Depression and Pain Perseverance Through Empowered Recovery Intervention NCT04091347

IRB Protocol

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1. Abstract

Older African American women experience disproportionate rates of chronic conditions in comparison to other groups. Pain, depressive symptoms, and frailty often co-occur in African American women aging with chronic conditions and this combination can lead to disability and poor quality of life. Addressing pain and depressive symptoms may improve or delay the progression to frailty. To our knowledge there is little work being done in this population to address both pain and depression. The Depression and Pain Perseverance through Empowered Recovery (DAPPER) program is person directed and will consist of 8 nurse visits during which the nurse assesses each participant for pain, depression, and frailty, then implements a manualized individually tailored intervention. The data collection visits, and nurse visits will take virtually. We propose a pilot trial that is a wait list randomized control pilot to test the acceptability and obtain a preliminary effect size for the intervention. We will recruit 64 (≥age 50) African American women who report pain intensity of 3 or higher that interferes with their activities, depressive symptoms lasting more than two weeks, are pre frail or frail, and live in the community/are not institutionalized. The sample will be recruited through the PI's previous study, community recruitment flyers distributed virtually, and word of mouth campaigns. Participants will be randomized into either the intervention or the wait list control group. Once the intervention group has completed their visits, the wait list control group will begin their visits. All participants will be offered the same information and format of nurse visits. The nurses will systematically tailor the content of the visits to the participants' risk profile and goals based on protocols. All participants will be assessed at the start of the study, at 12 weeks, and 24 weeks. The primary outcomes will be pain, depressive symptoms, and frailty status. Other endpoints include goal attainment, stress (cytokines), self-report, self-efficacy, and communication with health care providers. We will also examine the acceptability of the intervention using intervention compliance and one-on-one qualitative interviews. This study will offer either virtual or in person visits based on the preference of the participants.

2. Objectives

The aims of this pilot project are to 1) test the Depression and Pain Perseverance through Empowered Recovery (DAPPER) program for feasibility and acceptability. Specifically, we will 1) test the effect size of DAPPER on pain and depressive symptoms from baseline to 12 weeks (compare intervention to wait list control group) and then at 24 weeks to compare the intervention group to wait list control group once again, 2) estimate preliminary effect sizes for DAPPER in reduction of frailty, and 3) measure effect sizes and feasibility of measuring cytokines.

This study is being supported through funding from the Harold Amos Medical Faculty Program and the Johns Hopkins Older Adults Independence Pepper Center.

3. Background

BACKGROUND AND SIGNIFICANCE

African American women experience higher rates of comorbid conditions and related health consequences than other racial/ethnic groups. [1,2] Among the health consequences that African American women differentially face are pain, depressive symptoms, and frailty. Pain, depressive symptoms, and frailty can occur in a multi-directional cycle.

Pain and Depression

Pain and depression frequently co-occur among older adults with comorbidities and can exacerbate one another; [3]treatment is needed to avert frailty, disability, and mortality. [4, 5] In older adults it can be difficult to treat both pain and depressive symptoms. Older adults are not only at high risk for side effects from pharmacological interventions but also often don't experience full relief from them; [6] hence, it is vital that non-pharmacological mechanisms are developed to treat the pain-depression cycle among older adults.

The intersection of race, gender, and age put older minority women at an increased risk of experiencing undertreated depressive symptoms and pain that can significantly diminish their quality of life. [7, 8] Depressive symptoms among African Americans are more severe than other racial/ethnic groups.[9] Although half of adults with depressive symptoms undergo treatment, only 45% of African Americans with depressive symptoms undergo treatment.[9] African Americans experience higher rates of pain[10,11] and are prescribed pain medications less often than non-Hispanic Whites.[7] Some antidepressant medications, opioids, and NSAIDS can improve depression and decrease pain among older adults/older African Americans; however, they may experience high rates of side effects from these medications.[12]Hence, non-pharmacological pain interventions can be combined with pharmacological interventions[13]to help alleviate pain and depressive symptoms in older African American women.

Frailty and Pain

African American women experience higher rates of disability and frailty than non-Hispanic Whites or African American men. [2,14,15] Among many potential mechanisms underlying this disparity, pain is a factor that is amenable to interventions. [16-18] Frailty increases the perils of experiencing chronic pain; [17,19,20] whereas, chronic pain can contribute to frailty by increasing a risk of decreased activity and gait speed. [21-23] Pain has been identified as a modifiable factor that may improve frailty, if addressed. [24] Pain management in older frail women improves quality of life. [20]

Frailty and Depression

People with depression are at a fourfold increase of experiencing frailty. [25] Increases in both frailty and depression are related to higher odds of nursing home admissions and higher risks for falls. [26] Depressive symptoms may impact activity levels, energy, and nutrition, which all play a role in the etiology of frailty. Depressive symptoms may be a modifiable factor that could have an impact on frailty in older African American women.

Older African American women are crucial to target for intervention not only because of their heightened frailty prevalence, but because they are at higher risk of pain than other racial/ethnic groups and African American men. [10,11,27,28] Additionally, the relationship and outcomes of pain, depressive symptoms, and frailty are exacerbated in older women. [29].

Gaps in the Literature Addressing Pain, Depressive Symptoms, and Frailty

Communication: According to research**,** African Americans experience difficulties in communicating with their health care providers. [30-32] Ghods and colleagues reported that among 109 adults with depressive symptoms, African Americans had less rapport building with their health care providers and less depressive symptom related statements than non-Hispanic White counterparts. [33] In another study, researchers identified that among African American and non-Hispanic Whites with musculoskeletal pain that discussions about pain with their primary health care were sparse and communication about chronic pain was often challenging. [34] Hansson and colleagues (2018) conducted focus groups with health care providers and identified that there were challenges in communication among health care providers and frail older adults. [35]Interventions that include coaching and education strategies that target communication can be effective in improving communication between African Americans and their primary health care providers. [30,36] Studies show that a communication intervention has the potential to improve patients' communication with health care providers [37] and results in better health management. [38]

Non-pharmacological Strategies: There is limited data on culturally appropriate, non-pharmacological strategies to manage depressive symptoms, pain, and frailty within older African American women. To our knowledge non-pharmacological studies targeting pain have not shown significant improvements in African Americans, [39] or showed improvement in depression but had small numbers of African Americans in the sample. [40]

