STUDY PROTOCOL

Digital Health Platform (DHP) to Deliver Mindfulness as a Stress Management Intervention Leveraging Electronic (SMILE) Health Records for Racial and Ethnic Populations During the COVID-19 Pandemic: Clinical Trial

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Digital Health Platform (DHP) to Deliver Mindfulness as a Stress Management Intervention Leveraging Electronic (SMILE) Health Records for Racial and Ethnic Populations During the COVID-19 Pandemic: Clinical Trial

Protocol Number*: 23-0154

National Clinical Trial (NCT) Identified Number: [Not yet assigned]

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Sponsor: University of North Carolina, Chapel Hill

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23 January 2024

CONFIDENTIALITY STATEMENT

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STATEMENT OF COMPLIANCE

The trial will be carried out in accordance with International Council on Harmonisation Good Clinical Practice (ICH GCP) and the following:

- United States (US) Code of Federal Regulations (CFR) applicable to clinical studies (45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56, 21 CFR Part 312, and/or 21 CFR Part 812).

National Institutes of Health (NIH)-funded investigators and clinical trial site staff who are responsible for the conduct, management, or oversight of NIH-funded clinical trials have completed Human Subjects Protection and ICH GCP Training.

The protocol, informed consent form(s), recruitment materials, and all participant materials were submitted to the IRB for review and approval. Approval of both the protocol and the consent form(s) must be obtained before any participant is consented. 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(s) will be IRB approved; a determination will be made regarding whether a new consent needs to be obtained from participants who provided consent, using a previously approved consent form.

INVESTIGATOR'S SIGNATURE

The signature below constitutes the approval of this protocol and provides the necessary assurances that this study will be conducted according to all stipulations of the protocol, including all statements regarding confidentiality, and according to local legal and regulatory requirements and applicable US federal regulations and ICH guidelines, as described in the *Statement of Compliance* above.

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1 PROTOCOL SUMMARY

1.1 SYNOPSIS

Title: Digital Health Platform (DHP) to Deliver Mindfulness as a Stress Management Intervention Leveraging Electronic (SMILE) Health Records for Racial and Ethnic Populations During the COVID-19 Pandemic: Clinical Trial

Grant Number: *5R01MD017051*

Study Description: The goal of this clinical trial is to evaluate the SMILE app, a Digital Health Platform (DHP), that will deliver a mindfulness intervention, designed to mitigate COVID related stress. Additionally, the SMILE app will remotely collect self-reported psychological and physiological metrics of mental health and autonomic regulation. Study participants are adults who self-identify as African American, Black and/or Latino, and who have clinically significant levels of anxiety. This is a three-arm clinical trial that will test intervention (1) an instructor-administered Mindfulness-Based Stress Management training through an internet-delivered, interactive, group-based approach (MTIA), and (2) self-administered Mindfulness training through a study-developed mHealth app (MAPP), against a wait-list control group (WLC).

Objectives*:

Aim 1: Establish the effectiveness and durability of an 8-week Mindfulness DHP intervention. We will focus on two constructs important to mental health and hypothesize that:

A) Anxiety, self-report stress and quality-of life measures will significantly improve when comparing:
  A.1) Pre-to-post intervention, and;
  A.2) Control vs. intervention groups over 8 weeks and at 1-month follow-up.

B) Arousal, autonomic indices of HRV (reflecting parasympathetic activation) will significantly improve, when comparing:
  B.1) Pre-to-post intervention, and;
  B.2) Control vs. intervention groups over 8 weeks and at 1-month follow-up.

Aim 2: Establish the sustainability of two Mindfulness DHP interventions utilizing retention, mHealth usage (frequency), and participant satisfaction.

Aim 3: Exploratory Aim. Examine associations between COVID-19 related stress, mental health outcomes, and HRV. Examine the extent to which COVID-19 related stress and mental health symptoms are linked to HRV at baseline and how that relationship changes over time.

Endpoints:

Primary Endpoints:

1. GAD-7 Anxiety Scale Anxiety

Time Frame1: trajectory of change pre-intervention to end-intervention (8 weeks measured at 2-week intervals)
Time Frame 2: Pre-intervention to follow-up (12 weeks)

Secondary Endpoints:

2. COVID-19 Stress Scale (shortened) Stress

Time Frame1: trajectory of change pre-intervention to end-intervention (8 weeks measured at 2-week intervals)
Time Frame 2: Pre-intervention to follow-up (12 weeks)

3. Perceived Stress Scale (PSS) Stress

Time Frame1: pre-intervention to end-intervention (8 weeks)
Time Frame 2: Pre-intervention to follow-up (12 weeks)

4. Posttraumatic Growth Inventory (PGI) Stress

Time Frame1: pre-intervention to end-intervention (8 weeks)
Time Frame 2: Pre-intervention to follow-up (12 weeks)]

5. PTSD Checklist for DSM-5 (PCL-5)

Time Frame1: pre-intervention to end-intervention (8 weeks)
Time Frame 2: Pre-intervention to follow-up (12 weeks)]

6. Center for Epidemiologic Studies Depression Scale (CES-D) Depression

Time Frame1: pre-intervention to end-intervention (8 weeks)
Time Frame 2: Pre-intervention to follow-up (12 weeks)

7. Connor-Davidson Resilience Scale (CD RISC) Resilience

Time Frame1: trajectory of change pre-intervention to end-intervention (8 weeks measured at 2-week intervals)
Time Frame 2: Pre-intervention to follow-up (12 weeks)

8. Mental Health Quality of Life (MHQoL) Quality of Life

Time Frame1: pre-intervention to end-intervention (8 weeks)
Time Frame 2: Pre-intervention to follow-up (12 weeks)

9. Brief COPE Scale Coping

Time Frame1: pre-intervention to end-intervention (8 weeks)
Time Frame 2: Pre-intervention to follow-up (12 weeks)

10. Parasympathetic activity measured by high-frequency heart rate variability (HF-HRV)

Time Frame1: pre-intervention to end-intervention (8 weeks)

Time Frame 2: Pre-intervention to follow-up (12 weeks)

11. Autonomic activity measured by heart period
Time Frame1: pre-intervention to end-intervention (8 weeks)
Time Frame 2: Pre-intervention to follow-up (12 weeks)

12. Vagal efficiency measured using HF-HRV and heart period coupling
Time Frame1: pre-intervention to end-intervention (8 weeks)
Time Frame 2: Pre-intervention to follow-up (12 weeks)

Other Pre-specified Outcome Measures:

13. Participant Retention Attrition calculation
Time Frame: end of study

14. Participant adherence
Time frame: pre-intervention to end-intervention (8 weeks)

15. Short Form Health Survey (SF-12) Physical Health
Time Frame1: pre-intervention to end-intervention (8 weeks)
Time Frame 2: Pre-intervention to follow-up (12 weeks)

16. Adult PROMIS Short Form Sleep
Time Frame1: pre-intervention to end-intervention (8 weeks)
Time Frame 2: Pre-intervention to follow-up (12 weeks)

17. Cognitive and Affective Mindfulness Scale - Revised (CAMS-R) Mindfulness practice
    Time Frame1: trajectory of change pre-intervention to end-intervention (8 weeks measured at 2-week intervals)
Time Frame 2: Pre-intervention to follow-up (12 weeks)

18. Client Satisfaction Questionnaire – Internet
    Timeframe: Post-intervention, week 8

Study Population:	The study will recruit participants 18-99 years old living in North Carolina that self-identify as African American, Black, Hispanic and/or Latino of any sex that demonstrate symptoms of anxiety, as determined based on the GAD-7 screening measure (score between 8-14). Anticipated enrollment: 404 participants.
Phase* or Stage:	3

Description of Sites/Facilities Enrolling Participants:	Various informatics tools will be used in this project such as Carolina Data Warehouse for Health (CDW-H) for primary source of electronical health record, RedCap hosted by NC TraCs as the database management tool, Tableau for analytics and visualizations. The primary statistical computing will be performed using R. Other statistical tools such as SAS and G-Power will be applied as needed. The High-Performance Computing (HPC) nodes using both CPUs and GPUs in UNC Information Technology Services (UNC ITS) are also available to perform high throughput data analysis.

Description of Study Intervention:

Participants will be assigned to 1 of 3 arms of the study: **M**indfulness-based stress management **t**raining through an internet-delivered, **i**nteractive, group-based **a**pproach (MTIA) intervention, MAPP intervention, or wait-list control. All participants will be mailed a device with the SMILE app installed, and the equipment for recording cardiac data in the home. All participants will complete the baseline psychometrics measures and physiological stress test using the instructions provided on the SMILE app. Those assigned to the MTIA or MAPP intervention groups will then participate in their assigned intervention over the subsequent 8 weeks. During these 8 weeks, psychometric and physiological data will be completed biweekly for all participants. Three months following the initial baseline, all participants will complete a final psychometric/physiological evaluation.

All data collection will occur remotely and intervention sessions will be virtual (i.e., in participants' homes). Participants will be provided with a tablet loaded with the SMILE mHealth and a heart rate monitor and will view, or participate in, a virtual introductory tutorial on the use of the equipment. All psychological and physiological data will be collected via the SMILE mHealth app. Participants will be assigned to 1 of 3 groups (MTIA, MAPP, WLC), and all participants will complete each scheduled assessment, regardless of group assignment.

1. **Baseline assessment (week 0).** Participants will complete demographic and psychological questionnaires followed by a HRV assessment protocol. A questionnaire will be administered in the SMILE app immediately prior to beginning the heart rate monitoring portion of each research assessment. This questionnaire will assess use of caffeine, nicotine, prescription medications and OTC medications previous to beginning the heart rate monitoring portion of the research assessment, all of which may be important for covariate analyses Then they are asked to attach the heart rate monitor, and follow the instructions/model on the app to perform the following tasks:

   a. Stress test: an expanded Eriksen-Flanker Fish (E-F) test of executive function to provide cognitive stress to the subjects. The E-F task measures both attention and inhibitory control, both of which require parasympathetic inhibition to optimize performance. Performance measures are recorded to explore potential impacts of improved autonomic regulation on the task. The stressor task consists of a simple reaction time test wherein the subject must press a key on the keyboard that corresponds to the direction that a central arrow is pointing. The central the arrow is randomly flanked by either congruent (<<<<<) or incongruent stimuli (<<><<). The E-F test is a cognitive stressor that elicits vagal withdraw, allowing inhibition function quantification.

   b. Dynamic response test: an orthostatic test consisting of 3 min of rest in the seated position, slowly standing, 3 min of standing, slowly seating, and 3 min of seated. In addition to the demographic questionnaire, the psychological measures included in the baseline assessment are: GAD-7, COVID Stress Scale, Connor-Davidson Resilience Scale (CD RISC), Mental Health Quality of Life, brief coping

scale [COPE]), Perceived Stress Scale, Posttraumatic Growth Inventory (PTGI), sleep disturbance (Adult PROMIS Short Form), PTSD Checklist for DSM-5 (PCL-5), Center for Epidemiologic Studies Depression Scale [CES-D], Cognitive and Affective Mindfulness Scale-Revised (CAMS-R), and physical health (Short Form Health Survey [SF-12]).

2. Intervention (weeks 1-8). Participants assigned to the MTIA and MAPP groups will participate in the 8-week intervention. Both intervention programs are mindful meditative practices, designed to cultivate regulation of attention to present moment awareness, as well as develop mindfulness and awareness skills to improve coping and reduce stress, thereby lowering anxiety and increasing well-being. A description of each intervention is provided below:

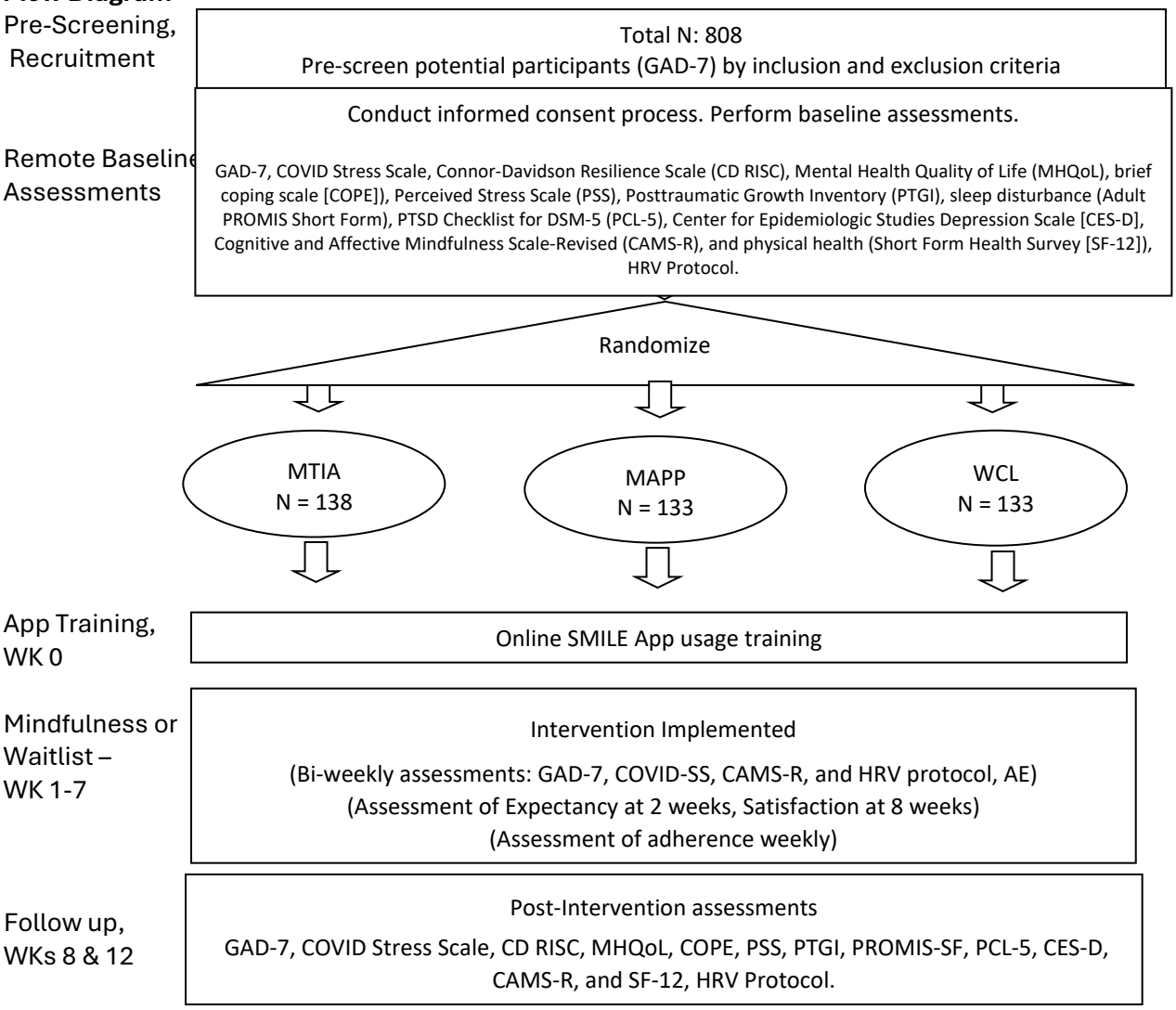
- **The M**indfulness-based stress management **t**raining through an internet-delivered, **i**nteractive, group-based **a**pproach (**MTIA**) **intervention** will incorporate the following elements: training in an 8-week, 90-minute per week, modified mindfulness program, which places additional emphasis on training which is feasible and relevant to race/ethnic groups, including: a) didactics on relevance to stress, coping and resilience, b) mindful compassion for self and others; c) mindful communication, including non-verbal mindfulness, mindful listening, and mindful speaking. The MTIA will be instructor led, internet-delivered (via Zoom), interactive, group-based mindfulness training intervention that will incorporate the training for approximately 9 persons in a group format, with outside-of session assignments.
- **The MindfulnessAPP (MAPP)** is a self-administered, internet delivered intervention developed by the SMILE study team. The MAPP intervention is designed to teach mindfulness skills so as to cultivate a state of mindful awareness. The MAPP is for individual use, with content that parallels that of the MTIA intervention. Each of the eight MAPP sessions will be composed of mindfulness exercises and didactics that correspond to the MTIA sessions. Since the MTIA weekly class will be 90 minutes in length, the MAPP assignments will recommend spending approximately 90 minutes per week covering the assigned lesson, but in a flexible format convenient for the participant. In addition, each session will contain mindfulness-based practice assignments generally ranging from 10 to 30 minutes per day. The total number of suggested days for completion will be 49 days, comparable to the time from start to finish of a traditional 8-week MTIA session; however, there will be flexibility within this individualized program.

3. **Assessments.** Biweekly during weeks 1-6, participants in all groups will be asked to complete assessments which include psychological questionnaires (GAD-7, COVID-SS, CAMS-R) and the same HRV assessment protocol as the baseline. Participants in both mindfulness groups will be asked to provide documentation of mindfulness practice. Eight week and follow-up assessment at week 12: participants in all groups

	will be asked to complete assessments which include psychological questionnaires (GAD-7, COVID Stress Scale, CD RISC, MHQoL, COPE, PSS, PTGI, PROMIS, PCL-5, CES-D, CAMS-R, and SF-12) and the same HRV assessment protocol as the baseline. *36 Months*
Participant Duration:	*12-14 Weeks from randomization to study completion*.

1.2 SCHEMA

Flow Diagram



1.3 SCHEDULE OF ACTIVITIES

	Pre-screening (Pre-	Screening / Consent / Training	Baseline Assessment	Week 2 Assessment	Week 4 Assessment	Week 6 Assessment	Week 8 Assessment	Follow-up Assessment (Week 12)
EMR (My UNC Chart) eligibility review ("UNC Message" sent)	X							
REDCap Eligibility Screening		X						
Consent Video and Consent document on REDCap		X						
Block Randomization		X						
Pre-loaded equipment and instructions mailing		X						
Online SMILE App usage training (given assignment)		X						
Demographics			X					
Remote Outcome Evaluation								
Psychological questionnaires (GAD-7, COVID-SS, CAMS-R)			X	X	X	X	X	X
Questionnaires (PSS, PGI, CESD, MHQoL, Brief COPE, CD-RISC PROMIS Sleep disturbance SF6a, SF-12, PCL-5)			X				X	X
Credibility/expectancy				X				
Satisfaction (Intervention groups)							X	
HRV assessment protocol (including review of medications, caffeine, nicotine use)			X	X	X	X	X	X
Adverse Events Reporting				X	X	X	X	X
Homework adherence (Twice weekly)				X	X	X	X	X

2 INTRODUCTION

2.1 STUDY RATIONALE

Hyperarousal and anxiety are hallmarks for racial/ethnic minorities facing COVID-19 related stress. Studies suggest that reduction of physiological arousal may prevent or reduce the likelihood of psychological distress, and development of clinical symptoms. Techniques such as mindfulness meditation and relaxation training have been associated with a reduction in hyperarousal and hold promise for decreasing COVID-19 related stress. Mindfulness training can increase heart rate variability (HRV), thereby helping to mitigate hyperarousal. Digital health platforms (DHP) hold promise to increase health equity by providing access and reach to a large numbers of racial/ethnic groups to ultimately offer targeted health services. By the end of the funding period, we will have tested the benefits of leveraging patient health records (PHR) to evaluate the effect of 2 virtually delivered mindfulness interventions vs. a wait-listed control on improving stress outcomes due to COVID-19 on race/ethnic groups, utilizing a DHP capable of collecting physiological and psychological predictors of mental health and demographics. We will have produced a DHP model for a Stress Management Intervention Leveraging Electronic health records (SMILE). The scientific premise of our proposal is that leveraging large numbers of PHRs will ultimately increase health equity by reaching populations of interest to offer a culturally sensitive DHP to provide targeted interventions informed by the individual's predictors of mental health.

