Feasibility of Mindfulness Meditation Training and Home Practice in Persons with Spinal Cord Injury: A Pilot Study

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Protocol Title:	Feasibility of Mindfulness Meditation Training and Home Practice in Persons with Spinal Cord Injury: A Pilot Study
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Name and address of the sponsor of the study:	National Institute of Health: National Center for Complimentary and Integrative Health
Population:	People with spinal cord injury
Number of Sites:	Single site
Study Duration:	Three years
Subject Duration:	12 weeks

General Information

The prevalence of debilitating chronic pain in people with spinal cord injury (SCI) ranges from 65-85%. Chronic pain after SCI contributes to anxiety, depression and diminishes the health-related quality of life (QOL). Pharmacological agents such as opioids are the primary therapeutic options to manage chronic pain after SCI, but are ineffective in relieving pain and associated with significant side effects. Mindfulness meditation training (MM) has been shown to improve mental and physical symptoms, including pain-related interference, in many studies of people without SCI who have chronic pain. However, these interventions are typically lengthy, expensive, and require in-person visits with a therapist, making them inaccessible to many people with SCI. Mounting evidence suggests that mobile apps may provide an effective and low-cost way to provide MM. Indeed, one recent study found that internet-based MM training led to reduced pain interference and improved mental health in people with SCI and chronic pain, suggesting app-based MM interventions may have promise in this population. However, this study used an intervention created by the researchers which is not currently available to the public for free, limiting large-scale dissemination. Additionally, the feasibility found in that study may not necessarily translate to that of an existing, publicly available app-based MM intervention among persons with SCI. Similarly, the feasibility of other app-based MM interventions for non-SCI populations may not translate to persons with SCI due to the specific physiological limitations experienced by a person with SCI.

Our multidisciplinary, interinstitutional team of investigators proposes to randomize 60 SCI patients experiencing chronic pain to practice audio-guided MM for **≥ 10 minutes daily for 6 weeks** using the free app "Mindfulness Coach" developed by the Department of Veteran Affairs, or to view health and wellness-related TED talks for **≥ 10 minutes daily for 6 weeks** on the free TED app (active control). Primary outcomes are the **feasibility and acceptability** of proposed interventions in people with SCI and chronic pain. Secondary outcomes include the feasibility of collecting patient-reported outcomes of pain, anxiety, depression, mindfulness, quality of life, stress, fatigue and sleep disturbance.

Given the great need for remotely delivered, low-cost chronic pain management and unique physiological limitations among persons with SCI, it is essential to determine the **feasibility** and **acceptability** of a free, publicly available app-based MM intervention prior to conducting a larger efficacy study. With the emerging use of telemedicine in this COVID-19 era, therapy-focused apps, and remote data collection are becoming increas ar making this line of inquiry

both **timely and innovative**. Furthermore, the app-guided MM intervention ha tial to facilitate self-

management of pain by persons with SCI, as the MM exercises can be practiced at the individual's preferred time and place. *The long-term goal* of this study is to improve pain management and QOL of people with SCI living with chronic pain by identifying affordable and accessible app-guided interventions which can be used as an adjuvant tool after SCI in conjunction with other treatments.

Background Information

Debilitating, persistent pain occurs in 65-85% of persons who sustain spinal cord injury (SCI) and one-third of them categorize their pain as severe.[1-3] Pain has been shown to negatively impact daily life beyond the functional consequences of SCI.[1 4 5]Additionally, chronic pain after SCI is associated with increased risk of developing anxiety, depression, and decreased quality of life (QOL).[6-9] Pharmacological agents, including opioids, anti-depressants, and anti-epileptics, have been recommended by the International Association for the Study of Pain to manage chronic pain after SCI.[10] However, these drugs have been reported to be ineffective in a survey completed by people with SCI.[11] Despite ineffective pain relief and significant side effects such as cognitive dysfunction, addiction, withdrawal, constipation, sedation, and paradoxically worsened pain, all of which may affect participation in life activities and decrease QOL[12-16], opioids and anti-epileptic medications are currently the primary therapeutic options for pain after SCI.[17] This often leaves people to cope on their own outside the healthcare system. There is a clear need for effective non-pharmacological interventions to help people with SCI manage their pain.

