Official Title: Feasibility Trial of a Mindfulness Based Intervention to Reduce Maladaptive Eating Behaviors in Youth with Type 1 Diabetes

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RESEARCH PROTOCOL

TITLE:
Feasibility Trial of a Mindfulness Based Intervention to Reduce Maladaptive Eating Behaviors in Youth with Type 1 Diabetes

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RESEARCH PLAN

A. Specific Aims

Aim 1. Develop adapted manuals and participant materials for BREATHE-T1D intervention and HealthEd-T1D comparison condition. We will conduct/analyze a series of structured, open-ended interviews with interdisciplinary T1D experts and adolescents with T1D to make adaptations to content/delivery (telehealth) of a BREATHE mindfulness group and HealthEd comparison group for adolescents with T1D. Our expected outcomes will be a mindfulness-based group program addressing negative affectivity and a didactic HealthEd control group, with teen workbooks and intervention manuals adapted specifically for youth with T1D.

Aim 2. Evaluate feasibility/acceptability of BREATHE-T1D and HealthEd-T1D. Our hypothesis is that we will be able to recruit participants, as measured by CONSORT tracking of recruitment, enrollment, and dropouts, to a 2-way pilot RCT involving randomization to BREATHE-T1D telehealth, or HealthEd-T1D. We will assess post-intervention follow-up rates by condition. We anticipate that both conditions will be acceptable, with surveys indicating high satisfaction and qualitative structured interviews informing final refinements. We hypothesize BREATHE-T1D telehealth will evidence the highest participation ($\geq$80%), with both conditions achieving $\geq$65%

attendance.

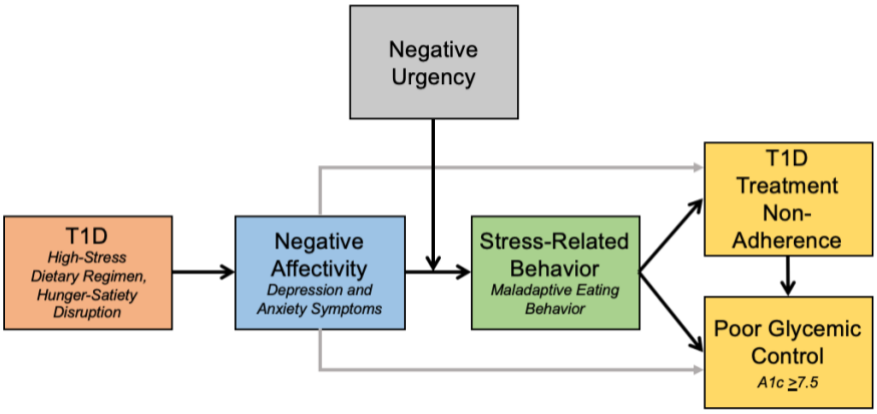
B. Background and Significance

Type 1 Diabetes in Adolescents. T1D is one of the most common childhood chronic illnesses, affecting 1 in every 400 youth under age 20 [1]. Rigorous daily medical regimens must be followed including multiple blood glucose checks, insulin injections, monitoring food choices and physical activity, maintaining snack availability for hypoglycemia, restocking medical supplies, and management of acute complications (ADA, 2011). National studies demonstrate that only 32% of youth aged 13-18 years and 18% of youth age 19 and older meet American Diabetes Association (ADA) targets for glycemic control, as compared to 56% of adults [2,3]. Additionally, up to 1/3 of young adults experience diabetes-related acute and chronic complications.[4] Thus, glycemic control significantly deteriorates across adolescence and continues into young adulthood.[5]. Adherence to diabetes prescribed regimen is critical in achieving glycemic control and reducing the risk of acute and long-term complications of diabetes [6].

Psychological Well-being and T1D in Adolescents

Although there are multiple reasons for the observed decline in T1D treatment adherence and glycemic control during adolescence, one significant and potentially modifiable risk factor is **negative affectivity**. As shown in ***Figure 1***, the conceptual model guiding the work is that the high-stress dietary regimen and disruption of physiological signals of hunger-satiety signals that are necessary burdens of T1D promote negative affectivity, including depression and anxiety symptoms.[7] Negative affectivity, in turn, is known to promote stress-related behavior, including maladaptive eating behavior, which commonly occurs in an effort to cope with unpleasant emotions.[7] Consequently, stress-related behavior leads to diminished treatment adherence and thereby, worsening of glycemic control.[7] In support of this model, there is a well-established association between T1D and increased risk for elevated depression and anxiety symptoms, with meta-analyses indicating that **40% of teens with T1D have elevated symptoms of depression or anxiety**, as compared to 20% in community samples of adolescents without T1D.[8,9] Depression and anxiety symptoms have been associated with greater risk of developing poor self-care and treatment non-adherence, and consequently, poor glycemic control.[8,10]

Figure 1. *Conceptual etiological model guiding the work*



Negative affectivity may impact treatment adherence and glycemic control through a variety of **stress-related behavioral mechanisms**; yet, maladaptive eating behavior appears to be particularly salient for youth with T1D, given the hyper-focus on food/calories and disruption of hunger-satiety signals that are central features of this chronic illness.[7] **Maladaptive eating behavior** refers to a spectrum of unhealthy eating and weight-control behaviors that include excessive dietary restriction, loss-of-control or binge eating, and specific to individuals with T1D, withholding post-prandial insulin.[11] Intentional insulin omission leads to acute weight loss, whereas regular insulin administration promotes weight gain. Overweight (BMI $\geq 85^{th}$ %ile for age/sex) and obesity (BMI $\geq 95^{th}$ %ile for age/sex) are increasingly common in youth with T1D, with 25% having overweight and 7% obesity.[12] Maladaptive eating behavior typically emerges during adolescence among youth with T1D, as well as those without T1D, and it is more common among adolescents with overweight/obesity.[13] Further, adolescents with T1D have very high rates of maladaptive eating relative to adolescents without T1D.[13] Specifically, 20% of adolescents with T1D report clinically significant maladaptive eating behavior, referring to symptoms that meet diagnostic criteria for an eating disorder, and an additional ~25% report subthreshold maladaptive eating, which is problematic but occurs less frequently and/or for a shorter duration than the diagnostic threshold.[13,14] Maladaptive eating behavior in adolescents with T1D is complicated, because one of the primary aspects of daily T1D treatment adherence requires a hyper-focus on food.[7] Youth with T1D must carefully monitor carbohydrate composition of meals and override hunger-satiety physiological signals in order to achieve adequate glycemic control. Of further concern, although maladaptive eating behavior is risky for all adolescents, risks to adolescents with T1D are high stakes. Maladaptive eating behavior interferes with treatment adherence[15] and increases risk of physical health complications.[13,14,16] **Thus, interventions in adolescents with T1D are needed to provide youth with alternative ways of coping with negative affectivity associated with their chronic illness**.

Further, although there are substantial data from longitudinal and experimental studies highlighting negative affectivity as a main contributor to stress-related behavior and health outcomes, contemporary models are increasingly recognizing the role of negative urgency as a key moderating influence in this chain.[17] **Negative urgency** is the propensity to act rashly when experiencing negative affectivity. Negative urgency is a core dimension of poor executive functioning and impulsivity, and this particular dimension seems to be especially important for adolescents.[18] Thus, our guiding etiological framework assumes that it is the combination of a propensity for negative urgency *and* the experience of negative affectivity that is mostly likely to lead to stress-related behaviors, including maladaptive eating, as an unhealthy form of coping in adolescents with T1D. From a developmental perspective, the timing of this phenomenon emerging in adolescence likely occurs because puberty is accompanied by significant increases in perceived stress, including stress related to the burden of T1D, and significant increases in negative affectivity.[19] For adolescents who are managing the added, major burden of T1D, adolescence is often a period when parental figures transfer more autonomy to youth for the management of their chronic disease.[20] What is more, the increase in negative affectivity is simultaneously occurring at a time in the lifespan when executive function has *not* reached maturation.[21] Indeed, adolescents, on average, behave significantly

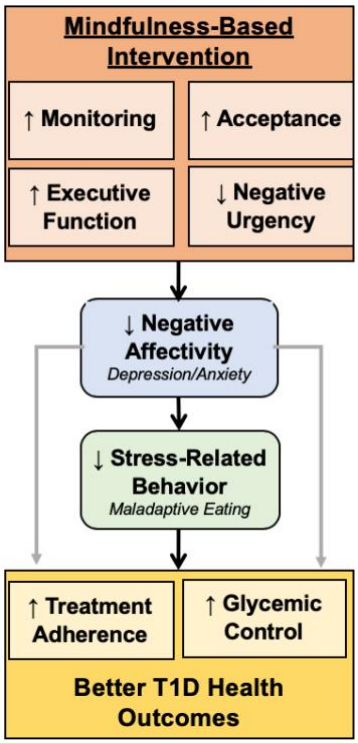
more impulsively than adults, particularly in the face of strong emotions.[22] In light of these considerations, there is strong evidence to suggest that **effective interventions to improve treatment adherence and glycemic control in adolescents with T1D will necessitate a developmentally-sensitive approach**. The dynamic changes in responsibility for disease management, increases in negative affectivity, and heightened maladaptive eating behavior render adolescence an ideal window of opportunity for interventions to optimize treatment adherence and prevent worsening of glycemic control in adolescents with T1D.