We will test our central hypothesis with a 3-arm randomized controlled trial. We will recruit 404 participants to be randomized to one of three arms: 1) an instructor-administered Mindfulness-Based Stress Management training through an internet-delivered, interactive, group-based approach (MTIA), 2) self-administered Mindfulness training through a study-developed mHealth app (MAPP), or 3) Waitlist control (WLC).

2.2 BACKGROUND

Hyperarousal and anxiety are hallmarks for racial/ethnic minorities facing COVID-19 related stress. Studies suggests that reduction of physiological arousal during and/or shortly after trauma exposure may prevent or reduce the likelihood of psychological distress, and the development of depressive or PTSD symptoms(1–5). Self-regulation, typically a subconscious process, can be enhanced by practice and conscious intervention through EBI. Techniques such as mindfulness meditation and relaxation training have been associated with a reduction in hyperarousal(5), serve as potential PTSD treatments(3,5), and hold promise for decreasing COVID-19 related stress. Mindfulness training has the ability to increase HRV(2,5), thereby helping to mitigate hyperarousal. DHP hold promise to increase health equity by providing access and reach to a large numbers of racial/ethnic groups to ultimately offer targeted health services.

By the end of the funding period, we will have tested the benefits of leveraging PHRs to evaluate the effect of 2 virtually delivered mindfulness interventions vs. a wait-listed control on improving stress outcomes due to

COVID-19 on race/ethnic groups, utilizing a DHP capable of collecting physiological and psychological predictors of mental health and demographics. We will have produced a DHP model for a Stress Management Intervention Leveraging Electronic health records (SMILE). The scientific premise of our proposal is that leveraging large numbers of patient portals/patient health records (PHRs) will ultimately increase health equity by reaching populations of interest to offer a culturally sensitive digital health platform (DHP) to provide targeted interventions informed by the individual's predictors of mental health.

Digital health and Digital health disparities

The concept of digital health has been evolving since 2000: 1) initially it included internet-focused applications and media to improve medical content, commerce, and connectivity; 2) then it expanded to include a broader set of scientific concepts and technologies (e.g., genomics, artificial intelligence, analytics, wearables, mobile applications, and telemedicine); 3) now, digital health technologies are being applied more broadly in medicine to include diagnosis, treatment, clinical decision support, care management, and care delivery(6). As defined by the FDA, digital health includes categories such as mobile health (mHealth), health information technology (IT), wearable devices, telehealth and telemedicine, and personalized medicine(7). Hereafter, we will refer to digital health as Benefits of DHP were seen during COVID-19, when medical services promptly migrated to online formats and in some cases the use of patient portals was highly encouraged to access certain services (e.g., COVID-19 testing and vaccination). Ideally, such benefits should reach individuals equally; unfortunately, race/ethnic groups already affected by the digital divide(8–10), and minority health and health disparities(11–14) are facing magnified digital health disparities(13–16). A long history of health disparities (related to medical mistrust, etc.) have been magnified as medical care has translated into digital health arena (11) with one study finding that Black patients used mHealth portals 40% less than White counterparts(17). In contrast, a survey from late March 2020 estimated that Black respondents were more likely than Whites to report using telehealth because of the pandemic, particularly when perceiving the pandemic as a minor threat to their own health(18). Another study compared telehealth visits before and after the pandemic started: patients identifying as Non-Hispanic White, and Other represented a higher proportion of visits while all other groups (Black and Latino) were a smaller proportion of visits (P=0.006).(19) Fully remote mobile-based studies can attract a diverse participant pool including people from traditionally underserved communities in mental health care and research (e.g., Latino individuals).(20)

Mixed outcomes on self-report vs documented use of digital health technologies by Black and Latino individuals during the pandemic, highlight the potential and need for research on DHP to increase health equity. We propose the evaluation of a novel DHP model by fully leveraging digital health technologies, conducting the study completely virtually. We will utilize a statewide academic medical center patient portals/patient health records (PHRs) system for recruitment, a smart device with a mHealth app to capture psychophysiological predictors of mental health and a second app to virtually deliver mindfulness, and a wearable device (e.g., heart rate monitor).

Mindfulness.
Mindfulness meditation has been described as "a behavioral technique involving the intentional self-regulation of attention to present-moment experience, combined with release of cognitive fixation on thoughts (whether simple images or complex storylines) regarding the past or future(21,22). Through training in mindfulness, individuals learn to evoke and sustain a non-judgmental state of present-moment awareness(22,23). Figure 1. Depicts the three core practices taught by mindfulness(24). Research has shown that mindfulness training programs such as Mindfulness-based Stress Reduction, which also incorporate exercises to generate compassion for oneself and others, result in reduced stress, decreased anxiety(25,26), improved coping, and a host of improved physical and psychological health outcomes(25,27). Mindfulness training programs have been adapted and successfully utilized for a wide range of conditions, populations, and cultures, including in health-care environments. Studies in care-giving settings have shown that mindfulness interventions can decrease perceived stress and improve coping skills, including decreased emotion-based coping and increased tolerance for uncertainty, as well as improve psychological well-being, quality of life(28,29), communication, interpersonal relationships, and resilience(30,31). Mindfulness training programs have been successfully adapted to distance-based formats, particularly involving use of the internet(32,33) and occasionally have incorporated smart-phone or telephone-delivered mindfulness training formats(34–37). Moreover, internet-based programming has been shown to overcome barriers of distance and access; there is still the need to evaluate personalized approaches (instructor guided vs self-paced) based on baseline mental health assessments. We are evaluating two mindfulness training programs vs. a control wait-list, 1) instructor administered, virtual, interactive, group-based mindfulness training (mindfulness training instructor administered - MTIA) and 2) self-administered mindfulness training through a mHealth app (mindfulness app - MAPP), to build resilience and mitigate stressors related to COVID-19 among racial/ethnic minorities.

Heart Rate Variability, Psychological resilience, Stress, and Anxiety.

The link between cognitive processes, autonomic control systems, and bodily processes (e.g., heart rate) is conceptualized in the polyvagal theory(38). Briefly stated, evolution of social primates required an increased capacity for autonomic inhibition via parasympathetic pathways. This cardiac vagal inhibition facilitates social functioning in safe environments where cooperation is beneficial to survival. The ability to self-regulate (i.e., calm oneself) is mediated by controlling both the parasympathetic (rest and restoration) and the sympathetic (stress) branches of the autonomic nervous system. Trauma can lead to triggering hyperarousal through the stress response or system shut-down, which can leave the autonomic system in a chronic state of reduced parasympathetic inhibition(38). Heart rate variability (HRV), the short-term variation in heartbeat time interval, is a measure of autonomic nervous system activity, with higher HRV indicating greater flexibility and ability to regulate emotional responses(38). It can thus be used to assess autonomic flexibility, the ability to regulate emotional responses, and link the stress response state to both mental health and reslience(39). Studies have found a significant association between PTSD and reduced levels on both high-frequency HRV (HF-HRV) and low frequency HRV (LF-HRV)(1–3,40,41). Resilience is defined as the ability to rebound or "bounce back" following adversity(42). An important aspect of the 'bouncing back' process is the return to a physiologic equilibrium indicated by higher resting HRV and a quicker recovery to resting heart rate following a stressor(42). In light of previous findings about the malleability of psychological resilience(43) and varied definitions of resilience(44), we take an incremental

theoretical approach to resilience(45) and view it as both a state and a trait that can be enhanced. For example, resilience has been found to be negatively associated with scores on the PTSD Checklist–Civilian Version (PCL-C)(46). There also seems to be a self-reinforcing mechanism, whereby resilience scores before treatment for PTSD predicted treatment outcomes, but treatment also increased resilience scores(47). Low resilience scores have also been associated with suicidality, problem alcohol use, depression, and physical health(48,49). In addition to standard scale measures of resilience, posttraumatic growth (PTG), coping, and social support are important covariates of mental health that have been associated with higher resilience(50). While widespread outbreaks of infectious disease like COVID-19 are associated with psychological distress and symptoms of mental illness(51), resilience may be a factor that leads some to post-traumatic growth in such challenging situations. HRV serves as both a measure of autonomic regulation and is a promising target for any intervention to improve mental health.

2.3 RISK/BENEFIT ASSESSMENT

2.3.1 KNOWN POTENTIAL RISKS

Mindfulness Intervention: Potential risks of mindfulness interventions are minimal. Emotional discomfort or distress may arise for some participants during mindfulness exercises or at home practice related to awareness of negative emotions, thoughts, or physical sensations. Similarly, early in the course of mindfulness training, individuals may experience mood swings. These symptoms are usually transient. Study staff will advise participants that they may avoid any practices that lead to more than transient discomfort. The relaxation experienced as part of mindfulness training is sometimes associated with transient sleepiness, lasting hours up to a day. We do not anticipate financial or risks to participants.

Psychological Assessment: Screening and self-report assessments contain questions regarding sensitive personal information. As a result, participants may become upset or embarrassed when recounting current or past distressing life events. This risk is necessary in order to assess anxiety symptoms.

Physiological Assessment: We anticipate a rare likelihood that a subject may find the chest strap heart monitor uncomfortable. We will provide the subjects with information on the care of the Polar H10 device, including the option to machine wash the straps, to help them maintain clean equipment during the study. These devices are routinely worn for longer duration under greater physical exertion by the athletes they are marketed towards (e.g., those training for a triathlon). With proper care, the likelihood of discomfort will be very small. However, if a subject finds it uncomfortable to continue to wear the device, we will remind them that participation is voluntary and they may withdraw.

Confidentiality: A breach of confidentiality could indicate to others a participant's psychiatric status, health history, or demographic data.

2.3.2 KNOWN POTENTIAL BENEFITS

We anticipate that the intervention will have **beneficial impact on COVID related anxiety and stress burden** by decreasing self-reported measures of distress and uncertainty and increasing self-efficacy and emotional wellbeing. We also expect to see a positive impact in resilience on autonomic nervous system balance. The larger Black and Latino community may benefit if the intervention is successful, because it will be a relatively low-cost, low-burden training program available to manage stress. Other benefits apply to future research efforts by clarifying methodological issues, such as acceptability of the intervention, participant accrual, research design of the mindfulness intervention, effect size estimation, and whether a definitive trial is warranted. The results may help others doing research in mind-body medicine improve their research methodology and choice of outcome measures for this underserved group.

Importance of the Knowledge to be Gained
It is likely that the results of this project will provide two important pieces of information. First, as stated above, results of this study will clarify issues of acceptance and enable refinement and tailoring of the mindfulness intervention and DHP to the Black and Latino population. This tailoring can improve sustainability of the intervention in clinical translation implement a low-cost intervention for populations with less access to stress reduction modalities and can also provide insight into personalized medicine and how could benefit most for intervention. Second, if the intervention shows promise, this study includes investigation of mechanisms of action with heart rate variability measures to examine relationship between physiological measures and emotional and physical health.

Finally, **knowledge gained** as a result of this proposed research could have a large impact due to the large number of individuals facing increased stress due to the COVID pandemic. It is anticipated that the importance of the knowledge to be gained far outweighs risks, which are minimal.

2.3.3 ASSESSMENT OF POTENTIAL RISKS AND BENEFITS

Emotional discomfort caused by study questions:
Participants will be advised to skip any questions that they do not wish to answer.

Emotional or psychological discomfort or distress (e.g. agitation, anxiety):
Emotional discomfort or distress is not uncommon in mindfulness practice and is often related to heightened awareness of negative emotions, thoughts or physical sensations. These occurrences are generally transient, can be managed with instructor guidance, and improve as the participant gains experience; moreover, as managing discomfort is essential to learning mindfulness and self-compassion skills (e.g. participants learn to notice and to be less reactive or avoidant of negative experiences) some level of emotional discomfort is important for progress.

To minimize the risk of severe or lasting psychological issues or reactions:

1. An experienced and certified mindfulness instructor will lead the MTIA sessions. A co-facilitator will attend in the event an AE occurs and the participants needs to be shifted to a breakout room (in Zoom) for specific guidance.

2. Participants will be encouraged throughout the sessions to confidentially discuss their experiences with the exercises, including any emotional difficulties, and will be prepared ahead of time to know what they may experience.

3. The beginning of each session will include time to discuss out-of-class practices. Participants will be engaged in problem-solving discussions and will become knowledgeable about coping skills to manage difficult emotions.

4. Participants will be given study contact information within their enrollment materials and will be encouraged to contact study staff should any negative changes in their emotional health occur during home practice or at any point during the study, or if difficulties arise that the participants feel uncomfortable discussing in the group setting.

5. Any reported new or increasing emotional health change will be detailed by study staff and communicated to the MPIs. The MPIs will determine the severity and relatedness of the event. For events that are more than mild, the MPIs may confer with an expert in the treatment of anxiety to offer the participant a list of relevant local resources as appropriate. Study staff will continue to monitor this participant during weekly sessions, documenting any resources accessed and to determine if emotional health symptoms have resolved.

Physical discomfort during sitting exercises:

Participants will receive instruction on posture and positioning during seated meditations and will be encouraged to move as needed during the exercise for maximal comfort.

Emotional harm due to breach of confidentiality:

Given the potentially sensitive nature of the information shared during group sessions, (e.g., emotional difficulties), the first intervention session includes a discussion regarding the importance of confidentiality. This means all participants agree that they will not discuss any of the information shared during class outside of the session.

All study questionnaires and audio recordings will be stored in a de-identified manner using study IDs and separately from any identifiable data. All data will be stored in password-protected, encrypted databases. Only UNC study personnel listed on the IRB application will have access to identifiable data and recorded content from MTIA sessions. All data reports will be de-identified and in aggregate.

3 3.0 OBJECTIVES AND ENDPOINTS

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS	PUTATIVE MECHANISMS OF ACTION
PRIMARY			
To determine the effectiveness of mindfulness training, delivered remotely either synchronously (MTIA) or asynchronously (MAPP) compared to a waitlist control in reducing **anxiety** among African American and Hispanic/Latino adults.	Anxiety is measured with the GAD-7 (Generalized Anxiety Disorder-7 question).	The GAD-7 is the most employed clinical measure of anxiety in the United States. Increased anxiety may result from COVID-related stress. This endpoint is expected to be causally related to the interventions.	Mindfulness training is expected to reduce arousal which leads to lower levels of stress and anxiety.
SECONDARY			
To determine the value of mindfulness training (MTIA or MAPP) compared to a waitlist control in reducing **COVID-related stress**.	COVID-19 Stress Scales shortened	Race/ethnic groups have been exposed to increased stressors throughout the pandemic that will continue to have a long-term impact on their quality of life. This variable may function as a mediator in the pathway between mindfulness training and anxiety.	Mindfulness training may mitigate the effects of stress on health-related quality of life.
To determine the value of mindfulness training (MTIA or MAPP) compared to a waitlist control in **increasing parasympathetic activity**.	High-frequency heart rate variability (HF-HRV) measured through a chest monitor	Mindfulness training is believed to increase parasympathetic tone. HF-HRV can be an objective measure of parasympathetic activity and the effectiveness of the training.	Increasing heart rate variability can mitigate hyperarousal, which, in turn can reduce stress and anxiety
To determine the value of mindfulness training (MTIA or MAPP) compared to a waitlist control in **increasing autonomic activity**.	Heart rate at rest, standing, and with stress measured through a chest monitor	Mindfulness training has been associated with lower heart rates.	Lowering heart rate can result in a diminished experience of stress.

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS	PUTATIVE MECHANISMS OF ACTION
To determine the value of mindfulness training (MTIA or MAPP) compared to a waitlist control in **increasing vagal efficiency**	Measured using HF-HRV and heart period coupling	Mindfulness training has been associated with increased vagal efficiency after a stressor.	
To determine the value of mindfulness training (MTIA or MAPP) compared to a waitlist control in increasing **resilience**.	Connor-Davidson Resilience Scale	Mindfulness has been associated with increased resilience.	
To determine the value of mindfulness training (MTIA or MAPP) compared to a waitlist control in reducing **PTSD symptoms**.	PTSD Checklist-Civilian version	Increased mindfulness has been associated with lower levels of PTSD symptoms	
To determine the value of mindfulness training (MTIA or MAPP) compared to a waitlist control in reducing **depressive symptoms**.	Cetner for Epidemiologic Studies Depression Scale	Increased mindfulness has been associated with lower levels of depressive symptoms.	
To determine the value of mindfulness training (MTIA or MAPP) compared to a waitlist control in reducing **perceived stress**.	Perceived Stress Scale—10 item	Mindfulness training has been associated with lower levels of perceived stress.	
To determine the value of mindfulness training (MTIA or MAPP) compared to a waitlist control in improving positive **coping**.	Brief COPE	Mindfulness training has been associated with positive coping strategies such as positive reframing.	
To determine the value of mindfulness training (MTIA or MAPP) compared to a waitlist control in improving **mental health quality of life**.	MH QoL	Increased mindfulness may be associated with improvements in quality of life related to self-image, mood, independence, relationships, daily activities, physical health, and optimism about the future.	
TERTIARY/EXPLORATORY			
To determine the value of mindfulness training (MTIA or MAPP) compared to a waitlist control in reducing **sleep disturbance.**	PROMIS Sleep Disturbance short form, 8a	Increased mindfulness has been associated with lower levels of sleep disturbance in some, but not all studies.	