Mindfulness meditation (MM) interventions have been identified as an effective pain management strategy.[18-21] Although considerable research has been conducted in other populations, only one study could be found that explored meditation in people with SCI who had chronic pain.[22-28] Furthermore, the majority of these interventions were lengthy and involved considerable face-to-face contact with a therapist, which may not be feasible for persons with SCI who face multiple barriers to accessing healthcare. In recent years, MM interventions delivered online and via mobile devices have proliferated and have been reported to be feasible, acceptable and effective at enhancing self-care practices across a broad range of diagnoses.[29] However, few publicly available online or app-based MM interventions have been the subject of empirical study.[30] Given the unique physiological limitations of an SCI population, determining the feasibility and acceptability of an existing, free, publicly available MM mobile-app to remotely manage chronic pain is essential among people with SCI[31] We propose a randomized clinical pilot study to evaluate the feasibility and acceptability of a mobile app-guided MM intervention compared to active control, i.e., health education (HE) condition in people with SCI who have chronic pain.

The proposed pilot randomized control trial (RCT) will determine the feasibility of a subsequent larger efficacy trial among people with SCI. Our ***long-term goal*** is to improve pain management and QOL of people with SCI living with chronic pain by identifying and evaluating app-guided interventions that are affordable and accessible and can be used as an adjuvant tool in conjunction with other treatments.

Objectives

Aim 1. To evaluate the feasibility of a 6-week app-guided MM intervention (daily sessions of ≥ 10 minutes 6 days/week) and HE condition (viewing daily TED Talks of ≥10 minutes 6 days/week) in people with SCI who have chronic pain. To achieve this aim, we will obtain the following data: a) Recruitment rate: the proportion of eligible people who provide consent, b) Adherence rate: the proportion of participants in MM and HE who complete the minimum recommended minutes (i.e., 60 minutes/week) of the MM or HE intervention; c) Retention rate: the proportion of participants in MM and HE who meet our criteria for adherence and complete the immediate post-intervention and 6-week follow-up assessment.

Aim 2. To examine the acceptability of a 6-week app-guided MM intervention and HE condition in people with SCI who have chronic pain. To achieve this aim, we will measure participant-reported satisfaction with the initial training to orient them to their randomly assigned condition and their satisfaction with the assigned home practice sessions at the end of 6 weeks (post-intervention).

Aim 3. To examine the feasibility of data collection procedures. We will collect measures of mindfulness, pain, anxiety, depression, and QOL and calculate the response rate for each measure at baseline, immediate post-intervention, and 6-week follow-up to evaluate the feasibility and acceptability of collecting these data.

Study Design

An RCT design will be used to evaluate the feasibility and acceptability of a 6-week app-based mindfulness meditation (MM) intervention (Table 1) and health education (HE; active control) condition in people with SCI who have chronic pain.

Study Population

Participants: We will screen potential participants using the following inclusion/exclusion criteria.

Inclusion Criteria: 1) At least 18 years of age, 2) Traumatic SCI of at least 6 months duration, 3) Chronic pain [defined as pain lasting at least 3 months with a pain intensity rating of 4 or higher on a 10-point visual analog scale], and 4) Understand spoken and written English sufficiently to provide informed consent, participate in the intervention and complete study surveys

Exclusion Criteria: 1) Lack of daily access to the internet using a smartphone or smart tablet, 2) Cognitive impairment (determined by their inability to demonstrate comprehension of informed consent by correctly answering 4 out of 5 questions pertaining to the study), 3) Significant visual/hearing impairment that does not allow the use of the MM and/or HE apps' audiovisual presentations, 4) Use of any kind of meditation more than once a week in the last 3 months, 5) Inabilityto provide or obtain an email address for communication with study staff, and 6) Inability to operate the app download or study related survey using a smartphone.

Study Procedures

Recruitment, Screening, and Consent: Participants will be recruited using a range of recruitment mechanisms designed to cast a broad net and reach a diverse sample of people with SCI. We will recruit locally through TIRR Memorial Hermann's (TIRR-MH) outpatient clinic, located in the heart of the Texas Medical Center, and outpatient rehabilitation facilities located throughout the Houston metropolitan area. We will post recruitment flyers at these locations and ask healthcare providers to inform patients by word of mouth, a Website with study information and a QR Code to access the website. We will include study announcements in our institutions/organizations' websites, social media outlets, and newsletters. We will also distribute our recruitment flyer through SCI support groups, the Veterans Association, the Unites Spinal Association groups, centers for independent living, and recreation and advocacy programs that serve people with SCI. In addition, we will recruit utilizing the TIRR-MH's Spinal Cord Injury and Disability (SCIDR) Registry, a national database of over 500 individuals with SCI who previously consented to be informed of future research opportunities. Included in this registry are men and women with traumatic SCI who participated in a recent national survey study on chronic pain, depression, and resilience. This study oversampled women with SCI; thus, we have ample access to women with SCI to ensure they are represented in the proposed pilot study. The team of investigators has an established network of organizations with whom we have successfully recruited in the past, and we are confident in our ability to recruit the proposed sample.

