Open Access Journal of Clinical Trials

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STUDY PROTOCOL

Evaluation of a Newly Developed Transdiagnostic Cognitive Behavioral Therapy Group to Promote Healthy Aging Among Older People with HIV: Study Protocol for a Pilot Randomized Controlled Trial

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Abstract: In the era of expanded access to effective antiretroviral therapy (ART), the life expectancy of the estimated 1.2 million people with HIV (PWH) in the United States has significantly increased. There is a timely need to develop and evaluate interventions for older PWH to improve their health and functioning. The primary objective of the present work was to describe the pilot trial methodology that aimed to evaluate the feasibility and acceptability of a transdiagnostic cognitive behavioral therapy (CBT) intervention for HIV and Symptom Management – "CHAMP" designed to promote healthy aging by way of decreasing psychological distress, health risk behaviors, and inflammation among older PWH. Ultimately, these data will be used to refine the intervention and study methods, and inform a future efficacy trial.

Keywords: aging, HIV, cognitive behavioral therapy, clinical trials methodology

Introduction

In the era of expanded access to effective antiretroviral therapy (ART), the life expectancy of the estimated 1.2 million people with HIV (PWH) in the United States has significantly increased.[1,2] Long-term HIV infection has incited new public health challenges, as older PWH are disproportionately affected by health complications associated with aging, including multi-morbid chronic diseases (eg, cardiovascular disease, non-AIDS-defining cancers, and type 2 diabetes), and declines in physical and cognitive functioning.[3–5] There is a timely need to develop and evaluate interventions for older PWH to improve and optimize their health and functioning.[6]

Long-term HIV infection, despite the use of effective ART, is associated with chronic immune activation. Immune activation includes elevated levels of circulating cytokines (eg, IL-6)[7,8] that have pleiotropic effects on systemic inflammation,[8] including the release of CRP into the bloodstream.[9,10] Inflammation is associated with incidence of age-related disease and functional decline.[11,12] Thus, older PWH may be disproportionately affected by age-related diseases due to chronic inflammation.

Psychological distress, inclusive of psychological disorders and subthreshold symptoms (eg, general distress, HIV-specific stress, and depressive and anxiety symptoms) is elevated among older PWH[13–16] and results in additional inflammation.[17–19] Specifically, psychological distress activates the immune system, sympathetic nervous system, and hypothalamic–pituitary–adrenal (HPA) axis.[20–24] Consistently, cohort and medical record studies have shown that

Received: 23 December 2023
Accepted: 12 April 2024
Published: 11 June 2024

individuals with a history of psychiatric disorders have significantly higher rates of age-related diseases and early mortality.[25,26]

Health risk behaviors, such as tobacco-smoking, hazardous alcohol consumption, physical inactivity, and poor diet quality have also been associated with age-related diseases, based on changes in circulating and epigenetic inflammatory biomarkers.[27–33] Further, there are bidirectional, and mutually reinforcing associations between health risk behaviors and psychological distress.[34–38] Thus, older PWH who are more likely to experience psychological distress and health risk behaviors may be a subpopulation disproportionately affected by inflammation and age-related health complications. Previous RCTs have found a small but significant decrease in inflammatory biomarkers (IL-6 and CRP) after the introduction of psychological interventions.[39] However, little is known about whether reducing psychological distress and associated health risk behaviors could mitigate the impact of chronic inflammation on age-related disease disparities among older PWH experiencing psychological distress.

There is strong evidence that cognitive behavioral therapy (CBT) effectively reduces psychological distress and improves health behaviors (eg, ART adherence) and outcomes (eg, viral load) in PWH.[40–45] CBT skills include cognitive restructuring (ie, changing maladaptive thinking patterns), activity scheduling, and problem-solving.[46–48] Contemporary CBT skills also include mindfulness (ie, purposively and non-judgmentally attending to the present moment),[49] metacognition (ie, awareness of one's thought process),[50] self-compassion (ie, extending compassion to one's self),[51] personal values, and acceptance (ie, active embracing subjective experiences).[46,47,52] Evidence indicates that traditional and contemporary CBT strategies reduce psychological distress, associated health risk behaviors, and related inflammation.[53] However, we are not aware of any published transdiagnostic CBT interventions designed for older PWH (Figure 1).

