorders, body image, and/or weight stigma will form the Yale Teen Power Advisory Board. The only requirement is that their age be 12-19 years old to correspond (approximately) to the age of participants in the clinical trials. There is no requirement that the adolescent be experiencing any eating disorder currently or in the past, and participants will not be considered ineligible unless there is a safety/privacy concern (current patient, current mental health problem that may worsen with discussion of eating disorder symptoms as they would be discussed in a classroom or educational setting; in our experience, this is exceedingly rare and easily identified by the PI or the parent). The teen advisory board will convene on Zoom and be completely voluntary.

General activities:

To establish group rapport, the Yale Teen Power Advisory Board will engage in general activities that are initiated by the group and/or focused on education, outreach, and advocacy.

Focus groups:
Adolescents will meet on zoom to participate in a focus group to provide feedback on future intervention development with teens in mind, and study findings. Adolescents will be paid for their participation ($10 per focus group per person plus a prize incentive, e.g., Teen Power tennis ball).

Focus groups will specifically address conducting treatment development research and disseminating results:

- Recruitment and retention of adolescents in studies.
- Feedback on potential community engagement activities (e.g., social media live events; workshops; health fairs) to increase awareness of clinical trial findings and their meaning.
- Examining and providing their perspective on all aspects of pilot RCT data (de-identified; not individual level) and results.

Focus groups will be with study investigators/staff. Specific questions to begin discussion will include:

- Which finding from the study is the most surprising to you? Least surprising?
- Do the findings from the study reflect what you thought would happen if your peers were in a treatment study?
- Is there a finding that you would want to know more about?
- What do you think we should research next?
- Which findings would you most want to share with others?
- Who would benefit from learning about the study findings? How should we tell them?

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Focus groups will be audio recorded and transcribed. If participants decline permission for recording, they can participate in general activities and can provide written responses to the focus group questions that will be shared anonymously with the group, but cannot be present at the focus group.

Assessments. Parents and adolescents will be assessed. At the beginning of treatment, adolescents will undergo a clinical assessment to confirm eligibility and to inform the course of treatment. Assessment batteries are guided by recommendations of *NIH ADOPT* workgroup on core measures (e.g., QEWP, EARLY, BRIEF, Kirby, PSS) (62-66). As well as established measures, acceptability (sessions attended; retention; patient/ clinician ratings of content), and adherence (e.g., homework completion), will be assessed. We will also gather clinical data on the patient's medical history prior to the study, which we will update as indicated in Table 2. Assessments will be the same for the open-series of patients during the treatment development phase as well as during the RCT phase, except that there will be no follow-up to the open-series of patients.

Assessment Training: Independent outcomes assessors will receive training in diagnostic interviews from investigators following well-established protocols used in previous projects. Once interviewers are certified in the measures (MINI and EDE), they will receive ongoing supervision to ensure consistent use and prevent drift.

TABLE 2: Assessment Batteries

	Baseline	Month 1	Month 2	Month 3	Post	Follow-Up (3 mo)
Adolescent assessment battery						
Established interviews:						
Eating Disorder Examination interview	*				*	
MINI Psychiatric Interview (MINI)	*					
Medical history	*					
Established survey measures:						
• Short UPPS (S-UPPS)	*				*	
• Amsterdam Executive Function Inventory (AEFI)	*				*	
• Kirby Delay Discounting	*				*	
• Sensitivity to Reward/Punishment (SRSPQ)	*				*	
• Questionnaire for Eating and Weight Patterns (QEWP-5)	*	*	*	*	*	*
• Eating Disorder Examination–Questionnaire (EDE-Q)	*	*	*	*	*	*
• Patient Health Questionnaire-9 (PHQ-9)	*	*	*	*	*	*
• Rosenberg Self-Esteem Scale (RSES)	*	*	*	*	*	*
• EARLY	*	*	*	*	*	*
• Pubertal Development Scale	*				*	*
• Perceptions of Teasing Scale (POTS)	*	*			*	*
• Weight-related Victimization	*				*	*
• Weight Bias Internalization Scale (WBIS-M)	*				*	*
• Brief Resilience Scale (BRS)	*	*	*	*	*	*
• Self-compassion Scale (SCS)	*	*			*	*
• CHAOS Scale	*	*			*	*
Anthropometric: BMI-z	*	*	*	*	*	*
Acceptability:						
• Treatment credibility	*					

• Ratings of session content		*	*	*	*	
Parent assessment battery						
Established survey measures:						
• Questionnaire for Eating and Weight Patterns (QEWP-5)	*	*	*	*	*	*
• Eating Disorder Examination–Questionnaire (EDE-Q)	*	*	*	*	*	*
• Child Feeding Questionnaire (CFQ)	*	*	*	*	*	*
• Perceived Stress (PSS)	*	*	*	*	*	*
• Accommodation Scale (AESED, FASA-DE)	*		*		*	*
• Fat Talk Questionnaire	*	* (child)			*	*
• Patient Health Questionnaire-9 (PHQ-9)	*	*			*	*
Anthropometric: BMI	*	*	*	*	*	*
Acceptability:						
• Treatment credibility	*					
• Ratings of session content		*	*	*	*	

Eating Disorder Examination (EDE) interview (67) for adolescents (10), the questionnaire version *(EDE-Q)* (68), and *Questionnaire for Eating and Weight Patterns (QEWP-5)* (69, 70) will assess disordered eating thoughts and behaviors (including binge/LOC eating). The EDE/EDE-Q and QEWP show good concordance (71-73), reliability (intra-class correlation .95-.99) and validity (74, 75).

MINI International Neuropsychiatric Interview-Version 7.0 (MINI) (76) is a brief structured interview for Axis I psychiatric disorders. Validation and reliability studies have supported the MINI, including good convergence with SCID (76). The MINI requires much less time than the SCID and reduces participant burden while providing adequate psychiatric data to characterize patients and determine exclusion criteria.

Short UPPS Scale (S-UPPS) is a reliable (α=.74-.88) 20-item measure of impulsive behavior, including negative urgency, lack of perseverance, lack of premeditation, sensation-seeking, and positive urgency (77).

