Feasibility of the Mindfulness-Based Stress Reduction Intervention for Black Women Living With HIV

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Sponsor:
NCCIH

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State of Compliance

The trial will be conducted in accordance with the International Conference on Harmonisation Good Clinical Practice (ICH GCP) and the applicable United States (US) Code of Federal Regulations (CFR). The Principal Investigator will monitor for deviations from or changes to the protocol that are not in accordance with approval from the Institutional Review Board (IRB), except where necessary to eliminate an immediate hazard(s) to the trial subjects. All personnel involved in the conduct of this study have completed Human Subjects Protection and ICH GCP Training.

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

Study Synopsis

Title:	Feasibility of the Mindfulness-Based Stress Reduction (MBSR) Intervention for Black Women Living With HIV
Study Description:	Black women living with HIV are at higher risk for experiencing stressful life events which can lead to deleterious health outcomes. MBSR offers a complementary and integrative approach for reducing stress as a mechanism for improving health outcomes. This is a randomized control pilot test aims to explore if MBSR is practical in the target population.
Objectives:	To conduct a 2-armed pilot test of the behavioral intervention compared to the standard of care to assess the feasibility and acceptability of the adapted mindfulness intervention for Black women living with HIV.
Endpoints:	Feasibility of the intervention
Study Population:	Black women living with HIV
Phase:	Stage I: Feasibility and pilot testing
Description of Study Intervention:	The intervention consists of the following: (1) a series of eight weekly session of 2.5 to 3 hours; (2) a silent retreat during the sixth week; (3) daily home assignments including formal and informal mindfulness practices; and (4) didactic presentations on stress and the consequences of stress.
Study Duration:	The estimated study duration of the randomized pilot study (e.g., from IRB approval to screening to finishing the study) is approximately 18 months.
Participant Duration:	The estimated participant duration (e.g., from pre-survey to post-survey) is approximately 3 months.

Schedule of Activities

Procedures	**Pre-screening (consent)**	**Visit 1 (Week 1)**	**Visit 2 (week 2 ± 7 days)**	**Visit 3 (week 3 ± 7 days)**	**Visit 4 (week 4 ± 7 days)**	**Visit 5 (week 5 ± 7 days)**	**Visit 6 (week 6 ± 7 days)**	**Visit 7 (week 7 ± 7 days)**	**Visit 8 (week 8 ± 7 days)**	**Visit 9 (week 8 ± 7 days)**	**Visit 10 (week 9 ± 7 days)**	**Visit 11 (week 10 ± 7 days)**	**Visit 12 (week 11 ± 7 days)**
Eligibility via EMR review	X												
Informed consent	X												
Randomization		X											
Demographics survey		X											
MBSR components													
Orientation			X										
8-weekly sessions				X	X	X	X	X	X		X	X	
Retreat										X			
Post-intervention interview and survey													X

Purpose

The primary purpose is to assess the feasibility and acceptability of an adapted mindfulness intervention for Black women living with HIV. Please note that we are not seeking to determine the efficacy of the study. Slight deviations from the protocol are allowed with the goal of assessing efficacy in a future study.

Background

Black/African American women remain disproportionately burdened by the HIV epidemic in the United States (US), accounting for 70% of new HIV diagnoses among women and 60% of women living with HIV (WLWH). Black WLWH have *mortality rates 17 times higher* than rates observed for White WLWH [1]. Sustained HIV viral load (VL) suppression is vital for improving survival and quality of life (QOL). Two essential *self-care behaviors* for people living with HIV (PLWH) to achieve and sustain VL suppression and improve their health outcomes are adherence to antiretroviral therapy (ART) and adherence to scheduled medical visits [2, 3]. Medical visit adherence is suboptimal among all WLWH, and VL suppression rates among Black WLWH are notably lower compared to White WLWH, 73% compared to 91% [4], and *Black WLWH* are *nearly 3 times more likely* than White women not to achieve VL suppression when prescribed ART [4]. VL suppression among Black women continues to be below the global target, which is to have 90% of those treated to achieve a suppressed VL [4-6]. There is an urgent need for gender-specific and culturally tailored interventions that can help Black WLWH achieve VL suppression.