The primary objective of the present study was to evaluate the feasibility and acceptability of a transdiagnostic CBT intervention for HIV and Symptom Management – "CHAMP" – compared to an educational control in a sample of older PWH. While our primary outcomes were feasibility and acceptability, we also aimed to explore potential intervention

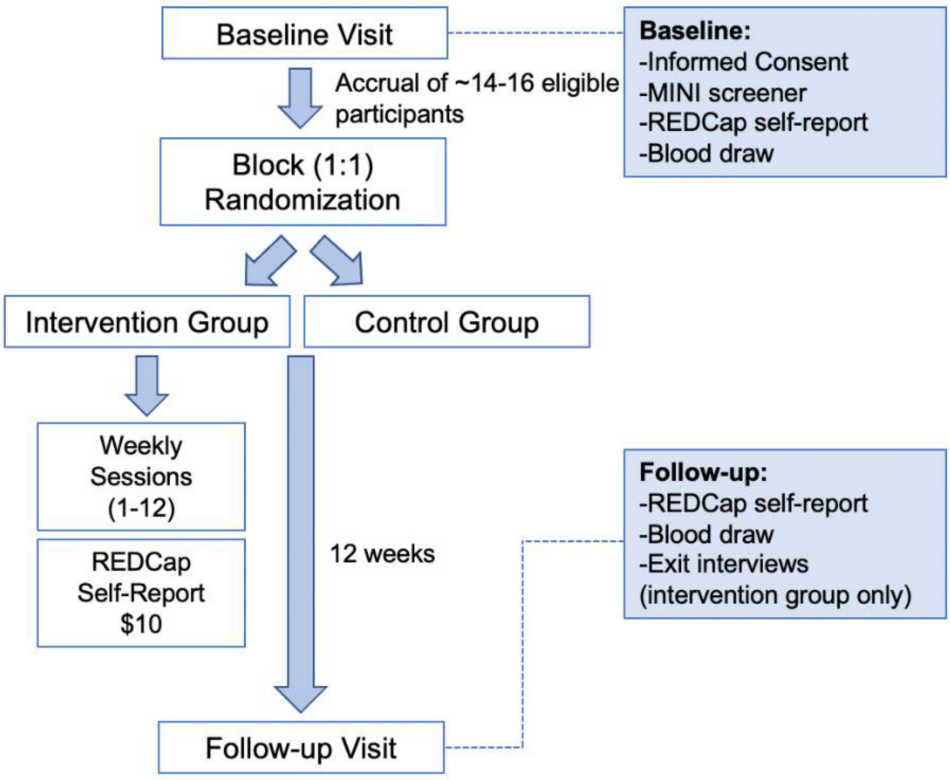

Figure 1 Study Flow Diagram.

effects on psychological distress, engagement in health risk behaviors, and inflammatory biomarkers (IL-6 and CRP). These pilot data were collected to refine the intervention and study methods and inform a future efficacy trial.

Methods

Study Design

Older adults living with HIV ($N = 30$) were recruited and enrolled from the Boston Metropolitan Area to participate in a trial on the effects of a novel, transdiagnostic CBT group intervention ("CHAMP") to promote healthy aging among older PWH by way of teaching skills to reduce psychological distress, and health risk behaviors. Potential participants were screened for initial eligibility on the phone. If initial eligibility criteria were met, participants attended a baseline assessment consisting of self-reported questionnaires (Research Electronic Data Capture [REDCap]),[54] clinician-administered Assessments, intravenous blood draw, and abstraction of medical record data related to HIV and other disease status. After the blood draw, participants were randomized (1:1) to CHAMP or educational control. Participants in CHAMP attended 12 weekly 60-minute group treatment sessions. Participants in the education control condition received a pamphlet on positive health behavior change: medication adherence, abstinence from substances, diet, and physical activity. All participants completed a follow-up assessment 12 weeks post-baseline (see Figure 1).