Amsterdam Executive Function Inventory (AEFI) is a brief questionnaire assessing executive functioning ability, such as attention, self-control, and self-monitoring. The construct validity and reliability are considered adequate (78).

Kirby Delay Discounting (79) will measure reward-based decision making by comparing relative values of immediate and delayed rewards; this is related to adult weight loss (63, 80) and youth binge eating (52). The Kirby yields stable scores at 5-weeks (r=.71) and 1-year (r=.63) (79).

Sensitivity to Punishment/Sensitivity to Reward Questionnaire (SPSRQ) (81) assesses reinforcement sensitivity, has been validated with people with eating disorders, and has a reliability of .75-.83.

EARLY is a 2-item questionnaire about self-weighing frequency and scale access (64, 82, 83).

Pubertal Development Scale (84) is a brief scale (7 items) for adolescent to self-report their pubertal status. It has shown concordance with parent- and teacher-report and is accessible to youth.

Patient Health Questionnaire-9 (PHQ-9) is a widely-used, brief measure of depression (85) developed with 6000 adults, validated with 2291 adolescents, showing good sensitivity and

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specificity (86).

Rosenberg Self-Esteem Scale (RSES) is used extensively and is a reliable (α=.88) measure of global self-esteem (87, 88) and has been used in work with adolescents and research on childhood obesity (89).

Self-Compassion Scale (SCS) (90) is a widely used measure of self-compassion and is reliable (α=.77-.78)

Perceptions of Teasing Scale (POTS) is an assessment of whether an individual has been teased and how teasing affected them (91). Reliability for the subscales ranges .66-.90.

Brief Resilience Scale (BRS) (92) is a 6-item measure of resilience with good reliability (α=.80-.91).

Weight Bias Internalization Scale-Modified (WBIS) (93) is an 11-item measure of weight-based self-stigma for children and adults across the weight spectrum. It is reliable (α=.90), has strong construct validity, and relates to eating pathology, body image, and self-esteem.

Weight-related Victimization is an unpublished measure developed by the UConn Rudd Center (which specializes in weight-related discrimination and stigma). These items examine different negative experiences related to weight for school-aged youth. It also examines how the weight-related victimization affects the child.

Child Feeding Questionnaire (CFQ) (94) will assess parent feeding practices (Restriction, Pressure to Eat, Monitoring) and attitudes (Perceived Responsibility, Concerns about Child Weight). The CFQ is reliable (α=.65-.91) and valid for work with diverse parents (95) seeking weight loss treatment for their children (96).

Perceived Stress (PSS) (97) has a reliable total score (α=.83), 6-week temporal stability (r=.81) and validity associated with health behaviors including eating (98).

CHAOS Scale (99) measures environmental processes within familial households, including perceive chaos, hubbub, and order. CHAOS has a reliable total score (α=.79) and a 12-month test-retest stability (r=.74).

Accommodation and Enabling Scale for Eating Disorders (AESED) (100) is a 33-item caregiver measure assessing family accommodation to the eating disorder. The measure is reliable (α=.77-.92). *FASA-DE* is a new version of the *Family Accommodation Scale for Anxiety Disorders (FASA) (101)* with adaptations specific to eating and weight that is being developed.

Fat Talk Questionnaire (FTQ) (102) is a measure of negative discussions about weight that the parent engages in; there are three subscales including fat talk about themselves (self), their child (child) or people with obesity (obesity). The measure has excellent reliability (α=.93).

Anthropometric measures: Height will be measured to the nearest 0.25 inch using a stadiometer or reported by parent/child. Weight will be measured to the nearest 0.1 pound using a digital scale provided to the patients for their home use. Height/weight data will calculate BMI (66). Adolescent BMI data will use CDC growth charts (age/sex-normed) to calculate BMI percentile, BMI z-score, and expected change in BMI (103).

Fitbit scale: All adolescents determined to be eligible will be given a Fitbit Aria Scale that they will

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be allowed to keep during and after the study. The scale is a smart scale that displays weight and syncs to Fitbit accounts that the study team will create for each participant. The adolescent patient and their parent will be asked to weigh themselves on the scale at each study data collection timepoint.

Ratings of Session Content. Patients and parents will be asked open-ended questions about the treatment during the treatment-development phase (examples listed below). Patients and parents will also rate session content on likert scales during both phases of the study.

- What did you not like about this treatment?
- What would you change?
- What was helpful about this treatment?
- What would you make sure to keep in the treatment?
- What were challenges in this program that were difficult to overcome?
- What advice would you give to someone starting treatment? To a clinician?

5. Genetic Testing N/A ☒

6. Subject Population: Provide a detailed description of the types of human subjects who will be recruited into this study.

Adolescents will be recruited using flyers in the community, primary care and other medical offices, and schools (104, 105). Our research facilities are local to these community spaces and should present minimal location-based barriers. Adolescents will have excess weight and regular binge/LOC eating without any contraindications (see inclusion/exclusion criteria) to be eligible for treatment.

7. Subject classification: Check off all classifications of subjects that will be specifically recruited for enrollment in the research project. Will subjects who may require additional safeguards or other considerations be enrolled in the study? If so, identify the population of subjects requiring special safeguards and provide a justification for their involvement.

☒Children	☐ Healthy	☐Fetal material, placenta, or dead fetus
☐Non-English Speaking	☐ Prisoners	☐Economically disadvantaged persons
☐Decisionally Impaired	☐ Employees	☐Pregnant women and/or fetuses
☐Yale Students	☐ Females of childbearing potential	

NOTE: Is this research proposal designed to enroll children who are wards of the state as potential subjects?
Yes ☐ No ☒

8. Inclusion/Exclusion Criteria: What are the criteria used to determine subject inclusion or exclusion?

Inclusion Criteria: To be included, adolescents must:

1. Be in the age range ≥12 years old and ≤17 years old;
2. Have a BMI that places them above the 85th percentile based on their age and sex;
3. Report 2 episodes of binge/LOC eating (feeling a loss of control while eating) per month for the past 3 months;
4. Be otherwise-healthy youth (i.e., no uncontrolled or serious medical conditions);
5. Read, comprehend, and write English at a sufficient level to complete study-related materials;

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6. Provide a signed and dated written assent prior to study participation;
7. Provide a signed and dated written consent from one parent prior to study participant; and
8. Be available for participation in the study for 7 months.