Interventions

Interventions to address treatment non-adherence and poor glycemic control in adolescents with T1D **must go well beyond standard-of-care T1D education**. Drawing on a combination of clinical experience, our guiding theoretical model, and extant scientific data, we anticipate that interventions should include: (i) explicit acknowledgement and acceptance of the burden of T1D, (ii) psychoeducation about negative affectivity during adolescence, (iii) provision of tools for self-monitoring and identification of unpleasant emotions, cognitions, and body sensations that commonly arise in adolescents with T1D, (iv) acceptance and tolerance of such unpleasant emotions, cognitions, and body sensations without acting rashly, and (v) coping skills for managing T1D stress and its concomitant, negative affectivity, which provide adolescents with healthier alternatives to maladaptive eating and that are tailored for adolescents with T1D who are required to carefully manage food intake. **As such, mindfulness-based intervention may be uniquely suited for the needs of adolescents with T1D**.

There has been rising scientific and clinical interest in mindfulness-based interventions to decrease negative affectivity[23,24] and improve physical health outcomes, including stronger treatment adherence and better chronic disease management.[25-27] A principal goal of mindfulness-based interventions is increasing dispositional mindfulness, referring to the propensity to pay attention on purpose to one's present-moment experiences with an attitude of non-judgment and equanimity.[28] From the framework of Monitor and Acceptance Theory,[29,30] mindfulness-based interventions are postulated to decrease negative affectivity and thereby, stress-related behavior through (i) increased attention to monitoring of present-moment experiences in combination with (ii) increased acceptance of experiences regardless of their valence. These mechanisms have been supported in recent dismantling studies.[29,31-33] We theorize that a mindfulness-based intervention will be particularly fitting for decreasing negative affectivity and decreasing stress-related behavior in adolescents with T1D. Enhanced monitoring and acceptance of thoughts, emotions, and body sensations as they unfold moment-to-moment is theorized to decrease negative affectivity through the therapeutic mechanisms of: (i) increased **monitoring** of thoughts, emotions, and body sensations, (ii) increased **acceptance** and equanimity with respect to thoughts, emotions, and body sensation, (iii) increased **executive function**, and (iv) decreased **negative urgency** (***Figure 2***).[30]

***Figure 2**. Mindfulness-based intervention conceptual model guiding the work*



Emerging studies of mindfulness-based interventions support the possibility that this therapeutic approach may distinctively help adolescents to flexibly deploy attention away from emotional and physical cues that prompt responding on "auto-pilot," including the use of maladaptive eating behavior to cope, and to respond alternatively with healthier coping strategies.[34,35]

A relatively small body of RCTs have evaluated mindfulness-based interventions in adults or emerging adults with diabetes, typically combining populations of adults with T1D and type 2 diabetes (T2D). These studies have shown moderate effects of mindfulness interventions for decreasing depression and anxiety symptoms, relative to waitlist, diabetes education, and treatment-as-usual controls, from post-treatment to 1-year follow-up.[36-43] Some of these RCTs also show significant effects of mindfulness interventions on improved glycemic control and overall health.[36,39,42,43] Yet, not all studies have found physical health benefits, particularly trials that included patients who already had adequate glycemic control.[36-38,40,41] **To our knowledge, no RCT study has evaluated a mindfulness-based intervention in adolescents with T1D.** Yet, mindfulness interventions may be especially valuable in adolescence, given marked developments in executive function and openness to new experience, which render this transitional period in the lifespan malleable.[22,44-47] Pilot and feasibility studies in diverse populations, including work conducted by our investigative team, support acceptability and credibility of mindfulness interventions in this age group.[23,48] Also, RCT studies support the efficacy of mindfulness interventions for lowering depression/anxiety in diverse samples of adolescents *without* T1D, with moderate effects compared to attention controls.[23] Preliminary RCTs also have found that mindfulness interventions decrease maladaptive eating in teens (*without* T1D) who are at risk for weight-related disorders and adverse metabolic health, as well as among adults with overweight/obesity.[38,40,49-51]

Development of a mindfulness-based intervention tailored for adolescents with T1D is a critical first step. Prior to efficacy testing, intervention development to adapt a mindfulness-based intervention for this unique chronic illness population is critical. There are **five main distinct considerations in adolescents with T1D** for adapting mindfulness-based training to address negative affectivity and stress-related behavior particularly maladaptive eating, in this population: (i) adolescents with T1D face potentially unpleasant physical and emotional sensations unique to T1D (e.g., hypoglycemia); (ii) T1D treatment adherence necessitates a heightened focus on eating and nutrition; (iii) T1D treatment adherence requires an overriding of physiological cues for hunger-satiety; (iv) T1D treatment adherence often results in higher body weight with appropriate insulin administration; and (v) many families have lengthy travel to receive specialty healthcare, suggesting novel delivery formats such as telehealth should be considered for feasibility, acceptability, and sustainability.

It is also essential to adapt and test feasibility/acceptability of a comparison, health education (HealthEd) didactic group program. Our investigative team has experience delivering HealthEd content, in an individualized delivery format, within T1D adolescent clinicals trials.[52] Separately, in adolescents *without* T1D, we have effectively used a general HealthEd group curriculum, matched to BREATHE for intensity, group format, and duration, to serve as a didactic control condition.[53,54] A comparison, HealthEd-T1D didactic group program is needed, which integrates the content relevant to T1D in a group delivery format. Vetting the viability of this approach with T1D experts and adolescents with T1D is critical, because establishing feasibility and acceptability of the control condition is required to enhance feasibility of recruitment, ensure acceptability of randomization to the control condition, and to minimize condition effects on attendance or confirm no cross-contamination or representation of mindfulness-based content between conditions, which could confound treatment effects in a subsequent efficacy trial.[55]

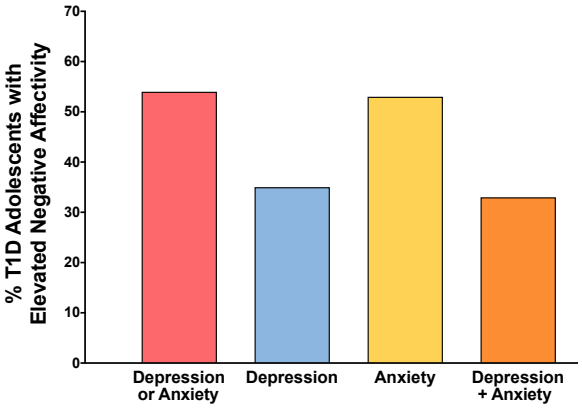
Current Study

The proposed study will develop the intervention with stakeholder input and conduct a preliminary feasibility and acceptability pilot. This study is essential for developing and evaluating both a mindfulness-based group curriculum (BREATHE-T1D) and a health knowledge control group (HealthEd-T1D) adapted for youth with T1D, in order to directly prepare for a future efficacy trial that can test the efficacy of a mindfulness-based group-based intervention on negative affectivity, stress-related behavior, treatment adherence, and glycemic control.