Specific Aims and Hypotheses

1. Assess the feasibility and acceptability of CHAMP, a novel multi-component group intervention including evidence-based transdiagnostic CBT content, developed for older PWH, and research Methods in a pilot randomized controlled trial (RCT). We hypothesized that CHAMP would meet a-priori benchmarks of feasibility and acceptability (outlined below).
2. Explore changes in a). psychological distress (ie, general distress, HIV-specific stress, and depressive and anxiety symptoms), b). health risk behaviors (ie, tobacco-smoking, alcohol use, sedentary behaviors, and poor diet quality), and c). inflammation biomarkers (ie, interleukin-6 [IL-6] and C-reactive protein [CRP]), in CHAMP versus the education control condition. We hypothesized that CHAMP would be associated with reductions in psychological distress, engagement in health risk behaviors, and inflammation.

Participants

Participants were 31 older adults living with HIV. Participants needed to meet the following eligibility criteria: 1). age ≥50 years, 2). HIV+ with an undetectable test result within the last 12 months (evidenced by medical chart or by participant providing test result); 3). prescribed effective ART (evidenced by medical chart or current ART prescription or pill bottle), 3). able to read and write in English, 5). able to provide informed consent, and 6). deemed psychiatrically stable based on a clinical interview.[55]

Procedures

The study was registered on clinicaltrials.gov (ID: NCT05434741). Enrollment to the RCT began on August 8, 2022, and ended on June 23, 2023. Although assessments and treatment were proposed to be delivered in-person, procedures were modified to allow for remote administration in response to the novel coronavirus pandemic. The trial consisted of a baseline assessment, 1:1 randomization, 12-session intervention period, and follow-up assessment. The Institutional Review Board at Mass General Brigham approved the study design and verbal informed consent process (see Figure 1). This trial complies with the Declaration of Helsinki.

We aimed to recruit up to 42–50 older PWH across three blocks (cohorts) (ie, approximately 14–16 people per block; see Figure 1) via referrals from care providers at the MGH Infectious Diseases (ID) clinic, leveraging a successful recruitment infrastructure. Additionally, we engaged in active recruitment efforts, including posting flyers in the MGH ID and Behavioral Medicine clinics and utilizing community-based recruitment strategies that have been fruitful in recruiting for other clinical intervention studies involving PWH (eg).[56,57] This combined strategy was to ensure optimal intervention group sizes of about 7–8 members and a balanced control group sample size.

Intervention Condition

The CHAMP intervention group was designed based on a clinically delivered group designed by and for people over 50 living with HIV. It was delivered in 12 weekly, one-hour sessions, facilitated by two therapists (at least one of whom was a licensed clinician). The intervention was delivered across three cohorts. It integrated transdiagnostic traditional CBT strategies, including 1). education on the links between thoughts, feeling, and behaviors, 2). cognitive restructuring, 3). behavioral activation, 4). goal-setting and problem-solving with third-wave CBT strategies, including 1). mindfulness (eg, breathing, and self-compassion practices), and 2). acceptance (eg, acknowledging and opening up to uncomfortable sensations). Specific skills were also incorporated to help promote health behavior change, which included information on physical activity and diet recommendations, skills for tracking food intake, and coping strategies for handling urges to use substances (or other unhealthy behaviors; eg, unhealthy eating).

All sessions began with a check-in on how each participant was feeling, completion of homework, and progress towards personal goals. All sessions ended with a review and summary of the session, and homework assignment. While each session specified homework designed to encourage practice of the skill(s) reviewed in session, this was purposively flexible, and participants were encouraged to practice any skill that was helpful for their personal goals. The session topics and corresponding worksheets included: 1). Domains of Healthy Aging 2). Stress and Anxiety 3). Adherence and Engagement in Primary/Preventative Care 4). Depression and Distress 5). Physical Activity 6). Self-Compassion 7). Substance Use 8). Accepting Uncertainty 9). Diet 10). Behavioral Activation and Self-Care 11). Frailty and Memory 12). Wrap-Up and Maintaining Gains (see Table 1).

