Intervention mapping to adapt a mindfulness-based intervention for adults with diabetes and emotional distress

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Sponsor: NCATS

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STATEMENT OF COMPLIANCE

The trial will be conducted in accordance with International Conference on Harmonisation Good Clinical Practice (ICH GCP) and applicable United States (US) Code of Federal Regulations (CFR). The Principal Investigator will assure that no deviation from, or changes to, the protocol will take place without prior documented approval from the Institutional Review Board (IRB), except where necessary to eliminate an immediate hazard(s) to the trial subjects. All personnel involved in the conduct of this study have completed Human Subjects Protection and ICH GCP Training.

The protocol, informed consent form(s), recruitment materials, and all subject materials will be submitted to the local Institutional Review Board (IRB) for review and approval. Approval of both the protocol and the consent form must be obtained before any subject is enrolled. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. All changes to the consent form will be IRB approved; a determination will be made regarding whether a new consent needs to be obtained from subjects who provided consent, using a previously approved consent form.

1 PROTOCOL SUMMARY

1.1 SYNOPSIS

Title:	Intervention mapping to adapt a mindfulness-based intervention for adults with diabetes and emotional distress
Study Description:	This study will pilot test the content of a Mindfulness-Based Diabetes Education program with adults who have type 2. The program integrates two evidence-based interventions – Mindfulness-Based Stress Reduction and Diabetes Self-Management Education. This pilot study will assess the acceptability, feasibility, and preliminary efficacy of the intervention. Participants' input will be used to adapt and improve the program to best fit the target study population.. This study will enroll up to 30 participants by the University of Alabama at Birmingham in conjunction with Cooper Green Mercy Healthcare Services Authority.
Objectives:	To pilot test an integrated Mindfulness-Based Stress Reduction/Diabetes Self-Management Education intervention in a small group of participants to assess acceptability and feasibility.
Endpoints:	Feasibility, Acceptability, Preliminary Efficacy
Study Population:	Adults with type 2 diabetes
Phase:	Single Arm Pilot Study
Description of Study Intervention:	This is a new program that combines Mindfulness-Based Stress Reduction and Diabetes Self-Management Education. If you enter and complete this study, you will be in this study for a total of 2 months. The Mindfulness-Based Diabetes Education program will be held weekly, in-person, in a group setting. Over 2 months, you will have eight weekly sessions for the program with a trained facilitator and other study participants. You will

	receive a schedule at the beginning of the program with the sessions outlined. The group sessions will occur every week. Approximately 5-10 participants will be assigned to each group.
Study Duration:	12 months
Subject Duration:	2 months

1.2 SCHEDULE OF ACTIVITIES (SOA)

Activity	**Activity Schedule**
Mindfulness-Based Diabetes Education program sessions	Weeks 1 to 8: meet weekly
Study assessment visits – 2	1. Enrollment assessment visit
	2. 8-week assessment visit
Focus Group – 1	1. Focus group

INTRODUCTION

1.3 STUDY RATIONALE

In this study, we will pilot an intervention (integrated mindfulness-based stress reduction and diabetes self-management education) in a small group of participants to assess acceptability, feasibility, and preliminary efficacy.

1.4 BACKGROUND

Type 2 diabetes is a chronic disease that is especially common in the Southeastern United States, affecting 14% of adults in Alabama. Low-income and racial/ethnic minority adults are disproportionately affected by type 2 diabetes. Managing type 2 diabetes requires patients to eat a healthy diet, exercise regularly, take all medications as prescribed, and monitor their blood sugar, which can be challenging for many patients.

Patients with type 2 diabetes who have elevated diabetes distress are less likely to follow the recommended treatment or to have well-controlled diabetes. Although some existing treatments help to improve distress, these treatments do not consistently improve diabetes self-management or outcomes. Information about how other psychosocial factors is associated with diabetes distress is limited. Additionally, the temporal relationship between diabetes distress and diabetes self-management behaviors has not been clearly elucidated. A better understanding of how diabetes distress is associated with other psychosocial factors and diabetes self-management behaviors will allow for the development of more effective interventions.

We applied a systematic method to develop an intervention which integrates components of mindfulness-based stress reduction and diabetes self-management education. In this study, we will pilot test this intervention in a small group of participants to assess acceptability and feasibility.

1.5 RISK/BENEFIT ASSESSMENT

1.5.1 KNOWN POTENTIAL RISKS

All participants will be treated according to the highest ethical standards. No participant will experience a reduction in medical, or any other type of needed service (e.g., social or clinical) that are currently available to him/her. Participation may involve completing a questionnaire, semi-structured interviews, or participating in the pilot study intervention (Mindfulness-Based Diabetes Education). Semi-structured interviews and focus groups will be audio-recorded, but no unique identifiers will be used in the collection of their responses. No significant risks are anticipated with this portion of the research plan than otherwise experienced in day-to-day living. The participants may experience some discomfort in talking about personal health issues, emotional distress, or diabetes management.

Breach of Confidentiality. The main potential risk of this study is breach of confidentiality. This is one of the most common risks of participation in clinical research. Accordingly, our team has designed a strategy to protect participant confidentiality. All participants will be informed of study procedures and gauged for understanding of study tasks. In addition, study personnel will follow regulatory guidelines

for obtaining informed consent. All interviews and intervention activities will be conducted in a private space. For all participants, research data will be stored using a unique participant identification code (sequence number based on entry to the study) instead of names or other personal identifiers. Consent forms with links to participant study numbers will be kept in a locked file cabinet in a locked office with the PI (Dr. Presley) or research assistant. According to UAB regulatory policy, records relating to research, including informed consent documents, shall be securely retained for one year after completion of the research. All records shall be accessible for inspection and copying by authorized representatives of the department or sponsor agency at reasonable times and in a reasonable manner. All electronic study data are kept on UAB secure encrypted password protected servers, and will only be available to research personnel for this project. All study personnel will complete HIPAA and human subjects training in accordance with UAB Institutional Review Board policy.