C. Preliminary Studies

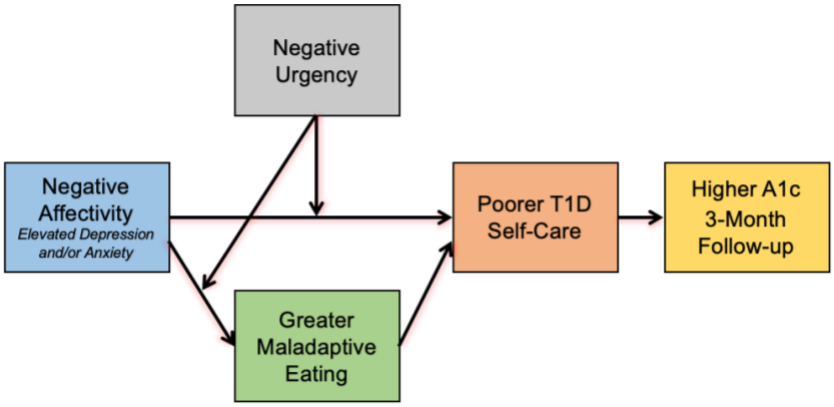
Negative affect/maladpative eating in adolescents with T1D at Children's National. Drs. Mackey (PI) and Streisand (Co-I) enrolled *N*=100 youth with T1D, 11-17y (*Mean* age=14y), in an observational, longitudinal study. The recruitment rate was 59% of eligible teens approached in clinic. Thus, our investigative team is **well-positioned to access the target population**. In preliminary analyses of this cohort, we were able to characterize rates of negative affectivity (***Figure 3***), maladaptive eating, and suboptimal glycemic control. Consistent with estimates from other cohorts of adolescents with T1D, **a majority (61%) of adolescents receiving T1D care at Children's National Hospital (Washington, DC) reported elevated symptoms of depression, anxiety, or both, and a considerable number (25%) report engaging in maladaptive eating behavior**. Also consistent with national statistics, **the vast majority (81%) of adolescents with T1D had poor glycemic control (A1c ≥7.5%)**.

Figure 3. *Rates of elevated depression, anxiety, and both types of negative affectivity among adolescents*



Further, preliminary analyses provide support for our conceptual model. Using path analysis, we found that negative affectivity, as reported by adolescents with T1D and their parents, predicted poorer self-care and higher A1c (worse glycemic control) 3 months later (***Figure 4***). In clinically meaningful terms, T1D teens with elevated depression and/or anxiety had a nearly 1% higher A1c at 3-month follow-up, controlling for baseline A1c, than those with no or low negative affectivity (*Mean* A1c 9.7% vs. 8.9%, *p*=.07). The effect of negative affectivity was partially explained by greater maladaptive eating behavior. Moreover, the connections of negative affectivity with maladaptive eating and self-care were moderated by negative urgency. Adolescents with T1D were most likely to report engaging in maladaptive eating behavior and poorer self-care in response to negative affectivity when they also were higher in negative urgency. **These data contribute to the overarching hypothesis for the current work: mindfulness-based intervention may be highly suitable for adolescents with T1D because its therapeutic targets include provision of coping skills for monitoring emotional states with an attitude of acceptance, increasing executive function, and decreasing negative urgency**.[38,40,48-51,56]

Figure 4. *Path analysis of observational data shows negative affectivity, combined with negative urgency, relates to poorer T1D self-care and higher A1c at 3-month follow-up, partially through greater maladaptive eating; model/all paths p<.05, controlling for age, sex, race/ethnicity, and socioeconomic status*

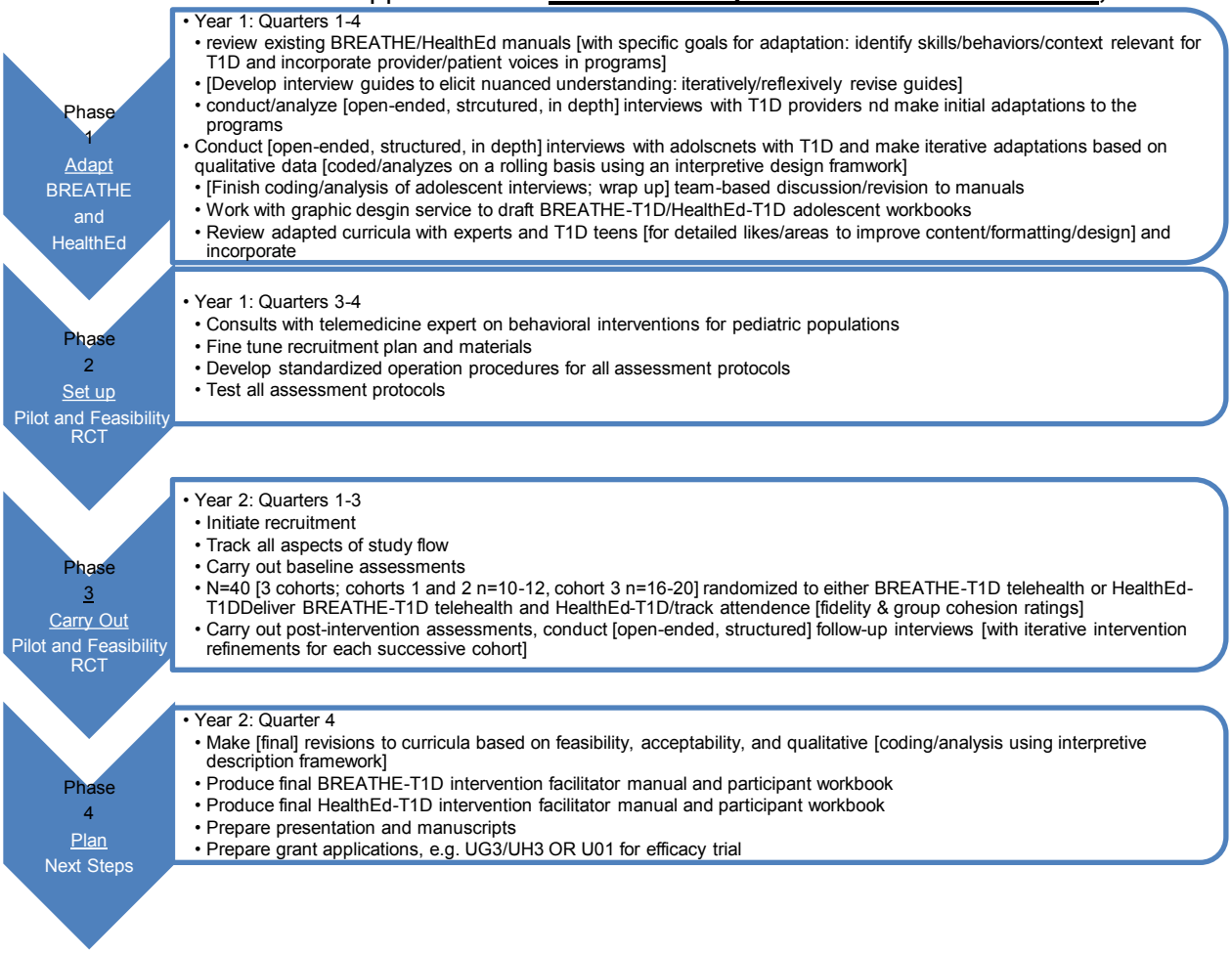


Intervention development in T1D. Drs. Mackey (PI) and Streisand (Co-I) recently completed an NIH-funded intervention development grant (DP3DK103998) to promote healthy eating and physical activity, in order to improve glycemic control in young children with T1D. This project employed the ORBIT model to [create a brand-new intervention from the ground up].[57] Interviews were initially conducted with 4 parents in the target population (parents of children ages 2-5y with T1D). Interviews used a semi-structured format with questions about adjustment to diagnosis, regimen, and areas of difficulty and strengths, with specific probes for eating behavior and physical activity. A stakeholder advisory board, including parents, professional experts in T1D care, and research consultants, was created. Once the initial program content was created, the research team contracted with a graphic designer to create a logo and visually appealing materials. The stakeholder advisory board was consulted for ongoing refinement and was sent drafts of the materials for review and feedback. Next, we carried out a small pilot study (*N*=10) to examine feasibility and acceptability of the intervention, approach, and assessment protocol. Minor adjustments were made and then a small pilot RCT (*N*=36) was conducted to evaluate feasibility and acceptability of the intervention as compared to usual care. Results indicated feasibility of recruitment in that 68% of contacted eligible candidates agreed to participate, feasibility of retention with 97% retained through 6-

month follow-up, and high acceptability/satisfaction, as 100% perceived the program had a positive impact on their child's T1D management and 84% would recommend the program to other parents and were glad that they participated. **These data indicate the unique expertise of the study team to systematically develop T1D behavioral interventions that are feasible and acceptable using a similar framework proposed in the current study**.