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS	PUTATIVE MECHANISMS OF ACTION
To determine the value of mindfulness training (MTIA or MAPP) compared to a waitlist control in increasing **perceived growth post trauma**.	Post-traumatic Growth Inventory	Increased mindfulness has been associated with positive reappraisal which may lead to experiences of post-traumatic growth	
PROCESS			
To determine the value of the MTIA intervention compared with MAPP on **retention** of participants in the study	The number of participants who continue their participation to the end of the trial	Low rates of retention brings the results of the trial into question.	
To determine the value of the MTIA intervention compared with MAPP on **the adherence** of participants to the study protocol	The number of participants who complete all assigned study procedures. In the intervention groups, this includes mindfulness practice	Adherence to study procedures is an important measure of engagement.	
To determine the value of the MTIA intervention compared with MAPP on **the credibility of the interventions and expectancy for success**	HEAL Treatment Expectancy v1.0 short form, 6 questions	The credibility of the intervention and its expectancy for success in reducing anxiety may have an impact on the way that participants complete self-report measures.	
To determine the value of the MTIA intervention compared with MAPP on **the satisfaction** of participants with the interventions	Client Satisfaction Questionnaire - Internet	Satisfaction is a pre-defined measure for comparing the sustainability of the two intervention groups	
To determine the value of mindfulness training (MTIA or MAPP) compared to a waitlist control in increasing **mindfulness**.	Cognitive and Affective Mindfulness Scale-Revised	Mindfulness training should increase self-reported mindfulness in participants by the end of the training period.	
To ensure that the HRV data is interpretable, the HRV protocol assesses medication, caffeine, and nicotine use.	Questions about current medications, last use of caffeine, and last use of nicotine.	HRV is influenced by medications, caffeine, and nicotine.	
SAFETY			

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS	PUTATIVE MECHANISMS OF ACTION
To monitor study participants for **adverse events** and changes in medications that could influence heart rate variability	Bi-weekly adverse events survey	Monitoring participants with subclinical anxiety is essential to participant safety	

4 STUDY DESIGN

4.1 OVERALL DESIGN

This 4-year randomized controlled, single site trial entails the adaptation of two mindfulness interventions vs. wait-list control accompanied by HRV-based metrics to test the effects of the interventions on mental health endpoints. In addition, the intervention will examine the effect of the frequency and length of at home practice on anxiety and resilience in a sample of race/ethnic minorities. Inclusion criteria will be based on self-reported clinical symptoms of anxiety (GAD-7). Participants will be trained in one of two Mindfulness protocols: instructor administered (MTIA) or self-administered (MAPP), while a third control group is waitlisted (WLC). All groups will complete psychological scales and perform HRV assessments at baseline, weekly for 8 weeks, and at the 3-month follow-up. The trajectory of change will be measured via biweekly collection of anxiety and resilience scores by the SMILE mHealth app during 8 weeks and later at 1-month follow-up.

Our proposed stage 1 DHP study will test the effectiveness of MTIA and MAPP on anxiety, in comparison with a delayed control group; and within group pre-post intervention. We will conduct a 3-arm randomized controlled trial of 404 participants (138 in MTIA, 133 in MAPP, and 133 in WLC). Randomization will involve an adaptive algorithm in R software blocked by cohort, gender, ethnicity, and baseline anxiety. Once all members of a cohort are assembled, the study ids will be sent to a statistician not involved with recruitment to make the algorithm-defined treatment assignments. We will collect psychometrics of mental health (e.g., anxiety) and physiological metrics of autonomic regulation (e.g., HRV) at baseline (Aim 3), biweekly during the 8-week intervention (and for 8 weeks after randomization to the mindfulness app or wait-list control), and 12-weeks follow-up.

In Aim 1, We hypothesize that the mindfulness interventions will result in significant improvements in anxiety, quality of life, and parasympathetic activation when comparing pre-to-post intervention and comparing the intervention groups (MTIA, MAPP) to the wait-list control post-intervention and at 4 weeks post intervention. In Aim 2, we hypothesize that the MTIA group will be more sustainable with higher retention rates, adherence and mindfulness practice rates, and participant satisfaction. In Aim 3, we explore the associations between stress and mental health symptoms and heart rate variability both at baseline and over time.

4.2 SCIENTIFIC RATIONALE FOR STUDY DESIGN

A goal of the study is to increase access to interventions that reduce stress and may improve anxiety in populations that experience health disparities. Mindfulness training has been shown to reduce stress and anxiety and has been tested in group settings using telehealth technologies. However, it is unknown if a comparable mindfulness app would be beneficial. Hence, the study aimed to test these interventions against a waitlist control group that is not expected to show any improvements. A waitlist control group is felt to be appropriate in this situation as there is no standard of care for mild Covid-related (situational) stress and anxiety.

4.3 JUSTIFICATION FOR INTERVENTION

The MTIA intervention will be delivered online (Zoom platform) in a group setting with a highly trained mindfulness instructor. The platform is chosen as the most accessible and widely used platform during the pandemic. Many mindfulness interventions transitioned to this format when the pandemic began. The comparison intervention based on an app that is developed by the study team is chosen to be comparable to the MTIA instruction. The MAPP is developed with the same intervention materials and using recordings from the same mindfulness instructor as the MTIA.

Initially, the use of an existing app, Headspace, was planned. However, in the interim between proposal submission and funding, the Headspace app changed—it was expanded to address other modalities for addressing mental health problems in addition to mindfulness training. Because the study team would be unable to limit participant's exposure to material consistent with the MTIA, it became necessary to develop a new app. Both interventions provide mindfulness training weekly over 8 weeks which is the most tested duration of mindfulness training in the literature. Based on our previous experience with telehealth interventions, we have shortened the length of each session to 75-90 minutes—it is very difficult for people to sit in a Zoom session for much longer than an hour. Both interventions were adapted for underserved populations based on the extensive experience of Dr. Gaylord in working with mindfulness with African Americans. Other study team members (e.g., Dr. Davila and Dr. Gallego Perez) addressed issues relating to cultural acceptability in Hispanic and Latinx populations.

To have evaluable data, participants must participate in at least two heart monitoring and questionnaire sessions.

4.4 END-OF-STUDY DEFINITION

In the intervention groups, a participant is considered to have completed the study if he/she/they have completed the baseline assessment, at least 5 intervention sessions, and at least the 8-week and 12-week follow-up assessments. Completers in the wait-list group will have completed the baseline assessment and at least the 8-week and 12-week follow-up assessments. We are hoping for completion of assessments at 2, 4, and 6 weeks as well.

5 STUDY POPULATION

5.1 INCLUSION CRITERIA

To be eligible to participate in this study, an individual must meet all of the following criteria:

1. Provision of signed and dated electronic informed consent.
2. Stated willingness to comply with all study procedures and lifestyle considerations and availability for the duration of the study.
3. Participants of any gender; Age 18-99 years old
4. Self-identify as African American, Black, Hispanic and/or Latino.
5. Demonstrate symptoms of anxiety, as determined based on the GAD-7 screening measure (score between 8 and14)
6. Willingness to adhere to the study regimen.
7. Living in North Carolina
8. Able to change positions (stand and sit)

5.2 EXCLUSION CRITERIA

Individuals with heart disease, stroke, dementia, autism, genetic and psychiatric disorders are excluded due to the impact of these disorders (or the medications for their treatment) on heart rate variability. Individuals who are already practicing mindfulness regularly are less likely to benefit. Those with behavioral problems severe enough for treatment center stay may not be appropriate for a group intervention. An individual who meets any of the following criteria will be excluded from participation in this study:

1. Current, or history of, heart disease
2. History of stroke or dementia
1. Diagnosis of movement disorders, such as Parkinson's Disease, or paralysis
2. Diagnosis of genetic disorders, such as Down Syndrome or Fragile-X syndrome
3. Diagnosis of autism
3. Diagnosis of schizophrenia, psychosis, dissociative disorder, mania/bipolar disorder, major depression, or a personality disorder

4. History of serious mental or behavioral health problems requiring a hospital or treatment center stay within the past 12 months.
4. Taking cardiac medications (other than blood pressure medications)
5. Taking seizure medications
6. Currently taking opioid medications or supplements
5. Practice of formal mindfulness for more than 15 minutes/day for 4 or more days/week over the past 6 months

5.3 LIFESTYLE CONSIDERATIONS

During this study, participants are asked to:

- Refrain from consuming caffeine for 3 hours prior to Heart Monitoring session.
- Refrain from consuming alcohol for 12 hours prior to Heart Monitoring session.

5.4 SCREEN FAILURES

Screen failures are defined as participants who consent to participate in this study but are not subsequently assigned to the study intervention or entered in the study. Individuals who do not meet the criteria for participation in this trial (screen failure) because of their GAD-7 score that is likely to change over time may be rescreened. They may not be rescreened if other exclusion criteria are present.

5.5 STRATEGIES FOR RECRUITMENT AND RETENTION

To assure recruitment we have the support of the North Carolina Translational and Clinical Science Institute (NC TraCS) responsible for the Carolina Data Warehouse for Health (CDW-H). The CDW-H is a central data repository containing clinical, research, and administrative data sourced from the UNC Health Care System (UNCH). NC TraCS will provide access to the population of interest through the UNCH patient portals for dissemination of the study and recruitment of participants.

Our goal is to recruit UNCH patients with active My UNC Chart. Participants will be self-identified African American, Black and Latino (a/e/x), English speakers (able to read and understand English), adults (18 and older) registered in the UNCH PHRs and active in the My UNC Chart portal. The NC Tracs Informatics Team will oversee the process for reviewing My UNC Chart records to provide recruitment information to potentially eligible individuals. Subjects will be contacted via My UNC Chart Message, email or mailed letter, depending on contact information provided in CDW-H. If these strategies are insufficient to meet recruitment goals, we will employ targeted advertising in markets frequented by Hispanics/Latinos or Blacks/ African Americans as identified by the NCTraCS community engagement teams and our collaborators.

Recruitment materials have been reviewed by the NCTraCS community engagement teams and modifications have been made to ensure that the materials are broadly appealing to Hispanics/Latinos and Black/African Americans of all ages and genders.

The recruitment notification will include a link to a REDCap form to complete an eligibility screening in REDCap. Aggregate responses to the screening questions will be communicated to the potential participant. Those who screen in will be invited to review the consenting procedures.

We anticipate that approximately 800 individuals will need to screen to achieve a sample size of 404. Based on our experience with prior mindfulness studies, we expect that 60-70% of the sample will identify as cis-gender women. Based on the demographics of our patient population, we expect that 75-85% will identify as Black/African Americans and that the average age of participants will be between 40 and 60. Technological barriers may prevent some older adults from attending. We are hoping to enroll 30 eligible participants each 6 weeks to meet our enrollment goals.

Incentives for participation include compensation for study measurement sessions. Each time participants complete the set of questionnaires and heart rate variability session; they will be given $20. Completion of all assessments will result in $120 in compensation.

6 STUDY INTERVENTION(S) OR EXPERIMENTAL MANIPULATION(S)

6.1 STUDY INTERVENTION(S) OR EXPERIMENTAL MANIPULATION(S) ADMINISTRATION

6.1.1 STUDY INTERVENTION OR EXPERIMENTAL MANIPULATION DESCRIPTION

Based on evidence from previous mindfulness studies, we believe that this intervention holds promise of making a significant impact on reducing anxiety, stress and improving coping and resilience in minority populations.

1) The MTIA intervention will incorporate the following elements: training in an 8-week, 60-minute per week, modified mindfulness program, which places additional emphasis on training which is feasible and relevant to race/ethnic groups, including: a) didactics on relevance to stress, coping and resilience, b) mindful compassion for self and others; c) mindful communication, including non-verbal mindfulness, mindful listening, and mindful speaking. The MTIA will be instructor led, internet-delivered, interactive, group-based mindfulness training intervention that will incorporate the training for approximately 9 persons in a group format, with outside-of-session assignments delivered via Zoom. Intervention details can be found in the Instructor's Manual of Proceures (IMOP).

2) The MAPP intervention will be internet-delivered through the study-developed mHealth SMILE app, and self-administered is a self-administered, internet delivered intervention developed by the SMILE study team. The MAPP intervention is designed to teach mindfulness skills so as to cultivate a state of mindful awareness. The MAPP is for individual use, with content that parallels that of the MTIA intervention. Each of the eight MAPP sessions will be composed of mindfulness exercises and didactics that correspond to the MTIA sessions. Since the MTIA weekly class will be 90 minutes in length, the MAPP assignments will recommend spending approximately 90 minutes per week covering the assigned lesson, but in a flexible format convenient for the participant. In addition, each session will contain mindfulness-based practice assignments generally ranging from 10 to 30 minutes per day. The total number of suggested days for completion will be 49 days, comparable to the time from start to finish of a traditional 8-week MTIA session; however, there will be flexibility within this individualized program.

Administration and/or Dosing

The MTIA intervention is led by a highly qualified mindfulness instructor with 8 weekly, 90-minute training sessions over Zoom with 7-9 other individuals. Individuals will participate from their homes or other locations that they choose. They will be advised to participate from a private room if possible. They will be sent an electronic tablet with Zoom downloaded to facilitate their participation. The tablet will include a participant manual with descriptions of the intervention sessions and with links to recorded practice guides. The instructor will use an intervention manual to guide the sessions. An assistant will be present for each session.

The MAPP intervention is developed to be similar to the MTIA and will include videotaped guidance by the MTIA instructor. The biggest differences between the two interventions is that the MAPP will be self-paced and will not include participation in a group. Full engagement with the app is designed to take 90 minutes altogether each week.

6.2 FIDELITY

6.2.1 INTERVENTIONIST TRAINING AND TRACKING

The instructors for the intervention will be those trained in mindfulness-based stress reduction (MBSR) through an approved training program. Instructors will work closely with Dr. Gaylord for training in this modified MBSR intervention and will have an **instructors' manual** (IMOP) to guide their intervention delivery. Preference will be given to instructors who are fully certified in MBSR and who identify as a member of the Black/African American community or the Hispanic/Latino community.

The MTIA intervention sessions will be recorded, and the audio recordings will be saved to a secure site managed by the university (Teams). The fidelity monitor will listen to the first and 7th weeks of the intervention and a randomly selected session from weeks 2-6 or 8. The fidelity monitor will compare the instructor's presented material to the instructor manual and will rate the degree to which the instructor covered the planned material (did not cover, partially covered, fully covered). The fidelity monitor will communicate results of the fidelity assessments to Dr. Gaylord. Dr. Gaylord will discuss the assessments with the

instructor so that deviations from the manual can be addressed. Dr. Gaylord will review the audio files as needed.

6.3 MEASURES TO MINIMIZE BIAS: RANDOMIZATION AND BLINDING

The study plans to implement cohort randomization. As soon as 24-30 participants are recruited and found eligible, the list of Study Ids will be sent to one of the study statisticians. The statistician is not involved in participant recruitment or management thereby preserving blinded allocation. The statistician will run the randomization program that is designed to balance participants by gender, ethnicity, and degree of baseline anxiety as measured in the GAD-7. The randomization program is implemented in R software using a modification of the miniRand package called 'cohortRand'. Details are available in Section 9 along with links to the GitHub documentation for cohortRand. The allocation list will be sent back to the study coordinator who will record the allocation in the data management software, REDCap. Another member of the team, the fidelity monitor, will confirm the allocation for each participant. The study coordinator will notify participants of their group assignment 1-2 weeks prior to the beginning of each cohort. The blinded research assistant will not have access to the files related to reminders or to allocation information. Access can be controlled through the REDCap data capture site and limited to unblinded staff.

Due to the nature of the interventions, blinding of participants after randomization is not possible. However, participants will be told that the study will be testing two mindfulness interventions for reducing anxiety in Blacks/African Americans and Hispanics/Latinos. Participants will complete a credibility/expectancy questionnaire after the interventions are described to ensure that they view the chances that the interventions will be successful equally. Self-report questionnaires necessarily will be unblinded but the lack of blinding is not expected to influence the objective measures based on heart rate monitoring. Most study staff will be unblinded due to the need to send reminders to participants based on their intervention group. However, the staff at RTI managing most of the data collection will be blinded to allocation and at least 2 of the four statisticians will be blinded. Dr. Heilman will also be blinded.

6.4 STUDY INTERVENTION/EXPERIMENTAL MANIPULATION ADHERENCE

Each cohort will be randomized individually with blocking for gender, ethnicity, and high or low anxiety level. This procedure necessitates that the composition of each cohort is tracked and that imbalances are minimized. Study participants are expected to complete all study questionnaires and heart rate variability assessments. However, they will not be considered lost to follow up until they miss three scheduled assessments in a row.

Adherence to the MTIA intervention is tracked through attendance logs assessed by the study coordinator or fidelity monitor at the beginning of each class. The staff will record attendance in REDCap. Adherence to the MAPP intervention is tracked via the app. The app will record when participants open each MAPP

component. Participants in both intervention groups will record their mindfulness practice twice weekly via a survey sent through REDCap. A survey will also ask participants about any new symptoms they are experiencing.

All participants will complete the full set of questionnaires and heart rate variability sessions at baseline, at the end of the intervention period (~8 weeks) and 4 weeks later (~12 weeks). They will also be asked to complete a limited set of questionnaires and the heart rate variability sessions 2 weeks into the intervention period, 4 weeks into the intervention period, and 6 weeks into the intervention period in each cohort. Completion of these milestones are tracked in the SMILE app.

6.5 CONCOMITANT THERAPY

For this protocol, participants may not take medications that interfere with the heart rate variability assessments. These medications include most cardiovascular drugs and anti-seizure medications. Participants with cardiovascular disease will be screened out. We will ask participants weekly during the study if they have added any new medications in the AE assessment survey.

6.5.1 RESCUE THERAPY

NA

7 STUDY INTERVENTION/EXPERIMENTAL MANIPULATION DISCONTINUATION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

7.1 DISCONTINUATION OF STUDY INTERVENTION/EXPERIMENTAL MANIPULATION

When a participant discontinues from the MTIA or the MAPP but not from the study, remaining study procedures will be completed as indicated by the study protocol if the participant agrees. If a clinically significant finding is identified (including, but not limited to changes from baseline) after enrollment, the investigator (PI Heilman) or qualified designee (Safety Monitor) will determine if any change in participant management is needed. Any new clinically relevant finding will be reported as an adverse event (AE).

The data to be collected at the time of study intervention discontinuation will include the following:

- The reason(s) for discontinuing the participant from the intervention, and methods for determining the need to discontinue
- If the participant is due to complete assessments within 2 weeks of being discontinued from the study intervention, those assessments will be administered at the time of discontinuation; if the next scheduled assessments are more than 2 weeks from the discontinuation date, the discontinued participant

will wait for the next scheduled assessment. Thereafter, the participant will be included in all future scheduled assessments, even though not participating in the intervention.

Participants may choose to discontinue attending the MTIA classes at any time. Reasons for discontinuing may include family needs, work schedule changes, personal illness, or other reasons making planned attendance more difficult. Participants may be asked to discontinue attending the classes if they are disruptive or if the instructor notices a change in their level of distress. The instructor will discuss the situation with PI Gaylord and a determination of the safety of their continued participation will be made. The participant will be referred for assessment as needed, and the Safety Monitor will be notified.

If a participant misses more than two MTIA classes, the study coordinator will contact them to ascertain if they intend to continue and if not, why they are discontinuing their participation. The study coordinator will ask if the participant remains willing to complete the research assessments or wishes to withdraw from the study altogether. If the participant is willing, all study assessments, including AE assessments, will be sent to them to complete.

Participants may choose to discontinue using the MAPP at any time. They will be asked to notify the study staff of their intention to discontinue. Reasons for discontinuing the use of the MAPP will be solicited and recorded. Permission to continue study follow-up will be requested.

7.2 PARTICIPANT DISCONTINUATION/WITHDRAWAL FROM THE STUDY

Participants are free to withdraw from participation in the study at any time upon request.
An investigator may discontinue a participant from the study for the following reasons:

- Significant study intervention non-compliance, unless varying compliance is an aspect of the study objectives
- Lost-to-follow up; unable to contact subject (see **Section 7.3, Lost to Follow-Up**)
- Any event or medical condition or situation occurs such that continued collection of follow-up study data would not be in the best interest of the participant or might require an additional treatment that would confound the interpretation of the study
- The participant meets an exclusion criterion (either newly developed or not previously recognized) that precludes further study participation

The reason for participant discontinuation or withdrawal from the study will be recorded on the End of Study Case Report Form (CRF). Subjects who sign the informed consent form and are not randomized and do not receive the study intervention will not be replaced. Subjects who sign the informed consent form and are randomized and receive the study intervention, and subsequently withdraw, or are discontinued from the study, will not be replaced.