In all of these recruitment activities, we will share our study announcement and/or recruitment flyer and invite those interested to contact the project research coordinator (RC) by email or phone for additional information and/or to schedule a screening interview. Additionally, the recruitment flyer will contain a QR code, which will open a survey that will ask the participant to enter their phone number and email address so that the research coordinator may contact them. The RC will follow up with interested individuals by phone and conduct an initial eligibility screening (i.e., whether they meet the inclusion and exclusion criteria). For eligible individuals, the RC will email them a link to an online informed consent form (via REDCap), review informed consent with the study candidate over the phone, and answer any questions. The RC will then ask individuals to provide written online consent, using a mouse or stylus, in the signature box of the online consent form. The RC will email a copy of the consent form to individuals who provide consent for their personal records. All screening, enrollment, and consent materials and procedures will be reviewed with our community advisors prior to implementation to ensure they are easy to understand and are optimally accessible. For eligible individuals who do not consent to the study, the RC will inquire about and document the reason for refusal and thank them for their time.

Baseline assessment: After consent is obtained, the RC will text and email a RedCap link to complete a 30-minute baseline assessment survey. All measures listed in the Measure section of the proposal will be collected via RedCap except the **International SCI pain basic data subset[96] (ISPBD version 2)** questionnaire**.** This measure is not validated for data collection by survey link and requires administration by a trained professional. Hence, this measure will be administered by the study personnel via phone interview or video conference who will be trained to administer the ISPBD by the PI (Korupolu). Participants who do not complete the survey imme receive an automated email,

followed a phone call (if needed) to assess if the participant experiencing any barriers to completing the survey. In addition to collecting outcome measures (see measures section), we will also collect information on demographic and disability characteristics including age, sex, gender, education level, employment status, marital status, etiology of injury, year of injury, level of injury, and completeness of injury.

Randomization: After completing the baseline assessment, eligible participants will be randomized in a 1:1 ratio to the mindfulness meditation (MM) or health education (HE) (active control) condition using the permuted blocks randomization with varying block sizes. We will stratify based on sex; thus, a random assignment will be conducted separately for men and women to ensure that women and men have comparable representation in the two conditions. Given literature suggesting sex-dependent differences, in pain and recovery from SCI, this randomization strategy reduces the risk that unequal sex distribution will potentially confound feasibility and acceptability ratings. It will also help us evaluate potential sex-related differences in adherence or satisfaction ratings in the two conditions.

Intervention: After randomization, the RC will schedule a 30-minute training session with the participant using Zoom. This one-on-one videoconference will describe their assigned condition (MM or HE), provide guidance on how to engage in the respective condition (i.e., how to download and use respective apps), and instruct participants on the frequency of engagement expected during the 6-week intervention period. We will develop a checklist of training components to ensure consistency in the delivery of the training by the RC.

MM Training and Intervention: Participants randomized to the MM condition will be provided with a unique invitation code that will allow them to download and use the free research version of the Mindfulness Coach app (available for iOS and Android platforms) developed by the Veteran Affairs National Center for PTSD[74]. If the app becomes unavailable on one of these platforms, the participants with that operating system will be provided with a loaner device (iPad) compatible with the Mindfulness Coach Explorer app. The study team/ RA will ship the loaner device to the participants. At the end of the six-week intervention, the RA will provide the return shipping label and request the participant to return the device using the prepaid shipping label. Participants will be informed of their responsibility to handle the loaner device carefully and adhere to the study guidelines for device usage and return.

The Loaner Device will be secured by taking the following measures-

1. Access Restriction: The loaner device provided for this study will be strictly limited to study use only. Access to the device will be restricted to authorized study personnel and participants involved in the research.
2. Apple Care+ Services: Apple Care+ services will be utilized to protect the loaner device from loss, damage, or failure to return. Apple Care+ covers up to two incidents annually, safeguarding the device against various risks.