Emotional Distress. Participants will complete the 17-item DDS measure after informed consent is obtained, which will be scored by study personnel to determine eligibility. Additionally, measures of emotional distress will be assessed at baseline and 2-month follow-up for intervention participants. The measures assess the level of diabetes distress and depressive symptoms that a participant is experiencing, these are not diagnostic tests. Our study measures will not ask about suicidality. Participants may experience emotional distress related to participating in the intervention, due to the focus on emotional distress. Participants will be informed that they may stop participation at any time if they feel uncomfortable. Additionally, if a participant appears to be in emotional distress, study staff will inquire as to the participant's well-being and whether they wish to stop the study visit or session. Participants who disclose potentially harmful information (e.g., suicidality) will be immediately referred for an assessment by behavioral health at CGMHSA. All participants will be provided with a letter outlining services that details information on available mental health services at CGMHSA and low-cost resources available in Jefferson County.
Inconvenience. Participating in the study may inconvenience patients because of the time needed to collect data and participate in the intervention sessions.

Alternative Treatments and Procedures: All study participants, including those in the single-arm pilot intervention, will have full access to all available standard of care clinical services at CGMHSA, and are permitted to withdraw or refuse participation at any time.

1.5.2 KNOWN POTENTIAL BENEFITS

Participants may or may not benefit from the study. For participants in the pilot intervention, benefits may include improvement in emotional distress, diabetes self-management behaviors, and glycemic control. Risks to participants are related primarily to breach of confidentiality and emotional distress. As the risk to individual participants is small and potential benefits are significant, the risk/benefit ratio is favorable.

2 STUDY DESIGN

2.1 OVERALL DESIGN

This is a single-arm pilot study of Mindfulness-Based Diabetes Education (an integrated mindfulness-based stress reduction and diabetes self-management education intervention) in adults with type 2 diabetes who receive care at a safety-net healthcare system. Participants will complete baseline and 2-

month assessments, as well as a focus group after study completion. Program will be delivered over 8-weekly group educational sessions, in-person with 5-10 participants per group.

2.2 END OF STUDY DEFINITION

Date of final visit for participant follow up assessment.

3 STUDY POPULATION

3.1 INCLUSION CRITERIA

Inclusion criteria:

- age 19-64 years
- diagnosis of type 2 diabetes
- receipt of care at CGMHSA (one or more visits to primary care or diabetes clinic within the prior year)

3.2 EXCLUSION CRITERIA

Exclusion criteria:

- non-English speaking
- currently pregnant
- personal history or prior diagnosis of bipolar disorder, schizophrenia, or psychosis

3.3 SCREEN FAILURES

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3.4 STRATEGIES FOR RECRUITMENT AND RETENTION

Study participants will be recruited from Cooper Green Mercy Health System Authority (CGMHSA). At CGMHSA, a report of patients who have been referred to diabetes education from 2017-2020 was generated to identify potential study participants. Letters will be mailed to participants (letters included), followed by a phone call to inform them of the study (phone script included), conduct screening listed below, and if participants are interested to schedule a study visit.

Additionally, potential participants may be identified through screening in the CGMHSA diabetes clinic or primary care clinic. CGMHSA clinicians will provide contact information (names, phone numbers) for potential participants seen in diabetes or primary care clinics who agree to be contacted about the study. Similar to the process described above, study personnel will call potential participants by phone to inform them of the study (phone scripts included), conduct screening listed below, and if participants are interested to schedule a study visit.

Study PI will inform CGMHSA primary care providers of the study and eligibility criteria (providing a study recruitment flyer); primary care providers will be asked to have any interested potential participants to contact study personnel at the number listed on the flyer.

If participants contact study personnel after seeing a study flyer or after learning of the study from their primary care provider, study staff will speak to potential participants by phone (upon call from potential participant or by returning a phone call to the potential participant), provide additional information about the study, conduct screening listed below, and if participants are interested to schedule a study visit. During the recruitment phone call, study staff will explain the research project.

4 STUDY INTERVENTION

4.1 STUDY INTERVENTION(S) ADMINISTRATION

4.1.1 STUDY INTERVENTION DESCRIPTION

We will recruit up to 30 participants to complete the pilot intervention, in groups of 5-10 participants. The program will be delivered in 8 weekly sessions of 1.5 to 2 hours duration each, for a total duration of 2 months. The pilot intervention will be delivered by study PI, Dr. Caroline Presley, who is an Internal Medicine-Pediatrics trained physician with training in delivery of mindfulness-based interventions. We have included the intervention manual with this amendment/revision. Program sessions will be recorded solely for the purposes of assessing fidelity to intervention content. Any identifying information will be removed from transcripts. The following table provides overview of session content with full details in the manual.