7.3 LOST TO FOLLOW-UP

A participant will be considered lost to follow-up if they miss three scheduled research sessions and study staff are unable to contact the participant after at least 5 attempts.

The following actions are taken if a participant fails to complete a study session:

- The site will attempt to contact the participant, reschedule the missed session if at least 1 week from the next scheduled session, counsel the participant on the importance of maintaining the assigned schedule and ascertain if the participant wishes to and/or should continue in the study
- Before a participant is deemed lost to follow-up, the investigator or designee will make every effort to regain contact with the participant (where possible, 5 contact attempts by phone/text or email over a period of 3 weeks). These contact attempts will be documented in the participant's medical record or study file.
- Should the participant 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.

8 STUDY ASSESSMENTS AND PROCEDURES

8.1 ENDPOINT AND OTHER NON-SAFETY ASSESSMENTS

Participants are to be recruited through the Carolina Data Warehouse for Health CDW-H) system at UNC Health. Participants who are free from cardiovascular and neuropsychiatric conditions (see inclusion and exclusion criteria) who are listed in the medical record as Black/African American or Hispanic/Latino (any race) will be sent a communication through the patient portal to introduce them to the study. (Note: a list of exclusionary diagnoses that were provided to the CDW-H are listed separately and can be provided.) Patients in the UNC Health system who have not signed up for the patient portal will be contacted by mail or email according to their preference stated in the system.

If interested in the study, patients may access the screening site set up in a secure environment (REDCap). On the screening site, they will be given additional information about the study as well as an opportunity to take the screening assessment. The screening questions mirror the eligibility criteria including a version of the GAD-7. Those who screen in will be asked for their contact information and for permission to use text and email for contact. They may proceed to the consenting section. The Consenting section includes a video describing the key points as well as the entire consent document. Participants may choose to read the entire consent at this time or to return and complete the consent document at a later date. On several pages of the consent document, participants are reminded that they can contact the study coordinator for questions.

Once they decide to proceed with the study, participants provide an electronic signature. The system sends a copy of the completed consent form to the participant. The study coordinator reviews each signed consent and documents the review.

Participants will be recruited in cohorts of 24-30 individuals. Consented participants will be told that it may be 2 months before randomization. They are sent a pre-randomization letter thanking them for signing up for the study and listing the compensation schedule. The letter will also remind them of the randomization plan and describe the three groups.

Up to 3 weeks prior to starting the intervention in each cohort, once 24-30 individuals have been consented, participants will be randomized into one of the three arms (MTIA, MAPP, WLC), and all participants will complete each scheduled assessment, regardless of group assignment. All data collection will occur remotely and intervention sessions will be virtual (i.e., in participants' homes). In a post-randomization packet, participants will be provided with a tablet loaded with the SMILE mHealth and a heart rate monitor and will view, or participate in, a virtual introductory tutorial on the use of the equipment. All psychological and physiological data will be collected via the SMILE mHealth app.

Upon receipt of the equipment, participants will be asked to test the heart rate monitor, prior to the baseline assessment, to familiarize themselves with placing the monitor and testing the heart rate signal. Instructions for placing the heart rate monitoring and testing will be provided in the SMILE app. In the event of problems, troubleshooting instructions will be provided, along with contact information for the researchers. These data will not be analyzed for research purposes, but will only be used to provide practice/feedback to the participants prior to the baseline assessment.

1) Baseline assessment (week 0). Participants will complete demographic and psychological questionnaires followed by a HRV assessment protocol. Immediately prior to beginning the HRV assessment, participants will be asked to complete a brief questionnaire regarding use of caffeine, nicotine, prescription medications and non-prescription medications. The HRV assessment protocol consists of asking participants to attach the heart rate monitor, and follow the instructions/model on the app to perform the following tasks:
    a. Stress test: an expanded Eriksen-Flanker Fish (E-F) test of executive function to provide cognitive stress to the subjects. The E-F task measures both attention and inhibitory control, both of which require parasympathetic inhibition to optimize performance. Performance measures are recorded to explore potential impacts of improved autonomic regulation on the task. The stressor task consists of a simple reaction time test wherein the subject must press a key on the keyboard that corresponds to the direction that a central arrow is pointing. The central the arrow is randomly flanked by either congruent (<<<<<) or incongruent stimuli (<<><<). The E-F test is a cognitive stressor that elicits vagal withdraw, allowing inhibition function quantification.
    b. Dynamic response test: an orthostatic test consisting of 3 min of rest in the seated position, slowly standing, 3 min of standing, slowly seating, and 3 min of seated.

    In addition to the demographic questionnaire, the psychological measures included in the baseline assessment are: GAD-7, COVID Stress Scale, Connor-Davidson Resilience Scale (CD RISC),

Mental Health Quality of Life, brief coping scale [COPE]),Perceived Stress Scale, Posttraumatic Growth Inventory (PTGI), sleep disturbance (Adult PROMIS Short Form), PTSD Checklist (PCL-5), Center for Epidemiologic Studies Depression Scale [CES-D], Cognitive and Affective Mindfulness Scale-Revised (CAMS-R), and physical health (Short Form Health Survey [SF-12]) **[Please note: All questionnaires will be attached to this protocol along with a brief description of and/or reference for their psychometric properties and scoring]**

2) Intervention (weeks 1-8). Participants assigned to the MTIA and MAPP groups will participate in the 8-week intervention. After the first week, they will be sent the HEAL expectancy questionnaire. Biweekly during weeks 1-6, participants in all groups will be asked to complete assessments which include psychological questionnaires (GAD-7, COVID-SS, CD-RISC, CAMS-R) and the same HRV assessment protocol as the baseline. Participants in both mindfulness groups will be asked to provide documentation of their mindfulness practice (if any) via RedCap surveys sent twice weekly. Participants in the intervention groups will also receive a question about their satisfaction with the mindfulness training with their check-in (mindfulness practice) surveys at 4 and 8 weeks.

3) 8-week and follow-up assessment at week 12: participants in all groups will be asked to complete assessments which include psychological questionnaires (GAD-7, COVID Stress Scale,CD RISC, MHQoL, COPE, PSS, PTGI, PROMIS, PCL-5, CES-D, CAMS-R, and SF-12) and the same HRV assessment protocol as the baseline.

8.2 SAFETY ASSESSMENTS

All participants will be asked to complete a brief questionnaire to assess their safety during their participation in this completely remote intervention. The safety questionnaire asks participants if, in the past 2 weeks, they have:

1) been hospitalized for any reason?
2) experienced any life-threatening events?
3) become physically disabled in some way?
4) experienced any new or worsening emotional health problems (for example, worry, nervousness, sadness, or stress)?
5) experienced any new or worsening physical health problems that you think might be related to being part of this study?

If their answer is yes to any of these questions, they are asked to explain and the staff is alerted.

To minimize the risk of severe or lasting psychological issues or reactions:

- An experienced and certified mindfulness instructor will lead the MTIA sessions. A co-facilitator will attend in the event an AE occurs and the participants needs to be shifted to a breakout room (in Zoom) for specific guidance.

- Participants will be encouraged throughout the sessions to confidentially discuss their experiences with the exercises, including any emotional difficulties, and will be prepared ahead of time to know what they may experience.
- The beginning of each session will include time to discuss out-of-class practices. Participants will be engaged in problem-solving discussions, and will become knowledgeable about coping skills to manage difficult emotions.
- Participants will be given study contact information within their enrollment materials and will be encouraged to contact study staff should any negative changes in their emotional health occur during the course of home practice or at any point during the study, or if difficulties arise that the participants feel uncomfortable discussing in the group setting.
- Any reported new or increasing emotional health change will be detailed by study staff and communicated to the MPIs. The MPIs will determine the severity and relatedness of the event. For events that are more than mild, the MPIs may confer with an expert in the treatment of anxiety to offer the participant a list of relevant local resources as appropriate. Study staff will continue to monitor this participant during weekly sessions, documenting any resources accessed and to determine if emotional health symptoms have resolved.

8.3 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

8.3.1 DEFINITION OF ADVERSE EVENTS

This protocol uses the definition of adverse event from 21 CFR 312.32 (a): any untoward medical occurrence associated with the use of an intervention in humans, ***whether or not considered intervention-related***.

The study team, led by the MPIs, will monitor all participants for 3 categories of events for all participants: adverse events (AEs), serious adverse events (SAEs) and unanticipated problems (UPs). These three categories are defined as follows:

Adverse event (AE): Any unfavorable and unintended change in physical or mental health status (i.e. new or worsening physical or mental health signs, symptoms, or disease) associated with participation in the study, regardless of whether it is considered related to the study.

8.3.2 DEFINITION OF SERIOUS ADVERSE EVENTS

Serious Adverse Event (SAE): Any AE that:

- Results in death
- Is life threatening, or places the participant at immediate risk of death from the event as it occurred
- Requires or prolongs hospitalization
- Causes persistent or significant disability or incapacity
- Results in congenital anomalies or birth defects
- Note: for this project, ALL SAEs would be considered unanticipated

Note: for this project, ALL SAEs would be considered unanticipated

8.3.3 CLASSIFICATION OF AN ADVERSE EVENT

8.3.3.1 SEVERITY OF EVENT

This study uses the following AE grading scale:

- Mild: An experience that is transient and requires no special treatment or intervention. The experience does not generally interfere with usual daily activities. In this study, an example includes mild emotional distress that persists after a Mindfulness session has ended.
- Moderate: An experience that is alleviated with simple therapeutic treatments. The experience impacts usual daily activities. In this study, an example includes moderate emotional distress requiring counseling.
- Severe: An experience that requires therapeutic intervention. The experience interrupts usual daily activities. In this study, an example includes anxiety symptoms requiring pharmacological intervention or withdrawal from the study. If any hospitalization (or prolongation of hospitalization) is required for treatment, it becomes an SAE.

This study uses the following AE attribution scale:

- Not related: The AE is clearly not related to the study procedures (i.e., another cause of the event is most plausible and/or a clinically plausible temporal sequence is inconsistent with the onset of the event).
- Possibly related: An event that follows a reasonable temporal sequence from the initiation of study procedures, but that could readily have been produced by a number of other factors.
- Related: The AE is clearly related to the study procedures.

This study uses the following AE expectedness scale:

- Unexpected: nature or severity of the event is not consistent with information about the intervention in the protocol or consent form
- Expected: event is known to be associated with the intervention under study

8.3.3.2 RELATIONSHIP TO STUDY INTERVENTION/EXPERIMENTAL MANIPULATION

All adverse events (AEs) will have their relationship to study procedures, including the intervention, assessed by an appropriately-trained clinician based on temporal relationship and his/her clinical judgment. The degree of certainty about causality will be graded using the categories below.

- **Related** – The AE is known to occur with the study procedures, there is a reasonable possibility that the study procedures caused the AE, or there is a temporal relationship between the study procedures and the event. Reasonable possibility means that there is evidence to suggest a causal relationship between the study procedures and the AE.
- **Possibly Related** --– There is some evidence to suggest a causal relationship (e.g., the event occurred within a reasonable time after administration of study procedures). However, other factors may have contributed to the event (e.g., the participant's clinical condition, other concomitant events). Although an AE may rate only as "possibly related" soon after discovery, it can be flagged as requiring more information and later be upgraded to "related", as appropriate.
- **Not Related** – There is not a reasonable possibility that the study procedures caused the event, there is no temporal relationship between the study procedures and event onset, or an alternate etiology has been established.

8.3.3.3 EXPECTEDNESS

Unexpected: nature or severity of the event is not consistent with information about the intervention in the protocol or consent form.
Expected: event is known to be associated with the intervention under study

A clinician with appropriate expertise in anxiety 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 procedures.

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

Extant literature to date suggests that standardized 8-week mindfulness-based group interventions are generally well tolerated with minimal risks in non-clinical adult populations. Emotional discomfort may occur as a transient, and often therapeutic, side effect.

However, given that course content can bring up difficult emotions, we will monitor for changes in health every 2 weeks throughout the study, as outlined below. The instructor in the MTIA arm also monitors participants for changes in emotional health. We will also ask participants to report any changes in their physical health that may be related to their participation in the study, with the exception of transient discomfort during sitting practices. Examples of potentially relevant, although unlikely, physical health changes include: headaches, body or joint aches, or an injury occurring during mindfulness practice. Participants will be encouraged to report any adverse event that they believe may be related to the interventions.

8.3.5 ADVERSE EVENT REPORTING

In order to facilitate the reporting of potential AEs to study staff, the following procedures will be in place:

1. During the 8-week intervention period, participants will be engaged in weekly group discussions about home practice, challenges to practice, and well-being. Any participant endorsing difficulties that the course facilitators feel are potentially beyond transient or typical will be approached privately to gather details.
2. Participants will be given study staff contact information, including study phone and e-mail addresses. Participants will be encouraged to contact study staff in the event of psychological or potentially relevant physical health concerns.
3. Every two weeks during the intervention, study staff will administer a brief adverse event survey in the SMILE app (see Appendix A), with questions regarding any serious adverse events, changes in emotional health, and physical health changes possibly related to study participation in the previous week. Study staff will also notify the course instructor of the increased emotional distress so that extra support can be provided as needed.
4. Non-serious AEs are reported to the Safety Officer biannually and to the IRB annually.
5. Unexpected and Related AEs/UPs with increased risk. All AEs that are deemed 1) unexpected; 2) possibly or probably related to study participation; and 3) suggest increased risk for study participants will be reported to the NIH Program Officer, SO, and UNC IRB within 48 hours of becoming aware of the information, using each organizations' respective reporting formats. In these reports, the MPIs will identify any corrective action planned or already undertaken. The MPIs will follow any additional course of action recommended by the UNC IRB, NIH, and/or SO.

The study team member receiving information from participants about a potential AE related to the study will complete an Adverse Event Form (see Appendix B) in REDCap. Procedures after this point are detailed in Section 3 of this document.

8.3.6 SERIOUS ADVERSE EVENT REPORTING

Study staff will notify the MPIs immediately upon becoming aware of an SAE, regardless of possible relatedness to the study. In consultation with the MPIs, a trained member of the study team will be responsible for conducting an evaluation of a serious adverse event and shall report the results of such evaluation to the NIH and the reviewing Institutional Review Board (IRB) within 48 hours, but in no event later than 10 working days after the investigator first learns of the event. All other SAEs (not unanticipated or related) will be summarized and reported to the SO and the NIH Program Officer quarterly.

8.3.7 REPORTING EVENTS TO PARTICIPANTS

N/A

8.3.8 EVENTS OF SPECIAL INTEREST

N/A

8.3.9 REPORTING OF PREGNANCY

N/A

8.4 UNANTICIPATED PROBLEMS

8.4.1 DEFINITION OF UNANTICIPATED PROBLEMS

An incident, experience, or outcome that meets the definition of an UP generally will warrant consideration of changes to the protocol or consent in order to protect the safety, welfare, or rights of participants or others. Other UPs may warrant corrective actions at a specific study site. Examples of corrective actions or changes that might need to be considered in response to an UP include:

- Modification of inclusion or exclusion criteria to mitigate the newly identified risks
- Implementation of additional safety monitoring procedures
- Suspension of consenting/enrollment of new participants or halting of study procedures for consented/enrolled participants
- Modification of informed consent documents to include a description of newly recognized risks
- Provision of additional information about newly recognized risks to previously consented/enrolled participants.

Unanticipated problems (UPs) 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 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.

8.4.2 UNANTICIPATED PROBLEMS REPORTING

The investigator will report unanticipated problems (UPs) to the reviewing Institutional Review Board (IRB) and to the lead principal investigator (PI) and to the Safety Officer. 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 and to the DCC/study sponsor/funding agency within <insert timeline in accordance with policy> of the investigator becoming aware of the event
- Any other UP will be reported to the IRB and to the DCC/study sponsor/funding agency within <insert timeline in accordance with policy> of the investigator becoming aware of the problem
- All UPs should be reported to appropriate institutional officials (as required by an institution's written reporting procedures), the supporting agency head (or designee), and the Office for Human Research Protections (OHRP) within <insert timeline in accordance with policy> of the IRB's receipt of the report of the problem from the investigator

*See **CD Section 8.4.1** for additional example text applicable for devices.*

8.4.3 REPORTING UNANTICIPATED PROBLEMS TO PARTICIPANTS

N/A.

9 STATISTICAL CONSIDERATIONS

9.1 STATISTICAL HYPOTHESES

Brief Summary:

The goal of this clinical trial is to evaluate the SMILE app, a Digital Health Platform (DHP), that will deliver a mindfulness intervention, designed to mitigate COVID related stress. Additionally, the SMILE app will remotely collect self-reported psychological and physiological metrics of mental health and autonomic regulation. Study participants are adults who self-identify as African American, Black and/or Latino, and who have clinically significant levels of anxiety.

The study aims are:

- Aim 1: Establish the effectiveness and durability of an 8-week Mindfulness DHP intervention. The investigators will focus on two constructs important to mental health and hypothesize that: A) Anxiety, self-report stress and quality-of-life measures will significantly improve when comparing: A.1) Pre-to-post intervention, and; A.2) Control vs. intervention groups over 8 weeks and at 1-month follow-up. B) Arousal, autonomic indices of HRV (reflecting parasympathetic activation) will significantly improve, when comparing: B.1) Pre-to-post intervention, and; B.2) Control vs. intervention groups over 8 weeks and at 1-month follow-up.

- Aim 2: Establish the sustainability of two Mindfulness DHP interventions utilizing retention, usage (frequency), and participant satisfaction. The investigators hypothesize that MTIA will be more sustainable than MAPP because the interactive, instructor-guided group model will create an environment of community and accountability.

- Aim 3: Exploratory: Examine associations between COVID-19 related stress, mental health outcomes, and HRV. Examine the extent to which COVID-19 related stress and mental health symptoms are linked to HRV at baseline and how that relationship changes over time.

Participants will be assigned to 1 of 3 arms of the study: MTIA intervention, MAPP intervention, or wait-list control. All participants will be mailed a device with the SMILE app installed, and equipment for recording cardiac data in the home. All participants will complete the baseline psychometrics measures and physiological stress test using the instructions provided on the SMILE app. Those assigned to the MTIA or MAPP intervention groups will then participate in their assigned intervention over the subsequent 8 weeks. During these 8 weeks, psychometric and physiological data will be completed biweekly for all participants. 3 months following the initial baseline, all participants will complete a final psychometric/physiological evaluation.

- Primary Endpoint(s): The primary endpoint is anxiety as measured by the GAD-7 scale, a commonly used clinical anxiety measure. We hypothesize that both intervention groups will show significant improvements compared to baseline at 8 weeks and 12 weeks. We further hypothesize that, compared to the wait-list control group, the mean anxiety for participants in the MTIA group and the MAPP intervention groups will show a significantly greater reduction in anxiety at the end of the intervention and at 12 weeks. Our null hypothesis is that neither intervention group will show a significant reduction in anxiety either compared to baseline or compared to the control group.

