IRB Study Number: 20201202
Version 4.02, Date: 11/10/2021

Full Protocol Title: Preventing Cognitive Decline in HIV-infected Latinos through a Culturally Tailored Health Promotion Intervention (HOLA)

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PI Name: Daniel E. Jimenez, Ph.D.

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1) Protocol Title

Preventing Cognitive Decline in HIV-infected Latinos through a Culturally Tailored Health Promotion Intervention (HOLA)

2) IRB Review History*

This protocol has not been submitted for review by an external IRB.

3) Objectives*

The project will conduct a pilot single-arm trial with Latinos living with HIV (LWH) to assess feasibility, acceptability, and preliminary effects on cognition for a fully powered randomized trial (R01).
Specific Aim 1: To determine feasibility and acceptability of HOLA, adapted to incorporate a cognition focus, aimed at improving cognitive functioning among older Latinos LWH and incorporating activity tracking (Fitbit);
Specific Aim 2: To explore whether HOLA will produce changes in cognitive functioning between baseline and post-test (16 weeks);
Specific Aim 3: To explore whether HOLA will produce changes in activity, psychosocial functioning (depression, anxiety, social support) or biomarkers of cognition (myokines/cytokines [IL-15], adipokines [irisin and adiponectin], neurotrophic factors [BDNF, IGF-1 VEGF]) between baseline and post-test; and APOE e4 carrier status (a genetic risk for dementia) baseline only.
Specific Aim 4: To explore whether changes in activity, psychosocial functioning or cognitive biomarkers correlate with changes in cognition, while accounting for genetic risk for dementia (APOE e4 carrier status).

4) Background*

Advancements in the treatment of HIV over the past two decades have greatly improved the longevity and health of people living with HIV (LWH). However, neurocognitive impairment among people LWH continues to be common and impactful and is observed in up to half of persons LWH. Non-pathological cognitive impairments are found in numerous aging studies and HIV studies. Although HIV-related dementia is not as prevalent with the advent of Antiretroviral Therapy (ART), adults with HIV remain susceptible to both cortical and subcortical insults that produce cognitive impairments. In 1,555 adults with HIV from across the United States, Heaton et al. found 52% experienced measurable cognitive impairments with 33%, 12%, and 5% experiencing Asymptomatic Neurocognitive Impairment, Mild Neurocognitive Disorder, and Mixed Neurocognitive Disorder, respectively. Such cognitive impairments may be attributable to factors such as: the death of glial cells caused by HIV; elevated cortisol levels and inflammation caused by HIV; age- and HIV-associated comorbidities; and ART-induced metabolic complications such as hypercholesterolemia and insulin resistance. For example, Justice et al. found a

high prevalence of cognitive impairments (e.g., speed of processing, memory) in middle-aged and older veterans with HIV. Both viral burden and older age are significant predictors of such cognitive impairment. Studies have also found cognitive declines and changes in brain functioning in adults with HIV as early as 1 year following infection. These declines occur across cognitive domains but are most often observed in speed of processing. Latinos LWH may be uniquely at risk for deleterious neuropathological and neurocognitive sequelae within the context of aging. Ethnic differences on cognitive impairments were evident across the domains of memory, executive functioning, and speed of information processing. Most of the neurocognitive domains in which there were significant ethnic differences are among the most commonly impacted by HIV in the combination ART era and are linked with problems in everyday functioning in people LWH. Furthermore, depression among older Latinos LWH has been reported at five times the level in the general population and is fueled by stigma and resultant loneliness due to rejection and withdrawal. Depression has been identified as an independent risk factor for cognitive impairment among older adults LWH. Thus, there is a growing population that is particularly vulnerable to dementia due to the co-occurrence of HIV, depression, and aging-related cognitive impairments.

5) Inclusion and Exclusion Criteria*

Inclusion Criteria:
The following conditions must be met for study eligibility:

- are Latino (self-identified);
- are age 50+;
- are HIV infected but are virologically suppressed (viral load <200 copies/mL);
- volunteer informed consent;

Exclusion Criteria:
Individuals meeting any of the following criteria will not be eligible to participate in the study:

- have diagnosis of any neurodegenerative disorder or dementia (Parkinson's disease, Alzheimer's disease, vascular, frontotemporal dementia, etc.) or significant cognitive impairment as indicated by a Telephone Interview for Cognitive Status (TICS) score less than or equal to 30;
- have other conditions that could impact cognitive functioning or testing (e.g., legally blind or deaf), currently undergoing radiation or chemotherapy, a history of brain trauma with a loss of consciousness greater than 30 minutes.
- have contraindications to physical activity outlined in the American College of Sports Medicine standards or severe medical illness that

precludes them from safely participating in a health promotion intervention.

- are unable to complete 10-meter walk test.
- have plans to move outside of the Miami metropolitan area within the next 6 months or are not living in stable housing (e.g. group home).