Self- Management Interventions: Self-Management interventions have been successful at addressing conditions such as depression and physical function among older adults. Self-management is defined as the tasks or strategies that are conducted within the living environment that promote health by addressing conditions or symptoms across five core areas: problem solving, decision making, resource utilization, partnerships with healthcare providers, and taking action. A self-management behavioral activation intervention that has effectively treated depressive symptoms in older African Americans is the Get Busy Get Better/Beat the Blues intervention (NIMH, RO1 MH 079814, PI :Laura Gitlin). [41,42] Get Busy Get Better included 208 community dwelling African Americans with depressive symptoms in Philadelphia. The intervention included up to ten visits by licensed social workers over 4 months. [42] The visits included ongoing education about depression and related treatment for depression. [42] The participants did set their own goals (decision making) and the education and treatment (problem solving) assisted them with achieving these goals. Another intervention, the Community Aging in Place, Advancing Better Living for Elders (CAPABLE) study (NIH, R01-AG040100, PI: Sarah L. Szanton), is a person directed tailored program in which participants set their own goals (decision making) and work with occupational therapists and nurses (partnerships with healthcare providers) to use individually tailored strategies (problem solving) to meet their self-selected goals. [43,44]The participants select goals from areas related to physical function as well as pain management, depression, falls, and communication with health care providers. [45]CAPABLE shows improvement in physical function, pain, depression, and disability outcomes. CAPABLE has been replicated in 28 sites in 14 state including statewide in Massachusetts. [43,45] To our knowledge, there have been no tailored self-management person directed interventions that address a group of conditions such as pain, depressive symptoms, and frailty among older African American women.

Development of DAPPER: Given the need for a tailored self-management intervention targeting pain, depressive symptoms, and frailty in older African American women, the gaps in the current literature, and documentation of successful interventions, we have developed an intervention. The proposed intervention is called Depression and Pain Perseverance through Empowered Recovery (DAPPER). We are adapting the Get Busy Get Better intervention by adding components (e.g. nurse visits and person directed goals) from the CAPABLE study for this intervention. We will further develop the intervention through this pilot test. Specifically, we are using the structured visits and visit content guidelines from Get Busy Get Better. We are also using the model of nurse visits from CAPABLE in which the participants are universally assessed,

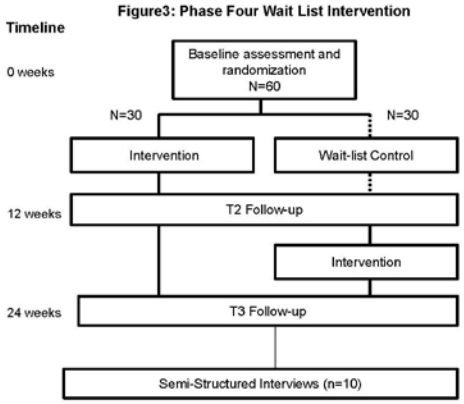
and their goals address the areas that are assessed. In DAPPER, the participants work with nurses to incorporate strategies surrounding communication with health care providers and non-pharmacological strategies that will help them meet their identified health goals surrounding pain and depressive symptoms. Through addressing these goals, we hope to impact frailty outcomes. Given the participants may have different types of pain and severity of depressive symptoms they will need individualized goals and tailored strategies to meet their goals. **The structure of the intervention, number of visits, and content of each visit remains the same across all participants. We have seen this model prove successful in the CAPABLE study.** [43,45]

Investigators:

The PI (Dr. Taylor) has had training in intervention research and has experience recruiting and conducting research in minority women aging with chronic disabling conditions. [46,47] Dr. Szanton (Co Investigator) was the principal investigator for the successful CAPABLE intervention[43], which is being used across the country and in Australia. Dr. Szanton now oversees the translation of CAPABLE and is involved with several other funded intervention clinical trials. Dr. Szanton has served as Dr. Taylor's post-doctoral mentor and now is her formal faculty mentor. Dr. Melissa Hladek (Co Investigator) has expertise in biomarkers and stress. She will conduct all training on the heart rate variability measures and will be analyzing data related to heart variability. She will also assist with data storing, handling, and analysis of cytokines. The data analyst will be a member of the Johns Hopkins School of Nursing Center for Innovative Care in Aging. They will assist with randomization, data management, and data analysis throughout the duration of the study. Dr. Jin Joo will serve as a consultant on the study. She is a psychiatrist with expertise in depression in older African Americans and minorities. We will consult Dr. Joo regarding any participants with severe depression and/or suicidal ideations.

Approach

4.a Theoretical Framework: Self-regulation theory is the theoretical framework for this study. Self-regulation theory involves two tenets: 1) participants manage their response based on their experiences (experiences with pain, depression, and frailty treatments) and knowledge of an event and 2) participants' goals are to maintain comfort and decrease the negative effects of an illness (pain depression and/or frailty) on their lives. [48,49] The intervention is participant centered and participant driven. This means that the participants' experiences and existing knowledge about pain, depressive symptoms, and frailty will drive the goals that they set. For example, a participant may have experienced pain, depression symptoms, and frailty; she is no longer able to go work in her garden. Her goal may be to be able to garden again. This would provide comfort, decrease the effects of these three conditions, and potentially improve her symptoms.



Design overview of the study: The design of the study is outlined in the above figure. The outcomes will determine effect sizes on the intervention's effect on pain and depressive symptoms. Outcomes will be measured at 12 weeks (compare intervention and wait list control group) and at 24 weeks (look at outcomes for wait list control group and outcomes over time for intervention group). Goal attainment will be measured at 12 weeks and 24 weeks. At 24 weeks, we will also conduct virtual semi-structured one on one individual interviews with participants to determine feasibility and acceptability. The intervention group (n=30) will start the study and will receive eight nurse visits that will be focused on decreasing pain, depressive symptoms, and meeting participant selected goals set in these areas. The wait list control group will receive monthly calls by a study team member to ensure their contact information

has not changed. Data collection, nurse visits, and interviews will be completed via Zoom video calls. Zoom is a HIPAA compliant virtual meeting software used for telehealth purposes. The study will include either in person or virtual visits depending on the preference of the participants. The study team completing in person visits have all been fully vaccinated and will wear personal protective equipment at visits. In addition, study team will screen all research participants for symptoms of COVID based on the Johns Hopkins University of Medicine including fever, cough, sore throat, shortness of berath, acute loss of tase or smell, headache, vomiting or nausea, new fatigue or runny nose in the last 72 hours. The study team will reschedule if participants exhibit any of these symptoms at a later date when participants are symptom free for 72 hours or have a negative Covid-19 test.