- Secondary Endpoint(s): For each of the secondary endpoints listed in Section 3.0 (See table), we hypothesize that, compared to the control group, the mean (or median value as appropriate) for each measure will show improvement at the end of the intervention period.

9.2 SAMPLE SIZE DETERMINATION

Power analysis was primarily informed by psychological variables (Aim 1.A), which are more common outcomes in published studies, then expected power was applied to the HRV outcome (Aim 1.B). To conduct the power analysis for Aim 1.A, recent studies of app-based mindfulness mediation were surveyed for effect sizes for treatment effects on stress, irritability, and psychological wellbeing measures. Effect size were calculated and adjusted for correlations of pre and post scores where possible. Between-group standardized mean differences varied depending on outcome, but small-to-medium effect size of Cohen's d =. was observed for outcomes compared to psychoeducation, waitlist, and assessment-only control groups(32,52). Aiming for 80% power, an alpha level of 0.05, and expected effect size of between subjects Cohen's d=0.4, we calculated that 100 participants will be needed per condition at the final time point to detect an effect of this size using a 2-sided independent-samples t-test. We expected that there would be a correlation among outcomes for participants in the same class within the MTIA intervention arm, as observed in our previous study (ICC=0.021), which can influence power to detect effects between groups(53). Using that intra-class correlation estimate and an average of 9 subjects per group, we calculated that we would need a sample of 117 subjects at the final time point for the MTIA arm to meet the previously defined power criteria for Aim 1.A. For Aim 1.B, the target sample size would also provide more than 97% power to detect HRV changes equal to those found in a prior study (Cohen's d = .55138); even with expected 10% physiological data loss due to mechanical error or signal noise as is common in physiological studies. Given an expected pre-post retention rate of 85% for MTIA group and 75% for MAPP and WLC groups, we estimate we would require recruitment of 138 participants in the MTIA group and 133 participants in each of the MAPP and WLC groups. We do not expect to have 80% power for each of the exploratory analyses.

9.3 POPULATIONS FOR ANALYSES

Our primary analysis will consist of a modified intention-to-treat analysis that will retain all participants randomized to the intervention groups who attended at least one intervention session (MTIA) or interacted with the MAPP at least once. In addition, among all randomized participants, this includes individuals with at least one post-baseline assessment. Our justification for this approach is that it is common when one or more arms include an individually randomized group because participants may not be available to attend the intervention after waiting for the cohort to begin.

We will also conduct an analysis using all randomized participants (standard Intention-to-treat) and a sensitivity analysis including only participants who attend 5 or more MTIA sessions, access the MAPP on 5 weeks, and complete the 8-week and 12-week assessments (per-protocol population).

9.4 STATISTICAL ANALYSES

9.4.1 GENERAL APPROACH

The analysis will include descriptive statistics of the study population consisting of means and standard deviations for continuous variables and percentages for categorical variables. Variables will be checked for normality. Transformations common for the variable will be employed as indicated. All analyses will control for age, gender (woman vs. not), ethnicity (Hispanic/Latino vs. not), and baseline anxiety. Control for age and gender is indicated due to their strong associations with the endpoints. Analyses will use two-tailed tests with a p-value of 0.05 considered statistically significant.

9.4.2 ANALYSIS OF THE PRIMARY ENDPOINT(S)

The primary outcome, The GAD-7 scale, is measured at baseline, 2 weeks, 4 weeks, 6 weeks, 8 weeks and 12 weeks. The analysis will be conducted using mixed effects models. Modeling will examine within-group changes in outcome variables between intervention groups. The main effect of interest will be treatment (group) X time interaction effects. Within-individual correlations will be modeled using random intercepts. The addition of random slopes will be tested. Model comparisons will be conducted using likelihood ratio tests for nested models and Akaike and Bayes Information Criterion (AIC and BIC) for non-nested models In the MTIA condition, random intercepts will be used to adjust for cohort differences. Fixed effects will include gender (woman vs. not), ethnicity group (Hispanic/Latino or not), and age.

Treatment X time differences will be assessed using an omnibus test (F-test) with a null hypothesis that there is no treatment X time effect among the three treatment arms. If the difference of treatment effect is significant at the 0.05 level, we will then examine individual group contrasts with the control group as the reference category.

The primary analysis, using the modified intention-to-treat, uses mixed effects models that are robust to missing data.

9.4.3 ANALYSIS OF THE SECONDARY ENDPOINT(S)

Analysis of the psychological endpoints relies on scales and will be assessed using the same procedure as described above for the GAD-7. For variables with fewer assessment time points, a multiple regression model may be employed. A complete Statistical Analysis Plan will be developed prior to the database lock.

For HRV analyses] and mean heart period [HP]), we will include within-timepoint observations at the 15-second epoch level, with labels for each observation along three dimensions (time, visit, and subject). Multiple-level modeling will be used to test for differences in the dynamic behavior of HP and High frequency HRV (HF_HRV) across time. In the case that the variability of either HP or HF_HRV is too great at the 15-second epoch level, we will apply a triangular smoothing algorithm with a span of 3-5 epochs to stabilize the estimates of both HP and HF_HRV. Vagal efficiency (VE) will be calculated over all epochs spanning the posture conditions. HRV analyses will include fixed effects for BMI and time-varying covariates for medication use, caffeine, tobacco, alcohol, and time of day.

The Aim 2 sustainability variables include1) retention (withdrew vs. not, measured by proportions); 2) usage (measured by a) attendance and b) homework completion in the MTIA group and by a) app

interaction—opening pages—b) and homework completion in the MAPP group); and 3) satisfaction with the intervention as measured by a Likert scale question. Retention is analyzed with a chi square statistic (or logistic regression). The analysis of usage will depend on the distributions. Prior to the database lock, we will examine usage distributions to determine if a t-test is possible or if a different type of analysis (e.g., Poisson model) will be needed. Satisfaction will be compared with a t-test or nonparametric test, as indicated.

9.4.4 SAFETY ANALYSES

N/A

9.4.5 BASELINE DESCRIPTIVE STATISTICS

Baseline characteristics will be calculated for each intervention group. These include demographic variables and baseline levels for the study endpoints. In addition, we will examine groups defined by their adherence to the protocol: participants who withdraw after attending at least one class or interacting with the app at least once compared to those who have 2 or more interactions with the intervention. Also, we will compare characteristics of completers and non-completers.

9.4.6 PLANNED INTERIM ANALYSES

NA

9.4.7 SUB-GROUP ANALYSES

Subgroup analyses will depend on the distribution of the overall sample by age, gender, and ethnicity. Subgroup analyses will be addressed in the formal SAP.

9.4.8 TABULATION OF INDIVIDUAL PARTICIPANT DATA

Individual participant data will be listed by measure and time point.

9.4.9 EXPLORATORY ANALYSES

A goal of the study is to understand the relationships between the psychological and quality-of-life variables and the heart rate variability assessments. We will examine the correlations among the variables at baseline and over time. Models under consideration include structural equation models that can consider the correlations among the psychological variables.

10 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1 REGULATORY, ETHICAL, AND STUDY OVERSIGHT CONSIDERATIONS

10.1.1 INFORMED CONSENT PROCESS

10.1.1.1 CONSENT/ASSENT AND OTHER INFORMATIONAL DOCUMENTS PROVIDED TO PARTICIPANTS

Informed Consent Process
Potential participants will access the screening site on REDCap. After the study is described, they will have an opportunity to agree to screening electronically. If they do not agree, they will be thanked and no further contact will be made. Participants who agree to screen will complete an electronic screening questionnaire. The questionnaire aggregates some of the exclusionary conditions to preserve participant confidentiality. It also includes a GAD-7 to ensure that participants score between 8 and 14. If they screen in, they will be given an opportunity to allow themselves to be contacted by text or email. This is important since most people no longer answer the telephone if they do not recognize the number. They are also given an opportunity to complete the consent for the study either at the time of screening or later.

10.1.1.2 CONSENT PROCEDURES AND DOCUMENTATION

A video of the consenting process is provided as well as the entire written consent form in an electronic format on REDCap. The participants can stop at any time and contact the study coordinator for more information or to answer questions. Once they have read the entire consent, participants may sign the form electronically (finger or mouse) and provide the date and their typed name. Study personnel will review the consent and screening form and sign off.

The consent materials are provided in English only since the interventions are currently only available in English. However, the study employs research assistants who are fluent in Spanish should participants prefer to discuss the consenting process in Spanish.

10.1.2 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 study participants, investigator, funding agency, and regulatory authorities. If the study is prematurely terminated or suspended, the Principal Investigator (PI) will promptly inform study participants, the Institutional Review Board (IRB), and sponsor/funding agency and will provide the reason(s) for the termination or suspension. Study participants 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 participants
- Insufficient compliance of study staff to the protocol (ie, significant protocol violations)
- Data that are not sufficiently complete and/or evaluable
- Determination that inadequate recruitment indicates futility

The study may resume once concerns about safety, protocol compliance, and data quality are addressed, and satisfy the funding agency, sponsor, IRB, Food and Drug Administration (FDA), or other relevant regulatory or oversight bodies (OHRP, DSMB).

10.1.3 CONFIDENTIALITY AND PRIVACY

Participant confidentiality and privacy is strictly held in trust by the participating investigators, their staff, the safety and oversight monitor(s), and the sponsor(s) and funding agency. This confidentiality is extended to the data being collected as part of this study. Data that could be used to identify a specific study participant will be held in strict confidence within the research team. No personally identifiable information from the study will be released to any unauthorized third party without prior written approval of the sponsor/funding agency.

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

The study participant's contact information will be securely stored at each clinical 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, Institutional policies, or sponsor/funding agency requirements.

Study participant research data, which is for the purposes of statistical analysis and scientific reporting, will be transmitted to and stored at the University of North Carolina at Chapel Hill. This will not include the participant's contact or identifying information. Rather, individual participants and their research data will be identified by a unique study identification number. The study data entry and study management systems used by clinical site research staff will be secured and password protected. At the end of the study, all study databases will be de-identified and archived at the UNC Dataverse.

Measures Taken to Ensure Confidentiality of Data Shared per the NIH Data Sharing Policies
It is NIH policy that the results and accomplishments of the activities it funds should be available to the public (see httpsngrants.nih.gov/policy/sharing.htm). The PI will ensure all mechanisms used to share data will include proper plans and safeguards for the protection of privacy, confidentiality, and security for data dissemination and reuse (e.g., all data will be thoroughly de-identified and will not be traceable to a specific study participant). Plans for archiving and long-term preservation of the data will be implemented, as appropriate.

Certificate of Confidentiality
To further protect the privacy of study participants, the Secretary, Health and Human Services (HHS), has issued a Certificate of Confidentiality (CoC) to all researchers engaged in biomedical, behavioral, clinical or

other human subjects research funded wholly or in part by the federal government. Recipients of NIH funding for human subjects research are required to protect identifiable research information from forced disclosure per the terms of the NIH Policy (see *https://humansubjects.nih.gov/coc/index*). As set forth in 45 CFR Part 75.303(a) and NIHGPS Chapter 8.3, recipients conducting NIH-supported research covered by this Policy are required to establish and maintain effective internal controls (e.g., policies and procedures) that provide reasonable assurance that the award is managed in compliance with Federal statutes, regulations, and the terms and conditions of award. It is the NIH policy that investigators and others who have access to research records will not disclose identifying information except when the participant consents or in certain instances when federal, state, or local law or regulation requires disclosure. NIH expects investigators to inform research participants of the protections and the limits to protections provided by a Certificate issued by this Policy.

Participants in the group intervention, the MTIA, will be reminded to keep confidential all information related to other participants. Audiotapes stored at UNC will be destroyed once the data is analyzed for fiedelity.

10.1.4 FUTURE USE OF STORED SPECIMENS AND DATA

NA

10.1.5 KEY ROLES AND STUDY GOVERNANCE

Principal Investigator	**Principal Investigator**	**Principal Investigator**	**Safety Officer**
Susan Gaylord, Ph/d, Associate Professor	*Keri Heilman, PhD, Research Assistant Professor*	*Maria Davila, PhD*	Aysenil Belger, PhD
University of North Carolina at Chapel Hill	University of North Carolina at Chapel Hill	*Research Triangle international*	University of North Carolina at Chapel Hill
919-966-8586	*773-814-8725*	*224-323-3327*	*919-843-7368*
gaylords@med.unc.edu	*kheilman@email.unc.edu*	*mariad@rti.org*	*aysenil.belger@unc.edu*

Study Staff and participants can report any concerns about the study to the Institutional Review Board of the University of North Carolina at Chapel Hill.

10.1.6 SAFETY OVERSIGHT

This study has three main safety oversights:

- The MPIs, Dr. Susan Gaylord, Dr Maria Davila and Dr Keri Heilman, are responsible for day-to-day oversight of study protocols and will ensure safety procedures are followed.
- Safety Officer (Aysenil Belger)
- The UNC IRB

1. Frequency of Data and Safety Monitoring

Data on AEs and UPs will be collected on an ongoing basis from study start to study completion.

General AE Procedures. The project manager or study staff will report all AEs to the MPIs monthly using the Adverse Event Reporting Form, after having gathered all necessary details. Study staff will report AEs that are more than mild and possibly related to study participation to the MPIs right away. Together the MPIs will determine the severity and the relatedness of the AE and will confer with the SO as needed. If the AE is serious and/or unexpected, possibly related to study participation, and suggests increased risk for participants, the procedures outlined below will also be followed.

AE reports will be collected by the project manager or study staff, summarized and de-identified**. A summary report of all AEs to date will be sent to the MPIs and the SO annually.**

As per UNC IRB guidelines, all AEs will be reported to the UNC IRB during the yearly study review process.

Serious AE Procedures. The project manager or study staff will report all SAEs to the MPIs immediately upon becoming aware of the information. An adverse event reporting form will also be completed.

For all deaths, the MPIs will notify the NIH Program Officer, ISM, and UNC IRB within 24 hours of becoming aware of the information.

For all SAEs that are unanticipated and that are related to the intervention, the MPIs will notify the NIH Program Officer, SO, and UNC IRB within 48 hours of becoming aware of the information.

All other SAEs (not unanticipated or related) will be summarized and reported to the SO and the NIH Program Officer quarterly.

The MPIs will follow any additional course of action recommended by the NIH, UNC IRB or SO.

Unexpected and Related AEs/UPs with increased risk. All AEs that are deemed 1) unexpected; 2) possibly or probably related to study participation; and 3) suggest increased risk for study participants will be reported to the NIH Program Officer, SO, and UNC IRB within 48 hours of becoming aware of the information, using each organizations' respective reporting formats. In these reports, the MPIs will identify any corrective action planned or already undertaken. The MPIs will follow any additional course of action recommended by the UNC IRB, NIH, and/or SO.

The SO will meet in person (or virtually as needed) at least 5 times throughout the study to review the Data and Safety Monitoring Report: 1) prior to first enrollment; 2) after the first 2 cohorts; 3) after 6 cohorts have completed; 4) after 8 cohorts have completed; 5) at study completion.

Additional meetings (ad-hoc) will occur as requested by the MPIs for review of unexpected adverse events or any SAEs that occur. Any recommended changes by the SO will be submitted to the UNC IRB for approval.

2. Content of Data and Safety Monitoring Report

The content of the reports to be provided to the SO include:

- Study overview, protocols, and reporting forms
- Study timetable
- Recruitment, enrollment, and attrition statistics
- Enrollee demographics and preliminary outcome data
- End of intervention feedback session results
- Adverse events, unanticipated problems, as above

ClinicalTrials.gov Requirements: This project includes an applicable clinical trial that has been registered at ClinicalTrials.gov. Summary results, including adverse events, will be reported no later than one year after the final completion date of the study. Grant and progress report forms will include a certification that we have made all required submissions to ClinicalTrials.gov.

10.1.7 CLINICAL MONITORING

Dr Aysenil Berger (UNC Dept of Psychiatry) will serve as the Safety Officer.

Conflict of Interest for SO: The SO has no personal or professional affiliation with the study investigators or the intervention that could be perceived as a conflict of interest.

Protection of Confidentiality
Data will be summarized by study staff and presented to the SO 2 weeks prior to meeting to allow full review of data. All data will be de-identified using study ID number and/or presented in aggregate format.

SO Responsibilities
The SO will act in an advisory capacity to the MPIs and NIH. The SO will submit a report after each meeting that summarizes the state of the study and any recommendations. SO reports will be submitted to the UNC IRB and NIH staff.

The SO's responsibilities include:

1. monitoring participant safety via examination of AEs and UPs and preliminary outcome measures; make recommendations when safety issues arise.
2. evaluating the progress of the study, including reviewing inclusion/exclusion criteria, study enrollment and retention, and reasons for attrition.
3. reviewing procedures for maintaining the confidentiality of data; and
4. reviewing protocols for data collection, management, and analyses.

10.1.8 QUALITY ASSURANCE AND QUALITY CONTROL

Quality control (QC) procedures will be implemented as follows:

Informed consent --- Study staff will review both the documentation of the consenting process as well as a percentage of the completed consent documents. This review will evaluate compliance with GCP, accuracy, and completeness. Feedback will be provided to the study team to ensure proper consenting procedures are followed.

Electronic data --- Data will be initially captured in several places, all electronic. Most of the data will be captured on the SMILE app in the Digital Health Platform. The MPI (Davila) at RTI is responsible for assessing the data integrity from the app and for making deidentified data available to the analytic team. Audio recordings for fidelity assessments will be kept on the Microsoft Teams site. Homework compliance assessments and Adverse Event assessments will be recorded on the study REDCap site. Staff responsible for the REDCap assessments will be trained in data capture biannually. Data completion rates will be assessed by the fidelity monitor (REDCap) and the RTI MPI (SMILE app) at least every 3 months.

Intervention Fidelity — Consistent delivery of the study interventions will be monitored throughout the intervention phase of the study. Procedures for ensuring fidelity of intervention delivery are described in **Section 6.2.1, Interventionist Training and Tracking**.

Protocol Deviations – The study team will review protocol deviations on an ongoing basis (monthly) and will implement corrective actions when the quantity or nature of deviations are deemed to be at a level of concern.

Should independent monitoring become necessary, the PI will provide direct access to all trial related sites, source data/documents, and reports for the purpose of monitoring and auditing by the sponsor/funding agency, and inspection by local and regulatory authorities.

10.1.9 DATA HANDLING AND RECORD KEEPING

10.1.9.1 DATA COLLECTION AND MANAGEMENT RESPONSIBILITIES

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

Clinical data (including adverse events (AEs), concomitant medications, and expected adverse reactions data) will be entered into REDCap, a 21 CFR Part 11-compliant data capture system provided by the University of North Carolina at Chapel Hill. The data system includes password protection and internal quality checks, such as automatic range checks, to identify data that appear inconsistent, incomplete, or inaccurate. Clinical data will be entered directly from the source documents.