Adaptation

After the first intervention cohort, several modifications were made to the CHAMP content prior to the implementation of the second intervention cohort. First, session 6, which focused on self-compassion as a strategy to cope with stigma, was revised to instead focus on coping with self-conscious emotions. This decision was made because in the first group, the one-hour session did not allow a sufficient amount of time for each group member to share their deeply personal experiences of stigma, while also allotting time to review self-compassion and practice a mindful self-compassion exercise. Second, session

Table 1 Intervention Sessions

Session	Description of Session
All sessions began with a check-in on how each participant is feeling, completion of homework, and progress towards personal goals. All session ended with a review and summary of the session, and homework assignment. While each session specified homework designed to encourage practice of the skill(s) reviewed in session, this was purposively flexible, and participants were encouraged to practice any skill that was helpful towards their goals.	
1. Domains of Healthy Aging	Discuss the domains of healthy aging and what healthy aging means for each of the participants. Begin creating a goal for participating in the group.
2. Stress and Anxiety	Review common stress and anxiety symptoms. Introduce the Cognitive Behavioral Therapy (CBT) model. Explain how anxiety can get reinforced. Practice relaxation strategies: deep breathing, and progressive muscle relaxation. Discuss practices. Homework: practice relaxation
3. Adherence and Engagement in Primary/Preventative Care	Define treatment and medication adherence. Introduce SMART (specific, measurable, attainable, relevant, and time-bound) goals. Homework: create and carry out at least one SMART goal.
4. Depression and Distress	Review common depressive symptoms. Review the CBT model. Introduce cognitive restructuring. Provide a thought log sheet to track unhelpful thinking. Homework: practice cognitive restructuring using the log.
5. Physical Activity	Discuss what types of physical activity the participants currently or have engaged in previously. Review SMART goals. Introduce problem-solving. Provide a problem-solving worksheet. Homework: practice problem-solving using worksheet.

(*Continued*)

Table 1 (Continued).

Session	Description of Session
6. Self-Compassion	Define self-conscious emotions including guilt, shame, and embarrassment. Introduce self-compassion as a way of coping. Practice mindful self-compassion practice, "soften, soothe, and allow". Homework: practice self-compassion.
7. Substance Use	Discuss ways to understand and change unhealthy behaviors, such as substance use. Define high-risk situations and provide a worksheet to help identify high-risk situations. Define coping plans and provide a worksheet to practice creating a coping plan to manage high-risk situations. Introduce urge surfing as way of coping. Homework: identify high risk situation(s), and create coping plan, or practice urge surfing.
8. Accepting Uncertainty	Review the function of uncomfortable emotions such as fear, anger, and sadness. Discuss the benefit of acknowledging uncomfortable emotions, and situations. Provide a worksheet to practice acknowledging and tolerating uncertainty. Homework: practice acknowledging and tolerating uncertainty and uncomfortable emotions.
9. Diet	Review the Dietary Approaches to Stop Hypertension (DASH) eating plan. Introduce keeping a food records. Review SMART goals and problem-solving skills. Homework: practice food tracking.
10. Behavioral Activation and Self-Care	Introduce behavioral activation. Practice identifying activities that could improve one's mood. Provide a worksheet that details examples of various hobbies, social activities, and sensory experiences. Discuss self-monitoring with use of an activity log. Homework: practice using activity log
11. Frailty and Memory	Discuss what it means to get older for each individual. Discuss the benefits of opening up to age-related changes with "opening up versus struggling" worksheet. Discuss coping with loss and changes in functioning. Homework: practice using the worksheet.
12. Wrap Up and Maintaining Gains	Discuss maintaining gains and relapse prevention strategies. Review session 2–11 skills.

8, which focused on acceptance, was changed to focus on acknowledgement after several group members in the first group reported that the word "acceptance" conveyed approval of the context of psychological distress. Some expressed a reluctance to convey acceptance for unjust experiences or unmet needs (eg, discrimination, unmet subsistence needs such as unstable housing, etc). Additionally, some conveyed that this language was not conducive to thinking about change (eg, behaviors, life circumstances). Lastly, the original group size was intended to be between seven and ten members; however, we elected to start a group once we had five participants. This change allowed for more group discussion, which facilitated trust, social connection, and group cohesion, all of which were considered "active ingredients" of the intervention. Smaller revisions included adding more images to the intervention slides used in the session, as well as changing questions during the check-in to allow for group facilitators to better direct the conversation.