Exclusion Criteria: Prospective participants will be excluded if the adolescent:

1. Has a medical or psychiatric condition that would require hospitalization or intensive care (e.g., neurological disorder, psychotic disorders, suicidality);
2. Has a medical or psychiatric condition that would prohibit them from engaging in behavioral treatment or moderate physical activity (e.g., cardiovascular problems);
3. Has uncontrolled medical condition(s) (e.g., uncontrolled diabetes or hypertension);
4. Is pregnant or breastfeeding;
5. Is taking medication(s) or participating in treatment(s) that could influence weight or appetite;
6. Began taking hormonal contraceptives less than 3 months prior;
7. Has a developmental or cognitive disorder (e.g., autism spectrum disorder);
8. Has a concurrent feeding/eating disorder (e.g., bulimia nervosa); or
9. Is participating in another clinical research study.

9. How will **eligibility** be determined, and by whom?

Participants will be interviewed during an initial intake by a study clinician. The semi-structured investigator-based Eating Disorder Examination (EDE) interview (child version) will be used to determine binge/LOC eating episodes and to characterize eating-disorder psychopathology. The EDE along with the MINI psychiatric interview will also determine whether participants have any co-existing psychiatric conditions that require referrals, hospitalization or more intensive/different treatment.

Final determination of eligibility will be from the PI.

10. **Risks:** Describe the reasonably foreseeable risks, including risks to subject privacy, discomforts, or inconveniences associated with subjects participating in the research.

The primary risks of the treatment development research and pilot RCT are the behavioral interventions, the assessment procedures, and unknown treatment efficacy.

Cognitive-behavioral therapy (CBT) is an established treatment for psychiatric conditions and health behavior change. CBT is established and widely-used in research and clinical settings, for both youth and adults. The only foreseeable risks include some mild discomfort or embarrassment when discussing eating patterns, weight, or body image concerns. Previous controlled clinical trials conducted by the PI and study team with similar interventions with adult and adolescent participants have not reported problems. Any troublesome effects would be readily identifiable by the experienced study clinicians during repeated evaluations. Thus, the risks of the CBT interventions are judged to be minimal.

Research assessments are noninvasive and should add no substantial risk. The major disadvantages are the time taken to complete them and potential for a breach of confidentiality. Completion of the assessment interviews and surveys may cause some mild anxiety or embarrassment to some participants. Past experiences of the PI and study team indicate that the measures are acceptable to participants. Careful efforts aimed at maintaining confidentiality will be made (as described below).

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There is a chance that participants' eating concerns and overweight may fail to improve or may worsen during the study. Participants will be withdrawn from the study if their clinical condition deteriorates to a significant degree, and they will be provided with appropriate referrals.

11. Minimizing Risks: Describe the manner in which the above-mentioned risks will be minimized.

The study clinicians will be carefully trained and supervised by the PI. All study clinicians and study staff will have IRB and ethics training; because of their educational experience and training (e.g., in psychology), they can reasonably be expected to identify potential problems and to take appropriate action as medically indicated. The PI will be continuously available to the study clinicians to discuss any problems and to implement any needed interventions or offer appropriate referrals. The detailed assessments repeated during the course of treatment will allow for additional and ample opportunity to identify difficulties. In the event that a participant experiences undue distress, resources are available. If a study participant experiences any psychiatric symptoms or distress (e.g., depressive symptoms or suicidality) at any stage of study participation they will receive short-term treatment and support from the PI and study treatment team (which includes psychologists) and will be connected with a local emergency department and their physician or a therapist for ongoing care.

Participation may be in-person or remote (telehealth). For participants who participate remotely (i.e., during the COVID pandemic), all participants will complete a "Telehealth Safety Plan" with their clinician at session 1. This plan, recommended by the National Register of Health Service Psychologists for providers conducting telehealth, provides standard language around what to do in an emergency and what to do if a telehealth session is disconnected. The Telehealth Safety Plan also includes an interactive worksheet for the clinician to do with the participant to identify personally-relevant ways to get help. The participant and the clinician will both keep a copy of this plan. The plan will not be retained after the participant finishes the study.

Potential participants will be informed of alternative treatments, and if indicated or requested, appropriate referrals will be provided. Potential participants will also be informed that they may drop out of the study at any time.

To ensure confidentiality, all research records will be kept in locked files in the Department of Psychiatry at Yale School of Medicine. All research personnel will be trained and supervised around confidentiality issues. The training will include formal NIH or Yale IRB modules with testing certification as well as HIPAA guidelines to follow around confidentiality. All participants will be assigned a study number. Subsequently, participants will be identified only by that number and an encoded version of their initials (e.g., John Smith [adolescent] = JSMI-A). A list of numbers and the corresponding names will be maintained by the PI and stored in a locked research file. Any information published as a result of the study will be such that it will not permit identification of any participant. All information collected will remain confidential except when we are legally required to disclose such information by law. These circumstances include knowledge of abuse of a child or elderly person, threats of harm to self or others, and plans to harm to property.

Fitbit scale confidentiality: Study staff will create Fitbit accounts for participants when they are given the scale. Study ID, rather than name, will be used in the account. The most conservative privacy settings will be selected. Participants will be told, as described in the consent form, that their data will be accessed by study staff during the study treatment and follow up phase. Study staff will access the accounts created for the study to collect weight data, which will be recorded in study databases at Yale. After the follow up phase is completed, participants will be allowed to keep the

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scale and to connect the scale to a personal account or retain the use of the account we created for them. If they choose to keep the same account, they will be encouraged to change the log-in information. Weight data collected for the study will be aggregated for publication and presentation of results and will not identify individual participants. If participants do not want to use the Fitbit scale, they will have the option of receiving a non-smart scale and/or providing self-reported weight to study staff at data collection timepoints.

Focus interviews will be transcribed and audio records will be deleted at the end of the study. Other data will be stored in locked cabinets for 7 years after the final data are collected. Research records may be audited by a regulatory agency within the federal government. Organizations that have a responsibility for protecting human subjects, including the Yale IRB (Human Investigation Committee), may have access to the research records. Additionally, the funding agency (NIH) may have access to the research records.