Table: Mindfulness-Based Diabetes Education Sessions and Content

Session	Session Content
1	• Introduction to mindfulness; body scan meditation • Introduction to behavior change and diabetes
2	• Role of perception, stress responses and reactivity; breath awareness meditation • Healthy eating module with mindful eating of healthy snack w/reflection on thoughts, emotions, physical sensations • Pleasant events calendar w/focus on events related to diabetes self-management
3	• Exploration of mind-body connections • Physical activity (PA) module, mindful walking with attention to thoughts, emotions, physical sensations related to PA • Unpleasant events calendar w/focus on events related to diabetes self-management
4	• Mindfulness as means to reduce negative effects of stress, mindful yoga • Healthy eating module • SMART goal setting focused on diabetes self-management
5	• Exploration of coping mechanisms, capacity for mindful responding; breath awareness meditation • Self-monitoring blood glucose module • SMART goal setting focused on diabetes self-management
6	• Integration of mindfulness into daily life; breath awareness meditation • Medication taking module • SMART goal setting focused on diabetes self-management

7	• Mindfulness and interpersonal communication; mindful walking • Problem solving module • SMART goal setting focused on diabetes self-management
8	• Focus on continued formal and informal practice; guided reflection • Framework for mindfulness and influence on diabetes

4.1.2 DOSING AND ADMINISTRATION

The program will be delivered in a group setting for 8 weekly sessions of 1.5 to 2 hours duration each, for a total duration of 2 months.

4.2 STUDY INTERVENTION COMPLIANCE

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4.3 CONCOMITANT THERAPY

No changes to participants' medication regimen will be made during the study. Participants will be instructed to continue taking medications prescribed by their healthcare provider. Additionally, participants who are engaged in mental health treatment, including psychotherapy, will be able to continue this treatment unchanged during their participation in this study.

5 STUDY INTERVENTION DISCONTINUATION AND SUBJECT DISCONTINUATION/WITHDRAWAL

5.1 DISCONTINUATION OF STUDY INTERVENTION

This study will be stopped prior to its completion if: (1) the intervention is associated with adverse effects that call into question the safety of the intervention; (2) difficulty in study recruitment or retention will significantly impact the ability to evaluate the study endpoints; (3) any new information becomes available during the trial that necessitates stopping the trial; or (4) other situations occur that might warrant stopping the trial.

5.2 SUBJECT DISCONTINUATION/WITHDRAWAL FROM THE STUDY

Subjects are free to withdraw from participation in the study at any time upon request.

An investigator may discontinue or withdraw a subject from the study for the following reasons:

- Significant study intervention non-compliance
- If any clinical adverse event (AE), laboratory abnormality, or other medical condition or situation occurs such that continued participation in the study would not be in the best interest of the subject

Subjects who sign the informed consent form and are randomized but do not receive the study intervention may be replaced. Subjects who sign the informed consent form, and are randomized and receive the study intervention, and subsequently withdraw, or are withdrawn or discontinued from the study, will not be replaced.

5.3 LOST TO FOLLOW-UP

A subject will be considered lost to follow-up if he or she fails to return for 2 scheduled visits and is unable to be contacted by the study site staff.

The following actions must be taken if a subject fails to be available for a required study visit:

- The site will attempt to contact the subject and reschedule the missed visit and counsel the subject on the importance of maintaining the assigned visit schedule and ascertain if the subject wishes to and/or should continue in the study.
- Before a subject is deemed lost to follow-up, the investigator or designee will make every effort to regain contact with the subject (where possible, 3 telephone calls and, if necessary, a certified letter to the subject's last known mailing address or local equivalent methods). These contact attempts should be documented in the subject's medical record or study file.
- Should the subject continue to be unreachable, he or she will be considered to have withdrawn from the study with a primary reason of lost to follow-up.

6 STUDY ASSESSMENTS AND PROCEDURES

6.1 STUDY ASSESSMENTS

Participants will complete assessment at baseline and 2 months. Assessments will include interviewer-administered measures. Participants will also participate in a focus group for acceptability following completion of the intervention. Process measures for feasibility will be tracked throughout the study.

Acceptability, focus groups:

- assessment of intervention content
- perceived positive or negative effects
- appropriateness of intervention duration and frequency
- barriers to engagement, suggestions to improve the intervention
- overall satisfaction

Feasibility of the intervention using process measures:

- percentage of screened participants who are eligible
- percentage of eligible participants who enroll
- distribution of participants by demographics (age, race, ethnicity, gender)
- number of sessions attended
- participant adherence to study tasks
- overall study retention

Preliminary efficacy: baseline and 2-month follow-up:

- diabetes distress (Diabetes Distress Scale)
- diabetes self-management behaviors (Adherence to Refills and Medications scale, Summary of Diabetes Self-Care Activities)

- glycemic control (A1C test results from electronic medical records)

6.2 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

6.2.1 DEFINITION OF ADVERSE EVENTS (AE)

Adverse event means any untoward medical occurrence associated with the use of an intervention in humans, whether or not considered intervention-related (21 CFR 312.32 (a)).

6.2.2 DEFINITION OF SERIOUS ADVERSE EVENTS (SAE)

An adverse event (AE) is considered "serious" if, in the view of either the investigator or sponsor, it results in any of the following outcomes:

- Death
- A life-threatening adverse event (of note, the term "life-threatening" refers to an event in which the subject was at risk of death at the time of the event, rather than to an event which hypothetically might have caused death if it were more severe)
- inpatient hospitalization or prolongation of existing hospitalization
- a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions
- or a congenital anomaly/birth defect.

Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse.