The utilization of access restriction measures and Apple Care+ services aim to minimize potential risks and enhance the overall security of the loaner device throughout the study duration."

Meditation Coach is an iOS- and Android-based app designed to deliver mindfulness training. The app is tailored to users who may be skeptical about meditation practices by providing simple instructions and brief meditation exercises. The app offers written information about mindfulness (e.g., sections on “What is Mindfulness?” and “Benefits of Mindfulness”) as well as 12 audio-guided meditations, with titles such as “Awareness of Breath,” “Awareness of the Body,” or “Mindfulness of Emotional Discomfort,” each lasting 8-13 minutes, with an average length of 10 minutes (Table 1 below). Users can engage in a “training plan” option in the app, which consists of 14 sessions each of which includes short readings about mindfulness and one guided meditation (sessions 1, 7, and 14 also include a self-assessment of the mindfulness experience). Users have the option of bypassing the training program and accessing the full list of 12 guided meditations, which is what participants in the present study will be encouraged to do. The app was developed for broad use, including but not limited to a Veteran population. The app transmits HIPAA compliant de-identified usage data to a secure server using methods approved under the VA’s Technical Reference Model.[97] The investigators will have access to this data in real-time on the VA App Connect dashboard, and will download usage data to our own secure servers monthly. During the initial training, the RC will assist the participant in downloading and using the app, and instruct the participant to select the “Awareness of the Breath” audio-guided meditation (approximately 8 minutes) to practice during the videoconference. The RC will encourage participants to listen to at least one, and ideally two, audio-guided meditation exercises each day for the next six weeks.

Figure 1. Mindfulness Coach App Interface

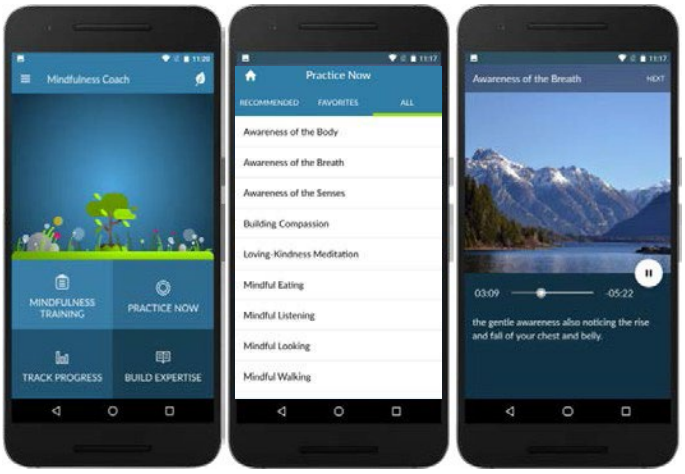
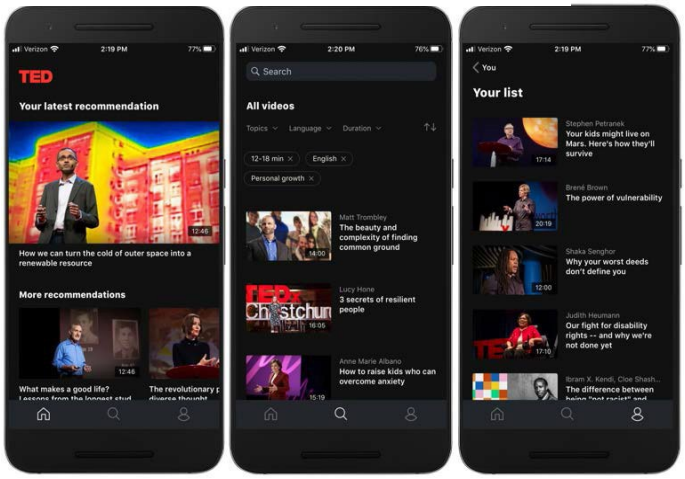


Figure 2. Active Control (TED) App Interface



Finally, the RC will orient participants to the "Track Progress" section of the app. The RC will ask participants to complete weekly logs of their MM practice (based on the record of their use they can view within the app) via a RedCap survery sent via email.[98] This is primarily to ensure a similar burden to participants in the HE condition, as the research team also will have access to app usage data for each participant from the app developers at VA's National Center for PTSD. Thus, compliance with the MM intervention will be assessed in two ways: via self-report in the weekly RedCap assessments and directly from app usage, which the research team can access in real-time on the VA App Connect dashboard. The research team will download this usage data to our own secure servers monthly and will examine the agreement between the two methods of usage data. We will also ask the participants to export the data from the app at the end of the post-intervention, which creates an email from the participant's email address to the study email with an Excel file attached that documents the participant's app usage. The research coordinator (RC) will provide the participants with an instruction guide to assist them in exporting the app usage data.