D. Research Design and Methods

Overview. The proposed approach is consistent with the ORBIT model of progressive behavioral intervention development.[57] Specifically, we propose to first adapt content/delivery format of an existing adolescent mindfulness-based group intervention, Learning to BREATHE, for adolescents with T1D ***using a rigorous qualitative data collection/analysis approach to intervention adaptation***.[58] Then, we will test the feasibility/acceptability of this adapted BREATHE-T1D group program delivered via telehealth, with the goal of identifying feasibility of delivery for a future efficacy trial. We also will adapt a health knowledge group-based program for teens with T1D (HealthEd-T1D) to serve as a didactic, non-overlapping comparison condition that will be designed to have viable feasibility/acceptability. The figure below displays the flow and estimated time frame of the approach. For **Phase 1 "Adapt BREATHE and HealthEd,"** we will



utilize a rigorous, multistep, iterative process[58] to systematically assess, code, and integrate in-depth, qualitative feedback from T1D experts and teens with T1D on the curricula. In **Phase 2 "Set up Pilot and Feasibility RCT,"** we will finalize the BREATHE-T1D and HealthEd-T1D manuals/ workbooks, consult with a telemedicine expert to establish standard operating procedures for telehealth delivery of BREATHE-T1D, finalize recruitment materials, and establish assessment standard operating procedures. In **Phase 3 "Carry out Pilot and Feasibility RCT,"** we will carry out a 2-way pilot RCT in *N*=40 adolescents, 12-17y, with ≥1-year duration of T1D, randomized to BREATHE-T1D delivered via telehealth, or HealthEd-T1D. We will track all elements of study flow and carry out a mixed-methods evaluation of feasibility and acceptability. In **Phase 4 "Plan Next Steps,"** we will make final refinements to BREATHE-T1D and HealthEd-T1D and study protocols based upon Phase 3 results, disseminate results, and prepare a grant application that directly builds upon the R34 findings. Specific elements of each phase are described below:

1. **Phase 1: Adapt BREATHE and HealthEd**: Phase 1 will focus on [initial] tailoring of BREATHE for adolescents with T1D. This phase will include a rigorous qualitative data collection and coding/analysis approach to intervention adaptation[58] using the inputs of interdisciplinary T1D healthcare/provider experts and adolescent patients with T1D to adapt and refine BREATHE-T1D. Also, we will use experts' and patients' inputs to adapt a credible and feasible HealthEd comparison group adapted for adolescents with T1D. The foundation for these adaptations will be our existing, manualized BREATHE and HealthEd group programs:

a) **Learning to BREATHE**: Learning to BREATHE is a mindfulness-based group program derived from mindfulness-based stress reduction[28] and adapted for adolescents by incorporating experiential activities and guided discussions to teach standard mindfulness skills.[59] Each letter in BREATHE acronym corresponds to a theme: **B**: Body, **R**: Reflections, **E**: Emotions, **A**: Attention, **T**: Tenderness, **H**: Habits (of Healthy Living), for overall goal of **E**: Empowerment. Example activities include breath awareness, body scanning, mindful eating, sitting meditation, loving-kindness practice, and gentle yoga. The original, published curriculum was designed to offer high flexibility in delivery timing and selection of exercises.[59] We previously developed a manualized version of BREATHE for consistency in timing and content,[48,53] but minimally modified content from its original format. Brief homework (~10 minutes/day), including formal (e.g., meditation audio-recordings) and informal practices (e.g., personalizing mindfulness in daily living), is assigned weekly. Teens are given digital meditation audio-recordings, a yoga mat, meditation cushion, homework log, and worksheets. Although BREATHE has not been delivered to adolescents with T1D, previous studies show it is well-liked by racially/ethnically diverse teens, including in our pilot studies delivering BREATHE to teens at-risk for weight-related disorders.[48,53] Speaking to its potential application for adolescents with T1D, data from our group and others show that BREATHE decreases depression symptoms and ameliorates insulin resistance up to 1-year later in pilot RCTs.[48,53,60-63]

b) **HealthEd**: The HealthEd curriculum will be derived primarily from a didactic manual that Dr. Streisand (Co-I) and colleagues developed as an educational control condition for delivery to adolescents with T1D (1R01DK121316-01; PI Jaser). This manualized program provides basic education on T1D that would be included as part of standard-of-care, including didactics on insulin administration, managing and prevention hypo/hyperglycemia, managing T1D at school, considerations for travel, and driving with T1D. The program requires adaptation for group delivery, and in doing so, we will draw on the delivery format of a HealthEd didactic group program, HeyDurham,[64] designed for providing health knowledge to middle and high school-age youth, which we have been using as a non-specific, control condition in behavioral

trials.[53,54] Also, because the original HealthEd-T1D manual was developed for parents, it is necessary to ensure content is relevant, credible, and acceptable to teens with T1D. Establishment of feasibility and acceptability of a control condition is necessary to facilitate recruitment and retention for a future, larger RCT.

c) **Qualitative design/analytic plan for intervention adaptation**: Trained interviewers will conduct structured, open-ended interviews with *N*=10 stakeholders, including *n*=3 interdisciplinary T1D healthcare experts, *n*=3 first wave adolescents with T1D, and n=4 second wave adolescents with T1D in order to gather in-depth, comprehensive information on how best to adapt BREATHE and HealthEd for specific delivery to adolescents with T1D. We will use a rigorous, multistep, iterative process, delineated by Rosen et al.,[58] for adapting BREATHE for the new target population and an interpretive description methodological framework will be used for analyses of qualitative data.[65] Participants will be purposefully sampled to ensure that diverse demographics are included in both stakeholder interviewees (e.g., discipline/area of T1D expertise) and adolescents (e.g., age, sex, race/ethnicity, insulin regimen). The first step will include interviews with healthcare experts to guide the initial adaptations to the manuals. Interview guides with healthcare experts will be designed to elicit a comprehensive understanding of providers' subjective experiences of adolescent T1D patient challenges with negative emotions, barriers and facilitators of T1D self-management, problematic eating behaviors observed in clinical care, and barriers and facilitators to using telehealth as a delivery method of clinical care in this population. We will then ask clinicians to review the BREATHE and HealthEd base programs and provide specific feedback and commentary regarding patient needs and face evaluation of the potential usefulness of the new programs.

   In parallel, we will create and adapt interview guides with teens with T1D. These will be designed to elicit a comprehensive understanding of teens' subjective experiences of negative emotions related to T1D and other key life domains, current coping strategies, unhealthy eating patterns/weight-control attempts, barriers and enablers to T1D treatment adherence and self-care, and desired support. As with clinicians, teens will be asked to comment on the base programs of BREATHE content/format/delivery mode and content/format of HealthEd. Three teens with T1D will complete interviews and review the base programs. Based on the feedback from healthcare experts and initial group of 3 teens, we will make specific adaptations to the BREATHE and HealthEd programs and any changes to the interview guide for teenagers. Next, we will conduct interviews and ask for comments on the first draft of the BREATHE-T1D and HealthED-T1D programs with the final 4 teens. Following these interviews, we will make any additional changes to BREATHE-T1D and HealthEd-T1D. We will then take this draft back to the stakeholders for any last review or comment. Based on our previous experience, we anticipate that specific changes will be needed regarding intervention content, examples, and specific discussion, which are an essential aspect of expert BREATHE intervention delivery (i.e., the discussion that is facilitated after experiential activities). For example, it may be critical to directly address awareness of physical sensations that adolescents with T1D may encounter when experiencing hypo/hyperglycemia or adapt the mindful eating exercise to reflect that hunger may not be the reason a teen with T1D is required to eat. As with our previous studies,[66] we have found that acceptability is increased when intervention materials are presented in an appealing and professional manner. Participant workbooks will be designed by a graphic design service to enhance appeal.