10.1.9.2 STUDY RECORDS RETENTION

Study documents will be retained for a minimum of 5 years after the last approval of a marketing application in an International Council on Harmonisation (ICH) region and until there are no pending or contemplated marketing applications in an ICH region or until at least 5 years have elapsed since the formal discontinuation of clinical development of the study intervention. These documents should be retained for a longer period, however, if required by local regulations. No records will be destroyed without the written consent of the sponsor/funding agency, if applicable. It is the responsibility of the sponsor/funding agency to inform the investigator when these documents no longer need to be retained.

10.1.10 PROTOCOL DEVIATIONS

This protocol defines a protocol deviation as any noncompliance with the clinical trial protocol, International Council on Harmonisation Good Clinical Practice (ICH GCP), or Manual of Procedures (MOP) requirements. The noncompliance may be either on the part of the participant, the investigator, or the study site staff. As a result of deviations, corrective actions will be developed by the site and implemented promptly.

These practices are consistent with ICH GCP:

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

It will be the responsibility of the MPIs to use continuous vigilance to identify and report deviations within 10 working days of identification of the protocol deviation, or within 10 working days of the scheduled protocol-required activity. All deviations will be addressed in study source documents, reported to NIMHD Program Official. Protocol deviations will be sent to the reviewing Institutional Review Board (IRB) per their policies. The MPIs will be responsible for knowing and adhering to the reviewing IRB requirements. Further details about the handling of protocol deviations will be included in the MOP.

10.1.11 PUBLICATION AND DATA SHARING POLICY

The MPIs will develop a policy for publication procedures and for resolving authorship issues.

This study will be conducted in accordance with the following publication and data sharing policies and regulations:

National Institutes of Health (NIH) Public Access Policy, which ensures that the public has access to the published results of NIH funded research. It requires scientists to submit final peer-reviewed journal manuscripts that arise from NIH funds to the digital archive PubMed Central upon acceptance for publication.

This study will comply with the NIH Data Sharing Policy and Policy on the Dissemination of NIH-Funded Clinical Trial Information and the Clinical Trials Registration and Results Information Submission rule. As such, this trial will be registered at ClinicalTrials.gov, and results information from this trial will be submitted to ClinicalTrials.gov. In addition, every attempt will be made to publish results in peer-reviewed journals. Data from this study may be requested from other researchers 2 years after the completion of the primary endpoint by contacting the UNC Dataverse. Considerations for ensuring confidentiality of these shared data are described in Section 10.1.3.

10.1.12 CONFLICT OF INTEREST POLICY

The independence of this study from any actual or perceived influence 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. The study leadership in conjunction with the Conflict of Interest Office at the University of North Carolina at Chapel Hill and NIMHD has established policies and procedures for all study

group members to disclose all conflicts of interest and has established a mechanism for the management of all reported dualities of interest.

10.2 ADDITIONAL CONSIDERATIONS

N/A

10.3 ABBREVIATIONS AND SPECIAL TERMS

AE	Adverse Event
ANCOVA	Analysis of Covariance
CFR	Code of Federal Regulations
CLIA	Clinical Laboratory Improvement Amendments
CMP	Clinical Monitoring Plan
COC	Certificate of Confidentiality
CONSORT	Consolidated Standards of Reporting Trials
CRF	Case Report Form
DCC	Data Coordinating Center
DHHS	Department of Health and Human Services
DSMB	Data Safety Monitoring Board
DRE	Disease-Related Event
EC	Ethics Committee
eCRF	Electronic Case Report Forms
FDA	Food and Drug Administration
FDAAA	Food and Drug Administration Amendments Act of 2007
FFR	Federal Financial Report
GCP	Good Clinical Practice
GMP	Good Manufacturing Practices
HIPAA	Health Insurance Portability and Accountability Act
ICH	International Council on Harmonisation
ICMJE	International Committee of Medical Journal Editors
IRB	Institutional Review Board
ITT	Intention-To-Treat
LSMEANS	Least-squares Means
MedDRA	Medical Dictionary for Regulatory Activities
MAPP	Mindfulness app
MOP	Manual of Procedures
MPIs	Multiple Principal Investigators

MTIA	Mindfulness-Based Stress Management training through an internet-delivered, interactive, group-based approach
NCT	National Clinical Trial
NIH	National Institutes of Health
NIH IC	NIH Institute or Center
OHRP	Office for Human Research Protections
PI	Principal Investigator
QA	Quality Assurance
QC	Quality Control
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SO	Safety Officer
SOA	Schedule of Activities
SOP	Standard Operating Procedure
UP	Unanticipated Problem
US	United States

10.4 PROTOCOL AMENDMENT HISTORY

*The table below is intended to capture changes of IRB-approved versions of the protocol, including a description of the change and rationale. A **Summary of Changes** table for the current amendment is located in the **Protocol Title Page**.*

Version	Date	Description of Change	Brief Rationale

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Appendix 1. Screening Questionnaire

Introduction

Introduction to the SMILE Study

Video: [Insert link to video]

Thank you for your interest in the SMILE study! Please watch the video below to learn more details about the study. After watching the video, you will have the opportunity to complete screening questions to see whether you qualify for the study.

Interest in screening

1) Thank you for watching the video! If you are possibly interested in participating in this research, please answer the questions on the following pages as accurately and honestly as possible so that we can determine if the study is a good fit for you. There are no right or wrong answers, and all information you provide will remain confidential.

◯ I am interested in hearing more about the study and agree to complete the following questions to see if I am eligible.

◯ I am not interested in this study and do not wish to complete the screening questions.

SMILE Study

First Name: _____

Last Name: _____

How did you hear about this study? _____

About you (5 questions)

How old are you? _____

Because all of our research materials and the training programs will be provided in English, are you able to read and write in English?

◯ Yes
◯ No

Do you consider yourself to be Black, African American, Hispanic or Latino?

◯ Yes
◯ No

Please select your racial and/or ethnic groups. Select all that apply to you.

☐ American Indian or Alaska Native
☐ Asian
• Black or African American
• Hispanic or Latino
• Native Hawaiian or other Pacific Islander
☐ White

During the research sessions, we will be measuring how your heart rate changes when you shift body positions. Are you able to shift from a seated position to standing? (using a cane or other aid to assist you is fine!)

◯ Yes
◯ No

(Your Health)

The next questions will help determine if you are a good fit for the research study.

Because certain health conditions can affect your heart rate, which we will be measuring during the research study, please provide a response to the following question to the best of your knowledge:

--Have you ever had heart problems other than high blood pressure?

-- Do you have a history of stroke or dementia (severe memory loss)?

--Do you have any movement disorders, such as Parkinson's Disease, or paralysis?"

--Do you have a diagnosis of a genetic disorders such as Down Syndrome or Fragile-X

syndrome? Would your answers to any of these questions be YES?

◯ Yes
◯ No

Because certain medications conditions can affect your heart rate, which we will be measuring during the research study, please provide a response to the following question to the best of your knowledge:

--Are you currently taking any heart medication (other than blood pressure medication)?

--Are you currently taking seizure medications? (These may be used to treat epilepsy or mental health or pain conditions).

(Examples of seizure medications also used for other conditions include lamotrigine, carbamazepine, valproic acid, pregabalin, gabapentin)

--Are you currently taking any opioid medications or supplements? (Examples of opioids include Percocet,

Codeine, Oxycontin, and Kratom) Would your answer to any of these questions be YES?

◯ Yes
◯ No

Because certain psychological or behavioral health conditions can affect your heart rate or can impact the results of the Mindfulness training program, please provide a response to the following question to the best of your knowledge:

--Do you have a diagnosis of autism?

--Do you have a history of serious mental or behavioral health problems requiring a hospital or treatment center stay within the past 12 months?

--Do you have a diagnosis of schizophrenia, psychosis, dissociative disorder, mania/bipolar disorder, major depression, or a personality disorder?

Would your answer to any of these questions be YES?

- ◯ Yes
- ◯ No

Prior experience with mindfulness

Because other practices of Mindfulness may affect our ability to test the effects of our specific version of Mindfulness, please provide a response to the following question:

Over the past 6 months, have you practiced formal mindfulness meditation for more than 15 minutes per day, for 4 or more days per week?

- ◯ Yes
- ◯ No

Appendix 2. Consent Form

REDCap introduction: "You are eligible to participate in the SMILE study! If you are interested in participating, please re-watch the Information Video before reading and signing the Consent document below. [insert link to Consent video]"

University of North Carolina at Chapel Hill
Consent to Participate in a Research Study and Addendum for Unencrypted Communication
Adult Participants

Consent Form Version Date: Version 3, 1/08/2024
IRB Study # 23-0154
Title of Study: Digital health platform (DHP) to deliver Mindfulness as a Stress Management Intervention Leveraging Electronic (SMILE) health records for racial and ethnic populations during the COVID-19 pandemic: Clinical Trial
Principal Investigator: Dr. Susan Gaylord
Principal Investigator Department: Physical Medicine and Rehabilitation
Principal Investigator Phone number: (919) 966-8586
Principal Investigator Email Address: susan_gaylord@med.unc.edu
Funding Source and/or Sponsor: National Institutes of Health (NIH)

Concise Summary

The purpose of this research study is to determine whether a training program can help you feel calmer and more relaxed during times of stress, worry or concern. The program we are testing is called mindfulness. Mindfulness training helps you learn to focus on what is happening here and now without judging your experience or getting lost in guilt about the past or worry about the future. Mindfulness training also includes learning how to treat yourself and others with kindness and compassion. In this research, we are creating mindfulness training programs that are geared specifically towards adults who are African American, Black, Hispanic or Latino. We will be testing 2 versions of an 8-week mindfulness training program—one delivered once weekly online by an instructor with a group of participants, and one delivered through an app. A third group will wait for 12 weeks prior to having access to the app. Results will be evaluated by asking you to complete questionnaires and record your heart rate using an app (i.e., the SMILE app) that is installed on a computer tablet we ship to your home. It may take 1-2 months for your part of the study to start after you join. The active part of the study takes about 3 months, which includes 8 weeks of a mindfulness training program and 4 weeks after the end of the training program. During that time, you will be asked to complete 6 research assessments using the tablet and heart monitor.

If you are interested in learning more about this study, please continue to read below.

What are some general things you should know about research studies?
You are being asked to take part in a research study. To join the study is voluntary.

You may choose not to participate, or you may withdraw your consent to be in the study, for any reason, without penalty.

Research studies are designed to obtain new knowledge. This new information may help people in the future. You may not receive any direct benefit from being in the research study. There also may be risks to being in research studies. Deciding not to be in the study or leaving the study before it is done will not affect your relationship with the researcher, your health care provider, or the University of North Carolina-Chapel Hill. If you are a patient with an illness, you do not have to be in the research study in order to receive health care.

Details about this study are discussed below. It is important that you understand this information so that you can make an informed choice about being in this research study.

You will be able to download a copy of this consent form. You should ask the researchers named above, or staff members who may assist them, any questions you have about this study at any time.

What is the purpose of this study?

For many people, particularly those who are African American, Black, Hispanic or Latino(a/e/x), the COVID pandemic has created an increase in economic, social and physical stress. The purpose of this research study is to see whether a home-based mindfulness training program, adapted for adults who are African American, Black, Hispanic or Latino, can help reduce everyday stress, concern or worry.

How many people will take part in this study?

Approximately 404 people at this institution will take part in this study.

How long will your part in this study last?

Your total participation in the study is approximately 4-5 months. Regardless of your group assignment, you will complete 6 research assessments using the tablet and heart monitor, each lasting 30-60 minutes. If you are assigned to group mindfulness training, you will meet once per week for 75-90 minutes over 8 weeks (about 2 months). If you are assigned to app-based mindfulness training, you will be encouraged to engage with training through the app for 60-75 minutes once per week for 8 weeks. You will also be encouraged to practice what you have learned every day for at least 10 minutes.

What will happen if you take part in the study?

Once you agree to be in the study (by signing the last page of this form), you may have to wait 1 month or two before you are assigned to a group. The researchers will randomly assign you to 1 of 3 groups (such as by flipping a coin) and you will not get to choose into which group you are placed. Once you are assigned to a group, we will mail the equipment that you need to your home. The equipment includes: (1) a computer tablet; and (2) a heart monitor. The tablet and heart monitor will already be set up for you with the SMILE app and you will be provided instructions to practice using the heart monitor. You will be asked to mail the equipment back (postage paid) in the provided packaging at the end of the study.

- ***Explanation of groups***

Group mindfulness training: In this version, you will attend online group sessions (via Zoom), guided by a mindfulness instructor.

App-based mindfulness training: In this version, you will not attend online group sessions. Instead, you will be given video presentations/instructions to complete mindfulness training sessions on your own.

Wait-group: if you are assigned to this group, you will not receive mindfulness training until after you complete your role in the research. At that time, you will be given access to the app-based mindfulness training, but no further research sessions will occur.

- ***Schedule***

The following is a schedule of sessions that will occur once you have been placed into a group. All sessions will be conducted while you are at home, and all participants in all groups will be asked to complete all 6 research assessments with the tablet and heart monitor. You will be compensated for completion of each research assessment. With your permission, we will send you reminders before each research assessment session.

Initial research assessment. This will include questionnaires about your age, marital status, and your health. It will also include wearing a heart monitor while playing a computer game and shifting your position from sitting to standing. This assessment will take approximately 60 minutes.

- If you are assigned to Group mindfulness training, you will meet with the group, including instructors for 60-75 minutes once a week for 8 weeks (about 2 months). You will be asked to complete shorter mindfulness exercises during the week as well.
- If you are assigned to the App-based mindfulness training program, you will be asked to view the videos on the app each week and complete the shorter mindfulness exercises.
- If you are assigned to the Wait group, you will complete the research assessments only.

Every 2 weeks during the 8 weeks (about 2 months) of the mindfulness training you will be asked to complete a short research assessment (about 30 minutes each). The short research assessment will include fewer questionnaires and the same heart monitoring as the initial research assessment.

At the end of the 8 weeks and again 1 month later, you will be asked to complete a slightly longer set of questionnaires along with the heart monitoring. These last research assessments will take approximately 45 minutes each.

- ***Questionnaires***

The questionnaires were selected as they may indicate whether the mindfulness training programs are having a positive effect on your life. The questionnaires include items related to COVID, stress, anxiety, concern, sleep, quality of life, and your impressions of the training programs. You will be provided with the option to skip questions that you do not want to answer. The questionnaires will be included in the SMILE app that is installed on the computer tablet that we will ship to you. You will keep the tablet for the duration of the program and return it in the prepaid shipping box.

If you are assigned to the Group-mindfulness training or the app-based mindfulness training program, you will be asked to complete additional bi-weekly brief questionnaires regarding your daily mindfulness practices. Additionally, at Week 2, you will be asked to complete a brief questionnaire

about your expectancy of the mindfulness program, and at Week 8, you will be asked to complete a brief questionnaire about your satisfaction with the training.

- ***Heart monitoring***

To test the effects of mindfulness training on your body's ability to relax, we would like to record your heart rates during 2 tasks: (1) during a brief computer game; (2) while you shift positions from sitting to standing up. In the SMILE app, you will be provided with instructions for how to use the included heart rate monitor, which will fasten around your chest like a belt. Before you begin each Heart Monitoring, you will be asked about your current medication use, and will be asked to refrain from alcohol (12 hours) and caffeine (3 hours).

What are the possible benefits from being in this study?
Research is designed to benefit society by gaining new knowledge. You may find that your mindfulness training helps you to reduce feelings of stress, tension, and worry.

What are the possible risks or discomforts involved from being in this study?
There is minimal risk to you for participating in the study. All research is subject to a risk of loss of privacy and confidentiality. We try to minimize this risk by including only study ID numbers on anything we collect from research participants.

For all participants, there is a risk that you will experience discomfort using the heart monitor. If you experience discomfort using the heart monitor, we ask that you contact the researchers for guidance.

Emotional discomfort or distress may arise during mindfulness training. This is due to an increased awareness of negative emotions, thoughts or physical sensations. This discomfort usually lasts a very short time and tends to go away entirely with increased mindfulness practice. However, you can contact the researchers and avoid any mindfulness practices leading to more than transient discomfort.

For the group mindfulness sessions, we will use Zoom, a videoconferencing program with end-to-end encryption. Although every reasonable effort is taken, confidentiality during internet communication cannot be guaranteed. It is possible that additional information beyond that collected for research purposes may be taken and used by others not associated with the study. If you are placed in the group mindfulness program, please note that other participants in the group will be able to see and/or hear you on the Zoom video. We ask that you respect the privacy and confidentiality of others in your group. You must agree not to reveal anything you learn from group discussions during the online sessions. To minimize risks, we will provide you with earbuds or earphones. You may also choose to be known by a nickname or made-up name during the training sessions.

What if we learn about new findings or information during the study?
You will be given any new information gained during the course of the study that might affect your willingness to continue your participation.

How will information about you be protected?
Participants will not be identified in any report or publication about this study. We may use de-identified data from this study in future research without additional consent. In addition, the National Institutes of

Health which funds this study requires that the information we collect from the study be shared with other researchers through a secure online research repository. The purpose of this sharing is for people in the future to be able to answer additional research questions. All of your personal identifiers will be removed from the data before being placed in the repository.

Although every effort will be made to keep research records private, there may be times when federal or state law requires the disclosure of such records, including personal information. This is very unlikely, but if disclosure is ever required, UNC-Chapel Hill will take steps allowable by law to protect the privacy of personal information. In some cases, your information in this research study could be reviewed by representatives of the University, research sponsors, or government agencies (for example, the NIH) for purposes such as quality control or safety.

With the permission of everyone in the group, we will record the group mindfulness training sessions (Sessions 1,2,3, and 7 or 8). The purpose of the recording is to ensure that the instructors are teaching mindfulness in the agreed-upon ways. Since the recording will occur via Zoom, a video and an audio recording will be automatically produced. The video recordings will be immediately deleted, and the audio recordings will be stored in a secure online site (Microsoft Teams) until they can be reviewed by the study fidelity monitors. The audio recordings will not be deleted until the end of the study, even if you or the researchers terminate your participation in the study early. You can request that audio recordings be turned off during times when you would like to share something that you do not want to be reviewed by the research team.

Please check one of the following:

_____ok to record me during the group mindfulness training sessions

_____not ok to record me during the group mindfulness training sessions

Alternatively, the group mindfulness sessions may be attended by the study fidelity monitor.

Names (or other identifiable information) will not be used or recorded on any of your data or questionnaire files. You will be assigned an ID number when you enroll in the study, and all files will be labeled with your ID number only. The master file that links name and ID will be stored on a password-protected computer at UNC, and will ONLY be accessible by individuals who are part of the research.

All data files will be stored on a secure cloud or network that can only be accessed by researchers on the study. Electronically-signed consent forms will be stored in REDCap and will only be accessible to UNC researchers who are involved in the research.

What is a Certificate of Confidentiality?

This research is covered by a Certificate of Confidentiality. With this Certificate, the researchers may not disclose or use information, documents or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings in the United States, for example, if there is a court subpoena, unless you have consented for this use.

The Certificate cannot be used to refuse a request for information from personnel of a federal or state agency that is sponsoring the study for auditing or evaluation purposes or for information that must be

disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law, such as mandatory reporting requirements for child abuse or neglect, disabled adult abuse or neglect, communicable diseases, injuries caused by suspected criminal violence, cancer diagnosis or benign brain or central nervous system tumors or other mandatory reporting requirement under applicable law. The Certificate of Confidentiality will not be used if disclosure is for other scientific research, as allowed by federal regulations protecting research subjects or for any purpose you have consented to in this informed consent document.