6.2.3 CLASSIFICATION OF AN ADVERSE EVENT

6.2.3.1 SEVERITY OF EVENT

For adverse events (AEs), the following guidelines will be used to describe severity:

- **Mild** – Events require minimal or no treatment and do not interfere with the subject's daily activities.
- **Moderate** – Events result in a low level of inconvenience or concern with the therapeutic measures. Moderate events may cause some interference with functioning.
- **Severe** – Events interrupt a subject's usual daily activity and may require systemic drug therapy or other treatment. Severe events are usually potentially life-threatening or incapacitating. Of note, the term "severe" does not necessarily equate to "serious."

6.2.3.2 RELATIONSHIP TO STUDY INTERVENTION

All adverse events (AEs) must have their relationship to study intervention assessed by the clinician who examines and evaluates the subject based on temporal relationship and his/her clinical judgment. The degree of certainty about causality will be graded using the categories below. In a clinical trial, the study product must always be suspect.

- **Related** – The AE is known to occur with the study intervention, there is a reasonable possibility that the study intervention caused the AE, or there is a temporal relationship between the study intervention and event. Reasonable possibility means that there is evidence to suggest a causal relationship between the study intervention and the AE.
- **Not Related** – There is not a reasonable possibility that the administration of the study intervention caused the event, there is no temporal relationship between the study intervention and event onset, or an alternate etiology has been established.

6.2.3.3 EXPECTEDNESS

The Principal Investigator will be responsible for determining whether an adverse event (AE) is expected or unexpected. An AE will be considered unexpected if the nature, severity, or frequency of the event is not consistent with the risk information previously described for the study intervention.

6.2.4 TIME PERIOD AND FREQUENCY FOR EVENT ASSESSMENT AND FOLLOW-UP

The occurrence of an adverse event (AE) or serious adverse event (SAE) may come to the attention of study personnel during study visits and interviews of a study subject presenting for medical care, or upon review by a study monitor.

All AEs including local and systemic reactions not meeting the criteria for SAEs will be captured on the appropriate case report form (CRF). Information to be collected includes event description, time of onset, clinician's assessment of severity, relationship to study product (assessed only by those with the training and authority to make a diagnosis), and time of resolution/stabilization of the event. All AEs occurring while on study must be documented appropriately regardless of relationship. All AEs will be followed to adequate resolution.

Any medical condition that is present at the time that the subject is screened will be considered as baseline and not reported as an AE. However, if the study subject's condition deteriorates at any time during the study, it will be recorded as an AE.

Changes in the severity of an AE will be documented to allow an assessment of the duration of the event at each level of severity to be performed. AEs characterized as intermittent require documentation of onset and duration of each episode.

The Study Coordinator will record all reportable events with start dates occurring any time after informed consent is obtained until 7 (for non-serious AEs) or 30 days (for SAEs) after the last day of study participation. At each study visit, the Study Coordinator will inquire about the occurrence of AE/SAEs since the last visit. Events will be followed for outcome information until resolution or stabilization.

6.2.5 ADVERSE AND SERIOUS ADVERSE EVENT REPORTING

All serious adverse events must be reported to the IRB according to regulatory requirements. The Principal Investigator will immediately report to the sponsor any serious adverse event, whether or not considered study intervention related, including those listed in the protocol or package insert and must include an assessment of whether there is a reasonable possibility that the study intervention caused the event. Study endpoints that are serious adverse events (e.g., all-cause mortality) must be reported in accordance with the protocol unless there is evidence suggesting a causal relationship between the

study intervention and the event (e.g., death from anaphylaxis). In that case, the investigator must immediately report the event to the sponsor.

All serious adverse events (SAEs) will be followed until satisfactory resolution or until the Principal Investigator deems the event to be chronic or the subject is stable. Other supporting documentation of the event may be requested and should be provided as soon as possible.

6.3 UNANTICIPATED PROBLEMS

6.3.1 DEFINITION OF UNANTICIPATED PROBLEMS (UP)

The Office for Human Research Protections (OHRP) considers unanticipated problems involving risks to subjects or others to include, in general, any incident, experience, or outcome that meets **all** of the following criteria:

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

6.3.2 UNANTICIPATED PROBLEM REPORTING

The investigator will report unanticipated problems (UPs) to the reviewing Institutional Review Board (IRB). The UP report will include the following information:

- Protocol identifying information: protocol title and number, PI's name, and the IRB project number;
- A detailed description of the event, incident, experience, or outcome;
- An explanation of the basis for determining that the event, incident, experience, or outcome represents an UP;
- A description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the UP.

To satisfy the requirement for prompt reporting, UPs will be reported using the following timeline:

- UPs that are serious adverse events (SAEs) will be reported to the IRB within 10 working days of the investigator becoming aware of the event.
- Any other UP will be reported to the IRB within 10 working days of the investigator becoming aware of the problem.

7 STATISTICAL CONSIDERATIONS

7.1 STATISTICAL HYPOTHESES

- Primary Efficacy Endpoint(s):

No formal hypothesis testing given small sample size.

- Secondary Efficacy Endpoint(s):

7.2 SAMPLE SIZE DETERMINATION

Sample size considerations:
Based on recruitment for prior studies at CGMHS conducted by Dr. Cherrington, we anticipate it will be feasible to recruit 30 adults to participate in the pilot intervention. We provide a power calculation to further justify our sample size. Assuming a standard deviation of 1.8% for the change in HbA1c (from baseline to 2-month follow-up), which was obtained from results of a prior intervention study in adults with type 2 diabetes recruited from CGMHS, a sample size of 30 participants, a two-sided paired t-test, and a significance level of 0.05, we will have 80% power to detect changes in HbA1c (from baseline to follow-up) of 1.0% and greater as being statistically significant.62 This calculation was performed using nQuery Advisor + nTerim, version 3.