Since the second and third intervention cohorts, additional revisions were considered for future iterations of this work. First, the team discussed strategies to improve group attendance. For example, attendance contracts were considered where participants would agree to attend at least 9 of 12 (75%) sessions. Rolling group admission was also considered, such that recruitment, and enrollment would occur continuously throughout the study period. This would mean participants could join at any session and exit the group once they had completed all 12 sessions. This strategy of a rolling group might better allow for the scheduling of makeup sessions, or participants attending previously missed sessions in the next cycle. However, this strategy would require consistent enrollment in future groups. Second, while session 8 was designed to focused on acknowledging both uncomfortable emotions and tolerating uncertainty, the team considered refining this session to focus on emotions and distress tolerance skills to increase clarity for participants.

Education Control Condition

Participants were given an educational pamphlet that reviews health behaviors important to healthy aging. Topics include 1). adherence to medication and medical appointments, 2). low-sodium diet, 3). One hundred and fifty minutes of weekly moderate physical activity, 4). elimination of substance use, including alcohol (available upon request).

Therapist Training and Supervision

The first CHAMP group was facilitated by the principal investigator (PI; AB) and co-investigator (Co-I; JF), both licensed clinical psychologists with expertise in the included evidence-based content. The second and third groups were facilitated by the Co-I (JF), and a practicum student in a master's level mental health counseling program. The student completed weekly trainings to review and practice teaching the CHAMP content via review of the intervention manual and participant facing PowerPoint slides, with the AB and JF prior to the start of the group. During the group, weekly supervision meetings were held to ensure competency and fidelity.

Assessments

Data collection included self-reported questionnaires, clinician administered interviews, and biospecimens (ie, intravenous blood draws).

Screening

Participants were asked to provide standard demographic information (ie, name, contact information, age, sex, race/ethnicity, level of education, etc)., HIV status, current use of antiretroviral medications and viral load status, and comfort with the English language at baseline.

Feasibility

Collected Feasibility data included rates of recruitment and effort required to recruit the sample (eg, number of staff hours), as well as the number of screenings conducted, proportion eligible, proportion who agree to enroll, and attendance patterns. *Feasibility of recruitment*: Enrollment rate of ≥70% of those who are eligible. *Feasibility of assessment*: Completion of ≥75% of scheduled group sessions.

Acceptability

Collected Acceptability was assessed with a satisfaction evaluation survey that has been used with similar samples and includes items such as: "How likely are you to recommend this group to a friend living with HIV?" and "How comfortable were you providing biological data as part of the research study?"

Psychological Distress and Health Risk Behaviors

Exploratory outcomes included measures of general stress (K10[58] and Perceived Stress Scale [PSS]),[59] HIV-specific stress (HIV/AIDS Stress Scale),[60] depressive (Patient Health Questionnaire – 9 [PHQ-9])[61] and anxiety (Generalized Anxiety Disorder – 7 [GAD-7])[62] symptoms, tobacco-smoking (Fagerstrom Test for Nicotine Dependence [FTND]),[63] hazardous alcohol use (Alcohol Use Disorder Identification Test [AUDIT]),[64] physical inactivity (Physical Activity and Sedentary Behavior Questionnaire [PASBQ]),[65] and poor diet (Dietary Risk Assessment [DRA]).[66] Please see associated citations for scoring guides for each measure listed.

