Behavioral Approaches to Reducing Diabetes Distress and Improving Glycemic Control (EMBARK)

NCT04016558

Study Protocol

8/10/2019

Behavioral Approaches to Reducing Diabetes Distress and Improving Glycemic Control (EMBARK)

Project Summary. Diabetes Distress (DD) is the personal, often hidden side of diabetes: it reflects the unique emotional burdens and strains that individuals with diabetes may experience as they struggle to keep blood glucose levels within range7. When high, DD can have a major, negative impact on disease management and glycemic control9. High DD is characterized by frustration, feeling overwhelmed, and feeling hopeless and discouraged by the unceasing demands of diabetes. DD is also linked to an individual's beliefs, expectations, current life situation, and personal and social resources10-27.

There have been very few systematic interventions directly aimed at reducing DD among adults with T1D. Furthermore, systematic reviews4,5 conclude that, of the few interventions to date, most attempt to reduce DD only indirectly by providing diabetes education and/or enhancing disease management. These interventions, which have yielded only modest improvements in HbA1c, rarely address the powerful and persistent underlying affective experience of DD, and the direct impact of high DD on disease management.

The proposed study is a 3-arm, 12-month RCT to test the added value of a DD-targeted (TunedIn) intervention vs. a unified DD and management intervention (FixIt), relative to a traditional, educational/behavioral-management intervention (StreamLine). Each of the 3 arms will follow a separate, standardized protocol. All participants will receive 3 months of intervention with 9 months of subsequent follow-up (12 months total). We will examine models of disease-management behaviors as mediators of associations between DD and HbA1C, and explore the directions of longitudinal associations among DD, disease management and HbA1c.

Aims & Hypotheses:

Primary Specific Aim 1 Hypothesis 1. Improvement in primary (HbA1C, Diabetes Distress) and secondary (frequency of hypoglycemia, emotion regulation measures) outcomes from baseline to 12-month follow-up will be greater in TunedIn relative to StreamLine, and greater in FixIt relative to either TunedIn or StreamLine.

Primary Specific Aim 2 Hypothesis 1 (Mediation Hypothesis). *Decreases* in DD will be significantly associated with *decreases* in HbA1C within each of the 3 intervention groups over 12 months. Associations between changes in DD and changes in glycemic control will be explained by changes in disease-management mediators (e.g., increased blousing) across all 3 intervention groups. In exploratory analyses, we will examine the direction of associations as presented in the conceptual models in Figure 3.

Secondary Specific Aim 1 Hypothesis 1 (Moderator Hypothesis). Differences in primary and secondary outcomes between FixIt and TunedIn will be qualified by: (a) patient characteristics (with stronger positive effects for younger age and patients with shorter T1D duration), (b) both baseline emotion regulation (ER) skills and level of DD (with stronger positive effects for patients with poorer ER skills and higher DD), and (c) baseline cognitive-processing constructs (with stronger positive effects for patients with lower problem-solving skills and diabetes knowledge).

Secondary Specific Aim 2 Hypothesis 1 (Cost-effectiveness). FixIt and TunedIn will be more cost-effective than StreamLine in terms of improvements in primary and secondary outcomes.

Research Design: This is a 3-arm, 12-month randomized comparison trial (baseline N=118 per arm) to test the added value of a DD-targeted intervention (TunedIn) vs. a unified DD and management intervention (FixIt), relative to a traditional, educational/behavioral-management intervention (StreamLine) to reduce diabetes distress and improve glycemic control in adults with type 1 diabetes. Additionally, the implementation costs and per-participant program costs will be calculated.

Each of the 3 arms will follow a separate, standardized protocol. All participants will receive 3 months of intervention with 9 months of follow-up (12 months total).

Background & Significance: Diabetes distress (DD) refers to the often hidden emotional burdens, stresses, and worries that result from managing a demanding, progressive, chronic disease like type 1 diabetes (T1D)1. DD is highly prevalent (42% with elevated DD)2; is distinct from clinical depression3; tends to be chronic, rather than episodic2; and has been significantly associated with poor self-care behavior and glycemic control4-8. Thus, there is growing evidence of associative and causative linkages among DD, self-management, and glycemic control, making DD a significant clinical problem.