12. Data and Safety Monitoring Plan: Include an appropriate Data and Safety Monitoring Plan (DSMP) based on the investigator's risk assessment stated below. (Note: the HIC will make the final determination of the risk to subjects.)
    a. What is the investigator's assessment of the overall risk level for subjects participating in this study? Minimal risk
    b. If children are involved, what is the investigator's assessment of the overall risk level for the children participating in this study? Minimal risk
    c. Include an appropriate Data and Safety Monitoring Plan. Examples of DSMPs are available here http://your.yale.edu/policies-procedures/forms/420-fr-01-data-and-safety-monitoring-plans-templates for
        i. Minimal risk
        ii. Greater than minimal

    d. For multi-site studies for which the Yale PI serves as the lead investigator: n/a

The treatment interventions and assessment protocols are well-established and pose primarily low risks to participants. The DSMP for the proposed pilot RCT focuses on close monitoring by the PI in conjunction with an independent Safety Monitor. Excessive adverse events and/or any serious events (should they occur) will be reported promptly to the NIH and to the Yale School of Medicine IRB (Human Investigation Committee). Other (less serious) adverse events will be reported to the IRB periodically during regular reporting periods. In addition to the DSMP, the Yale IRB reviews all aspects of the study protocol (including progress and problems) minimally once per year.

Monitoring for the safety of participants and the integrity and quality of data will be the responsibility of the PI, the study team, and the Yale IRB (Human Investigation Committee).

The PI will be responsible for monitoring the safety of participants and the integrity and quality of data for the proposed pilot RCT, executing the DSMP, and complying with reporting requirements to the NIH and Yale IRB.

Qualifications and responsibilities of the Safety Monitor.
The Safety Monitor for this trial will be Mahnoosh (Mona) Sharifi, MD, MPH. Dr. Sharifi is an Assistant Professor of Pediatrics in the section of General Pediatrics at Yale, and practices as a general pediatrician at the Yale Pediatric Primary Care Center. Dr. Sharifi is an experienced pediatrician with substantial clinical research and clinical expertise with adolescents and families, including those with obesity. Dr. Sharifi is not involved in the study design or clinical intervention or

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related to any chain of command. As Safety Monitor, Dr. Sharifi will review the reports sent by the PI and will determine whether there is any corrective action, trigger of an ad hoc review, or stopping rule violation that should be communicated to the study PI, the IRB at the Yale School of Medicine, and the NIH.

Risk Assessment

This is a behavioral (NON-medication) RCT that does not involve multiple sites, treatment blinding, or high-risk interventions. Although the pilot RCT does include vulnerable individuals (adolescents 12-17 years old), the risks associated with the proposed pilot RCT, including the cognitive-behavioral treatment and assessment protocols, are judged to pose minimal risks to participants. Therefore, we provide the following plan for monitoring the safety of participants and the integrity and quality of data:

Measurement and Reporting of Data Integrity and Quality

The PI is responsible for monitoring the data, assuring protocol compliance, and conducting the safety reviews. During the review process, the PI will evaluate whether the study should continue unchanged, require modification/amendment, or close to enrollment.

The PI, in consultation with Dr. Grilo (Primary Mentor), will provide a summary of the DSMP report to the NIH as part of the annual progress report and to the Yale IRB on a yearly basis as part of the annual re-approval process. The DSMP reports will include Subject accrual, Treatment completion rates, Interim analyses, and Adverse and serious adverse events. These reports will be discussed with the mentoring team during regular meetings and sent to the Safety Monitor for review. The frequency of data review is summarized in the following table:

	Data Type	**Frequency of Review by PI**	**Frequency of Review by PI and Safety Monitor**
1	Subject accrual	Monthly	Annually
2	Treatment completion rates (retention/attrition)	Quarterly	Annually
3	Interim analyses	Twice Yearly	Annually
4	Adverse and serious adverse event rates	As needed	Annually
5	Checklist for Safety Monitor	NA	Annually

The PI, the Institutional Review Board (IRB) and/or the Safety Monitor have the authority to stop or suspend the study or require modifications.

Subject Accrual

Subject accrual reviews will help to assure that subjects are being enrolled (accrued) at a rate necessary to meet the recruitment goals in general and with regard to racial/ethnic diversity. Subject accrual rates will be discussed with the PI monthly and annual accrual rates will be reported by the PI to the Safety Monitor to determine if any corrective action is needed to meet the recruitment goals.

Treatment Completion Rates

Retention, attrition and completion rates will be carefully tracked and reviewed. This will be done quarterly to highlight any possible concerns and will be reviewed formally with the PI and Safety Monitor annually. Differential dropout across treatments and/or higher than expected dropout will be reviewed to determine whether any problems are present and what, if any, corrective action needs to be taken. “Trigger points” for corrective action, as described below, include: 35% (“low alert”), 40% (“mid alert”), 45% (“high alert”), and 50% (“extreme alert”). With early alerts to problems, action

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would be taken to avoid higher level alerts; if a higher-level alert should arise, more drastic actions would be taken.

It is possible that baseline differences between the treatment conditions, excessive attrition, and/or missing data will limit the value of the data analysis, and hence knowledge to be gained from this study. For these reasons, interim analyses will be conducted twice yearly. Baseline differences, if present, will be considered in relation to potential effects on the power to detect differences in the primary outcomes. If these effects were to develop and be sizeable, alterations to the randomization schedule would be considered. Such effects would be evaluated and discussed by the PI and mentors, and plans would be communicated to the NIH and Yale IRB. To address excessive attrition and missing data, the following actions would be taken at the "trigger point" for each level of alert:

1) Low-level alert (35%): Review of potential problems by PI and review of procedures for supervision of study clinicians.
2) Mid-level alert (40%): Meeting between PI and senior study team members to discuss approaches to minimize further dropouts.
3) High-level alert (45%): Meeting between PI and senior study team members to determine further alterations to study protocol to complete the study with no further losses.
4) Extreme-level alert (50%): In the unlikely event that a 50% dropout rate occurs prior to the mid-study time point, the PI and senior study team members would convene to discuss the usefulness of continuing the study.