2. **Phase 2: Set up Pilot and Feasibility RCT**: The protocol will be submitted to the IRB for approval prior to data collection. Data collection procedures will be finalized with input from the expert panel and adolescents with T1D to ensure that measures capture essential factors and are feasible to administer and complete.

a) **BREATHE delivery mode**: We will create 1 adaptation of BREATHE-T1D. The format will be BREATHE-T1D telehealth. This approach will use a telehealth delivery platform, Zoom, currently in use by the telehealth division and CNH providers for a variety of behavioral/medical treatments. Zoom allows for groups to occur via video so that each member can see the others, mimicking the experience of an in-person group. We anticipate that BREATHE-T1D manual/teen workbook will require minimal-to-no modifications in order to deliver the program via Zoom.

b) **Finalize standard operating procedures**: Written standard operating procedures, with accompanying checklists, will be finalized for all aspects of the pilot RCT. An amendment will be submitted to the IRB, as needed, based upon protocol revisions and adaptations for BREATHE-T1D telehealth and HealthEd-T1D. All research staff will be trained in protocols, complete/update CITI trainings in responsible conduct of research, and prepare/test REDCap databases for surveys and data management.

c) **Train interventionists**: Interventionists will be master's or doctoral level clinicians who have experience working with teens with T1D. Interventionists will participate in a comprehensive 3-day training to learn BREATHE-T1D and HealthEd-T1D. Training will be led by Drs. Mackey (PI), Streisand (Co-I), and Shomaker (Co-I). Drs. Mackey and Streisand have expertise in behavioral T1D interventions. Dr. Shomaker has expertise in BREATHE delivery and training/supervision. Training will be conducted virtually, and it will include presentations of theoretical/empirical background, review of BREATHE-T1D and HealthEd-T1D intervention manuals/teen workbooks, modeling of session elements, and role-play using mock-groups. Telehealth protocols and delivery methods will be practiced.

3. **Phase 3: Carry out Pilot and Feasibility RCT**:

a) **Participants**: We will recruit a total *N*=40 participants for *n*=20 in each arm of the intervention from the ~700 adolescents seen through the CNH T1D clinic annually]. Participants will be included on the basis of the following criteria: (i) age 12-17y, (ii) T1D, with at least 1-year duration of illness, (iii) negative affectivity, defined as clinically elevated scores (T-score ≥55 indicating at least mild depression/anxiety symptoms on either the PROMIS short form-depression and/or anxiety scales), similar to criteria used in our previous studies in this patient population,[67] and recommended for use in clinic screening procedures in youth with T1D,[68]] (iv) English-speaking, (v) no cognitive or developmental delays which would interfere with their ability to participate in the study, and (vi) have no other serious medical conditions (e.g., cystic fibrosis, cancer). Participants with Spanish-speaking parent will not be excluded; consent and parent surveys will be translated into Spanish and an interpreter will be utilized for delivery of consent. Participants will not be excluded based upon insulin regimen or method of measuring blood glucose. Participants will not be excluded based on receiving outside psychological support, but treatment outside of the study will be carefully tracked and controlled for in analyses.

b) **Recruitment**: Participants will be recruited using a variety of approaches that have been highly successful in previous studies conducted by Drs. Mackey (PI) and Streisand (Co-I) in youth with T1D. Success of these approaches for the particular pilot RCT will be tracked to inform a future efficacy trial. Strategies will include: (i) direct mailings, emails, and phone calls to participants who, based upon an electronic medical record review, appear to be eligible, based upon age, health status/diagnoses, and (ii) in-person approach of teens and parents at T1D clinic appointments who are in the target age range. Potentially interested participants will be screened for depression and anxiety and will be invited to enroll if they meet the criterion for elevated (T-score ≥55) depression and/or anxiety. Although recruitment feasibility must be tested for the current 2-way intervention protocol, our team has a strong history of

recruitment/retention for clinical trials in youth with T1D, with a recruitment rate of 71% in a prior trial targeting an adolescent T1D population.[69]

c) **Baseline assessment**: Following the pre-screen, participants who are interested and eligible will be met at the clinic most convenient for them. The endocrinology division at CNH sees patients across 6 different outpatient clinics across Maryland, Virginia, and DC. Baseline assessments will be done via telehealth for maximum flexibility for participants or can be done in person to coincide with a quarterly endocrinology healthcare visit. At this telehealth visit, they will complete a virtual informed consent process, complete baseline questionnaires, and participate in an orientation visit, which we have found in previous studies results in strong retention and participation rates. They will receive a $50 ClinCard for completion of this assessment and study-specific retention items (e.g., study logo water bottle).

d) **Group participation**: A computerized randomization sequence will be created by the data manager in randomly permuted blocks. After completion of baseline assessments, allocation will be performed by the study coordinator using REDCap, which conceals the sequence. Teens will be randomized to BREATHE-T1D telehealth or HealthEd-T1D. As shown in ***Table 1***, we will aim for *n*=5 youth/group and interventions will be run in parallel. If scheduling is difficult, we will recruit up to 12 for each of the first two cohorts and allow for two groups of 3 per intervention condition in order not to delay interested candidates and have enough per group. We will still maintain an overall n of 40, adjusting the numbers in the final cohort based on what we have in cohorts 1 and 2. Based upon our base BREATHE and HealthEd manuals, we anticipate that group duration will be ~6 consecutive weeks, 1-hour/week during non-school hours, with potential for duration/frequency modifications based on the adaptation phase.

Table 1. *Estimated timeline for pilot and feasibility RCT of N=40 adolescents with T1D*

Quarter 1	Quarter 2	Quarter 3	Quarter 4
Recruitment Cohort 1 *n*=10-12	**Recruitment** Cohort 2 *n*=10-12	**Recruitment** Cohort 3 *n*=16-20	
Baseline assessment Cohort 1	**Baseline assessment** Cohort 2	**Baseline assessment** Cohort 3	
Cohort 1 *BREATHE-T1D telehealth n=5-6* *HealthEd n=5-6*	**Cohort 2** *BREATHE-T1D telehealth n=5-6* *HealthEd n=5-6*	**Cohort 3** *BREATHE-T1D telehealth n=8-10* *HealthEd n=8-10*	
	Follow-up assessment [& program revisions] Cohort 1	**Follow-up assessment [& program revisions]** Cohort 2	**Follow-up assessment [& final refinements]** Cohort 3

All sessions will be audio-recorded and reviewed by Dr. Shomaker (Co-I) on a weekly basis for intervention fidelity and interventionist competence using structured rating scales. Feedback will be provided in weekly live supervision meetings led by Drs. Streisand and Shomaker with facilitators. These protocols previously have been successful as evidenced by strong ratings of adherence, competence, and absence of cross-contamination.[54,70-72] Attendance and home practice will be tracked at each session. Adolescents will report homework completion to facilitators, and also will record completion of home practices on journal logs for BREATHE-T1D (telehealth), and complete satisfaction/acceptability measures following each session. Group cohesion will be evaluated by two independent raters' review of audio-recorded sessions using the Therapy Process Observational Coding System-Group Cohesion scale, which shows good psychometric properties.[73] To assess credibility, adolescents will report at session 1 their perceived likelihood that stress, mood, and T1D health can be improved.[74] Descriptions of cohesion/credibility by arm will inform optimization

of facilitator training and intervention delivery. Adolescents will also report on program acceptability at the end of each session.

e) **Post-intervention follow-up assessment**: Within 4 weeks after intervention completion, adolescents will complete surveys online. At post-intervention, all adolescents will complete an open-ended, structured interview to query about their subjective experiences of group cohesion, facilitator alliance, and perceived relevance and utility of the program. After coding *n*=3 BREATHE-T1D telehealth interviews, and *n*=3 HealthEd-T1D interviews, Co-I and qualitative expert, Dr. Kelly will develop a coding manual for two trained raters to code the remainder of the following qualitative post-intervention adolescent interviews. Dr. Kelly will oversee coding through regular audits. To assure rich and meaningful information, we will make iterative adjustments to interview guides as needed and maintain regular communication and systematic discussion among interviewers, data analysts, and investigators.

   Based on the feedback received in cohorts 1 and 2, additional modifications will be made to BREATHE-T1D and HealthEd-T1D as indicated for cohort 3. Changes can be made in real time between each cohort as needed. To carry out these iterative adaptations to the interventions, after each set of *n*=5 interviews per arm, qualitative findings will be reviewed by the team to determine if there are needed, minor adjustments or tweaks to the BREATHE and/or HealthEd modules for the subsequent cohort(s). Teens will receive a $75 ClinCard to complete the first set of post-intervention follow-up assessments, including surveys and the interview. Participants will be paid an additional $50 for completing the second set of post-intervention follow-up assessment at 3 months post-intervention, which consists of the same set of online questionnaires completed at baseline. Trained research assistants will complete medical record reviews to extract HbA1c as an indicator of glycemic control from the immediate endocrine visit that follows the final intervention session.

f) **Measures**: To assess feasibility and acceptability of all intervention conditions and the assessment protocol, we will carefully track recruitment, retention, participation, fidelity, acceptability, and key constructs of interest to be measured in a future efficacy trial. ***Table 2*** provides an overview of measures and assessment.