DAPPER Protocol

Inclusion/Exclusion Criteria

Inclusion criteria: 1) self-reported pain ≥3 out of a 0 -10 scale that has lasted longer than 3 months and keeps them from doing at least one activity that they would like, 2) Self-Identify as African American/Black female 3) non-institutionalized and living in the community Maryland, Virginia or Washington DC area. 4) score a 5 or higher on the PHQ9 (depression measure) at least two times during a two week period (screening call and then at first data collection visit via video), 5) pre-frail (one or two criteria on frailty phenotype) or frail (three or more of the criteria on frailty phenotype), 6) at least one ADL or IADL limitation Exclusion Criteria: 1) Hospitalized > 3 times in the last year, 2) participating in physical therapy, 3) have a terminal diagnosis (<1 year expected survival), 4) ≥ moderate intellectual impairment (5-7 errors) based on the Short Portable Mental Status Questionnaire (SPMSQ), 5) Unable to understand or speak English

We will recruit participants from the PI's Communication Behaviors and Development of Pain and Depression Intervention among Older African American Women (IRB000170533) study. This study consisted of focus groups for the development of the DAPPER intervention. We will only contact participants who agreed to be contacted for future studies. We will contact these participants by phone and ask them if they are interested in participating in the intervention (please see the phone script). If participants agree to this, we will screen them on the phone at this time.

Recruitment will also be conducted via mass marketing. A study team member will identify organizations (e.g. churches, senior high rises) that have established partnerships with the Johns Hopkins School of Nursing Center of Innovative Care in Aging, the Johns Hopkins Center for Health and Aging, and the Johns Hopkins Geriatric Services Frailty registry. The study team will provide each site (Maryland AARP, senior high rises, African American hair salons, etc.) director with flyers. We will send the flyers via email to distribute on social media sites or distribute to mailing lists. We will send messages through Johns Hopkins MyChart for recruiting to patients who have demographics that match the study inclusion criteria. We will not send recruitment messages to individuals who have opted out of receiving them. We will also provide flyers to health care providers of older adults and/or chronic pain patients. We will also use "Word of Mouth" campaigns – volunteers & ambassadors, clinics, and personal contacts. The potential participants will be instructed to contact the research team if they are interested in participating in the research study. A study team member will screen the potential participant and explain the study over the phone. If the individual is eligible a study team member will arrange a video visit to re-screen, explain the study again, ask the participant understanding of the study, and give them an opportunity to ask questions. If the potential subject wishes to participant, the study team member will obtain consent either

by delivering the consents as a hard copy or via DocuSign and conduct the baseline questionnaire. If participants do not do a Docusign consent we will use the following process:

- After the consent designee and participant or LAR review the consent form, the participant or LAR is offered the opportunity to ask any questions and have those questions answered.
- The participant (or LAR) will sign and date/time the paper copy of the informed consent document.
- The consent designee must verify the participant or LAR physically signed the consent document either by viewing via video conference, obtaining a photo of the complete signed consent document; or obtaining verbal confirmation from the participant that she signed the consent form or agreed to participate electronically.
- The signed document is then mailed, emailed, photo/scanned to text or faxed to the consent designee.
- If the signed consent is provided as an electronic copy (dropped off at their place of residence) emailed ,photo/scanned to text, or faxed), the participant or LAR must return the original signed document on their first in person visit or by mail if there is no in person visit.
- If the signed consent form is mailed to the consent designee by the participant or LAR, The IRB-approved consent designee will sign their copy which they possess after the participant has acknowledged signature on their copy. Once the participants original copy is received the consent designee copies will be attached to make a single document.
- If the participant signed consent form is provided immediately by electronic format (emailed, faxed or photo/scanned to text, once received, the IRB-approved consent designee signs, dates/times this informed consent document.

We will provide participants with password protected ZOOM links for all meetings.
We will distribute flyers to the Maryland AARP, senior housing residents, African American hair salons, and on Facebook local group and organization sites. A study team member will obtain necessary permission from administrative staff at all locations before any flyers are distributed via postal mail or email.

We will randomize participants to each group with the following process. 1) Once we find potentially interested participants through the above referral sources, we will telephone screen for eligibility and explain study procedures. 2) If eligible by phone, the research assistant will re-screen, re-explain the study, obtain consent (via DocuSign or hard copy), and conduct the baseline data collection. 4) If participants qualify for the study after this visit, within 48 hours of the baseline interview, we will randomize using a computer-based assignment scheme and communicate the assignment to participants by letter. An employee of the Johns Hopkins Center of Innovative Care in Aging will be unblinded and will complete the randomization for the project. 5) The person assigned to randomize will inform the nurses of the participants' group (intervention or control). 7) The nurses will contact the participant within one week to schedule the first appointment.

The wait list control group will have data collectors schedule a Zoom video visit with them. The same data will be collected for the intervention group. Participants in the wait list control group will not start the DAPPER intervention until the intervention group has completed the study. The wait list control group will receive monthly phone calls to confirm contact information.

Data Collectors: The data collectors have been trained to obtain baseline and outcome measures of each participant. The data collectors will collect baseline and outcome data and are responsible for teaching the participants how to collect saliva samples. The data collectors will call participants to schedule the first Zoom video call. The data collector will call/log on at the mutually agreed time. The data collector will complete the questionnaire booklet with the participant and complete the frailty phenotype measurements

with the participant. If the participants meets the criteria for frailty, pain, and depression, enrollment in the study will continue. Upon completion of the nurses' visits, the data collectors will schedule a final visit with participants.

Research Nurses: An RN is the appropriate professional to conduct the visits because of the training in assessment skills, and knowledge base in physiology, medications, and patient education in pain and depressive symptoms. [50] The nurses have been trained on the protocol. The nurses will call the participants to schedule the first visit. The nurses will meet with participants via Zoom video calls during a mutually agreed upon time. The nurses will work with participants to set goals surrounding pain and depressive symptoms. The goals will be participant driven and documented by the nurse. The nurse will then work with the participant to identify strategies to work on three goals.