There have been very few systematic interventions directly aimed at reducing DD among adults with T1D. Furthermore, systematic reviews by Sturt et al.4and Schmidt et al.5conclude that, of the few interventions to date, most attempt to reduce DD only indirectly by providing diabetes education and/or enhancing disease management. These interventions, which have yielded only modest improvements in HbA1C (see below), rarely address the powerful and persistent underlying affective experience of DD, and the direct impact of high DD on disease management. Very few address the unique, specific needs of T1D adults. Of 41 studies reviewed by Sturt et al., only five focused on T1D30-34, and only one included a single session on emotion-focused coping30. Findings indicated improvements in self-efficacy and empowerment, but only a 0.4% reduction in HbA1C. Schmidt et al. reported one additional study targeting T1D (van der Ven, 200535). This study (N=107) compared Cognitive Behavioral Therapy (CBT) vs. Blood Glucose Awareness Training (BGAT) (both groups attended 6, 2-hour sessions). The CBT group reported higher self-efficacy, reduced depression and anxiety symptoms, and reduced DD compared to BGAT, but no group differences were reported in disease management or HbA1C. We found only a few additional studies that assessed DD or mood among T1D adults35-40. Median sample size for these studies was small, and all used 4-8 group-delivered or web-based CBT intervention sessions. Five of the six showed short-term reduced DD, but only three reported statistically significantly improved glycemic control36-38, and even in these studies, improvements were modest. Only one study with a limited sample size (N=33) focused on the emotional side of diabetes37. Findings indicated significantly reduced symptoms of depression and anxiety, but only a 0.3% reduction in HbA1C.

In summary, (i) few studies have measured DD directly and have identified the explicit sources of DD among T1D adults; (ii) the content of interventions have often been focused solely on education and behavior change, with DD change often considered a secondary outcome; (iii) no studies have used an integrated framework that addressed DD-related emotions and cognitions, and none have addressed how they directly influenced diabetes management and glycemic control; and (iv) very few studies included T1D adults with high baseline DD and HbA1C, making it difficult to identify interventions that reduce both DD and HbA1C and determine their relationships. This study builds upon this literature by addressing each of these issues directly.

Recruitment. Adults with T1D will be recruited by partnering with academic clinics' research registries and community-based organizations. Partnering organizations will send e-mails and/or social media posts to their members. Patients who are eligible and interested during telephone screening will be emailed a link to a secure electronic consent and online baseline survey, with a copy of the consent emailed for their records. Patients who are eligible following completion will be sent a pre-paid slip to

collect HbA1C at a local laboratory to confirm HbA1C eligibility. HbA1C collection will be 5.0ml of whole

Follow up will occur at 3, 6, and 12 months following Group Meeting 1, and procedures will be the same for each group. Participants will be emailed a link to a secure online follow up survey, plus a pre-paid slip to collect HbA1C at a local laboratory. HbA1C collection will be 5.0ml of whole blood.

Interventions:

1. **StreamLine** (management strategy)

2. **TunedIn** (DD-targeted strategy)

3. **FixIt** (unified strategy)

Each of the 3 study arms will selectively include: (a) a group workshop (8-10 participants), (b) real-time online video group meetings and (c) individual phone/video calls or face-to-face meetings with the interventionist (summarized in Table 1).

StreamLine (management strategy) is an education/disease management program that focuses directly on identifying and resolving specific BG problems; no DD-related component is included. StreamLine focuses on systematic methods to identify and resolve specific BG problems, primarily through changes in carbohydrate consumption, and basal and bolus insulin use. Participants will attend a brief, 4-hour didactic non-interactional meeting with a certified diabetes educator (CDE) and, using standardized BG data, will learn how to employ a 5-point BG management system to identify and resolve BG problems (e.g., excursions, lows) that have the greatest HbA1C or hypoglycemia impacts: (1) utilizing BG pattern data, and (2) examining basal insulin rates, (3) frequency of blousing, (4) timing of bolusing, and (5) amount of insulin bolused. Participants will leave the session to record 3 days of structured, seven-point glucose testing, ether through continuous glucose monitoring (CGM) or finger stick (participants' own devices; these will not be provided by the study) during the following week. They will then meet individually (face to face, phone/video, 30 minutes) with their CDE to review their BG data, identify a specific BG problem, and adjust their current management to resolve the problem, using the 5-point program. Four additional individual participant/facilitator meetings (face to face, phone/video, 30 minutes) will occur at approximately two to three-week intervals to best support individualized and participant-tailored management-change efforts. If incidicated by the facilitator and/or clinical supervisors, based on participant need, an additional one to two individual contacts may be scheduled during the intervention period.