7.3 STATISTICAL ANALYSES

7.3.1 GENERAL APPROACH

Given our small sample size and the resultant lack of precision of an estimate of effect size, we will not estimate efficacy based on outcome measures. In addition, we will not be testing formal statistical hypotheses.

7.3.2 ANALYSIS OF THE PRIMARY EFFICACY ENDPOINT(S)

Initial proposed analysis: To estimate effect size of the pilot intervention, we will perform paired t-tests to study the change in the primary outcome, A1C, and secondary outcomes, diabetes distress and diabetes self-management behaviors, from baseline to post-intervention. Analysis of covariance will be used to examine baseline to 2-month changes in primary and secondary outcomes while controlling for potential covariates of interest, such as demographics or disease severity. Distributions of continuous outcome variables will be examined for normality using box plots, stem and leaf plots, and normal probability plots. Variables that are determined to be non-normally distributed will be transformed or analyzed using non-parametric tests, such as Wilcoxon signed-rank test. All statistical tests will be two-sided using a significance level of 0.05. Statistical analysis will be completed using SAS, version 9.4 or later.

Analysis plan: We will generate descriptive statistics, including frequency distribution tables for categorical variables, as well as means, medians, standard deviations, and interquartile ranges for continuous variables, including diabetes distress.

7.3.3 ANALYSIS OF THE SECONDARY ENDPOINT(S)

We will also generate descriptive statistics, including frequency distribution tables for categorical variables, as well as means, medians, standard deviations, and interquartile ranges for continuous variables, for feasibility measures.

Qualitative methods will be applied to data collected participants related to acceptability.

7.3.4 SAFETY ANALYSES

Descriptive statistics, primarily frequency distribution tables for categorical variables, will be generated for any adverse events.

7.3.5 BASELINE DESCRIPTIVE STATISTICS

Descriptive statistics, primarily frequency distribution tables for categorical variables, will be generated to characterize participants. We will also generate descriptive statistics, including frequency distribution tables for categorical variables, as well as means, medians, standard deviations, and interquartile ranges for continuous variables.

8 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

8.1 REGULATORY, ETHICAL, AND STUDY OVERSIGHT CONSIDERATIONS

8.1.1 INFORMED CONSENT PROCESS

8.1.1.1 CONSENT/ASSENT AND OTHER INFORMATIONAL DOCUMENTS PROVIDED TO SUBJECTS

Consent forms describing in detail the study intervention, study procedures, and risks are given to the subject and written documentation of informed consent is required prior to conducting study screening procedures. A separate screening consent form will not be used.

8.1.1.2 CONSENT PROCEDURES AND DOCUMENTATION

Informed consent is a process that is initiated prior to the individual's agreeing to participate in the study and continues throughout the individual's study participation. Consent forms will be Institutional Review Board (IRB)-approved and the subject will be asked to read and review the document. The investigator will explain the research study to the subject and answer any questions that may arise. A verbal explanation will be provided in terms suited to the subject's comprehension of the purposes, procedures, and potential risks of the study and of their rights as research subjects. Subjects will have the opportunity to carefully review the written consent form and ask questions prior to signing. The subjects should have the opportunity to discuss the study with their family or surrogates or think about it prior to agreeing to participate. The subject will sign the informed consent document prior to any procedures being done specifically for the study. Subjects must be informed that participation is voluntary and that they may withdraw from the study at any time, without prejudice. A copy of the informed consent document will be given to the subjects for their records. The informed consent process will be conducted and documented in the source document (including the date), and the form signed, before the subject undergoes any study-specific procedures. The rights and welfare of the

subjects will be protected by emphasizing to them that the quality of their medical care will not be adversely affected if they decline to participate in this study.

8.1.2 STUDY DISCONTINUATION AND CLOSURE

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to regulatory authorities. If the study is prematurely terminated or suspended, the Principal Investigator (PI) will promptly inform study subjects and the Institutional Review Board (IRB), will provide the reason(s) for the termination or suspension. Study subjects will be contacted, as applicable, and be informed of changes to study visit schedule.

Circumstances that may warrant termination or suspension include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to subjects
- Demonstration of efficacy that would warrant stopping
- Insufficient compliance to protocol requirements
- Data that are not sufficiently complete and/or evaluable
- Determination that the primary endpoint has been met
- Determination of futility

Study may resume once concerns about safety, protocol compliance, and data quality are addressed, and satisfy the IRB.

8.1.3 CONFIDENTIALITY AND PRIVACY

Subject confidentiality and privacy is strictly held in trust by the participating investigators and their staff. Therefore, the study protocol, documentation, data, and all other information generated will be held in strict confidence. No information concerning the study or the data will be released to any unauthorized third party without prior written approval of the Principal Investigator.

All research activities will be conducted in as private a setting as possible.

Representatives of the Institutional Review Board (IRB) may inspect all documents and records required to be maintained by the investigator, including but not limited to, medical records (office, clinic, or hospital) and pharmacy records for the subjects in this study.

The study subject's contact information will be securely stored at each site for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for as long a period as dictated by the reviewing IRB and/or Institutional policies.

Study subject research data, which is for the purposes of statistical analysis and scientific reporting, will be stored at the UAB Division of Preventive Medicine, Medical Towers offices. This will not include the subject's contact or identifying information. Rather, individual subjects and their research data will be identified by a unique study identification number. The study data entry and study management systems used by research staff will be secured and password protected.