Visits

Data Collection Visit One: The data collector will call or do video visit with patient in order to re-screen for criteria to be in the study. If participant meets criteria, the data collector will have participant sign a consent form.
We will be using DocuSign, the Institution's approved and 21 CFR Part 11-compliant software, to obtain a secure electronic signature. Once the IRB approves our consent form(s), we will use the IRB-approved consent form(s) as the base for the DocuSign template. The IRB-approved document will not be altered other than to overlay locations where signatures, initials, dates or other DocuSign fields will be added to create the study-specific DocuSign template.
We will send the consent to the participant via DocuSign, providing a participant-specific code in advance of sending the document via DocuSign, that will be required when the participant accesses and signs the consent. The consent discussion may take place via phone or video conference (e.g. Zoom). Participants will be given adequate time to consider the research study and ask questions prior to signing the consent form. When ready to sign, the participant will enter their code, verifying that the person signing the consent is the person that we spoke with previously, and sign the consent within the DocuSign system. (Note: For studies requiring multiple signatures, e.g. two parental signatures or if a witness is required, all individuals will receive codes in order to sign). Once the participant has electronically signed, the study team member obtaining informed consent will be notified that the electronic form is ready for his or her signature. Once signing is completed by all parties, both the study team and the participant can download the signed consent as a PDF. The study team will also have access to the audit log and the Certificate of Completion. The study team will load the signed consent into Epic.
After the informed consent process is completed, the IRB approved study team member files the consent document in the research record, including a note confirming the consent process. The data collector will verify if the participant has any questions regarding the consent form and verify the participant understands the consent form. The data collector will ensure that the participant reads the consent form and has a copy of the consent form. After the consent is completed, a formal assessment of outcomes will be done. The data collector will explain the process of saliva sample collection to the participant. We will not collect saliva samples from participants outside of Maryland. A kit will be dropped off to the participants with non-contact either at their door or given to front office. We will call and confirm participants receive the kits. The participants will be asked to store samples in their home refrigerator. If there is not a working refrigerator, the participants will be provided with a cooler and ice packs that will be replaced over the two days. When the participant is ready for the saliva sample to be picked up, they will notify us, and it will be picked up using protective gear (gown, gloves, and mask) without contact with participants and stored in the Johns Hopkins School of Nursing lab.

Final Data Collection Visit: At this visit, the data collector will enact the same protocol as at baseline.

Saliva Sample Visits: A member of the research staff will contact the participants to ask them a good time to pick up samples. The research staff member will arrive to participants home to pick up samples. Personnel picking up the samples will notify participants when they are arriving, and participants will place the sample outside the front door once the staff member pulls up or walks up to their home location. The staff member will label the specimens and take them directly to the Johns Hopkins School of Nursing refrigerator. Please see specifics below (laboratory studies) for further information about the collection and storage process of the saliva samples.

Nurse Visit One: The first nurse visit via Zoom video/call will consist of the nurse conducting an assessment of the participant's mental and physical health. The nurse will conduct education on depressive symptoms and pain. A booklet on both depression and pain will be left with the participant (see the intervention manual). This will be emailed or mailed to participants. Next, the nurse will assist the participant to set goals surrounding pain and depressive symptoms, and determination of [51, 52]strategies to be practiced for the next six visits.

After the participants have selected the goals the nurse will work with them to develop a plan of strategies. The strategies that the nurses will offer to work on with the participants will be evidenced-based and specifically target goals surrounding pain and depressive symptoms. For example, if a participant identifies she has arthritic pain the nurse would offer strategies effective for this type of pain such as heat therapy. If the participant agrees to this strategy, the nurse will identify the safest mechanism of heat therapy (e.g. warm gel packs) for the participant. The nurse would identify any contraindications (e.g. diabetic neuropathy). If no contraindications are identified, the nurse would purchase the gel packs using the funding for the study and would mail the packs to the participants. The nurse would teach the participant how to use the gel packs and then use the teach back method with the participant to ensure they know how to use them safely. This would be done via video visit. The participant would be able to call the nurse or PI with any questions or difficulties using any of the strategies. Examples of the strategies we plan to use include heat packs, tai chi exercises, [53,54] breathing exercises[55], and training in communication with health care providers[56,57] surrounding pain and depressive symptoms. The strategies will be individualized to meet the goals of the participants; however, the fidelity of the intervention will be maintained by the nurses being consistent in how the intervention is delivered and the structure of the visits. All participants will also have the same outcome measures.

Nurse Visits Two and Three: The next two visits will consist of the nurse working through each of the strategies. The nurse will discuss strategies with participants via video visits. The nurse will tailor the strategies and teach the participant the strategy at visits two and three.

Nurse Visit Four: At visit four the nurse will observe the participant performing the strategies (e.g. completing exercises in the home), discuss how the strategies are going, and reevaluate goals. Any accommodations or changes will be made at this visit.

Nurse Visit Five: At visit five the nurse will observe the participant doing strategies and assist with any changes.

Nurse Visits Six and Seven: At visits six and seven the nurse will evaluate the participant working on strategies and remind them of their goals.

Nurse Visit Eight: At visit eight the nurse will conduct a final assessment and goals will be assessed at that time. The nurse will reevaluate the goals with participants and ask them if they believe they met their goals, why or why not.

Measurements: We chose measures based on our experiences in community-based trials as well as those that met the following criteria: 1) possess known reliability and validity with older samples; 2) are sensitive to change from an intervention; 3) represent objective as well as subjective indicators of the domains we seek to impact. Finally, we sought to achieve a balance between psychometric quality and practical considerations such as respondent burden. Table 1 shows the instruments that will be used to measure outcomes.

Table 1- Instruments Measuring Main Outcome Variables

Outcomes	Instruments
Cognition (see inclusion/exclusion criteria)	Short Portable Mini Mental Status Exam [58]
Depressive Symptoms	Patient Health Questionnaire 9 and Patient Reported Health Outcomes (PROMIS) 57 [59,60]
Pain	PROMIS Pain Interference, Pain Intensity and Pain Behavior [61,62]
Communication	Patients' Reaction Assessment[63]
Comorbid Conditions	Charlson Comorbidity Index [64]
ADLS/IADLS	Katz [65]
Frailty	Frailty phenotype [66] Frail Scale [67] will be used to measure frailty.
Stress	Perceived Stress Scale [67]
Self-Efficacy	Coping and Self-Efficacy Scale [9]
Readiness to Change	Gitlin and Rose's Readiness to Change Rating System (Gitlin & Rose,)
Social Network Scale	Lubben Social Network Scale
IL6	Saliva Sample
TNF **α**	Saliva Sample
IL8	Saliva Sample
IL-1 ***β***	Saliva Sample
Goal Attainment	Subjective Report

The following instruments and a demographic questionnaire (e.g. age, SES, and education) will be administered to the participants' pre- and post-intervention.