TunedIn (DD-targeted strategy) utilizes exercises and scenarios of ER-based strategies that were effective in reducing DD in the OnTrack arm of T1REDEEM6, now greatly expanded in number and focused in intensity to be more comprehensive and inclusive to help participants observe how what they feel affects what they do regarding disease management. Taking advantage of the power of facilitated group interaction in reducing DD, participants in TunedIn will attend 2 highly interactive group workshops (6 hours followed by 2 hours), facilitated by a psychologist or social worker experienced in diabetes. Each will identify and discuss common emotional responses related to BG management (e.g., over-reacting, avoiding, lack of mindfulness). Between the two workshops (2 weeks), participants will
blood. For those patients who are unable to go to a local laboratory, we will provide a HbA1C home test kit mailed to their home address for their convenience and comfort. After blood sample is provided by patient (instructions are provided in each test kit), they will mail the kit back to the lab to be analyzed. Randomization of eligible participants will occur after baseline assessments. Sequential ID numbers will be generated and randomly assigned to the 3 study groups. Each participant will receive the next ID number, contained in a REDCap database. Block randomization stratified by clinical recruitment site will be used to ensure equivalent distributions in the three intervention study arms across sites.
complete a “feeling log,” a tool commonly used in ER-based programs, in which participants document.

FixIt (unified strategy) seamlessly integrates StreamLine and TunedIn. It makes use of the same highly interactive group discussion around affect management using ER techniques and affect logs used in TunedIn with the same 5-point glycemic-management program used in StreamLine. Thus, interconnected feelings and expectations are highlighted as problematic BG patterns are identified. To ensure the delivery of a balanced, integrated approach, FixIt will be co-facilitated by a psychologist/social worker experienced in diabetes (as in FixIt) and a CDE (as in StreamLine). Participants will attend 2 group workshops (6 hours followed by 4 hours), separated by 2 weeks. Between the 2 workshops, participants will record their BG data for 3 days and keep a parallel "affect log" to provide context. They will then meet face to face or through phone/video for 30 minutes with one of their 2 group interventionists to review the collected data and begin the process of identifying a specific glycemic problem, along with an action plan to address it. Full discussion of DD-related aspects of the plan will also be included to both enhance mindfulness and identify typical ER strategies that may reduce DD and ease problem resolution. At the second group session, these plans will be shared to shape the plan to make it more personally actionable. Participants will be further supported by: 3 online video group meetings (60 minutes, monthly) utilizing facilitated group discussion to review specific plans addressing behavioral and affective management for each participant, and 3 additional individual participant/facilitator meetings (face to face or phone/video, 30 minutes) to review BG data and the contextual and DD barriers to change. This strategy, therefore, combines the primary intervention modalities of StreamLine and TunedIn.

Measures

Telephone screening questions will document: age, years with T1D, age at diagnosis, insulin treatment (multiple-dose injection [MDI], CGM, insulin pump), co-morbidities and diabetes-related complications, and English language skills (attached). Self-reported surveys completed electronically will include the following measures:

• The **number of hypoglycemic episodes** will be assessed, including: frequency of symptomatic hypoglycemia (BG < 70 Mg/dL) in the past week and episodes of hypoglycemia in the past 6 months (or since last follow-up) requiring the assistance of another person or medication intervention (2 items)82.

• The **Type 1 Diabetes Distress Scale (T1DDS)**, an internally reliable, validated 28-item scale (alpha=.84)28 will be used to assess total DD plus 7 DD subscales: management, powerlessness, hypoglycemia, eating, friends/family, physician, and negative social perceptions.

• Depression symptoms will be assessed using the 8-item **Patient Health Questionnaire depression screener (PHQ-8)**74,75

• The personal ontrol subscale from the **Revised Illness Perception Questionnaire** (6 items; alpha=.80)87will assess participants' perceived control over their illness.

• The **Five Facet Mindfulness Questionnaire**88**,** a validated and widely used measure based on a factor analytic study of 5 independently developed mindfulness measures, will be used to assess: **non-judging of experience, and nonreactivity to inner experien**ce.

• We also will include the only validated diabetes-specific ER scales to assess self-compassion in the context of diabetes management (SCS-D, 19 items; alpha=.9490). Diabetes-specific self-compassion will be measured using the **Self-Compassion Scale - Diabetes (SCS-D)** (19 items; alpha=.94)90.

• **Missed insulin boluses** will be measured using self-reported numeric report of missed insulin boluses over a 7 day period.