It is possible that other situations could occur that might warrant stopping the trial. Any concerns would be discussed with appropriate parties (PI, Mentors, Safety Monitor, NIH, Yale IRB).

Measurement and Reporting of Adverse Events

Data on adverse events will be collected on an ongoing basis. Adverse events data will be monitored by the PI and reviewed with the Safety Monitor throughout the pilot RCT (see Table above).

This protocol presents minimal risks to the subjects and Unanticipated Problems Involving Risks to Subjects or Others (UPIRSOs), including adverse events, are not anticipated. In the unlikely event that such problems occur, Reportable Events (which are events that are serious or life-threatening and unanticipated (or anticipated but occurring with a greater frequency than expected) and possibly, probably, or definitely related) or UPIRSOs that may require a temporary or permanent interruption of study activities will be reported immediately (if possible), followed by a written report within 5 calendar days of the PI becoming aware of the event to the IRB. The PI will apprise study personnel of all UPIRSOs and adverse events that occur during the conduct of this research project through regular study meetings, and via email as they are reviewed by the PI.

Attribution of Adverse Events:

Adverse events will be monitored for each subject participating in the study and attributed to the study procedures by the PI according to the following categories:

a) Definite: Adverse event is clearly related to the study treatment or assessment procedure.
b) Probable: Adverse event is likely related to the study treatment or assessment procedure.
c) Possible: Adverse event may be related to the study treatment or assessment procedure.
d) Unlikely: Adverse event is likely not to be related to the study treatment or assessment procedure.
e) Unrelated: Adverse event is clearly not related to the study treatment or assessment procedure.

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Plan for Grading Adverse Events:
The following scale will be used to grade the severity of adverse events (should they occur) during the study:

a) Mild adverse event
b) Moderate adverse event
c) Severe adverse event

Plan for Determining Seriousness of Adverse Events:
In addition to grading adverse events, the PI will determine whether the adverse event meets the criteria for a Serious Adverse Event (SAE). An adverse event will be considered serious if it results in any of the following outcomes:

a) Death;
b) A life-threatening experience that results in in-patient hospitalization;
c) A persistent or significant disability or incapacity;
d) A congenital anomaly or birth defect; or
e) Any other adverse event that, based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition.

Plan for reporting events to the Yale IRB that are unexpected AND related AND involve risk of harm to subjects or others:
The PI will report to the IRB any incident, experience or outcome that meets ALL 3 of the following criteria:

1) Is unexpected (in terms of nature, specificity, severity, or frequency) given (a) the research procedures described in the protocol-related documents, such as the IRB-approved protocol and informed consent document and (b) the characteristics of the subject population being studied; and
2) Is related or possibly related to participation in the research (possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
3) Suggests that the research places subjects or others at greater risk of harm (including physical, psychological, economic, legal, or social harm) than was previously known or recognized.

Unanticipated Problems Involving Risks to Subjects or Others (UPIRSOs) may be medical or non-medical in nature, and include – but are not limited to – serious, unexpected, and related adverse events.

All related events involving risk but not meeting the prompt reporting requirements described above will be reported to the IRB in summary form at the time of continuing review. If appropriate, such summary may be a simple brief statement that events have occurred at the expected frequency and level of severity as previously documented.

Plan for reporting adverse events to the mentors, Safety Monitor, study team, and funding agency:
For the current study, the following individuals, funding, and/or regulatory agencies will be notified:

- Primary Mentor (Grilo) and Co-Mentor (Silverman);
- All Co-Investigators listed on the protocol; and
- National Institutes of Health.

The PI will review all adverse events upon completion of every study subject. The PI will evaluate the frequency and severity of adverse events and determine if modifications to the protocol or consent form are required.

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Procedures for providing follow up care:
Study participant safety will be monitored by the study team and reported to the PI at all visits and referrals will be provided if warranted and/or requested. If a study participant experiences any psychiatric symptoms or distress (e.g., depressive symptoms or suicidality) at any stage of study participation they will receive short-term treatment and support from the study treatment team (which includes psychologists) and will be connected to a local emergency department and their physician or therapist for ongoing care.

Other Potential Issues Relating to Stopping Rules for the Pilot RCT Include:

1) New Information: It is unlikely that any new information would become available during this trial that would necessitate stopping the trial. If new data become available, these will be evaluated.
2) Limits of Assumptions: It is possible that baseline differences between the treatment conditions, excessive attrition, and/or missing data could limit the value of data analysis. Baseline differences across treatment groups, if present, will be evaluated twice yearly and considered in relation to potential effects on the power to detect differences in the primary outcomes. If these effects were to develop and be sizeable, alterations to the randomization schedule would be considered. Any plans to alter the randomization scheme would be communicated to the NIH.
3) Limits of Rules: There are other situations that could occur that might warrant stopping the trial and/or including a section on the safety report entitled “Other situations that have occurred since the last safety report that warrant discussion” to allow for communication of concerns.

13. Statistical Considerations: Describe the statistical analyses that support the study design.

DATA ANALYSIS AND AIMS
Baseline demographic and clinical characteristics will be compared between treatment and control groups using chi-square tests for categorical variables (e.g., sex) and ANOVAs or Kruskal-Wallis tests for continuous variables (e.g., BMI z-score). Continuous variables will be examined for adherence to normality using probability plots and Kolmogorov-Smirnov tests. If normality is not satisfied and transformations do not achieve acceptable normality, alternative strategies (e.g., nonparametric) will be considered. Dropouts and completers will also be compared. Analyses will be intent-to-treat. Outcomes will be tested at the α=0.05 threshold.

Overall analysis strategy. Descriptive statistics will quantify change and mixed-effects models (106, 107) will compare treatments through post; 3-month follow-up will be exploratory. These models allow for different numbers of observations per participant, use all available data on each participant, account for clustered data observations, and are unaffected by data missing at random. A further advantage is the capacity to test and account for individual-difference contributions to treatment outcomes (108). This strategy provides flexibility in modeling the correlation structure of the data. In models for each outcome, we will include fixed effects of time and treatment and their interaction, and random subject-level effects. Because we cannot *a priori* predict the shape of the response over time, we will first treat time as categorical and then test for polynomial trends. We will consider different error structures (e.g., compound symmetry, autoregressive) and select the best-fitting structure based on information criteria. Data on all participants enrolled in the study will be used in mixed models. We will compare dropout patterns and if there are concerns of informative dropout and/or informative intermittent missing data, we will use pattern mixture models to perform sensitivity analyses to main analyses.