Outcomes:

Depressive Symptoms: During the delivery of this intervention, we will use two instruments the PHQ 9 and the PROMIS. We will use the PHQ 9 to measure depressive symptoms.[59] The PHQ9 includes 9 questions related to the DSM diagnostic criteria for major depression. [60] We will also use the Patient Reported Outcomes Measurement System (PROMIS) 57, which is an 8-item instrument that can be used to measure self-reported negative mood, view of self, and somatic symptoms. Utilizing both measures will

ensure we obtain an in-depth measure of depressive symptoms in our sample. These instruments that are easily transferrable to the clinical setting.[1]

Pain: Pain interference will be measured using the PROMIS Pain interference scale, which consists of six items from the PROMIS short form on pain interference.[61]The scores range from 6-30 with higher scores indicating more pain interference. Pain intensity will also be measured using one item from PROMIS Pain Intensity Instrument.[62] Scores range from 0-10 and higher scores indicate more intensity. The PROMIS pain behavior scale is used to measure self-reported external manifestations of pain.[71] The scores on PROMIS Pain Behaviors scale can range from 7-42 with higher scores indicating more pain behaviors.

Communication: The participants' perceived abilities to initiate communication with their primary health care providers will be measured using the Patients Reactions Assessment (PRA).[63] The PRA is a 15-item instrument used to measure the quality of patients' relationships with their health care providers and includes a subscale on the ability to initiate communication. The subscale on the instrument that measures perceived ability to communicate will be used; scores can range 0-35 with higher scores indicating higher perceived ability to communicate.

Comorbid Conditions: We will measure comorbid conditions with the Charlson Comorbidity Index.[3] The Charlson comorbidity index consists of 17 categories of chronic conditions including two subcategories for diabetes and liver disease. Comorbidities are based on mortality risk and severity of the disease; the scores for each disease range from 1-6. A final Charlson Comorbidity Index score is compiled; scores greater than or equal to five indicate more chronic conditions and increased risk of mortality.

Physical Function: Physical function will be assessed by measuring ADLs Katz ADL and Lawton's IADL measures.[65,73]On Katz's ADLS scores range from 0-6 with 6 indicating full function and a score of 2 or less indicating sever functional impairment. On Lawton's IADL instrument scores range from 0-8 and higher scores indicate better physical function. [74]

Frailty will be assessed by the physical frailty phenotype (includes gait speed, grip strength, BMI, and measures of physical activity and exhaustion).[66] The frailty phenotype is used to determine if a person is robust (score of 0), pre-frail (score of 1 or 2), or frail (score of 3-5). The Frail Scale will be used to measure frailty for virtual data collection visits.[67] The Frail Scale asks self-report questions about fatigue, resistance, ambulation, illnesses, and loss of weight.

Stress will be measured by perceived stress as it often accompanies depression and/or pain. We will measure using the perceived stress scale.[68] The scores can range from 0-40; higher scores indicate more perceived stress.

Self-efficacy is a large part of self-regulation. We are going to measure self-efficacy using the coping and self-efficacy scale.[68] The scores range from 0-26 with higher scores indicating more self-efficacy.

Readiness to change will be used to identify participants' readiness to change. The levels include 1-pre-contemplation, 2-contemplation, 3- preparation, and 4- action and maintenance. This will allow the nurses to identify where participants are on this scale and determine if strategies or goals need to be adjusted or reevaluated based on readiness to change scores.

Social Networks may be related to depressive symptoms and/or stress. We will measure social networks through the Lubben social network scale, which identifies social engagement with both family and friends. The scores can range from 0-60 with higher scores indicating more social engagement.

There is a growing body of literature demonstrating the relationship between inflammatory cytokines with pain, frailty, and depression. For example, inflammatory cytokines may play a very crucial role in pain transmission pathways.[74,75] Studies have shown a link between frailty as well as pain with IL-6 and Tumor Necrosis Factor Alpha.[76-78] The release of pro-inflammatory cytokines can lead to neuro inflammation, which can contribute to depression.[79,80]

We describe the cytokines we will measure below:

Interleukin-8 (IL-8): IL8 is a pro-inflammatory cytokine that is a used for neutrophil recruitment. It may increase with pain and depression.

Interleukin - 1β (IL- *1β*) IL 1β is a pro-inflammatory cytokine that affects cell vial binding cell surface IL-1R1 receptor. It increases neuronal excitability and may increase with pain and frailty.

Interleukin -6 (IL-6)is a pro-inflammatory cytokine that functions in inflammation and maturation of B cells. It is associated with an increase in pain, frailty, and depression.

Tumor Necrosis Factor-Alpha (TNF-α) is a pro-inflammatory cytokine which stimulates the NF-kB signaling pathway resulting in down-stream IL-6 production.[31] It is associated with an increase in pain and frailty.

Goal Attainment will be measured by asking participants if their goals are not met, partially met, or fully met. We will evaluate goal attainment at nurse visit five as well as the final visit (nurse visit 8).

Biomarker Procedures:

Salivary Biomarkers Specimen Collection: At the first data collection visit and last data collection visit, participants will complete saliva collection. Instructions will be given via phone or video. Then the participants will collect the samples themselves. Universal precautions will be used when handling salivary samples. Participants will be instructed to imagine they are chewing a favorite food, slowly moving their jaws in a chewing motion. While doing this, saliva will pool in their mouth. Next, they will gently force the specimen through a short plastic drinking straw into a vial. This passive drool method has been used extensively and has several advantages over a method including volume and less interference with salivary glands.[63] Careful instruction will be given with return demos at the first data collection video/phone visit and reminder instructions at the last data collection visit. Participants will be encouraged to collect specimens the next two days. Each participant will receive a set of pre-labeled, color-coded salivary sample collection tubes, and a similarly color-coded instruction sheet for sample collection times, either via mail, or drop-off at their door using no contact. Samples will be stored in a provided bag in the patient's freezer. Once the participants have completed the samples a study team member will contact them within 48 hours to schedule a pickup of the samples. Specimens will be picked up by the trained study staff using protective equipment including gloves and masks, then transported in a designated cooler to the lab facilities at Johns Hopkins University School of Nursing. Samples for salivary biomarkers will be placed into separate tubes and labeled for freezing at -80°C until batch assayed in duplicate for the respective measurements. Saliva samples will be measured using enzyme immunoassay (EIA) kits from Salimetrics (St. College, PA). A research assistant or the PI will pick up the samples and store in the appropriate freezer at the Johns Hopkins School of Nursing. Samples will be clearly labeled. After all participants have completed each saliva specimen collection (first and last visits) the specimens will be mailed via overnight service to Salimetrics to run in lab.