Active Control Training and Intervention: Active control in this study will be referred as a health education (HE) condition. Participants randomized to HE will be asked to download and use the free TED Talk app (available for iOS and Android platforms). Prior to the training, the RC will create a TED Talk account for each participant with a unique study ID (e.g., "SCIPainStudy01") and study-related password (e.g., "SCIPainStudy01"). Participants' TED Talk accounts used for the study will in no way be connected to any identifying information. Each participant's account will include a list of over 50 TED Talks or health education presentations related to the six broad categories of sleep, nutrition, mood, relationships, chronic pain, and health behaviors. These talks or presentations range from 4 to 18 minutes and were reviewed/selected by the investigator team. The RC will instruct them to watch or listen to these videos for ≥ 10 minutes daily for 6 days per week. The RC will ask participants to complete weekly logs of their TED Talk app use (based on the record or their use they can view within the app) via a RedCap survey sent via email. As it is not possible for the research team to directly assess usage from the TED Talk app, compliance with the HE intervention will be assessed from this self-reported data.

Weekly assessments: Following standard procedures used in previous intervention research projects to minimize attrition, the RC will send all participants an email andtext message at the end of each week of the intervention period to encourage them to maintain their participation and will include a link to a brief (<10 minute) RedCap survey to assess pain intensity and interference (0-10 visual analogue scale), depression (patient Health Questionnaire-2; PHQ-2)[99], and anxiety (Generalized Anxiety Disorder-2; GAD-2)[100] and their daily app use.

Post-Treatment and 6-Week Follow Up Assessment: At the end of the 6-week intervention period and 6-weeks post-intervention period (i.e., 12 weeks post-baseline), the RC will send participants a text message and an email with a link to a 30-minute RedCap survey (see measures section for full list). The **International SCI pain basic data subset[96] (version 2)** questionnaire which requires data collection by phone interview, will be collected separately. If the participant does not complete the post- treatment or follow-up assessments within 5 days of receiving the RedCap link, if participant does not complete the assessment within a few days, the RC will initiate email reminders followed by a phone call to remind them

about completing the assessment.

Post-Study Adherence Barrier Survey: After completion of the study (post 12 weeks, the participants who did not use the app at all or used less than the recommended minutes(<45 minutes), the RC will send the participant a text message and an email with a link to a <less than 5-minute survey to get better understanding and information about the barriers and challenges the participant faced to use the app less than recommended minutes or not at all.

Participant Compensation: Participants will be reimbursed for completing baseline assessment ($25), immediate post-intervention assessment ($25), and 6-week follow up assessment ($25). Additionally, participants will be reimbursed for completing the brief weekly surveys at the end of each week during the intervention period ($10 for each weekly assessment completed).

Community Advisory Board Involvement: To ensure this program of research is in line with the needs and priorities of individuals living with SCI-related chronic pain, we have assembled a panel of individuals with SCI and chronic pain to serve on a Community Advisory Board (CAB) through the duration of the study. The CAB will regularly meet with the study investigators, individually and in group settings, to provide input on each step of the research process (see Timeline). As part of the proposed study's innovation is examining the feasibility/acceptability of a publicly available MM app, the CAB will *not* be providing feedback on the app itself. However, the CAB will provide feedback on all other elements of the study, including beta-testing and providing feedback on the relevance, accessibility, and practicality of materials and methods. Proposed PI (Korupolu) will moderate twice-yearly CAB teleconferences in year 1-2 and one meeting in year 3. In Year 1 meetings we will gather feedback on the assessments (i.e., the online survey accessibility, wording, etc.), recruitment materials (i.e., recruitment flyers and emails), video-conference orientation to conditions, and the initial feedback from the 8 participants run as part of the internally funded pilot trial. The study team will revise the study materials as necessary based on CAB feedback. Year 2 meetings (two meetings) will focus on providing the CAB with updates on recruitment and study progress, and discussion of any challenges. Year 3 meeting will focus on a discussion of study findings related to feasibility (i.e., recruitment, adherence, and retention rates) and acceptability (i.e., responses to the program evaluation questionnaire including responses to open-ended questions asking for suggested revisions), how to revise study procedures for a subsequent efficacy study and where to share/present findings to ensure dissemination that is of direct benefit to the SCI community.