There were three points during this study when suicidality was assessed: baseline and follow-up self-report questionnaires inquired about how often participants experience suicidal thoughts (PHQ-9) and suicidal thoughts/attempts related to HIV/AIDS (HIV/AIDS Stress Scale), and the baseline diagnostic interview inquired about lifetime and current suicidality. The REDCap Alerts & Notification feature ensured that the two licensed psychologist investigators (AB and JF) received immediate notice of endorsed suicidality on self-report questionnaires. The clinical research coordinator (CRC) simultaneously reviewed questionnaires in real time. Either the AB or JF completed a real-time risk assessment and evaluated the participant for active suicidality and psychiatric stability. Appropriate steps were protocolized to enable appropriate next steps based on this assessment, including calling 911 or instructing the participant to go to the nearest emergency room if necessary.

Biospecimens

Blood samples were collected to explore inflammation biomarkers (ie, IL-6 and CRP) at both baseline and follow-up research visits according to the MGH Performance Criteria. The CRC completed an institutionally based phlebotomy training program consisting of two hours of informational videos, a one hour hands-on didactic lesson, and five shadowing hours with a trained coordinator taught by the Division of Clinical Research. After training, the CRC conducted intravenous blood draws in an office laboratory space using two 10 mL collection tubes. The CRC transported the samples to a −80-degree freezer for storage the same day, where they were stored until the samples were sent for testing.

Exit Interviews

Consistent with prior research,[67] all intervention group members completed a 20 minute exit interview between approximately weeks 12 and 16 to examine perceptions of the intervention content, dosage, delivery, and study methods. The exit interviews were conducted by the CRC, and not one of the interventionists to reduce potential response bias. Participants were asked to describe barriers and facilitators to study participation and recommended how the study protocol might be modified to better meet their needs. These interviews were qualitatively analyzed.

Data Analysis

Consistent with the literature on the role and interpretation of pilot data,[68] the focus of this study was to establish feasibility and acceptability of the CHAMP intervention. All planned preliminary analyses were meant to inform the subsequent efficacy trial with the acknowledgement that this pilot RCT was under-powered.

Qualitative Analysis

All qualitative exit interviews were digitally audio-recorded, transcribed verbatim, and transferred to Dedoose. This program is designed for the storage, coding, retrieval, and analysis of qualitative data. We followed the stages of thematic analysis.[69] Two complementary coding schemes were used: 1). *descriptive*, which uses words or short phrases to summarize passages of data and 2). in vivo, in which actual language from participants is used to name concepts and themes. Extensive analytic memos were written after each exit interview was conducted, coded, and throughout the analysis process to reflect on code choices, emergent themes and patterns, and conceptual models. Finally, the data were *themed*, in which the final sets of codes were transformed into more descriptive themes to organize recurrent meanings.

Quantitative Analysis

Given the small sample size, all feasibility and acceptability estimates were imprecise. Summary statistics were median (interquartile range [IQR]) or percentages with exact (Clopper-Pearson) confidence intervals. For *feasibility*, we planned to describe the rate of recruitment, effort required (eg, number of staff hours) to recruit the sample, number of screenings conducted, proportion of eligible screens, proportion of eligible screens who agreed to enroll in the study, and number of sessions attended. For *acceptability*, we planned to describe median (IQR) acceptability ratings.

Exploratory Analyses

We planned to summarize between group differences using median (IQR) for inflammation biomarkers (IL-6 and CRP), general (K10 and PSS)[59] and HIV-specific stress (HIV/AIDS Stress Scale);[60] depressive (PHQ-9)[61] and anxiety (GAD-7)[62] symptoms; tobacco-smoking (FTND);[63] hazardous alcohol use (AUDIT);[64] sedentary behaviors (PASBQ);[65] HIV medication adherence (HIV-ASES); and poor diet (DRA).[66] Statistical significance was assessed using a Wilcoxon Signed-Rank test. For measures with an established clinical cut-off, we compared using a McNemar's test.

Status Update

As of October 5th, 2023, 40 participants were screened for the study; 31 gave verbal consent to participate in the study, completed a baseline assessment, and 30 were randomized; and 27 completed follow-up visits. Our current attrition rate is approximately 13% (three withdrew or were considered lost to follow-up).