Data Analysis. Descriptive statistics will be computed for baseline characteristics, initially testing for differences between: (1) intervention arms and (2) patient dropouts vs. non-dropouts. Patient-level demographic and disease status covariates will be screened in bivariate analyses and included in multivariate analysis if they are related to the outcome at $p < .20$, significantly differ between treatment arms, or are associated with dropout. Correlations among variables within each area of secondary outcomes and moderators (see measures above) will be examined, and redundant measures will be combined or eliminated to avoid multicollinearity. In the event normality assumptions are not met, we will use transformations to normalize distributions, ordinal or Poisson regression where appropriate, and/or the appropriate link function (e.g., logit link for dichotomized measures)95-97. We will examine change in outcomes across groups will be evaluated by ANCOVA. In these models, the follow-up value is specified as the outcome, the baseline value as the covariate, and treatment group was a fixed effect. When the treatment group effect was statistically significant ($p < 0.05$), Helmert contrasts will be used to determine differences among the three groups. Missing values will be imputed with NORM software (version 2.0; The Methodology Center, Penn State, University Park, PA) (23,24) using multiple-imputation procedures to create a stable, complete data set. Parallel analyses will be performed with raw and imputed data sets. Hypothesis tests will be 2-sided with alpha set at .05. Goodness-of-fit tests and model-fitting diagnostics will be used to assess for influential points, outliers, over-dispersion, and heteroscedasticity, and to evaluate alternative model specifications.143

Intervention implementation costs on a per-participant basis, and training costs on a per-facilitator basis, will be calculated using activity-based costing methods. Costs for staff time will be assigned based on the prevailing national wage rate as reported in the Bureau of Labor Statistics' Occupational Outlook Handbook in the final year of intervention implementation92. All other costs will be adjusted for inflation

to constant U.S. dollars for the final year of implementation using the Bureau of Labor Statistics'

Sample size and power estimates are based on two-sided $a = 0.05$ and Student t tests on change from baseline to each follow-up point. Estimating a 20% attrition rate, a sample of 90 per group allows for detection of moderate effect sizes ($d = 0.47$ SD unit differences) equating to mean changes in DD of at least 0.36 and mean changes in HbA1c of at least 0.44%.

Inclusion criteria:

To be eligible to enter baseline assessment:

• Adult patients with T1D (confirmed by clinical history and/or anti-glutamic acid decarboxylase [GAD] antibody testing) on intensive insulin treatment;

• Diagnosis of T1D for at least 12 months that occurred at or below age 40;

• Age 19 years or older;

• Have a recent HbA1c of 7.2% or higher, or unable to recall most recent value;

• Not have started to use any new (to the participant) diabetes device (such as an insulin pump or continuous glucose monitor) in the past 6 months;

• Internet access through a computer or smart phone;

• Ability to speak/read English.

To be eligible to be randomized to receive an intervention (following baseline assessment):

• Type 1 Diabetes Distress Scale (T1DDS) mean score 2.0 or higher;

• HbA1c 7.5 or higher.

Exclusion criteria:

• Documented psychosis, blindness, dementia, active dialysis, substance abuse, amputations, or severe functional deficits, or recent major surgery or hospitalization in the past year.

Consent process

During the telephone screening call, patients will be invited to give verbal consent to be screened for eligibility. Verbal consent will be documented by the researcher. Following determination of eligibility and interest, the study protocol will then be described to individuals. During the initial recruitment conversation, potential participants will be asked open-ended questions and they will be invited to repeat back their understanding of the study. Individuals will then be asked to report their name, mailing address, phone number, and email address.

Potential participants who wish to reflect upon participation outside of the screening telephone call will be offered a study fact sheet that summarizes the study procedures and timescales. Potential participants will be asked for their email address, which will only be used to send the fact sheet to the patient. The research staff will agree with the potential participant a time to continue the telephone conversation; potential participants will also be encouraged to telephone the research staff with any questions about participation.

Individuals eligible at the end of phone screening, and interested in participating, will be asked to give their contact details (including email address). A consent form will be emailed to the individual using DocuSign, which will indicate places where the individual should initial and sign the form. Once signed by the individual, a member of the research team will countersign the consent form. A copy of the signed consent will be emailed to the participant for their records. The consent process will additionally include a HIPAA authorization for release of records. As indicated on the form, these records will be

Consumer Price Index for Medical Care.93

limited to laboratory tests (HbA1c tests at the prescribed dates) and coming from either their electronic

The consent will include an additional request for consent (via DocuSign) for participants' contact details to be stored by the research team to allow participants to be informed about future research studies.

Risks & Benefits:

Risks are minimal. These risks, and strategies to address them, are described below.