Commercially available kits will be used for batch assay and each assay will be performed in duplicate. Duplicate assays that demonstrate a coefficient of variation greater than 15% will be reanalyzed. All data

will be de-identified. The sample will be identifiable by a unique generated code. The lab will be blinded and will not have information that could link the generate code to the study participant. Only the PI will have information that will link the unique generated code to the study participant.

Bio specimens for the study will be stored at Salimetrics Laboratory. Salimetrics Laboratory supports protocols by providing facilities, technical experience, and training for non-routine blood and urine biochemical analyses. Salilmetrics will also provide necessary kits for the saliva collection. After the saliva analysis is completed and analyzed (~2 years), we will evaluate whether to continue to store the specimens for an additional 3 years or to destroy them. If we decide to destroy the samples at the end of this period, the lab will thaw out the samples and pool them together, then dilute the sample with a bleach solution. This study does not plan to share the bio specimens with other investigators.

Participants will be able to withdraw consent to use their bio specimens, by contacting the PI and putting their request in writing. If a participant decides to withdrawal consent, the PI will contact the lab and the sample will be destroyed as described above.

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Fidelity Plan: The fidelity plan is based on the NIH Behavior Change consortium developed by national leaders. All of the nurses and data collectors have received training for the Beat the Blues/Get Busy Get Better Dapper Adaptation Protocol. They have all received training on how to measure frailty using the frailty phenotype. We will enhance fidelity through design elements (intervention is distinct and based on theory), training (using an intervention manual and having formal training), delivery (reminder calls the night before intervention sessions, measure fidelity through records of home sessions (by date and duration), checklists completed by study team members, direct observations concerning intervention engagement to evaluate receipt, and enactment (e.g. participants will show the exercises to the nurses). Ten percent of sessions will be audio taped which will be reviewed by the principal investigator using monitoring checklists developed for this pilot trial. The recordings will not be transcribed. When video visits are done the recordings will be recorded via digital recorder and not via the ZOOM recording feature. Feedback will be provided to each interventionist who will provide case presentations in supervisory sessions. Bi-weekly meetings with the data collectors, registered nurses, and the PI.

Data collection and management: We will use the Redcap data entry and management system, which is available to all Clinical Translation Science Award (CTSA) sites such as Johns Hopkins University. Data from screening, intervention sessions, and final data collection will be entered onto forms that the data manager will check for completeness and appropriateness. The data manager will send reports of missing or inappropriate entries to the PI every week for clarification and resolution. The details of the Data Safety and Monitoring plan are in the human subjects section.

Acceptability Qualitative Interviews: Upon completion of the intervention, the follow up interviews will be scheduled with 10 randomly selected participants from both the intervention and wait list control groups. These interviews will be done by a study team member. The interviews will be scheduled and completed with participants via phone or video. We will ask their thoughts on the intervention and ask for what worked and what did not. The interviews will be audio recorded with a digital recorder only. We will make sure that all information is in a locked file cabinet at Johns Hopkins School of Nursing. We will keep all audio recordings separate from documented person information. We will ask participants to avoid using names in the interviews. The audio recordings will be stored on an encrypted computer after the interviews are completed. The PI will review all transcripts and work with study team to identify themes surrounding intervention changes and conduct intervention mapping to refine the intervention for the next grant application. The audio recordings will be stored on an encrypted computer after the interviews are

completed. Production transcripts will transcribe the follow up interviews. The PI will review all transcripts and work with study team to identify themes surrounding intervention changes and conduct intervention mapping to refine the intervention for the next grant application.

As a additional portion of the study upon completion of the last data collection visit, we would like to call all of the participants who completed the intervention and verify their contact information in order to send them a handout with the study findings. We will verify their address/email and ask if they would like to receive the findings. In addition, we would like to ask participants follow up questions about their participation in the study (please see attached post follow interview guide). Follow up questions will also include acceptabilityand satisfication questions in goal attainment. We will also obtain consent for these interview questions using the attached consent script that we will verbally read to them. These interviews will take place via zoom, or telephone and will be recorded with a digital recorder. We will give participants the opportunity to send photos of any goals or changes that were made after completing the study. We will only use recordings for purpose of analyzing goals data and follow up questions. All recordings will be deleted after one year and stored on our encrypted server. Photos will not include any participant identifiers and photos and will not be used for dissemination of findings..

4. Drugs/ Substances/ Devices

N/A

5. Study Statistics

Sample size calculation and analysis of aims

Sample size: To calculate effect sizes for planning a definitive trial our sample size calculations were based on the need to pilot DAPPER for pain and depressive symptoms. We assume an attrition rate of 13% during the 16-week follow-up based on the CAPABLE trial. Based on these assumptions, an initial sample size of 64 participants (3 , 32in the intervention group and 32 in wait list control) would yield 52 participants (25 intervention, 25 wait list control) after attrition. It is unlikely we will detect a significant difference between the groups due to small sample size and limited follow-up.

Analytic approach:
For DAPPER, the outcomes will be improvement in pain, depressive symptoms, and communication with health care providers. A database will be created and stored on a password protected encrypted computer. Prior to conducting the analysis, the distribution of the data will be examined to determine if they meet the assumptions of the analytical model and to explore the pattern of missing data. The number of sessions attended will be computed as an indicator of acceptability. To test the effect of the intervention on outcomes (depressive symptoms, pain), generalized estimating equations will be used (GEE) with time, group, and the time x group interaction. We will not be sufficiently powered to detect a significant effect; interpretation of the results will be based on the effect size associated with the time by group interaction for each outcome. One advantage of GEE is it allows all participants' data to be included in the analysis, even those who do not complete the study, providing an intention-to-treat analysis. We will also conduct sensitivity analyses with completers only and compare the effect size to the ITT analysis to estimate the effect size when all participants adhere to the intervention.