Failure to achieve VL suppression and suboptimal ART and medical visit adherence among WLWH are associated with experiencing stressful and traumatic life events [7-21]. WLWH are more likely to report experiencing stressful and traumatic life events than both men living with HIV and non-infected women, [20, 22, 23] with Black women having higher rates of traumatic life events than White women [24]. Mindfulness-Based Stress Reduction (MBSR) offers a complementary and integrative approach to reducing stress and the potential for improving adherence to ART and medical visits, ultimately leading to VL suppression. MBSR, developed by Jon Kabat-Zinn [25], has demonstrated efficacy in improving stress management, physical and psychological symptoms [26-29], QOL [30], and coping [27, 31] among breast cancer survivors, female interpersonal violence survivors, and primarily White and non-Southern HIV patient populations. Efficacy data on the effects of MBSR on ART adherence are limited by high baseline adherence rates in published studies [26, 29]. Yet, MBSR has demonstrated efficacy in improving VL suppression in a primarily young male HIV patient population [31]. No studies to date have adapted a MBSR for Black WLWH aiming to reduce stress and improve ART and medical visit adherence. Thus, research is needed to culturally adapt the promising MSBR intervention to enhance HIV health behaviors and outcomes for Black WLWH, which has the potential to attenuate racial and gender disparities in HIV.

Study Aim

Conduct a two-arm randomized pilot test of the adapted intervention compared to usual care among 48 Black WLWH (24/arm) to assess the feasibility and acceptability of the adapted intervention.

Study Design

The study presented in this protocol is a pilot randomized controlled trial with two parallel groups and a primary endpoint of intervention feasibility. Participants will be randomized (1:1) allocation to either the control arm (usual care) or the experimental arm (MBSR).

Study Setting

Participants will be recruited from an academic ambulatory care clinic in the Southern US. The clinic provides comprehensive care to people living with HIV.

Inclusion and Exclusion Criteria

Inclusion Criteria
1) Cisgender females
2) HIV seropositive
3) 18 years of age or older
4) Able to speak English
5) An active patient at the study site
6) at least 1 HIV VL that is >500 copies/mL during the previous 12 months or one missed scheduled medical visit.

Exclusion Criteria
1) Unable to speak English
2) Appearing temporarily impaired (e.g., intoxicated), or
3) Unwilling to or legally able to provide informed consent.

Recruitment Procedures

We will use multiple methods for recruitment. Our primary method of recruitment is via a data query. Research staff will also run a data query of the outpatient HIV clinic EMR to produce a list of patients who meet the eligibility criteria. The list will be provided in the form of an Excel Spreadsheet that includes the patient's name, MRN, next scheduled clinic appointment, viral load and missed visit data for the previous 12 months, and phone number. Study staff will create a list of patients to approach at their clinic appointment to discuss the study. If the upcoming clinic appointments are not scheduled to occur soon, study staff will call potential participants using the recruitment script and ask if they are interested in participating. Once we have exhausted the list, if needed, we can then recruit using flyers or a data query. Once a potential participant calls about the study, a member of the study team will use the screening script to ask questions as well as review the

potential participant's HIV clinical data (CD4 and HIV viral load). We requested a partial waiver of authorization for recruitment and screening.

Once eligible has been determined and verbal informed consent has been given. We will randomize women to either the treatment condition (MBSR; n=24) or usual care condition (usual care; n=24). Participants will receive a phone call and or text message reminder 1-2 days prior to the session. If participants are not present at the time of the session, then a member of the research team will contact the participant via phone or text message.

Study Intervention

We recruit and randomize women to either the treatment condition (MBSR; n=24) or usual care condition (usual care; n=24). Participants will be randomized to the intervention or control group using an excel-based randomization algorithm that matched conditions based on age and missed scheduled medical visits. The control group will continue to receive usual care per the HIV treatment guidelines in a team environment. The academic health center's HIV primary care clinic has implemented a team-based model of care in which physicians, nurse practitioners, nurses, social workers, counselors, and nutritionists collaborate to provide high-quality, affordable care to each patient. We decided to use usual care as the control group because previous research has demonstrated that using a matched time and attention group may have non-study effects outside of the intervention that influence outcomes [32, 33]. In addition, the primary goal of this study is to assess the feasibility of MBSR for Black WLWH who are currently receiving evidence-based care. Thus, MBSR will be an addition to usual care, which makes usual care a valid control condition [34]. MBSR sessions received by the treatment group will include an orientation, about 8-weekly sessions, and a retreat. The orientation session will be approximately 3 hours and include an overview of MBSR and mindfulness practice and discussion. Sessions 1-8 will be approximately 2.5 hours and include a brief opening meditation practice, additional meditation practices (e.g., body scan, focused awareness, yoga, etc.), group discussion, and recommendations for home practice. The retreat will be approximately 5 hours on a mutually agreed day between regularly scheduled sessions, and the activities for the retreat include group mindful eating, reviewing previously learned meditation practices, learning new practices, and group discussion. All participants will complete a pre-and post-intervention survey for feasibility purposes, not to determine efficacy or pre/post-intervention changes. This practice is not allowed by NCCIH. The intervention delivery format was changed from face-to-face to videoconferencing because of University COVID policies, and IRB approval was obtained.