8.1.4 QUALITY ASSURANCE AND QUALITY CONTROL

The site will perform internal quality management of study conduct, data collection, documentation and completion. Quality control (QC) procedures will be completed by the Data Manager during data entry into the appropriate CRF. Any missing data or data anomalies will be communicated to the Study Coordinator for clarification/resolution.

Following written Standard Operating Procedures (SOPs), the monitors will verify that the clinical trial is conducted and data are generated are collected, documented (recorded), and reported in compliance with the protocol, International Conference on Harmonisation Good Clinical Practice (ICH GCP), and applicable regulatory requirements.

The site will provide direct access to all trial related sites, source data/documents, and reports for the purpose of monitoring and inspection by local and regulatory authorities.

8.1.5 DATA HANDLING AND RECORD KEEPING

8.1.5.1 DATA COLLECTION AND MANAGEMENT RESPONSIBILITIES

Data collection is the responsibility of the clinical trial staff at the site under the supervision of the Principal Investigator. The Principal Investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported.

All source documents should be completed in a neat, legible manner to ensure accurate interpretation of data.

Hard copies of source document worksheets will be used for recording data for each subject enrolled in the study. Data recorded in the case report form (CRF) derived from source documents should be consistent with the data recorded on the source documents.

8.1.5.2 STUDY RECORDS RETENTION

Study documents should be retained for a minimum of 3 years after the completion of the study. These documents should be retained for a longer period, however, if required by local regulations.

8.1.6 PROTOCOL DEVIATIONS

A protocol deviation is any noncompliance with the clinical trial protocol requirements. The noncompliance may be either on the part of the subject, the investigator, or the study site staff. As a result of deviations, corrective actions are to be developed by the site and implemented promptly.

These practices are consistent with ICH GCP:

- 4.5 Compliance with Protocol, sections 4.5.1, 4.5.2, and 4.5.3
- 5.1 Quality Assurance and Quality Control, section 5.1.1
- 5.20 Noncompliance, sections 5.20.1, and 5.20.2.

It is the responsibility of the Principal Investigator to use continuous vigilance to identify and report deviations within 10 working days of identification of the protocol deviation. Protocol deviations must be sent to the reviewing Institutional Review Board (IRB) per their policies. The Principal Investigator is responsible for knowing and adhering to the reviewing IRB requirements.

8.1.7 CONFLICT OF INTEREST POLICY

The independence of this study from any actual or perceived influence, such as by the pharmaceutical industry, is critical. Therefore, any actual conflict of interest of persons who have a role in the design, conduct, analysis, publication, or any aspect of this trial will be disclosed and managed. Furthermore, persons who have a perceived conflict of interest will be required to have such conflicts managed in a way that is appropriate to their participation in the design and conduct of this trial.

8.2 ABBREVIATIONS

AE	Adverse Event
ANCOVA	Analysis of Covariance
CFR	Code of Federal Regulations
CONSORT	Consolidated Standards of Reporting Trials
CRF	Case Report Form
DHHS	Department of Health and Human Services
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
ICH	International Conference on Harmonisation
ICMJE	International Committee of Medical Journal Editors
IRB	Institutional Review Board
LSMEANS	Least-squares Means
NCT	National Clinical Trial
NIH	National Institutes of Health
OHRP	Office for Human Research Protections
PI	Principal Investigator
QA	Quality Assurance
QC	Quality Control
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SOA	Schedule of Activities
SOP	Standard Operating Procedure
UP	Unanticipated Problem
US	United States

9 REFERENCES

CONSENT FORM TO BE PART OF A RESEARCH STUDY – PILOT STUDY

Title of Research: Intervention mapping to adapt a mindfulness-based intervention for adults with diabetes and emotional distress

UAB IRB Protocol #: IRB-300003578

Principal Investigator: Caroline Presley, MD MPH

Sponsor: UAB Center for Clinical and Translational Science, UAB Diabetes Research Center

General Information	You are being asked to take part in a research study. This research study is voluntary, meaning you do not have to take part in it. The procedures, risks, and benefits are fully described further in the consent form.
Purpose	The purpose of the study is to pilot test the content of a Mindfulness-Based Diabetes Education program with adults who have type 2 diabetes in order to get participants' feedback on the program. This information will be used to adapt and improve the program based on participants' input.
Duration & Visits	You will be in this study for up to 2 months. You are being asked to complete 2 study visits at enrollment and at 2 months, as well as to attend 1 focus group at 2 months. The study visits will last approximately 30-45 minutes, and participants will be asked to complete a questionnaire. The focus group will take approximately 60 minutes, and participants will be asked for their thoughts and feedback on the program. This study will provide a program called Mindfulness-Based Diabetes Education. This is a new program that combines a stress management and a diabetes self-management education program. It is an 8-week program with weekly meetings in-person, group meetings. Sessions will focus on education and strategies to improve diabetes self-management including healthy eating, physical activity, medication taking, self-monitoring, and will also include instruction and practice of mindfulness-based exercises to reduce stress.
Overview of Procedures	This study will include 2 study visits and a focus group that will be run by a trained facilitator to get participants' feedback on the Mindfulness-Based Diabetes Education program. If you are eligible and choose to participate, you will receive Mindfulness-Based Diabetes Education program.
Risks	The most common risks include breach of confidentiality, inconvenience, or emotional distress. You may experience minor pain or discomfort related to study activities; this is a minor risk and is reversible.
Benefits	You may or may not benefit from the study. This research may help develop an intervention and benefit future patient care.
Alternatives	Your alternative is not to participate in the research.