Acceptability of the intervention will be examined in multiple ways. We will examine percentages of people who stayed in each arm of the study and conduct numerous descriptive correlational analyses of the

association between the intervention compliance and other variables. These analyses will quantify intervention implementation by demographic and participant health variables. Analyses that utilize the post-randomization data (e.g. treatment compliance) [40-43] will be evaluated in supplementary analyses. We will distinguish non-compliance with intervention from attrition or loss to follow-up, i.e. missing data. We will also use the one-on-one qualitative interviews to examine acceptability of the intervention.

6. Risks

a. Medical risks, listing all procedures, their major and minor risks and expected frequency.

Minimal risks to study participants are expected. There is a chance participants may experience some discomfort, or fatigue in completing saliva specimen collections. Participants may become fatigued or emotionally distressed while completing battery of questions. When performing the frailty phenotype walking speed tests participants may stumble, fall, or become short of breath or fatigued. If strategies include any type of physical activity (e.g. tai chi exercises) participants may become short of breath, fatigued, or may experience pulled muscles or dizziness.

b. Steps taken to minimize the risks.

Participants can decline the saliva specimen collection or stop collecting specimens at any time. Participants can decline saliva collection or stop at any time. Participants can also decline to answer any of the survey questions. Research staff has been trained to interact with participants in a positive, non-judgmental manner that encourages honest communication and a partnership approach to study participation. Participants may decline the walking speed test, or any exercise strategies suggested by the nurse. The nurses have the necessary training to recognize respiratory distress and how to reduce falls (e.g. removal of clutter, assessing for dizziness and balance) via Zoom. The principal investigator will be made aware of any adverse reactions or events. Participants will receive a follow-up telephone call to assure that the reaction/event has resolved. If the reaction/event persists, a referral will be made to the participant's primary care provider for further evaluation.

Procedures for protecting against and minimizing potential risks:

If any physical problems emerge during any of the home visits, immediate medical attention will be sought for the participant. The risk of invasion of privacy will be addressed with participants during the informed consent process. All personnel involved in the study will be fully trained and certified in the protection of human subjects and HIPAA regulations. We will use a virtual video call software called Zoom. Zoom is encrypted, collects no protected health information (PHI) and any data transmitted during the call is destroyed when the call ends. It is both HIPAA and HITECH compliant.
This certification will be kept current throughout the study. As part of the informed consent process, participants will be notified of their rights pertaining to protected health information. Participants will be informed that they can stop the questionnaire and rest at any time. All study participants will be provided referral information to existing health services as in typical or usual care. Thus, participants have the information to access any services that they may perceive as necessary independent of their study participation.

The risk of breaching study participant confidentiality will be minimized by identifying all participants by code numbers, securing all data collected in locked files in the PI's office, and screening information to locked file cabinets with limited staff access. Pre-coded data collection instruments are prepared for use with study participants at each testing occasion. Identification numbers to assure subject confidentiality will be used. Only

one master log of subject names, addresses, telephone numbers, and study identification assignment will be maintained in a password protected computer program. Data collection will be on computer tablets that are password protected. Audio recording of nurse visits will be routinely conducted for fidelity and quality control review. These recordings will be identified by numbers only and stored in files on computers of the project coordinator and Dr. Taylor who will provide fidelity oversight of the interventionists. Access to these computer files will be password protected; recordings will not contain respondent name or other personal identifying information and will not be transcribed. Recordings will be used only for quality control and training purposes and then destroyed (deleted from computers) within one year of trial completion.

Plan for Data and Safety Monitoring: This study is partially funded through the Older Americans Independent Center (OAIC) Pepper Center at Johns Hopkins University. Data and safety reports will be reviewed by the OAIC Director and/or co-PI. In the yearly progress report to NIH, the OAIC Directors will certify that the principal investigator has read all data and safety reports, in addition to making sure all corrective actions have been taken where there were concerns and/or that no concerns were noted.
e.2 Verification of eligibility criteria: The OAIC'S Data and Safety Monitoring Board reviews all applications for OAIC support that are being considered for funding. The board will verify that the inclusion and exclusion criteria are acceptable, or they will recommend revisions.
e.3 Frequency of Data and Safety Monitoring: Reports are reviewed quarterly, in conjunction with review of OAIC supported investigator progress reports. The OAIC DSMB is convened every 6 months. Unscheduled reviews may be conducted if necessary, at the request of the OAIC Director, study PI, SO/DSMB, or NIA program official.
e.4 Content of Data and Safety Monitoring Reports: Reports include, at a minimum, study status; descriptions of all SAEs, AEs, UPs, and protocol deviations (including enrollment of an ineligible participant); and any abnormal laboratory, imaging, and other test results. The study PI will attest his/her knowledge to the list of SAEs, AEs, UPs, and protocol deviations completed or that no SAEs, AEs, UPs, and protocol deviations occurred.
The members of the DSMB will be available to offer advice and provide ad hoc consultation throughout the study period. There will be continuous investigator monitoring with prompt incident reporting to the OAIC, Johns Hopkins Internal Review Board, Robert Wood Johnson Foundation, and National Institute of Health (NIH). Evaluation of this trial will include periodic assessments of data quality, participant recruitment, accrual, and retention. All adverse events will be reported to the IRB and the chair of the DSMB within 48 hours if attributable to the study. Members of the DSMB may request an interim analysis of data, which will be presented by the trial biostatistician in a session closed to the PI. The minutes meetings of the DSMB will be reported to Robert Wood Johnson Foundation, NIH, and IRB.

Adverse Event (AE) Reporting: The DSMB will be notified by the principal investigator of any serious AE within 48 hours of initial notification to the project team. All members of the DSMB will receive copies of all safety reports at the time of submission to the IRB. In addition, a listing of AEs and their attribution (e.g., level of probability of being study related, intervention related, or unrelated to study or treatment) will be provided to the DSMB on a monthly basis. We do not anticipate any adverse reactions to the intervention. Based on our previous work and studies in this area by others, there is only a small risk that participants will become increasingly anxious to the point that it becomes an adverse event (e.g., harmful to self or others) as a consequence of the activity intervention or having a member of the research team in their home. However, interviewers/interventionists are well trained to manage this reaction or make an effective referral if necessary.