Potential Risks Versus Benefits

There are minimal risks associated with this study. We will discuss stressful life events and other potentially sensitive subjects such as personal history of depression and HIV. This may cause emotional or psychological distress, and we want you to tell us if you feel distressed. We can always request a break or stop the study visit, and we can get additional help for you from a clinic social worker, psychologist, or counselor. In addition,

we also ask you to perform mental tests that you may find difficult, uncomfortable, or embarrassing; however, these tests are designed to measure your peak mental abilities. For many individuals, as they want to do their best, it is normal to feel anxious or worried about not doing well on such tests. We just ask that you do your best, but please keep in mind that no one scores perfectly on these tests.

During the group discussions, we will ask you to refrain from using your name during the discussions and not discuss other participants with individuals outside the group. There is a risk that you may accidentally use your name during the session. A member of the research team will remove participants' names from the transcripts.

There are no guaranteed benefits directly to the participant. However, participants may notice improvements in awareness and increased knowledge of mindfulness.

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 or withdraw a participant from the study for the following reasons:

- Significant study intervention non-compliance
- If any serious adverse event (AE) or other medical condition or situation occurs such that continued participation in the study would not be in the best interest of the participant.

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

Lost to Follow-up

A participant will be considered lost to follow-up if she fails to return for two scheduled visits and cannot be contacted by the study staff.

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

- A study staff member will attempt to contact the participant to determine the reason for the missed visit, counsel the participant on the importance of attending scheduled study sessions, 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 a study staff member will make every effort to regain contact with the participant (where possible, up to 3 telephone calls).

- Should the participant continue to be unreachable, she will be considered to have withdrawn from the study with a primary reason of lost to follow-up.

Adverse Events

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

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

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

There is no expectation of any adverse events or outcomes related to participation in this study. Participating in behavioral interventions such as mindfulness interventions is considered minimal risk. All participants will be given access to contact a study team member and advised to report any adverse events to the study team immediately. The study staff members will not specifically ask about adverse events during the study visit or reminder calls. Study staff members will ask participants to share voluntarily the reason for any missed research visits.

The PI or a member of the study team will record death with start dates occurring any time after informed consent is obtained until 30 days after the last day of study participation. All serious adverse events must be reported to the IRB according to regulatory requirements.

Statistical Analysis Plan

We hypothesize that the mindfulness intervention will be feasible among Black women with HIV.

The primary endpoint for this study is feasibility, which will be measured by the feasibility of the intervention measure Field [35], which consists of four items measured on a 5-point scale ranging from "*Completely disagree*" (1) to "*Completely agree*" (5).

Our sample size considerations are based on information obtained by previous studies in terms of sample size for pilot projects [35, 36], successful feasibility studies of medication adherence in HIV patients [37, 38], and successful feasibility studies of MBSR in populations with chronic disease [39, 40]. Given the limited sample size and primary objective of this application, which is to assess the feasibility and acceptability of the adapted intervention in the target population, this study is not powered sufficiently to formally detect significant group differences. We will not use our data to estimate an effect size for a future larger-scale study due to the high degree of uncertainty of estimates from small samples and where multiple measures are examined [35]. However, we will use descriptive statistics to describe sample characteristics. Bivariate analysis will be conducted between groups using measures of effect size (e.g., Cohen's d, d-equivalent, odds ratios, etc.) and 95% confidence intervals around these measures.

Regulatory, Ethical, and Study Oversight Considerations

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

Informed consent is a process that is initiated prior to the individual's agreeing to participate in the study and continues throughout the individual's study participation. Consent forms will be Institutional Review Board (IRB)-approved, and the subject will be asked to read and review the document. The investigator or a member of the research team will explain the research study to the subject and answer any questions that may arise. A verbal explanation will be provided in terms suited to the subject's comprehension of the purposes, procedures, and potential risks of the study and of their rights as research subjects. Subjects will have the opportunity to carefully review the written consent form and ask questions prior to providing verbal consent. The subjects should have the opportunity to discuss the study with their family or surrogates or think about it prior to agreeing to participate. The subject will provide verbal informed consent, which will be witnessed and documented by a member of the study team prior to any procedures being done specifically for the study. Subjects must be informed that participation is voluntary and that they may withdraw from the study at any time, without prejudice. A copy of the informed consent document will be given to the subjects for their records. The rights and welfare of the subjects will be protected by emphasizing to them that the quality of their medical care will not be adversely affected if they decline to participate in this study.

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

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

Representatives of the IRB may inspect all documents and records required to be maintained by the investigator, including but not limited to, medical records (office, clinic, or hospital) and pharmacy records for the subjects in this study. The clinical study site will permit access to such records.

The study subject'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 and/or Institutional policies.

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

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

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

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