Purpose of the Research Study

We are asking you to take part in a research study to reduce stress and improve diabetes self-management in adults who have type 2 diabetes. Alabama is 3rd for diabetes among all 50 states in the United States which means about 14% of people in the state have diabetes. Diabetes distress is common with adults with type 2 diabetes and impacts diabetes self-management and blood glucose control. Currently, programs that improve both diabetes distress and diabetes self-management are lacking.

This study will pilot test the content of a Mindfulness-Based Diabetes Education program with adults who have type 2 diabetes in order to get participants' feedback on the program. The feedback will be used to improve and

adapt the program to best fit the target study population. The program integrates two evidence-based interventions – Mindfulness-Based Stress Reduction and Diabetes Self-Management Education. This pilot study will assess the acceptability, feasibility, and preliminary efficacy of the intervention. Participants' input will be used to adapt and improve the program. This study will enroll up to 30 participants by the University of Alabama at Birmingham in conjunction with Cooper Green Mercy Healthcare Services Authority.

Study Participation & Procedures

You have been screened and are eligible to participate in this research study. *Eligibility*: To be eligible to participate in this study, you need to complete a prescreening questionnaire, be 19 to 64 years of age, and meet eligibility requirements.

To enroll in this study, a questionnaire will be conducted. If you decide to participate in this study, you will attend a total of two study assessment visits including today's visit, as well as a one focus group. The study visits will take place at the beginning of the study and at 2 months. These visits will last about 30-45 minutes and take place in a private room at Cooper Green Mercy Healthcare Authority or Medical Towers at UAB or may be conducted by remotely by telephone or video-conference. Questionnaires include self-reported measures of your mood, stress, self-efficacy, social support, diabetes self-management behaviors, treatment satisfaction/burden. The following measures will be collected by trained research staff at each study assessment visit:

Measure	Description
Questionnaire	Questions about your mood, stress, self-efficacy, social support, diabetes self-management behaviors, treatment satisfaction/burden
Hemoglobin A1c Result	Study staff will obtain your most recent hemoglobin A1c result from your medical record. No other information will be obtained from your medical record.

The focus group will be held at the completion of the 2-month program and run by a trained facilitator. It will last approximately 60-minutes and will ask for participants' feedback on the program.

If you decide to participate, you will be assigned to receive the Mindfulness-Based Diabetes Education program. This is a new program that combines Mindfulness-Based Stress Reduction and Diabetes Self-Management Education. If you enter and complete this study, you will be in this study for a total of 2 months. The Mindfulness-Based Diabetes Education program will be held weekly, in-person, in a group setting. Over 2 months, you will have eight weekly sessions for the program with a trained facilitator and other study participants. You will receive a schedule at the beginning of the program with the sessions outlined. The group sessions will occur every week. Approximately 5-10 participants will be assigned to each group.

Group meetings will be held in person in a conference room at Cooper Green or at Medical Towers. Group meetings will last about 90 to 120 minutes each. Group sessions will focus on education and discussion about mindfulness-based exercises to reduce stress, as well as modules focused on healthy eating, physical activity, medication taking, self-monitoring to improve diabetes management. A trained interventionist will deliver each session. If you agree to join the study, the study will not make any changes to your medications.

Activity	Activity Schedule
Mindfulness-Based Diabetes Education program sessions	Weeks 1 to 8: meet weekly
Study assessment visits – 2	1. Enrollment assessment visit
	2. 8-week assessment visit
Focus Group – 1	1. Focus group

Risks and Discomforts

The risks for this study are low. You will be assigned to the Mindfulness-Based Diabetes Education program, as this is a pilot study testing a new intervention. This program may prove to be less effective or to have more side

effects than alternatives. If you enter this study, you will be asked to attend group meetings that focus on skills you need to reduce stress and improve your diabetes self-management. Risks include discomfort, a loss of confidentiality, minor pain, and inconvenience. You may feel some discomfort in talking about personal health issues, emotional distress, or diabetes management. You will only be asked to discuss what you feel comfortable sharing and you may choose not to share. Study staff will explain to all participants that what is said in group meetings is confidential. However, a risk for entering this program is loss of confidentiality. This risk is very small, as study staff follow rules to make sure your information is shared only with people who are supposed to have it. We take precautions to minimize the risk of loss of confidentiality including storing study information with a code only, there is no participant's name or other identifying information. Access to study information will be restricted to study personnel. Study information will be stored electronically on a secure, encrypted, password protected server. Program sessions will be audio-recorded to assess fidelity of the program; names or other identifying information will be removed from the transcripts and only study staff will have access to these.

You will be encouraged to make changes to your habits around your diabetes self-management (including healthy eating, physical activity, self-monitoring, medication taking) as well as to practice mindfulness exercises to reduce stress. You may feel tired or hungry when you first make these changes, but this is usually mild and often gets better with time. This study will include gentle, non-strenuous physical activity including walking and gentle yoga. Participants will be offered modifications based on their physical abilities. You could hurt yourself when exercising, such as spraining your ankle. On rare occasions, increased exercise can cause chest pain and undue shortness of breath. This is not common, and you will only be asked to make changes that are comfortable for you. Over 2-months, you will be asked to attend 2 study assessment visits, 8 group meetings, and 1 focus group. These study activities may be inconvenient and take time from your day-to-day activities. You will be assigned to the study program, which may prove to be less effective than alternatives.

Benefits
If you participate, you may experience reduced stress and improved diabetes self-management. Improved diabetes distress and diabetes self-management behaviors have benefits for diabetes outcomes and reduced risks of complications due to diabetes.