Primary Aims.

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Primary Aim 1 is to **test** the efficacy of adolescent CBT relative to the active control condition at post-treatment on clinical outcomes, including: (a) reduction in binge/LOC eating frequency (evaluated by the QEWP), and (b) reduction in weight (evaluated by BMI z-score). Significant time-by-treatment effects with significantly less adolescent binge/LOC eating and significantly reduced weight in adolescent CBT relative to the control condition will be considered supportive of these aims. Parallel analyses will also assess binge/LOC frequency reduction using the EDE; because this interview is only administered at baseline and post, this analysis will, by definition, occur among completers. Adolescent CBT is hypothesized to yield reduced binge/LOC eating frequency and weight reduction (i.e., weight loss or less excess weight gain) compared to the control group.

Primary Aim 2 is to **test** the acceptability and establish the feasibility of adolescent CBT. Descriptive statistics will quantify clinician/patient treatment ratings, sessions attended, and retention, and clinician adherence/competence through ratings of recorded sessions.

Secondary Aims.

Secondary Aim 1 is to **explore** the efficacy of adolescent CBT relative to active control: (a) reduction in disordered eating thoughts and behaviors (EDE-Q), (b) improvements in executive function (S-UPPS, Kirby), (c) improvement in psychosocial functioning (reduced depression, PHQ; improved self-esteem, RSES).

Secondary Aim 2 is to **explore** the durability and maintenance of treatment effects during short-term follow-up.

Secondary Aim 3 is to **explore** potential predictors of primary outcomes. Following Kraemer's (109) conceptual/statistical model for predictors, we will explore whether baseline characteristics predict treatment effects by testing for main effects and interactions in models for primary outcomes (specified above), including (a) adolescent executive function (S-SUPPS, Kirby), (b) self-weighing (EARLY), (c) parent BMI and disordered eating behaviors (EDE-Q/QEWP), and (d) parent feeding practices and attitudes (CFQ). Grilo et al (25) used this analytic strategy in earlier work.

Power Analysis and Justification of Sample Size. Results are anticipated to yield significant impact by providing effect sizes for grant applications to perform definitive studies comparing the new adolescent CBT treatment with existing interpersonal therapy for youth LOC. Power estimates for the pilot RCT were based on the comparison of CBT (n=25) and control conditions (n=25). Assuming a two-sided test at α=0.05 threshold, we have 80% power to detect clinically meaningful between-subjects (d=0.8) and within-subject effects within each group (d'=0.58). Even assuming 20% dropout, we still have 80% power to detect clinically meaningful effects (d=0.9 between-subjects and d'=0.66 within-subject). While power is limited given the pilot nature of the study, such effects are similar to effects observed in a prior study (31) that compared LOC eating between youth who received either interpersonal therapy or were in a control group. Thus, we have a reasonable chance of finding statistically significant differences between CBT and control, even in this pilot study.

SECTION II: RESEARCH INVOLVING DRUGS, BIOLOGICS, RADIOTRACERS, PLACEBOS AND DEVICES

If this section (or one of its parts, A or B) is not applicable, check off N/A and delete the rest of the section.

RADIOTRACERS ☒N/A

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DRUGS/BIOLOGICS ☒N/A

DEVICES ☒N/A

SECTION III: RECRUITMENT/CONSENT AND ASSENT PROCEDURES

1. Targeted Enrollment: Give the number of subjects:
   a. Targeted for enrollment at Yale for this protocol: 55
   b. If this is a multi-site study, give the total number of subjects targeted across all sites: n/a

2. Indicate recruitment methods below. Attach copies of any recruitment materials that will be used.

☒ Flyers	☒ Internet/web postings	☐ Radio
☐ Posters	☐ Mass email solicitation	☒ Telephone
☐ Letter	☒ Departmental/Center website	☐ Television
☐ Medical record review*	☐ Departmental/Center research boards	☐ Newspaper
☐ Departmental/Center newsletters	☒ Web-based clinical trial registries	☒ Clinicaltrails.gov
☒ YCCI Recruitment database	☒ Social Media (Twitter/Facebook):	
☒ Other: EPIC direct-to-patient		
☒ Other: messages to provider EPIC inbox		

* Requests for medical records should be made through JDAT as described at http://medicine.yale.edu/ycci/oncore/availableservices/datarequests/datarequests.aspx

3. Recruitment Procedures:

a. Describe how potential subjects will be identified.

Participants will be recruited using widespread media advertising, internet and printed materials throughout the community. The study will also be posted on the website for clinical trials at Yale and the Yale Program for Obesity, Weight, and Eating Research, and web-based clinical trials registries, such as Research Match.

b. Describe how potential subjects are contacted.

Pre-screening. Interested parents/adolescents will be screened briefly to determine whether the teen is likely to be eligible to participate in the study. If they seem potentially eligible and interested in the study, parents and their children will be scheduled for an initial assessment visit.

Initial Assessment. After initial contact, study clinicians (who have completed IRB training) will meet with potential participants to discuss the study, the treatments, the assessments, the follow-up period, and the informed consent procedures and forms.

EPIC Inbox Messages may be used to send information to providers about referring subjects to the treatment study. Providers, identified by JDAT, will receive the inbox message or email if they meet specific parameters (seeing patients under age 18). The following template will be utilized:

> Title of study, Phase or type of study: Cognitive-Behavioral Therapy for Adolescents with Binge Eating

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Principal Investigator: Janet Lydecker, Ph.D.

Study Contact: Janet Lydecker, Ph.D. Phone # 203-785-7210

Description:
We are recruiting teens for a cognitive-behavioral intervention for adolescents with binge eating.

About the treatment:
- We are treating BOTH binge eating and weight
- There is no cost to the patient, and no cost to their insurance
- Teens receive either cognitive-behavioral treatment or a healthy eating program
- Treatment lasts 4 months, and patients are followed up for 3 months after treatment ends.