Measures: The **primary outcomes** are feasibility (Aim 1) and acceptability (Aim 2) of the MM intervention and HE condition. **This study will use the National Center for Complimentary and Integrative Health (NCCIH) definition of feasibility and acceptability,** including whether participants can/will adhere to the protocol (recruitment, attend all visits, be able to perform or tolerate the intervention, complete study measures).[101]

Aim 1. To assess the **feasibility of participating** in a 6-week app-guided MM intervention (daily sessions of ≥ 10 minutes 6 days/week) and HE condition (viewing daily health education-related TED Talks of ≥10 minutes 6 days/week) in people with SCI who have chronic pain, we will collect the: a) **recruitment rate**: the proportion of eligible people who provide consent, b) **adherence rate**: the proportion of participants in each group who complete the minimum recommended minutes (i.e., 60 minutes/per week) of using the MM or HE app during the 6 weeks intervention, and c) **retention rate**: the proportion of participants in MM and HE conditions who meet our criteria for adherence and complete the baseline, immediate post-intervention and 6-week follow-up assessments.

Aim 2. To examine the **acceptability of participating** in a 6-week app-guided MM intervention (daily sessions of ≥ 10 minutes 6 days/week) and HE condition (active control), we will collect quantitative and qualitative patient-reported satisfaction with their video-conference training, their assigned app, and their assigned practice sessions. Quantitative satisfaction will be assessed using a program evaluation questionnaire that will assess their satisfaction with the app. This measure also allows participants to provide open-ended comments and suggestions. Additionally, the post-treatment assessment will contain open-ended questions to assess barriers to adherence, to inform strategies and to enhance compliance with the sessions in future studies.

Aim 3. To examine the **feasibility and acceptability of data collection procedures**, we will collect patient-reported measures of pain, depression, anxiety, mindfulness, and QOL and calculate the **r**[illegible]**e**: the proportion of participants in MM and HE conditions who complete the baseline, the immediat[illegible]vention, and the 6-week

follow-up assessments. Collecting these patient-reported outcomes will be determined to be feasible and acceptable if at least 70% of participants complete ≥ 70% of the assessment items.

The following patient reported outcomes will be collected at baseline and the immediate post-treatment and 6-week post-treatment follow up. These measures are included in this pilot trial to determine the feasibility and acceptability of collecting this data. If this pilot trial reveals that participation in the intervention and completion of these measures are feasible and acceptable, these measures will serve as primary outcome measures in a subsequent effectiveness trial.

Pain will be assessed using the **International SCI pain basic data subset[96] (version 2).** This pain measure is one of the CDEs recommended by the National Institute of Neurological Disorders and Stroke (NINDS) for measurement of pain in people with spinal cord injury. This measure collects information on the interference of pain with daily activities, mood and sleep. It also evaluates location, type of pain, the intensity of pain, duration of pain and treatment of pain for 3 worst pain problems reported by a person with SCI.

Pain-related distress will be assessed using the **Chronic Pain Acceptance Questionnaire** (CPAQ-R8), which consists of 8 items assessing acceptance of pain rated on a 0 (never true) to 6 (always true) scale to generate scores on two subscales: activity engagement and pain willingness. The CPAQ has been validated in patients with chronic pain.[107]

Brief Pain Catastrophizing Scale (Brief PCS) measures three aspects of catastrophic cognitions about pain-rumination, magnification, and helplessness. Each question has five response options ranging from 0 (not at all) to 4 (all the time) scale.

Depression will be measured by the eight-item **Patient Health Questionnaire** (PHQ-8),[108 109]which assesses each of the *Diagnostic and Statistical Manual of Mental Disorder-V* depression criteria, with the item assessing for suicidality removed. The PHQ-8 has strong psychometric characteristics.[109] This is a CDE proposed by NINDS for measuring depression in people with SCI.

Anxiety will be measured by the **General Anxiety Disorder-7** (GAD-7),[109 110] which assesses anxiety symptoms on a four-point scale and has strong psychometric characteristics. This is a CDE proposed by NINDS for measuring anxiety in people with SCI.