You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

Appointment reminders

To remind you of appointments, the study team would like to message you by text notifications. You may say "no" to receiving these messages and still participate in this study. If you say "yes", messages may contain personal information about you (e.g., your name, your participation in the SMILE study) and may be sent or received by the university's devices or in a method that is not able to be encrypted (protected) and there is the risk your information could be shared beyond you and the study team. This information may include information such as reminders and notifications to contact the study team.

If you wish to stop receiving unprotected communication from the study team or have lost access to your device, please notify the study team using the study contact information on the first page of this consent form. After the study is complete and all research activities finished, or you withdraw from the study or request to stop receiving unprotected communication, you will no longer receive un-encrypted (un-protected) messages specific to this study.

_____ Yes, I consent to the study team utilizing my cell phone number for text messages for appointment reminders. Please provide your cell-phone # _____

_____ No, I do not consent to receive un-protected communication from the study team.

What will happen if you are injured by this research?

Even though the procedures in the study are low risk, all research involves a chance that something bad might happen to you. If you are hurt, become sick, or develop a reaction from something that was done as part of this study, the researcher will help you get medical care, but the University of North Carolina at Chapel Hill has not set aside funds to pay you for any such injuries, illnesses or reactions, or for the related medical care. Any costs for medical expenses will be billed to you or your insurance company. You may be responsible for any co-payments and your insurance may not cover the costs of study-related injuries.

If you think you have been injured from taking part in this study, call the Principal Investigator at the phone number provided on this consent form. They will let you know what you should do.

By signing this form, you do not give up your right to seek payment or other rights if you are harmed as a result of being in this study.

What if you want to stop before your part in the study is complete?
You can withdraw from this study at any time, without penalty. The investigators also have the right to stop your participation at any time. This could be because you have had an unexpected reaction, or have failed to follow instructions, or because the entire study has been stopped.

If you withdraw or are withdrawn from this study all data collected up until the point of withdrawal will be retained, however no additional information will be collected unless you provide additional written permission for further data collection at the time of your withdrawal.

Will you receive anything for being in this study?
You can receive up to $120 for completing all research sessions ($20 per session for 6 sessions). Payments will be made monthly after the researchers verify completion of data collection after each session.

Will it cost you anything to be in this study?
It will not cost you anything to be in this study.

Who is sponsoring this study?
This research is funded by the National Institutes of Health. This means that the research team is being paid by the sponsor for doing the study. The researchers do not, however, have a direct financial interest with the sponsor or in the final results of the study.

What if you have questions about this study?
You have the right to ask, and have answered, any questions you may have about this research. If you have questions about the study (including payments), complaints, concerns, or if a research-related injury occurs, you should contact the researchers listed on the first page of this form.

A description of this clinical trial will be available on www.clinicaltrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

What if you have questions about your rights as a research participant?
All research on human volunteers is reviewed by a committee that works to protect your rights and welfare. If you have questions or concerns about your rights as a research subject, or if you would like to obtain information or offer input, you may contact the Institutional Review Board at 919-966-3113 or by email to IRB_subjects@unc.edu.

Participant's Agreement:

I have read the information provided above. I have asked all the questions I have at this time. I voluntarily agree to participate in this research study.

_____
Signature of Research Participant

_____
Date

_____
Printed Name of Research Participant

_____
Signature of Research Team Member Obtaining Consent

_____
Date

_____
Printed Name of Research Team Member Obtaining Consent

REDCap message after the e-sign is complete:

"Thank you for consenting to participate in the SMILE Study! You will be contacted by the research team once we are ready to begin your role in the study. It may take up to 2 months before you are contacted."

Appendix 3. Outcome Measures

12.31 GENERALIZED ANXIETY DISORDER SCREENER (GAD-7)

Over the *last 2 weeks*, how often have you been bothered by the following problems?	Not at all	Several Days	More than half the days	Nearly every day
1. Feeling nervous, anxious or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Worrying too much about different things	0	1	2	3
4. Trouble relaxing	0	1	2	3
5. Being so restless that it is hard to sit still	0	1	2	3
6. Becoming easily annoyed or irritated	0	1	2	3
7. Feeling afraid as if something awful might happen	0	1	2	3
	Total Score			
8. If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?	Not difficult at all	Somewhat difficult	Very difficult	Extremely difficult

Scoring and Interpretation:

GAD-7 Score	Provisional Diagnosis
0-7	None
8+	Probable anxiety disorder

References:

- Spitzer RL, Kroenke K, Williams JB, Lowe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Archives of internal medicine. May 22 2006;166(10):1092- 1097. PMID: 16717171
- Kroenke K, Spitzer RL, Williams JB, Monahan PO, Lowe B. Anxiety disorders in primary care: prevalence, impairment, comorbidity, and detection. Annals of internal medicine. Mar 6 2007;146(5):317-325. PMID: 17339617
- Lowe B, Decker O, Muller S, et al. Validation and standardization of the Generalized Anxiety Disorder Screener (GAD-7) in the general population. Medical care. Mar 2008;46(3):266-274. PMID: 1838884

12.32 CONNOR-DAVIDSON RESILIENCE SCALE

*For each item, please mark an "**x**" in the box below that best indicates how much you agree with the following statements as they apply to you over the last **month**. If a particular situation has not occurred recently, answer according to how you think you would have felt.*

Reference: Connor KM, Davidson JR. Development of a new resilience scale: the Connor-Davidson Resilience Scale (CD-RISC). Depress Anxiety. 2003;18(2):76-82. doi: 10.1002/da.10113. PMID: 12964174.

12.33 BRIEF - COPING ORIENTATION TO PROBLEMS EXPERIENCED INVENTORY (BRIEF-COPE)

COPING ORIENTATION TO PROBLEMS EXPERIENCED INVENTORY (BRIEF-COPE) – NOVOPSYCH

The following questions ask how you have sought to cope with a hardship in your life. Read the statements and indicate how much you have been using each coping style.

	I haven't been doing this at all	A little bit	A medium amount	I've been doing this a lot
1. I've been turning to work or other activities to take my mind off things.	**1**	**2**	**3**	**4**
2. I've been concentrating my efforts on doing something about the situation I'm in.	**1**	**2**	**3**	**4**
3. I've been saying to myself "this isn't real".	**1**	**2**	**3**	**4**

4. I've been using alcohol or other drugs to make myself feel better	**1**	**2**	**3**	**4**
5. 5I've been getting emotional support from others.	**1**	**2**	**3**	**4**
6. I've been giving up trying to deal with it.	**1**	**2**	**3**	**4**
7. I've been taking action to try to make the situation better.	**1**	**2**	**3**	**4**
8. I've been refusing to believe that it has happened.	**1**	**2**	**3**	**4**
9. I've been saying things to let my unpleasant feelings escape.	**1**	**2**	**3**	**4**
10. I've been getting help and advice from other people.	**1**	**2**	**3**	**4**
11. I've been using alcohol or other drugs to help me get through it.	**1**	**2**	**3**	**4**
12. I've been trying to see it in a different light, to make it seem more positive.	**1**	**2**	**3**	**4**
13. I've been criticizing myself.	**1**	**2**	**3**	**4**
14. I've been trying to come up with a strategy about what to do.	**1**	**2**	**3**	**4**
15. I've been getting comfort and understanding from someone.	**1**	**2**	**3**	**4**
16. I've been giving up the attempt to cope.	**1**	**2**	**3**	**4**
17. I've been looking for something good in what is happening.	**1**	**2**	**3**	**4**
18. I've been making jokes about it.	**1**	**2**	**3**	**4**
19. I've been making jokes about it.	**1**	**2**	**3**	**4**
20. I've been doing something to think about it less, such as going to movies, watching TV, reading, daydreaming, sleeping, or shopping.	**1**	**2**	**3**	**4**
21. I've been accepting the reality of the fact that it has happened.	**1**	**2**	**3**	**4**
22. I've been expressing my negative feelings.	**1**	**2**	**3**	**4**
23. I've been trying to find comfort in my religion or spiritual beliefs.	**1**	**2**	**3**	**4**
24. I've been trying to get advice or help from other people about what to do.	**1**	**2**	**3**	**4**

25. I've been learning to live with it.	**1**	**2**	**3**	**4**
26. I've been thinking hard about what steps to take.	**1**	**2**	**3**	**4**
27. I've been praying or meditating	**1**	**2**	**3**	**4**
28. I've been making fun of the situation.	**1**	**2**	**3**	**4**

"Scores are presented for three overarching coping styles as average scores (sum of item scores divided by number of items), indicating the degree to which the respondent has been engaging in that coping style.

1. = I haven't been doing this at all
2. = A little bit
3. = A medium amount
4. = I've been doing this a lot

A normative percentile is presented based on data from a non-clinical sample of athletes (Poulus et al., 2020). Interpretation by way of normative percentile helps contextualise results in comparison to typical responses of regular individuals.

In addition, a clinical percentile is presented which compares responses to clients receiving outpatient mental health services (Hegarty & Buchanan, 2021). A percentile of 50, for example, represents an average score for a client in psychological therapy, whereas a percentile of 90 indicates that the respondents scored higher than 90 percent of other individuals in treatment.

During interpretation it is most helpful to look at the pattern of responding across the three subscales. Consistently low scores on all subscales may indicate either:

1. The respondent does not feel they have many stressors to cope with. For example, that life is stress free.
2. A lack of reflective capacity or resistance to disclose personal information.
3. The respondent does not have many coping skills.

- **Problem-Focused Coping** (Items 2, 7, 10, 12, 14, 17, 23, 25)
  Characterised by the facets of active coping, use of informational support, planning, and positive reframing. A high score indicates coping strategies that are aimed at changing the stressful situation. High scores are indicative of psychological strength, grit, a practical approach to problem solving and is predictive of positive outcomes.
- **Emotion-Focused Coping** (Items 5, 9, 13, 15, 18, 20, 21, 22, 24, 26, 27, 28)
  Characterised by the facets of venting, use of emotional support, humour, acceptance, self-blame, and religion. A high score indicates coping strategies that are aiming to regulate emotions associated with the stressful situation. High or low scores are not uniformly associated with psychological health or ill health, but can be used to inform a wider formulation of the respondent's coping styles.
- **Avoidant Coping** (Items 1, 3, 4, 6, 8, 11, 16, 19)
  Characterised by the facets of self-distraction, denial, substance use, and behavioural disengagement. A high score indicate physical or cognitive efforts to disengage from the stressor. Low scores are typically indicative of adaptive coping." See link above for reference.

Carver, C. S. (1997). You want to measure coping but your protocol'too long: Consider the brief cope. International journal of behavioral medicine, 4(1), 92-100.

Dias, C., Cruz, J. F., and Fonseca, A. M. (2012). The relationship between multidimensional competitive anxiety, cognitive threat appraisal, and coping strategies: A multi-sport study. Int. J. Sport Exerc. Psychol.10, 52–65. doi: 10.1080/1612197X.2012.645131

Hegarty, D., Buchanan, B. (2021, June 25). THE VALUE OF NOVOPSYCH DATA – NEW NORMS FOR THE BRIEF-COPE. NovoPsych. *https://novopsych.com.au/news/the-value-of-novopsych-data-new-norms-for-the-brief-cope/*

Eisenberg, S. A., Shen, B. J., Schwarz, E. R., & Mallon, S. (2012). Avoidant coping moderates the association between anxiety and patient-rated physical functioning in heart failure patients. Journal of behavioral medicine, 35(3), 253-261.

Poulus, D., Coulter, T. J., Trotter, M. G., & Polman, R. (2020). Stress and Coping in Esports and the Influence of Mental Toughness. *Frontiers in Psychology*, *11*, 628. https://doi.org/10.3389/fpsyg.2020.00628

12.34 COVID-19 STRESS SCALES

The following asks about various kinds of worries that you might have experienced over the past seven days. In the following statements, we refer to COVID-19 as "the virus".

		0 Not at all 1 Slightly 2 Moderately 3 Very 4 Extremely
Danger	d1	I am worried about catching the virus
Danger	d2	I am worried that basic hygiene (e.g., handwashing) is not enough to keep me safe from the virus
Danger	d3	I am worried that our healthcare system is unable to keep me safe from the virus
Danger	d4	I am worried that I can't keep my family safe from the virus
Danger	d5	I am worried that our healthcare system won't be able to protect my loved ones
Danger	d6	I am worried that social distancing is not enough to keep me safe from the virus
Contamination	c1	I am worried that people around me will infect me with the virus
Contamination	c2	I am worried that if I touched something in a public space (e.g., handrail, door handle), I would catch the virus
Contamination	c3	I am worried that if someone coughed or sneezed near me, I would catch the virus
Contamination	c4	I am worried that I might catch the virus from handling money or using a debit machine
Contamination	c5	I am worried about taking change in cash transactions
Contamination	c6	I am worried that my mail has been contaminated by mail handlers

In the following statements, we refer to COVID-19 as "the virus". Please read each statement and indicate how frequently each problem has been for you during the past seven days.

		0 Never 1 Rarely 2 Sometimes 3 Often 4 Almost always
Traumatic stress	t1	I had trouble sleeping because I worried about the virus
Traumatic stress	t2	I had bad dreams about the virus
Traumatic stress	t3	I thought about the virus when I didn't mean to
Traumatic stress	t4	Disturbing mental images about the virus popped into my mind against my will
Traumatic stress	t5	I had trouble concentrating because I kept thinking about the virus
Traumatic stress	t6	Reminders of the virus caused me to have physical reactions, such as sweating or a pounding heart

Taylor, S., Landry, C. A., Paluszek, M. M., Fergus, T. A., McKay, D. & Asmundson, G. J. G. Development and initial validation of the COVID Stress Scales. Journal of Anxiety Disorders.72 (2020)

12.35 COGNITIVE AND AFFECTIVE MINDFULNESS SCALE-REVISED

Instructions: People have a variety of ways of relating to their thoughts and feelings. For each of the items below, rate how much each of these ways applies to you.

1. It is easy for me to concentrate on what I am doing.
- ◯ 1 - Rarely/Not at all
- ◯ 2 - Sometimes
- ◯ 3 - Often
- ◯ 4 - Almost Always

---

2. I am preoccupied by the future.
- ◯ 1 - Rarely/Not at all
- ◯ 5 - Sometimes
- ◯ 6 - Often
- ◯ 7 - Almost Always

---

3. I can tolerate emotional pain.
- ◯ 1 - Rarely/Not at all
- ◯ 2 - Sometimes
- ◯ 3 - Often
- ◯ 4 - Almost Always

---

4. I can accept things I cannot change.
- ◯ 1 - Rarely/Not at all
- ◯ 2 - Sometimes
- ◯ 3 - Often
- ◯ 4 - Almost Always

---

5. I can usually describe how I feel at the moment in all considerable detail.
- ◯ 1 - Rarely/Not at
- ◯ 2 -Sometime
- ◯ 3 - Often
- ◯ 4 - Almost Always

---

6. I am easily distracted.
- ◯ 1 - Rarely/Not at all
- ◯ 2 - Sometimes
- ◯ 3 - Often
- ◯ 4 - Almost Always

---

7. I am preoccupied by the past.
- ◯ 1 - Rarely/Not at all
- ◯ 2 - Sometimes
- ◯ 3 - Often
- ◯ 4 - Almost Always

---

8. It's easy for me to keep track of my thoughts and all feelings.
- ◯ 1 - Rarely/Not at
- ◯ 2 - Sometim
- ◯ 3 - Often
- ◯ 4 - Almost Always

---

9. I try to notice my thoughts without judging them.
- ◯ 1 - Rarely/Not at all
- ◯ 2 - Sometimes
- ◯ 3 - Often
- ◯ 4 - Almost Always

---

10. I am able to accept the thoughts and feelings I have.

- ◯ 1 - Rarely/Not at all
- ◯ 2 - Sometimes
- ◯ 3 - Often
- ◯ 4 - Almost Always

11. I am able to focus on the present moment.

- ◯ 1 - Rarely/Not at all
- ◯ 5 - Sometimes
- ◯ 6 - Often
- ◯ 7 - Almost Always

12. I am able to pay close attention to one thing for all a long period of time.

- ◯ 1 - Rarely/Not at
- ◯ 2 - Sometim
- ◯ 3 - Often
- ◯ 4 - Almost Always

Feldman, G., Hayes, A., Kumar, S., Greeson, J., & Laurenceau, J. P. (2007). Mindfulness and emotion regulation: The development and initial validation of the Cognitive and Affective Mindfulness ScaleRevised (CAMS-R). Journal of Psychopathology and Behavioral Assessment, 29(3), 177-190. Note that original scale was 12 items, but the original items 2 and 7 were deleted as less useful than the remaining 10.

12.36 POST TRAUMATIC GROWTH INVENTORY

Indicate for each of the statements below the degree to which this change occurred in your life as a result of the crisis/disaster, using the following scale.

0 = I did not experience this change as a result of my crisis.
1 = I experienced this change to a very small degree as a result of my crisis.
2 = I experienced this change to a small degree as a result of my crisis.
3 = I experienced this change to a moderate degree as a result of my crisis.
4 = I experienced this change to a great degree as a result of my crisis.
5 = I experienced this change to a very great degree as a result of my crisis.

Possible Areas of Growth and Change	0	1	2	3	4	5
1. I changed my priorities about what is important in life.						
2. I have a greater appreciation for the value of my own life.						
3. I developed new interests.						
4. I have a greater feeling of self-reliance.						
5. I have a better understanding of spiritual matters.						
6. I more clearly see that I can count on people in times of trouble.						
7. I established a new path for my life.						
8. I have a greater sense of closeness with others.						
9. I am more willing to express my emotions.						
10.I know better that I can handle difficulties.						
11.I am able to do better things with my life.						
12.I am better able to accept the way things work out.						
13.I can better appreciate each day.						
14.New opportunities are available which wouldn't have been otherwise.						

15.I have more compassion for others.						
16.I put more effort into my relationships.						
17.I am more likely to try to change things which need changing.						
*18.*I have a stronger religious faith.						
19.I discovered that I'm stronger than I thought I was.						
20.I learned a great deal about how wonderful people are.						
21.I better accept needing others.						

The Post Traumatic Growth Inventory (PTGI) is scored by adding all the responses. Individual factors are scored by adding responses to items on each factor. Factors are indicated by the Roman numerals after each item below. Items to which factors belong are not listed on the form administered to clients.