SURVEY ASSESSMENTS

The survey scales used for baseline and follow up assessments are non-invasive and the emotional, social, and legal risks seem quite minimal; in fact the study team has used most of the assessment measures in previous research, including a prior, similar study, without incident. Participants will be informed during recruitment and consent that they may skip any questions that cause discomfort, and cease participation in the study at any time. The use of online survey tools will allow participants to complete assessments at a convenient time and location of their own choosing.

LABORATORY ASSESSMENTS

Although it is not feasible to utilize participants' routinely collected HbA1c results, due to incompatibility with survey timings, participants will be able to select a contracted community laboratory service of their choosing. Participant confidentiality will be maintained through the use of coded blood draw requisitions that do not use any participant identifiable information. We do request obtaining consent from participants to request their current HbA1c result from their provider in the event that they do not complete one or more follow up blood draws.

The blood draws that participants will be asked to undertake are equivalent to those routinely undertaken by patients' as part of their ongoing diabetes care and are expected to cause minimal discomfort and risk. However, blood draws carry a risk of pain, bruising and fainting, and a rare risk of infection from the blood draw.

Participant confidentiality will be assured during the blood draw by the use of their unique, coded study ID as the sole identifier on the lab slips.

GROUP MEETINGS (IN PERSON OR WEB-BASED)

The group meetings pose a minimal risk for breaching participant confidentiality or privacy. The in-person group meetings will be held in a private meeting location at UCSF. Online web meetings will be held in a location of participants' choosing; they will be reminded to select a private location to safeguard their own and other attendees' privacy.

Material covered during the meetings will be generalizable to all attendees. Before and during the group meetings all participants will be informed and reminded of meeting ground rules and etiquette for maintaining confidentiality, respect and order during the meetings/

MEDICAL ISSUES

Although participants will not be instructed or expected to change how they manage their diabetes during the course of the study, they will receive education, information, and suggestions about strategies to manage blood sugar levels. Participants will be advised on a regular basis to review any possible changes they would like to make to their diabetes management regimens with their endocrinologist and/or other health care providers. In the event that participants report any medical concerns, for example more frequent occurrences of hypoglycemic episodes, they will be telephoned health records or a local laboratory (Quest diagnostics). Quest diagnostics specifically requires a HIPAA authorization form. The same procedure including DocuSign as outlined for the consent form above will be used for the HIPAA authorization form. Permission will be sought during the phone call to share the information with appropriate members of participants' healthcare team(s). Dr. Masharani will also be on call during the intervention period to address and clinical questions or concerns raised by participants or the intervention facilitators.

DEPRESSION AND OTHER PSYCHOLOGICAL ISSUES

Participants identified as reaching criteria for depression on the PHQ survey (a score of 15 or above) will be telephoned and sent a letter (see modified previously approved depression protocol, attached). This protocol encourages participants to seek care from a health provider for their symptoms and screens for suicide risk (which escalates additional referral to a senior investigator or emergency services, as required). Permission will be sought during the phone call to share the information with appropriate members of participants' healthcare team(s). Drs. Fisher and Polonsky will also be on call during the intervention period to address and questions or concerns raised by participants or the intervention facilitators about participants' psychological wellbeing.

If a participant seeks help for medical or psychological issues from project staff, they will be referred to appropriate resources at their respective health care settings. A senior investigator with clinical experience will be on-call during participant assessments and interventions to deal with potential clinical issues that may arise.

All study procedures are the minimum necessary to meet study objectives, with steps taken to mitigate risks. The research team has sufficient expertise and experience to conduct the research, and the sample size is sufficient to yield useful results.

CONSENT

Consent to participate is an ongoing process. During the initial recruitment conversation when the research assistant describes the study, they will invite participants to ask questions and ask them to repeat back to us their understanding of the study. Participation in the project will not affect the patient's clinical care in any way, and participants may withdraw consent at any point during their involvement.

MEDICAL AND PSYCHOLOGICAL CONCERNS

The protocols for addressing any emerging concerns is described above.

CONFIDENTIALITY

We will only collect the minimal personal information that is absolutely essential to research activity. All information will be coded and securely stored, with access solely granted to the investigators and study staff.

ECONOMIC HARMS

Participants will not bear the costs of any study procedures.

BENEFITS

Possible immediate and/or direct benefits to participants and society at large include:

• Knowledge may be gained about their health and health conditions

• Feeling of contribution to knowledge in the health or social sciences field

Payment

Participants will be paid for each of the 4 assessments (but not for the interventions) using gift cards on an incremental scale, as follows:

Stage	**Survey**	**Labs**	**Total**
Baseline	$20	$20	$40
3 months	$25	$30	$55
6 months	$30	$35	$65

9 months	$35	$45	$80
$240			