Alternatives
The alternative to study participation is that you may choose not to take part at all. There are other available diabetes self-management education programs that are not associated with this research study. You may discuss these alternative treatment options with your primary care provider.

Confidentiality and Authorization to Use and Disclose Information for Research Purposes
Federal regulations give you certain rights related to your health information. These include the right to know who will be able to get the information and why they may be able to get it. The study doctor must get your authorization (permission) to use or give out any health information that might identify you.

What protected health information may be used and/or given to others?
All medical information, including but not limited to information and/or records of any diagnosis or treatment of disease or condition, which may include sexually transmitted diseases (e.g., HIV, etc.) or communicable diseases, drug/alcohol dependency, etc.; all personal identifiers, including but not limited to your name, social security number, medical record number, date of birth, dates of service, etc.; any past, present, and future history, examinations, laboratory results, imaging studies and reports and treatments of any kind, including but not limited to drug/alcohol treatment, psychiatric/psychological treatment; financial/billing information, including but not limited to copies of your medical bills; any other information related to or collected for use in the research study, regardless of whether the information was collected for research or non-research (e.g., treatment) purposes; records about any study drug you received or about study devices used; and consent forms from past studies that might be in your medical record.

Who may use and give out information about you?
Information about your health may be used and given to others by Dr. Caroline Presley, the study doctor, and study staff. They might see the research information during and after the study.

Who might get this information?
All Individuals/entities listed in the informed consent document(s), including but not limited to, the physicians, nurses and staff and others performing services related to the research (whether at UAB or elsewhere). Your information may also be given to the sponsor of this research. "Sponsor" includes any persons or companies that are working for or with the sponsor, or are owned by the sponsor, or are providing support to the sponsor (e.g., contract research organization).

Information about you and your health which might identify you may be given to:

- the Office for Human Research Protections (OHRP)
- the U.S. Food and Drug Administration (FDA)
- the UAB Diabetes Research Center, a sponsor of this research
- National Institute of Diabetes, Digestive, and Kidney Diseases (NIDDK), a sponsor of this research
- the University of Alabama at Birmingham - the physicians and staff working on the research study (whether at UAB or elsewhere); the UAB IRB and its staff

Why will this information be used and/or given to others?
Information about you and your health that might identify you may be given to others to carry out the research study. The sponsor will analyze and evaluate the results of the study. In addition, people from the sponsor and its consultants will be visiting the research site. They will follow how the study is done, and they will be reviewing your information for this purpose.

What if I decide not to give permission to use and give out my health information?
By signing this consent form, you are giving permission to use and give out the health information listed above for the purposes described above. If you refuse to give permission, you will not be able to be in this research.

May I review or copy the information obtained from me or created about me?
You have the right to review and copy your health information. However, if you decide to be in this study and sign this permission form, you will not be allowed to look at or copy your information until after the research is completed.

May I withdraw or revoke (cancel) my permission?
Yes, but this permission will not stop automatically. The use of your personal health information will continue until you cancel your permission.

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor. If you withdraw your permission, you will not be able to continue being in this study.

When you withdraw your permission, no new health information which might identify you will be gathered after that date. Information that has already been gathered may still be used and given to others. This would be done if it were necessary for the research to be reliable.

Is my health information protected after it has been given to others?
If you give permission to give your identifiable health information to a person or business, the information may no longer be protected. There is a risk that your information will be released to others. Including others outside of UAB, without your permission.

Voluntary Participation and Withdrawal
Whether or not you take part in this study is your choice. There will be no penalty if you decide not to be in it. If you decide not to be in the study, you will not lose any benefits you are otherwise owed.
You are free to withdraw from this study at any time. Your choice to leave the study will not affect your relationship with this institution. Contact the study personnel if you want to withdraw from the study.

Cost of Participation
There will be no cost to you for taking part in the Mindfulness-Based Diabetes Education program and the study. The program and visits related to this study will be provided to you at no cost during the 2-month study period.

Payment for Participation
You will be paid $25 for the completion of the initial study assessment including a questionnaire. You will be paid $25 after completing the 2-month visit and $15 for the focus group at the end of the program. The total payment you may receive is $65. If you do not finish the entire study, you will only be paid for visits completed up to the time you decide to stop taking part in the study. Ask the study staff about the method of payment that will be used for this study (e.g., check, cash, gift card, direct deposit).

Payment for Research-Related Injuries
UAB, UAB Center for Clinical and Translational Science, and UAB Diabetes Research Center have not provided for any payment if you are harmed as a result of taking part in this study. If such harm occurs, treatment will be provided. However, this treatment will not be provided free of charge.

Significant New Findings
You will be told by the study doctor or the study staff if new information becomes available that might affect your choice to stay in the study.

Questions
If you have any questions, concerns, or complaints about the research or a research-related injury including available treatments, please contact the study doctor. You may contact Dr. Caroline Presley at 205-934-7609.

If you have questions about your rights as a research participant, or concerns or complaints about the research, you may contact the UAB Office of the IRB (OIRB) at (205) 934-3789 or toll free at 1-855-860-3789. Regular hours for the OIRB are 8:00 a.m. to 5:00 p.m. CT, Monday through Friday.

Legal Rights
You are not waiving any of your legal rights by signing this consent form.

Signatures
Your signature below indicates that you have read (or been read) the information provided above and agree to participate in this study. You will receive a copy of this signed consent form.

_____

Signature of Participant Date

_____

Signature of Person Obtaining Consent Date