Who to refer:
- Adolescents between 12-17 years old
- BMI >85th percentile
- *We will assess binge eating*

To refer a patient who may be eligible:
- The **teen or parent** can call: (203) 785-7210 or email: teenpower@yale.edu
- The **teen or parent** can request information: http://m.yale.edu/teenpower
- **Direct-to-provider**: email Dr Lydecker at janet.lydecker@yale.edu

c. Who is recruiting potential subjects?

PI and study staff will be recruiting potential participants.

4. Assessment of Current Health Provider Relationship for HIPAA Consideration:
Does the Investigator or any member of the research team have a direct existing clinical relationship with any potential subject?
☐Yes, all subjects
☐Yes, some of the subjects
☒No

If yes, describe the nature of this relationship. *Write here*

5. Request for waiver of HIPAA authorization: (When requesting a waiver of HIPAA Authorization for either the entire study, or for recruitment purposes only. Note: if you are collecting PHI as part of a phone or email screen, you must request a HIPAA waiver for recruitment purposes.)
Choose one:
☐ For entire study
☒ For recruitment/screening purposes only
☐ For inclusion of non-English speaking subject if short form is being used and there is no translated HIPAA research authorization form available on the University's HIPAA website at hipaa.yale.edu.

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i. Describe why it would be impracticable to obtain the subject's authorization for use/disclosure of this data:
ii. If requesting a waiver of **signed** authorization, describe why it would be impracticable to obtain the subject's signed authorization for use/disclosure of this data:

Potential participants will initially call us in response to advertisements, at which time, if they seem eligible, we will schedule them for an initial assessment and collect contact information. If potential participants elect to participate, they would then provide informed consent including HIPAA authorization as described at their initial intake visit.

The investigator assures that the protected health information for which a Waiver of Authorization has been requested will not be reused or disclosed to any person or entity other than those listed in this application, except as required by law, for authorized oversight of this research study, or as specifically approved for use in another study by an IRB.

Researchers are reminded that unauthorized disclosures of PHI to individuals outside of the Yale HIPAA-Covered entity must be accounted for in the "accounting for disclosures log", by subject name, purpose, date, recipients, and a description of information provided. Logs are to be forwarded to the Deputy HIPAA Privacy Officer.

6. **Process of Consent/Assent:** Describe the setting and conditions under which consent/assent will be obtained, including parental permission or surrogate permission and the steps taken to ensure subjects' independent decision-making.

   After initial screening and preliminary determination of eligibility, study clinicians (who have completed IRB and ethics training) will meet with potential participants for an initial intake appointment. At the intake, study clinicians will discuss the study and all procedures, treatments, and risks and obtain written informed consent from one parent and assent from the adolescent. All prospective participants will be free to decide whether or not to participate and enrolled participants are free to withdraw from the study at any time. Alternative treatments (both psychosocial and pharmacological options) will be discussed and referrals offered if requested. Written informed consent from parents, and assent from adolescents, will be obtained after they have the opportunity to discuss and address all questions with a study clinician and/or the PI. As talk therapy or educational materials on healthy eating are minimal risk, and both the treatment and active control conditions are likely to provide some direct benefit to the adolescent, only one parent signature will be obtained.

7. **Evaluation of Subject(s) Capacity to Provide Informed Consent/Assent:** Indicate how the personnel obtaining consent will assess the potential subject's ability and capacity to consent to the research being proposed.

   With all participants, we will describe the study verbally during the consent process and allow participants to ask any questions they might have. To ensure understanding, we will use open-ended questions with all participants to ask that they paraphrase the nature of the research and what they are being asked to do as part of the study, and also summarize the potential risks and benefits of the study.

8. **Non-English Speaking Subjects:** Explain provisions in place to ensure comprehension for research involving non-English speaking subjects. If enrollment of these subjects is anticipated, translated copies of all consent materials must be submitted for approval prior to use. n/a

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9. **Consent Waiver: In certain circumstances, the HIC may grant a waiver of signed consent, or a full waiver of consent, depending on the study.** If you will request either a waiver of consent, or a waiver of signed consent for this study, complete the appropriate section below.

☐Not Requesting any consent waivers

☒Requesting a waiver of signed consent:

☒ Recruitment/Screening only *(if for recruitment, the questions in the box below will apply to recruitment activities only)*

☐ Entire Study (Note that an information sheet may be required.)

For a waiver of signed consent, address the following:

- Would the signed consent form be the only record linking the subject and the research? YES ☒ NO ☐
- Does a breach of confidentiality constitute the principal risk to subjects? YES ☒ NO ☐

OR

- Does the research pose greater than minimal risk? YES ☐ NO☐
- Does the research include any activities that would require signed consent in a non-research context? YES ☐ NO ☐

☐ Requesting a waiver of consent:

☐ Recruitment/Screening only *(if for recruitment, the questions in the box below will apply to recruitment activities only)*

☐ Entire Study

For a full waiver of consent, please address all of the following:

- Does the research pose greater than minimal risk to subjects?
  ☐ Yes *If you answered yes, stop. A waiver cannot be granted.*
  ☐ No
- Will the waiver adversely affect subjects' rights and welfare? YES ☐ NO☐
- Why would the research be impracticable to conduct without the waiver? *Write here*
- Where appropriate, how will pertinent information be returned to, or shared with subjects at a later date? *Write here*

SECTION IV: PROTECTION OF RESEARCH SUBJECTS

Confidentiality & Security of Data:

1. What protected health information (medical information along with the HIPAA identifiers) about subjects will be collected and used for the research?

Height, weight, medical and psychosocial history will be collected and used for research.