Table 2*. Summary of key constructs and measures of Phase 3: Pilot and Feasibility RCT*

Construct	Measure	Interval
Recruitment Feasibility/ Acceptability	# screened per month # enrolled per month # weeks to form cohort 3 group % eligible who enroll	Study initiation through completion of recruitment by CONSORT guidelines
Intervention Feasibility	% sessions attended by condition recorded by intervention facilitator	Weekly/intervention phase
Intervention Acceptability	Teen survey satisfaction ratings Teen qualitative interview	Weekly/intervention phase Post-intervention follow-up
Intervention Fidelity	PI/Co-I structured ratings of BREATHE-T1D and HealthEd-T1D adherence & competence	Weekly/intervention phase
Retention Feasibility/ Acceptability	% complete post-treatment follow-up	Post-intervention follow-up

Assessment Feasibility	% assessments with missing vs. complete data	Baseline; post-intervention follow-up
Dispositional Mindfulness	Teen report on Mindful Attention Awareness Scale; Five-Factor Mindfulness Questionnaire	Baseline; post-intervention follow-up
Negative Affectivity	PROMIS short forms Depression/ Anxiety subscales	Baseline; post-intervention follow-up
Maladaptive Eating Behavior	Diabetes Eating Problems Survey – Revised	Baseline; post-intervention follow-up
Negative Urgency	Teen report on UPPS-P – Negative Urgency Subscale	Baseline; post-intervention follow-up
Treatment Adherence	Self-Care Inventory	Baseline; post-intervention follow-up
Glycemic Control	Hemoglobin A1c derived from the patient electronic medical record	Baseline; post-intervention follow-up
Diabetes Distress	Teen report on Problem Areas in Diabetes-Teen	Baseline; post-intervention follow-up

Data Analysis

Statistical Design and Power

Overview:

The first aim of the study is to carry out a series of iterative structured, open-ended interviews with key stakeholders in order to adapt an evidence-based, mindfulness group intervention, Learning to BREATHE, to be tailored to the distinctive needs of adolescents with type 1 diabetes (BREATHE-T1D). We also will adapt a didactic T1D health education program for delivery as a group-based control program matched for time and attention (HealthEd-T1D). The second aim is to assess the feasibility and acceptability of 2 adolescent group-based conditions: 1) BREATHE-T1D, delivered via telehealth, and 2) HealthEd-T1D, delivered via telehealth. We will determine the feasibility and acceptability of recruitment, assessment, retention, and each group condition. Together, these data will be essential for informing the final interventions, protocols, and design of a future efficacy trial of BREATHE-T1D for adolescents with T1D. The qualitative portions add patient voice to intervention adaptation and optimization, ensuring that the interventions to be tested and the outcomes to be measured as part of a larger efficacy trial will be meaningful, valuable, and helpful for adolescents.[75] Consistent with NCCIH's policy for the conduct of pilot studies, no preliminary analyses of efficacy are planned; yet, the study does include piloting of the measures of predictors, outcomes, and hypothesized mechanisms of the mindfulness-based intervention, BREATHE-T1D, in order to determine if measure administration is feasible and acceptable to adolescents with T1D for use in a future efficacy trial.

Aim 1:

Qualitative design/analytic plan for intervention adaptation. Structured, open-ended interviews will be conducted with a total of *N*=10 stakeholders, including *n*=3 interdisciplinary T1D healthcare experts and *n*=7 adolescents with T1D in order to adapt BREATHE and HealthEd for specific delivery to adolescents with T1D. Using interpretive description methods,[65] participants will be purposefully sampled to ensure that diverse demographics are included in both stakeholder interviewees (e.g., discipline/area of expertise) and adolescent participants (e.g., age, sex, race/ethnicity, insulin regimen, glycemic control). Trained research staff will conduct interviews using an interview guide. Interview guides will be developed by the investigative team, which now includes an

expert in qualitative research methods and interpretive description, Dr. Katherine Kelly (Co-I), who has successfully collaborated with Co-I Dr. Randi Streisand on previous mixed-methods studies in pediatric T1D.[76]

The first step in this process will include interviews with healthcare experts to guide the initial adaptations to the manuals. Interview guides with healthcare experts will be designed to elicit a comprehensive understanding of providers' subjective experiences of adolescent T1D patient challenges with negative emotions, barriers and enablers to T1D treatment adherence and self-care, problematic eating behaviors observed in clinical care experience, and barriers and enablers to using in person healthcare and telehealth as a delivery method of clinical care in this population. We will then ask clinicians to review the BREATHE and HealthEd base programs and provide specific feedback and commentary regarding patient needs and face evaluation of the potential usefulness of the new programs based on their clinical experience with adolescents with T1D. We will query T1D healthcare experts about intervention formatting and design; ask them to highlight sections that they particularly liked; ask them to highlight sections that they particularly did not like, thought were unclear, or thought could be improved; and query as to whether providers perceive that any important content is missing.

The second step that will happen in parallel with the provider interviews is that we will be creating and adapting interview guides with adolescents with T1D. These guides will be designed to elicit a comprehensive understanding of adolescents' subjective experiences of negative emotions related to T1D and other key life domains, current coping strategies, unhealthy eating patterns/weight-control attempts, barriers and enablers to T1D treatment adherence and self-care, and desired support. As with clinicians, teens also will be asked to comment on the base programs of BREATHE content/format/delivery mode and content/format of HealthEd. We will initially have *n*=3 teens with T1D complete these interviews and review the base programs.

Third, based on the feedback from the 3 healthcare experts and the initial group of 3 teens with T1D, we will make specific adaptations to the BREATHE and HealthEd programs and any changes, as indicated, to the interview guide for teenagers to elicit more information on emergent themes and/or to fill in more depth/detail about particular topic areas. Following revisions to the teen interview guides, we will conduct interviews and ask for comments on the first draft of the BREATHE-T1D and HealthED-T1D programs with *n*=4 new teens with T1D. Finally, findings from these 4 teens will result in additional changes made to BREATHE-T1D and HealthEd-T1D. We will then take this second draft back to the stakeholders for a last review and comment.

All interviews will be audio-recorded; interviewers also will take extensive field notes. Interviews will be transcribed verbatim for qualitative analyses using Atlas.ti. Dr. Kelly (Co-I; qualitative expert) will initially code *n*=3 healthcare expert and *n*=3 adolescent interviews using interpretive description.[65] The PI Dr. Eleanor Mackey then will review and validate initial coding. Coding results will be reviewed by the entire investigative team and adjustments will be made to the interview schedule as indicated to assure that rich, descriptive findings are being elicited. Subsequent interviews will be analyzed on a continuous basis, as soon as they are transcribed. To assure the greatest efficiency in completing qualitative analyses/coding, Dr. Kelly will complete analysis of these initial

interviews. We adopt an interpretive description framework because it employs an inductive constant comparative analysis that produces in-depth conceptualizations of interviews.[65] This qualitative analysis method is purposefully flexible so that relevant new findings can inform subsequent interviews creating a robust and efficient analysis. This qualitative analytic approach, in combination with regular, planned communication and discussion among the investigative team about interviews/analyses, will ensure that we derive the richest information from stakeholder interviews in order to adapt BREATHE-T1D and HealthEd-T1D.[58] See figure below for illustration of full process.

How Aim 1 qualitative data/analysis will inform the adaptation of BREATHE. Qualitative data/analysis will provide critical information on the specific mindfulness-based skills and contextual factors that will be most important for mindfulness-based training in adolescents with T1D. Qualitative data collection/analysis is ideally suited for intervention adaptation because it allows for both confirmation of anticipated changes to intervention content that will be necessary (e.g., matching themes with existing BREATHE content) as well as emergent or unanticipated information to optimize an intervention for the target population through additional changes to content or creation of new content. Based on our previous experience, we anticipate that specific changes will be needed regarding intervention content, examples that are provided in experiential activities (e.g., case study in module on stress and attention, or ways we practice kindness or meanness to ourselves), and specific discussion of areas of stress/concern for adolescents with T1D, which are an essential aspect of expert BREATHE intervention delivery (i.e., the discussion that is facilitated after experiential activities). For example, it may be critical to directly address awareness of physical sensations that adolescents with T1D may encounter when experiencing symptoms of hypo/hyperglycemia, adapt the mindful eating exercise to reflect that hunger may not be the reason a teen with T1D is required to eat, or other unique experiences teens with T1D note that will be important to modify or use to highlight specific aspects of the BREATHE curriculum.