Discussion

This protocol paper described the development, Adaptation, and pilot RCT of the CHAMP intervention for PWH who are over 50 years-old. The conception of this trial stemmed from the strong emerging evidence of the utility of transdiagnostic, multicomponent CBT approaches for mitigating age-related health decline[70–72] and the mechanisms (eg, inflammation) underlying these health disparities among OPWH.[73–75] The CHAMP intervention targets inflammation, in part, by focusing on traditional and contemporary transdiagnostic CBT skills (eg, cognitive restructuring, activity scheduling, mindfulness, and self-compassion)[46–48,52] to help reduce psychological distress, and health risk behaviors.[53]

Further, we outlined our research plan for assessing feasibility, acceptability, and preliminary efficacy of the intervention on psychological distress, engagement in health risk behaviors, and inflammation. Specifically, this pilot trial utilized a mixed methods design to reiteratively refine the intervention and pilot methods, aligned with both the ORBIT,[76] and Stage model[77] for intervention development. By reiteratively refining the intervention based on participant feedback from qualitatively analyzed exit interviews, we were enabled to make changes to the intervention content and pilot trial methods to better suit the needs of the study population, and as such, increase the feasibility and acceptability. This, as well as piloting quantitative data analysis plans, are a critical methodological strength for informing the planned efficacy trial of the CHAMP intervention to reduce psychological distress, engagement in health risk behaviors, and inflammation among older PWH.

This protocol may also inform the development and evaluation of other evidence-based psycho-behavioral interventions for OPWH. For example, this protocol produced training tools that could be disseminated for future use. These tools included a refined intervention manual, 12-week slide deck that tailored conventional and contemporary CBT strategies to OPWH, and worksheet-based homework assignments associated with each session. Further, the qualitative feedback that guided the adaptations to the CHAMP program, highlighted important recommendations for future intervention development work. First, behavioral skill-based interventions designed for older PWH should consider ensuring sufficient time for participants to share their emotionally laden experiences (eg, experiences of stigma or discrimination) while preserving sufficient time for the planned evidence-based content and skills. Additionally, for interventions involving people who may disproportionately experience discrimination or stigma and/or have unmet subsistence needs (eg, unstable housing) careful attention to language in relation to "acceptance" is important. Additionally clarity and rephrasing may be necessary to avoid conveying that it is psychologically advantageous to endorse problematic realities. Using alternative language such as "acknowledgement" may more effectively convey the benefits of nonjudgmental awareness of the present moment.

Despite its many strengths, this protocol also needs to be considered in the context of study limitations. These include a relatively small sample size ($n=31$), the inclusion of a non-attention matched control group, and limited control over confounds with respect to biomarker data collection. While the sample size, selection of control group, and biomarker data collection methods are consistent with the intentions of pilot trial data (ie, to establish feasibility and acceptability, rather than efficacy),[68] they do limit the conclusions that we are able to draw from the data. For example, with respect to biomarker data collection, the time of collection was not recorded and participants were not required to fast prior to the appointment, which may impact the results. Given that fasting can result in lower interleukin-6 [IL-6] and C-reactive protein [CRP] levels,[78] this may be important to account for in future studies.

Conclusion

The feasibility, acceptability, and preliminary efficacy findings of this pilot RCT were intended to inform the planned efficacy trial of the CHAMP intervention. The mixed methods design allowed for the continuous adaptation of the intervention materials to the study population's needs. Our outlined adaptations, design, and measurement strategies may also inform other studies involving similar populations and our study materials can be disseminated for future use. In conclusion, the described pilot RCT as well as the CHAMP intervention more broadly have the potential to improve the health and well-being of people aging with HIV.

Acknowledgments

We would like to thank all participants in this study. Additionally, we would like to thank the generous support of the Chong Jin Park Innovative Early Career Pilot Award in Aging and Palliative Care and the Center for Aging and Serious Illness at Massachusetts General Hospital.

Funding

This work was supported by Massachusetts General Hospital's Chong Jin Park Innovative Early Career Pilot Award in Aging and Palliative Care [PI Batchelder] and by the National Heart, Lung, And Blood Institute of the National Institutes of Health under Award Number K23HL167650 (PI Foley).

Disclosure

The authors report no conflicts of interest in this work.

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