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HIPAA identifiers to be collected:

☒ Names
☒ All geographic subdivisions smaller than a State, including: street address, city, county, precinct, zip codes and their equivalent geocodes, except for the initial three digits of a zip code if, according to the current publicly-available data from the Bureau of the Census: (1) the geographic unit formed by combining all zip codes with the same three initial digits contains more than 20,000 people, and (2) the initial three digits of a zip code for all such geographic units containing 20,000 or fewer people is changed to 000.
☒ Telephone numbers
☒ E-mail addresses
☒ All elements of dates for dates related to an individual, including: birth date

2. How will the research data be collected, recorded and stored?

To ensure confidentiality, all research records will be kept in locked files in the Department of Psychiatry at Yale School of Medicine. All research personnel will be trained and supervised around confidentiality issues. The training will include formal NIH or Yale IRB modules with testing certification as well as HIPAA guidelines to follow around confidentiality. All participants will be assigned a study number. Subsequently, participants will be identified only by that number and an encoded version of their initials (e.g., John Smith [adolescent] = JSMI-A). A list of numbers and the corresponding names will be maintained by the PI and stored in a locked research file. Any information published as a result of the study will be such that it will not permit identification of any participant. All information collected will remain confidential except when we are legally required to disclose such information by law. These circumstances include knowledge of abuse of a child or elderly person, threats of harm to self or others, and plans to harm to property.

Data will be stored in locked cabinets for 7 years after the final data are collected. At the end of the study, participants will only be identified by their study number. Research records may be audited by a regulatory agency within the federal government. Organizations that have a responsibility for protecting human subjects, including the Yale IRB (Human Investigation Committee), may have access to the research records. Additionally, the funding agency (NIH) may have access to the research records.

3. How will the digital data be stored? ☐CD ☐DVD ☐Flash Drive ☐Portable Hard Drive ☒Secured Server ☐Laptop Computer ☐Desktop Computer ☐Other

4. What methods and procedures will be used to safeguard the confidentiality and security of the identifiable study data and the storage media indicated above during and after the subject's participation in the study?

See above, the patients will only be identified by a number on any digital data files. Individually identifiable health information will be protected in accordance with the Health Insurance Portability and Accountability Act of 1996.

All portable devices must contain encryption software, per University Policy 5100. If there is a technical reason a device cannot be encrypted please submit an exception request to the Information Security, Policy and Compliance Office by clicking on url http://its.yale.edu/egrc or email it.compliance@yale.edu

5. What will be done with the data when the research is completed? Are there plans to destroy the identifiable data? If yes, describe how, by whom and when identifiers will be destroyed. If no, describe how the data and/or identifiers will be secured.

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Data will continue to be stored in locked cabinets in limited access areas until the legal requirement for storage has been met. Electronic data files will be password protected. Electronic data files will include code numbers only – i.e., will not contain patient identifying information.

6. If appropriate, has a Certificate of Confidentiality been obtained?

   Yes (NIH-funded study)

SECTION V: POTENTIAL BENEFITS

Potential Benefits: Identify any benefits that may be reasonably expected to result from the research, either to the subject(s) or to society at large. (Payment of subjects is not considered a benefit in this context of the risk benefit assessment.)

The study may have no direct benefit to the subject for their participation in this study. The cognitive-behavioral treatment is known to be helpful to some adults with binge-eating disorder and obesity, but we do not know if it will be help teens with binge eating. We anticipate that some of the knowledge from this study will be used to improve treatments for adolescents and to increase our understanding of binge eating.

SECTION VI: RESEARCH ALTERNATIVES AND ECONOMIC CONSIDERATIONS

1. Alternatives: What other alternatives are available to the study subjects outside of the research?

   Alternatives include community referrals for interpersonal processing therapy or weight management by a pediatrician.

2. Payments for Participation (Economic Considerations): Describe any payments that will be made to subjects, the amount and schedule of payments, and the conditions for receiving this compensation.

   Parents and adolescents will be paid for assessments (each: Mo. 1=$25; Mo. 2=$25; Mo. 3=$25; Post=$50; Follow-up=$25).

   Participants who complete the focus interview will receive $20 each.

3. Costs for Participation (Economic Considerations): Clearly describe the subject's costs associated with participation in the research, and the interventions or procedures of the study that will be provided at no cost to subjects.

   Psychological assessment and treatment will be provided at no cost to participants, their insurance, health plan benefits nor other third party payer.

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4. In Case of Injury: This section is required for any research involving more than minimal risk, and for minimal risk research that presents the potential for physical harm (e.g., research involving blood draws).

    a. Will medical treatment be available if research-related injury occurs?

    Yes. Referrals for treatment will be made.

    b. Where and from whom may treatment be obtained?

    As this study is behavioral (non-medication), there is minimal risk of injury. If the participant is injured as a direct result of participation in this research study, referrals for treatment will be made. If a study participant experiences any psychiatric symptoms or distress (e.g., depressive symptoms or suicidality) at any stage of study participation they will receive short-term treatment and support from the study treatment team (which includes psychologists) and will be connected to a local emergency department and their physician or therapist for ongoing care.

    c. Are there any limits to the treatment being provided?

    If the participant is injured as a direct result of participation in this research study, the treatment will be determined by the medical provider(s).

    d. Who will pay for this treatment?

    The participant or participant's insurance carrier will be billed for the cost of this treatment. There are no plans to compensate the participant for physical or mental disability, lost wages, or any other losses or damages occurring over the long term or if an injury becomes apparent after participation in the study has ended. However, by agreeing to participate in this research study, the participant is not waiving or giving up any legal rights to seek compensation. Participants who believe they have been injured should contact the Principal Investigator immediately.

    e. How will the medical treatment be accessed by subjects?

    Referrals will be provided.

IMPORTANT REMINDERS

Will this study have a billable service? Yes ☐ No☒

Are there any procedures involved in this protocol that will be performed at YNHH or one of its affiliated entities?
Yes ☐ No ☒

IMPORTANT REMINDER ABOUT RESEARCH AT YNHH

Please note that if this protocol includes Yale-New Haven Hospital patients, including patients at the HRU, the Principal Investigator and any co-investigators who are physicians or mid-level practitioners (includes PAs, APRNs, psychologists and speech pathologists) who may have direct patient contact with patients on YNHH premises must have medical staff appointment and appropriate clinical privileges at YNHH. If you are uncertain whether

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the study personnel meet the criteria, please telephone the Physician Services Department at 203-688-2615. By submitting this protocol as a PI, you attest that you and any co-investigator who may have patient contact has a medical staff appointment and appropriate clinical privileges at YNHH.

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