Sample size justification. Based upon our past experience[76] and recommended guidelines,[77] a total sample size of *N*=10 total stakeholders is anticipated to achieve informational redundancy.

Aim 2:

Statistical design/analytic plan. *N*=40 adolescents with T1D will be recruited for a pilot RCT of BREATHE-T1D delivered via telehealth, and HealthEd-T1D delivered via telehealth. The following table provides an overview of measures and methods of assessment for Aim 2:

Construct	Measure	Interval	Expected Outcome
Recruitment Feasibility/ Acceptability	# screened per month # enrolled per month # weeks to form cohort 3 group % eligible who enroll	Study initiation through completion of recruitment by CONSORT guidelines	30 screened per month 5 enrolled per month 12 weeks to form cohort 3 groups ≥80% eligible enroll after screen

Intervention Feasibility	% sessions attended by condition recorded by intervention facilitator	Weekly/intervention phase	≥80% attend ≥80% of BREATHE-T1D telehealth ≥80% attend ≥65% of HealthEd-T1D
Intervention Acceptability	Teen survey satisfaction ratings Teen qualitative interview	Weekly/intervention phase Post-intervention follow-up	≥80% liking/credibility/relevance/utility ratings ≥4 (1=not at all to 5=extremely) Themes indicative of liking/credibility/relevance/utility
Intervention Fidelity	Mackey/Shomaker structured ratings of BREATHE-T1D and HealthEd-T1D adherence and competence	Weekly/intervention phase	≥8 scores on adherence and competence ratings (1=poor to 10=exceptional) for all 3 intervention conditions
Retention Feasibility/ Acceptability	% complete post-treatment follow-up	Post-intervention follow-up	≥80% complete post-treatment follow-up
Assessment Feasibility	% assessments with missing vs. complete data	Baseline; post-intervention follow-up	<5% missing data for assessments administered to participants
Dispositional Mindfulness	Teen report on Mindful Attention Awareness Scale; Five-Factor Mindfulness Questionnaire	Baseline; post-intervention follow-up	<5% missing data for assessments administered to participants <10% will display worsening across conditions
Negative Affectivity	Teen report on PROMIS short forms Depression/ Anxiety subscales	Baseline; post-intervention follow-up	
Maladaptive Eating Behavior	Diabetes Eating Problems Survey – Revised	Baseline; post-intervention follow-up	

Negative Urgency	Teen report on UPPS-P – Negative Urgency Subscale	Baseline; post-intervention follow-up	
Treatment Adherence	Self-Care Inventory	Baseline; post-intervention follow-up	
Glycemic Control	Hemoglobin A1c derived from the patient electronic medical record	Baseline; post-intervention follow-up	<10% will display increased A1c across conditions
Diabetes Distress	Teen report on Problem Areas in Diabetes-Teen	Baseline; post-intervention follow-up	

g) **Feasibility**: The primary focus of the feasibility assessment will be to demonstrate that a recruitment, participation, and retention can meet pre-defined targets. To evaluate feasibility, a CONSORT table and descriptive statistics regarding recruitment, retention, data completeness, and fidelity will be generated by intervention group. Feasibility will be determined overall by meeting recruitment targets and rates of agreement to participate in the study. Retention, participation, and fidelity by group will be examined for meeting feasibility criteria (>80% retention, >80% sessions attended, >80% of homework completed, 80% fidelity of intervention delivery). Feasibility indicators also will be evaluated for differences between group conditions in order to determine if one program is more feasible. For participants lost to attrition in each cohort, baseline characteristics and research coordinator feedback will be evaluated to determine how recruitment rates may be improved.

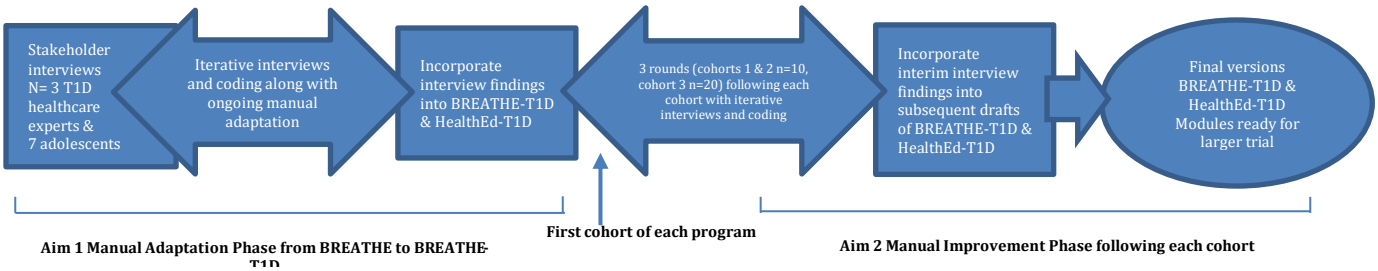
h) **Acceptability**: To evaluate acceptability quantitatively, descriptive data will be generated of post-intervention satisfaction surveys overall and by group condition. Acceptability will be determined by a high level of satisfaction with participation, perceived utility of the intervention content, and perceived benefit from participation (>80% reporting that they were satisfied and perceived utility and benefit). Acceptability indicators will also be evaluated for differences between group conditions in order to determine if one is more acceptable.

Qualitative acceptability strand. At post-intervention, all adolescents will complete an open-ended, structured interview to query about their subjective experiences of the intervention content, relationships with facilitators/other group members, home practice completion, and enablers and barriers of making changes in coping with negation emotions, eating behaviors, and T1D treatment adherence. After coding *n*=3 BREATHE-T1D, telehealth interviews, and *n*=3 HealthEd-T1D interviews, Dr. Kelly will develop a coding manual to be used by 2 trained coders, who have expertise in qualitative analysis, to code the remainder of the following qualitative post-intervention adolescent interviews. Dr. Kelly will oversee coding through regular audits. To assure rich and meaningful information, we will make iterative adjustments to interview guides as needed and maintain regular communication and systematic

discussion among interviewers, data analysts, the qualitative expert (Kelly), and experts in adolescents with T1D and behavioral interventions (Mackey & Streisand), eating (Mackey & Shomaker) and BREATHE (Shomaker).

Based on the feedback received in cohorts 1 and 2, additional modifications will be made to BREATHE-T1D and HealthEd-T1D as indicated for cohorts 2 and 3. Specifically, to carry out these additional, iterative adaptations to the interventions, after each set of *n*=5 interviews, qualitative findings will be reviewed by the team to determine if there are needed, minor adjustments or tweaks to the BREATHE and/or HealthEd modules for the subsequent cohort(s).

Figure depicting qualitative strand of the study to be carried out in Aims 1 and 2:



i) **Measurement**: Descriptive statistics using the measurements of hypothesized outcome and mechanism indicators will be used to look at variability in responses for each measure for utility of use in future trials (e.g., is there sufficient variability across participants to make it a worthwhile indicator of the proposed construct, do the measures correlate with one another in expected directions). Our primary pilot (and subsequent full-scale trial) assessments of improvement in measures will be a set of planned contrast comparisons using independent samples group t-tests with further validation using the non-parametric Wilcoxon rank sum test. These are:

   i) Comparison of the *n*=20 active treatment participants in BREATHE-T1D telehealth delivery to the *n*=20 HealthEd-T1D control arm participants on measures of feasibility (e.g., recruitment, dropout, data missingness, fidelity) and acceptability (e.g., satisfaction ratings) to determine if there are differences in feasibility or acceptability between BREATHE-T1D versus HeatlhEd-T1D.