Mindfulness will be assessed using the **Five Facet Mindfulness Questionnaire-Short Form** (FFMQ-15).[111]The FFMQ-15 is a 15-item measure that consists of five facets of mindfulness: observing, describing, acting with awareness, non-judging of inner experience, and non-reactivity to inner experience. The FFMQ-15 has shown strong psychometric properties in a variety of samples.[112 113]

Quality of Life will be measured using the **SCI-quality of life (QOL): Positive Affect and Well Being-Short Form** (PAWB-SF),[114 115] a 10-item scale developed to measure the impact of SCI on four domains of life, namely physical-medical, physical functioning, emotional, and social health. All PAWB-SF items were taken from the Neuro-QOL PAWB measure.[116] Items were calibrated based on data collected from the SCI sample, and the scores were transformed to the Neuro-QOL metric. This measure is a CDE proposed by NINDS for measuring the quality of life in people with SCI.

Perceived Stress Scale (PSS-4) is a self-reported questionnaire that was designed to measure the degree to which situations in one's life are appraised as stressful. A four-item scale was developed for measuring psychological stress. The PSS-4 determines how unpredictable, uncontrollable, and overloaded respondents find their lives. The scale also includes queries about current levels of experienced stress.

PROMIS Fatigue- Short Form 4a assesses a range of self-reported symptoms, from mild subjective feelings of tiredness to an overwhelming, debilitating, and sustained sense of exhaustion that likely decreases one's ability to execute daily activities and function normally in family or social roles. The fatigue short forms are universal rather than disease-specific. All assess fatigue over the past seven days. Each question has five response options ranging in value from one (not at all) to five (very much).

PROMIS Sleep Disturbance- Short Form 4a assesses self-reported perceptions of sleep quality, sleep depth, and restoration associated with sleep. This includes perceived difficulties and concerns with getting to sleep or staying asleep, as well as perceptions of the adequacy of and satisfaction with sleep. The Sleep Disturbance short form is universal rather than disease-specific. It assesses sleep disturbance over the past seven days. Each question has five response options ranging in value

from five (very poor) to one (very good).

Acceptance and Action Questionnaire (AAQ-2) measure of psychological inflexibility/experiential avoidance. **Acceptance and Action Questionnaire (AAQ-2**) contains 7 items and answers are given on a 7-point scale ranging from 1 (never true) to 7 (always true). High scores on the AAQ-2 are reflective of greater experiential avoidance and immobility, while low scores reflect greater acceptance and action.

Statistics:

Sample size: We plan to enroll a total of n=60 participants and randomize them 1:1 to the MM intervention group or the control group. Following the NCCIH guidance on pilot studies, we base this sample size on practical/budgetary considerations as well as the estimation precision for the feasibility and acceptability outcomes. For the proportions considered, the margin of error (MOE) would not exceed 17.9% when n=30 per arm. For example, when the true proportion is 75%, we could estimate it with an MOE of 15.5%. The planned sample size is also adequate for identifying potential unforeseen issues in the trial flow to facilitate improved planning for the subsequent larger trial.[117]

Analysis Plan: Most of the planned analyses are descriptive due to the pilot nature of the proposed study. Continuous variables will be summarized by mean and SD or median and quartiles as appropriate, and categorical variables will be summarized via frequency and percentages. Variables will be summarized both overall and separately for each randomization arm, following the intention-to-treat principle. We will also conduct subgroup analysis by sex for all outcomes.

Aim 1: The number of individuals screened, consented, and randomized per month will be presented, and we will use the CONSORT diagram to summarize the numbers and reasons related to recruitment, follow-up, and dropout. The main feasibility outcomes include recruitment rate, adherence rate and retention rate. a) Recruitment rate: the proportion of eligible people who provide consent (b) Adherence rate the proportion of participants in MM and HE condition who complete a minimum of 60 minutes/week assigned home practice sessions; (c) Retention rate: the proportion of participants in MM and HE condition who meet our criteria for adherence and complete the outcome assessments at baseline, immediate post-intervention and 6-week follow-up. We will summarize these outcomes by arm using frequency, percentage, and 95% confidence intervals. We will inspect these percentages relative to our feasibility targets. Next, we will obtain summary statistics by arm and by study week for the number of sessions completed, the number of days that the participants complete at least 1 session, and total duration of participation (i.e., time spent reviewing the mediation sessions or the TED talk sessions). These data are available in two data sources (i.e., email surveys and app usage data) for the MM Training arm, leading to two sets of variables. We will analyze both sets as well as their differences. For the active control arm (HE), we will summarize adherence data collected via weekly email surveys.