PTGI Factors

Factor I: Relating to Others
Factor II: New Possibilities
Factor III: Personal Strength
Factor IV: Spiritual Change
Factor V: Appreciation of Life

1. I changed my priorities about what is important in life. (V)
2. I have a greater appreciation for the value of my own life. (V)
3. I developed new interests. (II)
4. I have a greater feeling of self-reliance. (Ill)
5. I have a better understanding of spiritual matters. (IV)
6. I more clearly see that I can count on people in times of trouble. (I)
7. I established a new path for my life. (II)
8. I have a greater sense of closeness with others. (I)
9. I am more willing to express my emotions. (I)
10. I know better that I can handle difficulties. (III)
11. I am able to do better things with my life. (II)
12. I am better able to accept the way things work out. (Ill)
13. I can better appreciate each day. (V)
14. New opportunities are available which wouldn't have been otherwise. (II)
15. I have more compassion for others. (I)
16. I put more effort into my relationships. (I)
17. I am more likely to try to change things which need changing. (II)
18. I have a stronger religious faith. *(N)*
19. I discovered that I'm stronger than I thought I was. (III)
20. I learned a great deal about how wonderful people are. (I)
21. I better accept needing others. (I)

Calhoun, L. G. & Tedeschi, R. G. (2004). The foundations of posttraumatic growth: New considerations. *Psychological Inquiry. 15*, 93-102. Positive Psychology.com - Posttraumatic Growth (2021)

Tedeschi, R. G. & Calhoun, L G. (1996). The posttraumatic growth inventory: Measuring the positive legacy of trauma. *Journal of Traumatic Stress. 9,* 455-471.

Tedeschi, R. G. (2020). Growth after trauma: Five steps for coming out of a crisis stronger. *Harvard Business Review*. July-August

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12.37 POST-TRAUMATIC STRESS DISORDER CHECKLIST 5 (PCL-5)

Instructions: Below is a list of problems and complaints that people sometimes have in response to stressful life experiences. How much you have been bothered by that problem IN THE LAST MONTH.

		Not at all	A little bit	Moderately	Quite a bit	Extremely
1	Repeated, disturbing, and unwanted memories of the stressful experience?	**0**	**1**	**2**	**3**	**4**
2	Repeated, disturbing dreams of the stressful experience?	**0**	**1**	**2**	**3**	**4**
3	Suddenly feeling or acting as if the stressful experience were actually happening again (as if you were actually back there reliving it)?	**0**	**1**	**2**	**3**	**4**
4	Feeling very upset when something reminded you of the stressful experience?	**0**	**1**	**2**	**3**	**4**
5	Having strong physical reactions when something reminded you of the stressful experience (for example, heart pounding, trouble breathing, sweating)?	**0**	**1**	**2**	**3**	**4**
6	Avoiding memories, thoughts, or feelings related to the stressful experience?	**0**	**1**	**2**	**3**	**4**
7	Avoiding external reminders of the stressful experience (for example, people, places, conversations, activities, objects, or situations)?	**0**	**1**	**2**	**3**	**4**
8	Trouble remembering important parts of the stressful experience?	**0**	**1**	**2**	**3**	**4**
9	Having strong negative beliefs about yourself, other people, or the world (for example, having thoughts such as: I am bad, there is something seriously wrong with me, no one can be trusted, the world is completely dangerous)?	**0**	**1**	**2**	**3**	**4**
10	Blaming yourself or someone else for the stressful experience or what happened after it?	**0**	**1**	**2**	**3**	**4**
11	Having strong negative feelings such as fear, horror, anger, guilt, or shame?	**0**	**1**	**2**	**3**	**4**
12	Loss of interest in activities that you used to enjoy?	**0**	**1**	**2**	**3**	**4**
13	Feeling distant or cut off from other people?	**0**	**1**	**2**	**3**	**4**
14	Trouble experiencing positive feelings (for example, being unable to feel happiness or have loving feelings for people close to you)?	**0**	**1**	**2**	**3**	**4**
15	Irritable behaviour, angry outbursts, or acting aggressively?	**0**	**1**	**2**	**3**	**4**
16	Taking too many risks or doing things that could cause you harm?	**0**	**1**	**2**	**3**	**4**
17	Being “superalert” or watchful or on guard?	**0**	**1**	**2**	**3**	**4**

18	Feeling jumpy or easily startled?	**0**	**1**	**2**	**3**	**4**
19	Having difficulty concentrating?	**0**	**1**	**2**	**3**	**4**
20	Trouble falling or staying asleep?	**0**	**1**	**2**	**3**	**4**

Scoring the PCL-5 *PTSD Checklist for DSM-5 (PCL-5) - PTSD: National Center for PTSD (va.gov)*

- A total symptom severity score (range - 0-80) can be obtained by summing the scores for each of the 20 items.
- *DSM-5* symptom cluster severity scores can be obtained by summing the scores for the items within a given cluster, i.e., cluster B (items 1-5), cluster C (items 6-7), cluster D (items 8-14), and cluster E (items 15-20).
- Minimum threshold for change is suggested to be 5 points

References for the PCL-5

Weathers, F.W., Litz, B.T., Keane, T.M., Palmieri, P.A., Marx, B.P., & Schnurr, P.P. (2013).The PTSD Checklist for DSM-5 (PCL-5). Scale available from the National Center for PTSD at www.ptsd.va.gov.

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12.38 LEVEL 2—SLEEP DISTURBANCE SF 8B—ADULT*

If the measure is being completed by an informant, what is your relationship with the individual receiving care?

_____

In a typical week, approximately how much time do you spend with the individual receiving care?

_____hours/week

Instructions to patient: On the DSM-5 Level 1 cross-cutting questionnaire that you just completed, you indicated that *during the past 2 weeks* you (the individual receiving care) have been bothered by "problems with sleep that affected your sleep quality over all" at a mild or greater level of severity. The questions below ask about these feelings in more detail and especially how often you (the individual receiving care) have been bothered by a list of symptoms **during the past 7 days. Please respond to each item by marking (✓ or x) one box per row.**

						Clinician Use
In the past SEVEN (7) DAYS....						
	Not at all	**A little bit**	**Somewhat**	**Quite a bit**	**Very much**	
1. My sleep was restless.	❑ 1	❑ 2	❑ 3	❑ 4	❑ 5	
2. I was satisfied with my sleep.	❑ 5	❑ 4	❑ 3	❑ 2	❑ 1	
3. My sleep was refreshing.	❑ 5	❑ 4	❑ 3	❑ 2	❑ 1	
4. I had difficulty falling asleep.	❑ 1	❑ 2	❑ 3	❑ 4	❑ 5	
In the past SEVEN (7) DAYS....						
	Never	**Rarely**	**Sometimes**	**Often**	**Always**	
5. I had trouble staying asleep.	❑ 1	❑ 2	❑ 3	❑ 4	❑ 5	
6. I had trouble sleeping.	❑ 1	❑ 2	❑ 3	❑ 4	❑ 5	
7. I got enough sleep.	❑ 5	❑ 4	❑ 3	❑ 2	❑ 1	
In the past SEVEN (7) DAYS....						
	Very Poor	**Poor**	**Fair**	**Good**	**Very good**	
8. My sleep quality was...	❑ 5	❑ 4	❑ 3	❑ 2	❑ 1	
					Total/Partial Raw Score:	
					Prorated Total Raw Score:	
					T-Score:	

SCORING AND INTERPRETATION

Each item on the measure is rated on a 5-point scale (1=never; 2=rarely; 3=sometimes; 4=often; and 5=always) with a range in score from 8 to 40 with higher scores indicating greater severity of sleep disturbance. The clinician is asked to review the score on each item on the measure during the clinical interview and indicate the raw score for each item in the section provided for "Clinician Use." The raw scores on the 8 items should be summed to obtain a total raw score. Next, the T-score table should be used to identify the T-score associated with the individual's total raw score and the information entered in the T-score row on the measure.

Note: This look-up table works only if all items on the form are answered. If 75% or more of the questions have been answered; you are asked to prorate the raw score and then look up the conversion to T-Score. The formula to prorate the partial raw score to Total Raw Score is:

(Raw sum x number of items on the short form)
Number of items that were actually answered

If the result is a fraction, round to the nearest whole number. For example, if 6 of 8 items were answered and the sum of those 6 responses was 20, the prorated raw score would be 20 X 8/6 = 26.67. The T-score in this example would be that T-score associated with the rounded whole number raw score (in this case 27, for a T-score of 57.3).

The T-scores are interpreted as follows: Less than 55 = None to slight 55.0—59.9 = Mild

60.0—69.9 = Moderate

70 and over = Severe

Note: If more than 25% of the total items on the measure are missing the scores should not be used. Therefore, the individual receiving care (or informant) should be encouraged to complete all of the items on the measure.

Sleep Disturbance 8b
Short Form Conversion Table

Raw Score	T-score	SE*
8	28.9	4.8
9	33.1	3.7
10	35.9	3.3
11	38.0	3.0
12	39.8	2.9
13	41.4	2.8
14	42.9	2.7
15	44.2	2.7
16	45.5	2.6
17	46.7	2.6
18	47.9	2.6
19	49.0	2.6
20	50.1	2.5
21	51.2	2.5
22	52.2	2.5
23	53.3	2.5
24	54.3	2.5
25	55.3	2.5
26	56.3	2.5
27	57.3	2.5
28	58.3	2.5
29	59.4	2.5
30	60.4	2.5
31	61.5	2.5
32	62.6	2.5
33	63.7	2.6
34	64.9	2.6
35	66.1	2.7
36	67.5	2.8
37	69.0	3.0
38	70.8	3.2
39	73.0	3.5
40	76.5	4.4

*SE = Standard Error on T-score metric

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- Yu L., Buysse D.J., Germain A.,et al. **Development of short forms from the PROMIS™ sleep disturbance and sleep-related impairment item banks.** *Behav Sleep Med*. 2012; **10**: 6-24*https://doi.org/10.1080/15402002.2012.636266*

12.39 MENTAL HEALTH QUALITY OF LIFE

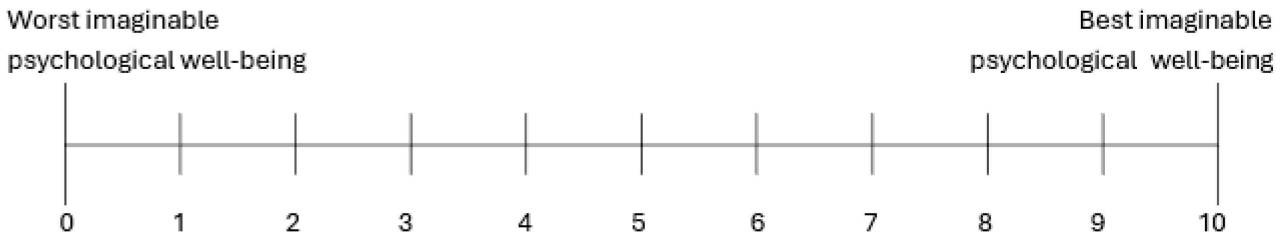
Please indicate below which statements best describe your situation **TODAY** by ticking **ONE** box in each of the seven subjects.

Self-image	
I think very positively about myself	
I think positively about myself	
I think negatively about myself	
I think very negatively about myself	
Independence *For example: freedom of choice, financial, co-decision-making*	
I am very satisfied with my level of independence	
I am satisfied with my level of independence	
I am dissatisfied with my level of independence	
I am very dissatisfied with my level of independence	
Mood	
I do not feel anxious, gloomy, or depressed	
I feel a little anxious, gloomy, or depressed	
I feel anxious, gloomy, or depressed	
I feel very anxious, gloomy, or depressed	
Relationships *For example: partner, children, family, friends*	
I am very satisfied with my relationships	
I am satisfied with my relationships	
I am dissatisfied with my relationships	

I am very dissatisfied with my relationships	
Daily activities *For example: work, study, household, leisure activities*	
I am very satisfied with my daily activities	
I am satisfied with my daily activities	
I am dissatisfied with my daily activities	
I am very dissatisfied with my daily activities	
Physical Health	
I have no physical health problems	
I have some physical health problems	
I have many physical health problems	
I have a great many physical health problems	
Future	
I am very optimistic about my future	
I am optimistic about my future	
I am gloomy about my future	
I am very gloomy about my future	

Psychological Well-being

On the scale below, please indicate with an X how you rate your psychological well-being. 0 represents the worst imaginable psychological well-being, while 10 represents the best imaginable psychological well-being.



van Krugten, F.C.W., Busschbach, J.J.V., Versteegh, M.M. *et al.* The Mental Health Quality of Life Questionnaire (MHQoL): development and first psychometric evaluation of a new measure to assess quality of life in people with mental health problems. *Qual Life Res* **31**, 633–643 (2022). https://doi.org/10.1007/s11136-021-02935-w

12.40 CENTER FOR EPIDEMIOLOGIC STUDIES DEPRESSION SCALE

Below is a list of the ways you might have felt or behaved. Please tell me how often you have felt this way during the **past week**. Circle **one** number on each line.

	During the Past Week			
	Rarely or none of the time (less than 1 day)	Some or a little of the time (1–2 days)	Occasionally or a moderate amount of time (3–4 days)	All of the time (5–7 days)
1. I was bothered by things that usually don't bother me	0	1	2	3
2. I did not feel like eating; my appetite was poor	0	1	2	3
3. I felt that I could not shake off the blues even with help from my family or friends	0	1	2	3
4. I felt I was just as good as other people	0	1	2	3
5. I had trouble keeping my mind on what I was doing	0	1	2	3
6. I felt depressed	0	1	2	3
7. I felt that everything I did was an effort	0	1	2	3
8. I felt hopeful about the future	0	1	2	3
9. I thought my life had been a failure	0	1	2	3
10. I felt fearful	0	1	2	3
11. My sleep was restless	0	1	2	3
12. I was happy	0	1	2	3
13. I talked less than usual	0	1	2	3
14. I felt lonely	0	1	2	3
15. People were unfriendly	0	1	2	3
16. I enjoyed life	0	1	2	3
17. I had crying spells	0	1	2	3
18. I felt sad	0	1	2	3
19. I felt that people dislike me	0	1	2	3
20. I could not get "going"	0	1	2	3

ITEM WEIGHTS	Items 4, 8, 12, & 16	3	2	1	0
	All other items:	0	1	2	3

SCORING: Score is the sum of the 20 item weights. If more than 4 items are missing, do not score the scale. A score of 16 or greater is considered depressed.

References

Lewinsohn, P.M., Seeley, J.R., Roberts, R.E., & Allen, N.B. (1997). Center for Epidemiological Studies-Depression Scale (CES-D) as a screening instrument for depression among community-residing older adults. *Psychology and Aging,* 12, 277- 287.

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12 .41 PERCEIVED STRESS SCALE (PSS-10)

The questions in this scale ask you about your feelings and thoughts during the last month. In each case, you will be asked to indicate how often you felt or thought a certain way.

In the last month, how often have you...

		Never	Almost Never	Sometimes	Fairly Often	Very Often
1	been upset because of something that happened unexpectedly?	**0**	**1**	**2**	**3**	**4**
2	felt that you were unable to control the important things in your life?	**0**	**1**	**2**	**3**	**4**
3	felt nervous and "stressed"?	**0**	**1**	**2**	**3**	**4**
4	felt confident about your ability to handle your personal problems?	**4**	**3**	**2**	**1**	**0**
5	felt that things were going your way?	**4**	**3**	**2**	**1**	**0**
6	found that you could not cope with all the things that you had to do?	**0**	**1**	**2**	**3**	**4**
7	been able to control irritations in your life?	**4**	**3**	**2**	**1**	**0**
8	felt that you were on top of things?	**4**	**3**	**2**	**1**	**0**
9	been angered because of things that were outside of your control?	**0**	**1**	**2**	**3**	**4**
10	felt difficulties were piling up so high that you could not overcome them?	**0**	**1**	**2**	**3**	**4**

- Cohen, S., & Williamson, G. (1988). Perceived stress in a probability sample of the United States. In S. Spacapan & S. Oskamp (Eds.), The social psychology of health: Claremont Symposium on applied social psychology. Newbury Park, CA: Sage.
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12.42 SHORT FORM SURVEY (SF-12)

The SF-12 is a copy-righted general quality of life measure that assesses 8 domains:

1. Limitations in physical activities because of health problems.
2. Limitations in social activities because of physical or emotional problems
3. Limitations in usual role activities because of physical health problems
4. Bodily pain
5. General mental health (psychological distress and well-being)
6. Limitations in usual role activities because of emotional problems
7. Vitality (energy and fatigue)
8. General health perceptions

1. Scoring results in two summary measures:

- Physical Component Summary (PCS)
- Mental Component Summary (MCS).

References:

- Ware Jr, John E., Mark Kosinski, and Susan D. Keller. "A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity." Medical care 34.3 (1996): 220-233.Validation Literature:
- Gandek, Barbara, et al. "Cross-validation of item selection and scoring for the SF-12 Health Survey in nine countries: results from the IQOLA Project." Journal of clinical epidemiology51.11 (1998): 1171-1178.
- Jenkinson, Crispin, et al. "A shorter form health survey: can the SF-12 replicate results from the SF-36 in longitudinal studies?." Journal of Public Health 19.2 (1997): 179-186.Additional Literature:
- Ware, John E., Susan D. Keller, and Mark Kosinski. SF-12: How to score the SF-12 physical and mental health summary scales. Health Institute, New England Medical Center, 1995.

12.43 HEAL Treatment Expectancy v1.0 – Short Form 6a

Please respond to each question or statement by marking one box per row.

		Not at all	A little bit	Somewhat	Quite a bit	Very much
TEX6199	I am confident in this treatment	☐	☐	☐	☐	☐
TEX6132	This treatment will be successful	☐	☐	☐	☐	☐
TEX6082	I feel good about this treatment	☐	☐	☐	☐	☐
TEX6221	I expect good outcomes from this treatment	☐	☐	☐	☐	☐
TEX6160	This treatment is right for me	☐	☐	☐	☐	☐
TEX6220	I value this treatment	☐	☐	☐	☐	☐

Reference

Greco CM, Yu L, Johnston KL, Dodds NE, Morone NE, Glick RM, Schneider MJ, Klem ML, McFarland CE, Lawrence S, Colditz J, Maihoefer CC, Jonas WB, Ryan ND, Pilkonis PA. Measuring nonspecific factors in treatment: item banks that assess the healthcare experience and attitudes from the patient's perspective. Qual Life Res. 2016 Jul;25(7):1625-34. doi: 10.1007/s11136-015-1178-1. Epub 2015 Nov 12. PMID: 26563249; PMCID: PMC4865446.

12.44 CLIENT SATISFACTION QUESTIONNAIRE-INTERNET

Instructions: Please indicate the degree to which you agree with the following statements about the mindfulness training program:

Item	Statement	Strongly disagree	Mildly disagree	Mildly agree	Strongly agree
1	The training I attended was of high quality.	1	2	3	4
2	I received the kind of training I wanted.	1	2	3	4
3	The training has met my needs.	1	2	3	4
4	I would recommend this training to a friend, if he or she were in need of similar help.	1	2	3	4

5	I am satisfied with the amount of help I received through the training.	1	2	3	4
6	The training helped me deal with my problems more effectively.	1	2	3	4
7	Overall, I am satisfied with the training.	1	2	3	4
8	I would come back to this training if I were to need help again.	1	2	3	4

Reference:

Boß L, Lehr D, Reis D, Vis C, Riper H, Berking M, Ebert DD. Reliability and Validity of Assessing User Satisfaction With Web-Based Health Interventions. J Med Internet Res. 2016 Aug 31;18(8):e234. doi: 10.2196/jmir.5952. PMID: 27582341; PMCID: PMC5023944.