Given that interviews for data collection and interventions via video, there is the potential for a member of our research team to encounter a potential emergency that is not related to study participation (e.g., dehydration, environmental risk, medical emergency). Following the emergence of the need to account for

such events in behavioral interventions differently than in medical/clinical studies,[58] we refer to such events as "alerts" and have well-developed procedures for their management. All alerts will be reported to the DSMB on a biannual basis. However, the reporting of alerts to the IRB of JHU is not required (see Chart below of potential alert events and plan for their management and reporting).

Recruitment, AE, and Alert Reports: Reports presented to the DSMB will include data on enrollment (study accrual by month; comparison of expected to actual enrollment; number of individuals screened, number eligible and number ineligible, number randomized by gender, AEs, and alerts. In addition, the DSMB will receive reports of the number of study participants who discontinue from the treatment group and/or the study and reasons for discontinuation. We propose that reports are provided to the DSMB twice yearly. However, the DSMB will decide upon the schedule of reports. In addition, the DSMB may request reports as needed as well as the unblinding of the data should they deem this necessary. If unblinded efficacy data is required, the biostatistician for this study (Dr. Zhang) will serve as a liaison between the PI, database, and the DSMB in order to assure that the PI and investigative team remains blinded.
Plan for reporting unanticipated problems or study deviations:

b.2. Protections Against Risk

The Principal Investigator will be notified of any adverse events. Participants will receive a follow-up telephone call to assure that the reaction has resolved. If the reaction persists, a referral will be made to the participant's primary care provider for further evaluation. In situations where there is initial severe distress or when the distress has not been resolved, if suicidal thoughts are present, we will immediately call 911 for further help and stay with the participant until help arrives. **If suicidal ideation or intent is identified, the study team member will follow the study's suicide protocol. The suicide protocol will utilize an adapted version of the Columbia Suicide Severity Rating Scale to assess mild, moderate or severe risk. If risk is mild study team will notify PI, provide mental health resource guide, advice to speak to their healthcare provider. If the risk is moderate, it will be the same as mild with expression of high concern and strong recommendation to seek care. If the risk is severe, the study team member will call 911 or suicide crisis number or escort to emergency room and immediately notify the PI. We will consult with Dr. Jin Joo on referrals and next steps for any all mild and moderate risk patients.** Furthermore, if any physical problems emerge during any of the visits, immediate medical attention will be sought for the participant.

If participants experience any physical problems during any portion of the study, immediate medical attention will be sought for the participant. See the table below regarding alert and actions to be taken.

Table 4

Alert	**Action Taken**
Medical Emergency: • Chest pains • Excessive bleeding • Fall and cannot get up • Difficulty breathing	If a member of the research team encounters any of these symptoms over the phone, the participant is put on hold and the PI will call 911 immediately. If the situation occurs within the home or during focus groups, the PI and/or research personnel will call 911 immediately and stay with the participant until help arrives. If participants engage in physical activity virtually, the nurse will assess every five minutes for shortness of breath or any pain at all. If participants verbalize this or shortness of breath is observed the nurses will ask

	participants to stop any physical activity.
Evidence of abuse	Evidence of physical abuse is follows: • Participant states to the PI/research staff that abuse occurs. • The RN observes physical evidence (e.g. black eye, black and blue marks arms/legs. The investigators will contact participants and strongly encourage him/her to contact his/her primary care provider and/or Adult Protective Services (phone number will be provided). Based on the situation, the PI may notify Adult Protective Services. The PI will complete an alert form. Note- The possibility of informing an agency about an abusive situation will be stated in the informed consent.
Extreme Home Hazards • Exposed electrical • External door missing or cannot be locked • Ceiling, floors caved in • No temperature regulation (e.g. no air or heat- must be extreme) • Major infestation	The investigators will refer participants to Baltimore City 311 who can refer participants to possible resources for home repairs and/or infestations.

All personnel involved in the study have been fully trained and certified in the protection of human subjects. This certification will be kept current throughout the study. Education in protection of human research participants: The investigators have completed the Johns Hopkins University School of Medicine Research Compliance course. All research personnel on the proposed study will complete the Johns Hopkins University (JHU) School of Medicine Research Compliance Course. The JHU course consists of the University of Minnesota Web modules on Informed Consent, the Consent Process, After Informed Consent, JHU School of Medicine module on local IRB requirements, and achievement of a passing score on the JHU Knowledge Assessment module. According to the policies of the JHU, approval for this research will be obtained from the JHU IRB office for research using human subjects. Participants will be assigned a code number on initial entry and only the code number will identify all subsequent questionnaires. Information needed for follow-up contact (names and addresses) will be kept separately from all other data.

Legal Risks such as the risks that would be associated with a breach of confidentiality:
The risk of breaching study participant confidentiality will be minimized by identifying all participants by code numbers and by securing all data collected in locked files in the PI's office and screening information at the senior center in areas with limited staff access. Pre-coded data collection instruments are prepared for use with study participants at each testing occasion. Identification numbers to assure subject confidentiality will be used. Only one master log of subject names, addresses, telephone number, and study identification assignment will be maintained on site in the locked PI's office. This log, in both hard copy and disk, will be stored in a locked filing cabinet separate from other identifying information. All completed data collection instruments are stored in locked filing cabinets.

Financial risks to the participants: There are no anticipated financial risks to the participants.

7. Benefits

Potential Benefits of the Proposed Research to Human Subjects and Others

Participants will receive study visits from a nurse and learn strategies to address pain and frailty syndrome as well as communication with providers.

There are no known direct benefits to participants, but possible benefits may include that participants will learn strategies to help improve their symptoms related to pain and depressive symptoms. Participants will also be contributing to important research that may help improve pain and depression outcomes among older African American women.

Importance of Knowledge to be gained

This study has the potential to add to the current body of literature on effective ways to address depression, pain, and frailty in community dwelling older African American women.

8. Costs

There are no costs to participants for participating in the study. We will compensate all participants, $20 (gift cards or cash) after completion of the final visit of study. We will also compensate the 10 participants selected for qualitative interviews at the end of the study with $10 (gift cards or cash). The funds that support the study will be used to purchase any materials for the strategies (e.g. heat therapy gel packs).

N/A

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