Aim 2: We will first derive item-specific summary statistics for the multiple-choice items in the program evaluation questionnaire by arm. Next, we will use mean, SD, and quartiles to summarize the total score. Qualitative data from the open-ended items on the program evaluation questionnaire will be analyzed using thematic analysis to identify themes of satisfaction and areas for future improvement.

Aim 3: We will calculate the response rate for each measure at baseline, immediate post-intervention, and 6-week follow up to evaluate feasibility and acceptability of collecting these data. For outcomes that are repeatedly measured, we will estimate the mean trajectory by arm using a (generalized) linear mixed model.

Additionally, descriptive analyses will be conducted for all variables collected. We will derive summary statistics for the patient outcomes by the arm and by time point (baseline, immediately after intervention, and six weeks after the intervention). Following the guidelines for feasibility studies, no statistical comparison or hypothesis testing will be conducted regarding the between-group differences in these measures.

Ethics: Please see the attachment protection of Human subjects document

Data handling and record keeping

Protection of subject privacy: Participants' confidentiality must be considered to ensure participant safety. Regarding

participants' data, the methods of responding to the self-report measures will be online (RedCap) and via phone interviews. Data collected by phone will be entered directly into RedCap by the RC. As such, participants will be reminded to take the battery of measures in a private location to ensure their confidentiality. No identifying data will be attached to the outcome measures. All participants will be assigned a participant ID number to enter on all online surveys to eliminate the need for personal information and allow the research team to match participants' baseline data with their follow-up data. The informed consent forms that include participant contact information will be kept separate to prevent persons not authorized from matching participants to their responses. The participant ID numbers linked with minimal identifying information will be stored on a secure server at the primary institution in a password-protected document that only authorized research team members may access. Once all data collection and data cleaning has been completed, with all participants' measures from each time-point combined, the data file with all identifying information will be destroyed. Finally, should any conflicts of interest be raised regarding participant safety or bias, the research team and community advisory board will meet to review this conflict and determine the appropriate response. Consultation may be used if necessary.

Database protection: Participant usage of the Meditation Coach app will be accessed through the app's dashboard, VA App Connect, which only investigators of the study will be able to access. This will allow us to generate invitation codes so that participants assigned to the MM condition will be able to use the research version of the Mindfulness Coach app and will allow us to download data for users (real-time access) in JSON files. We will use SAS code to extract the data. This data will be stored on our institutions' secured drive. The statistician from UTHealth will be provided access to these files per the institutional access policy. The password-protected deidentified files will be shared among investigators. Data will be stored on secure UTHealth desktops that can only be accessed using an institutional ID and password. A separate linking log with identifiable information will be stored on the institution's secured server. The RedCap survey results and reports are stored on UTHealth RedCap secure servers. A UTHealth email account is needed to log in. Excel spreadsheets used to tabulate and analyze data will be password protected and stored on protected UTHealth desktop computers located in locked project offices. As all data will be collected online (RedCap) or via phone interview and entered directly into RedCap by the research coordinator. Thus, we do not anticipate any usage or storage of any paper documents in this proposed study.

Quality control and assurance

Data quality and management: The investigators and study staff will review all data collection forms on an ongoing basis for data completeness and accuracy as well as protocol compliance. All data except the pain measure will be completed via RedCap by the participants. The pain measure will be collected via phone interview with a research assistant (RA), as this measure is not validated for collection via self-report. The RA will enter this data directly into RedCap during the phone interview. Additionally, while creating RedCap surveys to collect outcome data, we will restrict the entry of specific variables to prevent data entry errors. For example, the minimum age entry will be restricted to 18 per study inclusion criteria (participants' age will have already been verified as over 18 by the RC during the screening phone interview). The survey was carefully designed and tested multiple times to identify any potential issues with data collection with the input from Community Advisory Board. Additionally, we will audit the data for the first two months bi-weekly and then quarterly during the study period to prevent systematic errors.

Publication Plan

We acknowledge the importance of the timely release of scientific information and resources to the broader community. We are also aware of the policies and guidelines established by the NIH regarding the release of research results. Therefore, we plan to present the results generated by these studies at national and international conferences and publish the data in peer-reviewed journals in a timely fashion.

ATTACHMENTS

1. Updated Assessments (RedCap survey)
2. Updated Consent Document
3. Updated screening telephone script
4. Updated MM orientation tutorial slides
5. Updated TED talk orientation tutorial slides
6. Updated flyer