Sample size justification. For studies that can be considered both feasibility and pilot studies we approached sample size assessment for both. There are a range of thoughts on sample sizes needed to assess feasibility.[78] Julious et al.[79] recommend *n*=12 per group as a rule of thumb and justify this recommendation based upon rationale about feasibility and precision about the mean and variance. A paper provided by the United Kingdom National Institute of Health[80] recommends a total pilot sample size between *N*=30 and *N*=50. We also assessed the 80% completion rule (which is used for several of our feasibility outcomes). If we assume a chance response of 50% program completion, with a sample size of 15 (at alpha = 0.05 and 80% power), we can detect a difference of 80% completion or more. Therefore, we believe the proposed study will be powered to assess feasibility overall and by group condition.

Concerning the sample size assessment for pilot studies, we reference Cocks and Torgerson[81] who recommend using a total sample size of *N*=45 or more to detect a significant effect size of 0.25 or greater between 2 group conditions planned in the larger trial following the pilot study or to use a total sample size of *N*=30 to detect a significant effect size of 0.31 or greater between 2 group arms in the larger trial following the pilot study. Based upon our review of similar studies assessing glycemic control[82] and mindfulness-based intervention measures,[34] we believe these effects size are reasonable for our 3 planned 2-group comparisons regarding our primary aims of evaluating feasibility and acceptability.

E. Study Population:

There will be 90 total participants across both phases of study (3 diabetes team providers, 7 adolescents with T1D for the intervention development qualitative feedback, and 40 adolescent and caregiver dyads for the feasibility trial). Diabetes team providers (*n*=3) will be interviewed to provide feedback regarding the adaptation of BREATHE for use with adolescents with T1D. We will recruit a total N=40 participants for n=20 in each arm of the intervention. Participants will be included on the basis of the following criteria: (i) age 12-17y, (ii) T1D, with at least 1-year duration of illness, (iii) negative affectivity, defined as clinically elevated scores (T-score $\geq$55 indicating at least mild depression/anxiety symptoms on either the PROMIS short form-depression and/or anxiety scales) (iv) A1c >7.5%, (v) English-speaking, (vi) no cognitive or developmental delays which would interfere with their ability to participate in the study, (vii) are able and willing to complete questionnaires and intervention via the internet, (viii) do not have severe depression or active or recent (within the past two months) suicidal ideation and (viv) have no other serious medical conditions (e.g., cystic fibrosis, cancer). Participants with Spanish-speaking parent will not be excluded; consent and parent surveys will be translated into Spanish and an interpreter will be utilized for delivery of consent. Participants will not be excluded based upon insulin regimen or method of measuring blood glucose. Participants will not be excluded based on receiving psychological support outside of the context of the study, but treatment outside of the study will be carefully tracked and controlled for in analyses. The study will be nonselective in its recruitment and enrollment with respect to gender, race, and ethnicity.

F. Human Subjects

Adolescents and a primary caregiver will be recruited from the Child and Adolescent Diabetes Program at CNMC. Adolescents between the ages of 12-17 will be studied to capture both early and later development of eating disorder and disordered eating symptoms.

Participants will be recruited using a variety of approaches that have been highly successful in previous studies conducted by Drs. Mackey (PI) and Streisand (Co-I) in youth with T1D. Success of these approaches for the particular pilot RCT will be tracked to inform a future efficacy trial. Strategies will include: (i) direct mailings, emails, and phone calls to participants who, based upon an electronic medical record review, appear

to be eligible, based upon age, health status/diagnoses, A1c and (ii) in-person approach of teens and parents at T1D clinic appointments who are in the target age range. Potentially interested participants will be screened for depression and anxiety using the PROMIS scales and will be invited to enroll if they meet the criterion for elevated (T-score ≥55) depression and/or anxiety.

G. Risks and Side Effects:

There are no known psychological risks to subjects when providing feedback via qualitative interview or when filling out standardized psychological questionnaires. However, the questionnaires may contain questions that make the subjects feel uncomfortable in that they ask about their physical and psychological health. Additionally, we will be recruiting participants with elevations on measures of depression and/or anxiety. For participants by self-report responding that they are experiencing a clinically significant level of anxiety OR depressive symptoms (using the PROMIS short form – T > 55 cutoff for depression and for anxiety subscales), we will follow a protocol that has been effective in our prior studies. Additionally, adolescents report on disordered eating behaviors, including risky behaviors such as insulin withholding. The DEPRS will be screened for clinical cutoff and specifically for endorsing either of the two items that ask about insulin withholding. Specifically, all forms will be reviewed by the clinical research assistant within 24 hours of completion or in real time for screenings taking place in clinic or via zoom (and flagged if either the depression or anxiety scores are above the clinical cutoff (T-score > 55) or if the DEPRS is above the clinical cutoff AND/OR either of the insulin withholding items are endorsed). If the score is above the clinical cutoff or the insulin withholding items are endorsed, the study team will notify the family both that they are eligible for participation in the study, and also reminded of additional referrals for care, including the in-house diabetes psychologist and other community referrals. The PROMIS measures do not assess for suicidal ideation, and we will not be assessing this specifically given that it is outside of the scope of this trial. However, if suicidal ideation or intent is suggested during the course of any study interactions, the PI Dr. Eleanor Mackey, a licensed child clinical/pediatric psychologist, will be informed immediately via cell phone, and outreach to the parent and teen will be made. All research staff interacting with patients (e.g., research coordinator, research assistants) will be trained in our lab's risk assessment procedures. If deemed necessary, the teen will be referred for immediate mental health evaluation at the CNH Emergency Department. Our team of T1D psychologists maintains written protocols for all cases that necessitate a possible breach of confidentiality and for handling concerns that may arise such as suicidal ideation or self-harm. As we have done successfully in prior studies, we will monitor ongoing parent and teen reporting of the use of mental health support outside of the study either via usual care (e.g., seeing the in-clinic psychologist) or outside therapy/consultation or other behavioral health services. Paralleling national trends, most teenagers with T1D, even when screened and referred, do not seek regular therapy due to a variety of barriers. Thus, the interventions being offered, including the control condition, will likely offer more support and monitoring than adolescents would otherwise receive, even when they screen positively for depression/anxiety in diabetes clinic.

The primary potential source of risk in this study is the risk of gathering sensitive social, behavioral, and medical information. Data collection via the Internet will be conducted through secure applications (REDCap). The respondent burden for completion of questionnaires at each assessment point is approximately 20-40 minutes total.

Protection Against Risk. All members of the research team are currently trained in the ethical conduct of research, and will be required to uphold certifications throughout the project period. The plan for protecting privacy and confidentiality recognizes that the protection of privacy in studies involving sensitive data is of utmost importance. We will attempt to do this in several ways. We will emphasize the voluntary and confidential nature of the research as well as state the limits to confidentiality in the informed consent form, and again at the beginning of any qualitative interviews. All responses to interview items will be given by subjects in private. Internet data collection will occur through programs that have security features. We will minimize all communications that involve names or other identifying information. All clinically-relevant and study information will be kept in locked files in locked offices. Information about subjects will not be accessible to any non-authorized study personnel without the written consent of the subject. In all datasets we will use ID numbers only. A separate dataset linking names with ID numbers will be accessible only to authorized study personnel under the direction of the PI.

H. Benefits:

There are no known direct benefits to subjects to participating in this research. Those allocated to the BREATHE-T1D telehealth condition may gain skills in managing negative affect and ultimately improving diabetes management behaviors.

I. Outside Consultants/Collaborators

Lauren Shomaker, Ph.D., co-investigator, Colorado State University
Ann Davis, Ph.D., consultant, Children's Mercy Hospital

J. Contractual Agreements

None

K. Costs To Subjects:

None.

L. Conflicts Of Interest:

None.

M. Confidentiality:

All information collected as part of the study is confidential and will not be released to anyone to the extent permitted by law. To protect privacy, identification numbers will be used to identify all study information, and only authorized study personnel will have access to study records, with the permission of the PI. Each participant's identifying data will be separated from the study data and all clinically-relevant and study data will be stored in a password-protected database, on a password-protected computer, or in a locked filing cabinet in a locked office. Information about subjects will not be accessible to any non-authorized study personnel without the written consent of the participant.

N. Subject Compensation:

Participants in the intervention refinement phase will receive $20 in a Target gift card for their participation. Participants in the pilot intervention will receive money on their ClinCard at each data collection time point. Participants will be compensated with increasing amounts assessment completion (baseline $50, first follow-up $75, and second follow-up $50).

O. Facilities and Equipment

Data collection will take place in the Diabetes Care Complex at the Children's National Medical Center Shiek Zayed campus and surrounding regional outpatient clinics or online.

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