This study will include both men and women; no decision to exclude any person from this study will be based on gender. We do not expect there to be any difference in the number of women and men. This study will specifically target Latinos. Individuals from other ethnic backgrounds are excluded as the study intervention is specifically tailored to address and target the specific needs and preferences of older Latinos at increased risk for cognitive impairment.

6) Number of Subjects*

30 older Latinos age 50+ will be enrolled. Consistent with recommendations from biostatistical workgroups funded by NIH, this pilot study is not powered to test hypotheses. The proposed project builds upon recruitment and intervention infrastructure that is being used in other HOLA studies. Participants will not be replaced if withdrawn or lost to follow-up.

7) Study-Wide Recruitment Methods*

We will collaborate with another study, the Clinic Registry Project (IRB#20160911), which serves as a database, to contact eligible participants. They will provide us with contact information for participants in their study who have consented to be contacted by other studies. When contacting participants, the community health worker (CHW) will follow the phone script.

8) Procedures Involved*

Participants will be assessed at two time points (baseline and post intervention at 16 weeks) on measures of neurocognitive and psychosocial functioning. Blood will be collected to determine APOE (baseline only) and biomarkers of cognition (baseline and 16-weeks).

All participants will read and sign an informed consent. They will initially be provided with a verbal summary of the study and for those who appear to have problems reading the consent form it will be read aloud. Participant payments will be graduated. Participants will receive $25 on the first visit and $35 on the second visit (total of honoraria = $60). They will also be given the Fitbit tracking device to keep.

Prior to starting the baseline assessments, blood draws will take place at the CTRS . Approximately 20mL (2 tablespoons) of blood will be collected by a trained phlebotomist. Study staff will obtain biomarkers of cognition (myokines/cytokines [IL-15], adipokines [irisin and adiponectin], neurotrophic factors [BDNF, IGF-1 VEGF]) as well as apolipoprotein E (APOE) status, a genetic marker of dementia risk (baseline only).

Trained and certified bilingual research assistants (RAs) who have at least a bachelor's degree will conduct all assessments in private offices at the at the Soffer Clinical Research Building (CRB) or another location convenient to the participant where privacy can be protected. The neurocognitive testing will be conducted under the supervision of a neuropsychologist. Approximate administration time of the assessment will be 60 minutes.

Assessment Measures

Dementia Screen: The Telephone Interview for Cognitive Status (TICS) will be used to screen for dementia. A score of 30 or below indicates cognitive impairment.

Walking Ability: The 10-meter walk test will be used to evaluate walking ability, which has been used as a screening instrument to measure functional mobility and gait speed in physical activity interventions with older adults.

Demographics: The Center for Latino Health Research Opportunities (CLaRO) Demographics Form will be used to collect demographic information (e.g., gender, education, income, preferred language, country of origin, time in the US, etc.) and will include a list of all diagnosed medical conditions and medications.

Acculturation: The 24-item Bidimensional Acculturation Scale (BAS) will be used to measure acculturation.

Depression Severity: The 9-item Patient Health Questionnaire (PHQ-9) will be used to measure depression severity.

Anxiety Severity: The 7-item Generalized Anxiety Disorder (GAD-7) scale will be used to measure anxiety severity.

Social Support: Perceived social support will be measured using the 12-item Multidimensional Scale of Perceived Social Support (MSPSS).

Physical Activity: The 16-item Global Physical Activity Questionnaire (GPAQ) will be used to measure physical activity.

Processing Speed: Trails Making Test A will be used to measure processing speed.

Attention/Working Memory: The WAIS-IV Digit Span will be used.

Learning: Hopkins Verbal Learning Test-Revised (HVLT-R)

Memory: HVLT-R Delay

Verbal Fluency: Animal Fluency and Controlled Oral Word Association Test (COWAT)

Executive Function: Trails Making Test B

Motor: Grooved Pegboard (dominant and non-dominant)

Biomarkers of cognition: Myokines/cytokines (IL-15), adipokines (irisin and adiponectin), and neurotrophic factors (BDNF, IGF-1 VEGF)

Genetic risk factor for dementia (baseline only): Apolipoprotein E (ApoE)

Intervention Description: Content and Structure of HOLA

HOLA is a multi-component, health promotion intervention for older Latinos.

The first component consists of two manualized social and physical activation sessions. Prior to beginning the group walk phase, each participant will meet individually with a CHW for a 30 minute physical and social activation session to (a) educate potential participants about the goals of the intervention; (b) provide information surrounding cognitive functioning, age-related memory loss vs. dementia, difference between dementia and Alzheimer's disease, how their comorbidities impacted cognition, and ways they can prevent cognitive decline and the; (c) motivate participants to engage in physical activity; (d) increase participants' social activities (e) identify potential obstacles that may interfere with meeting the demands of the intervention; and (f) brainstorm ways to overcome these obstacles. Participants will again meet individually with the CHW for 30 minutes after week 8 to discuss progress of physical and social activity goals. In addition, during this session, the CHW goes over the ground rules for the intervention and reminds each participant that it is important that we create a comfortable environment where every member of the group is free to share thoughts, feelings and experiences. In order to do this, we ask that each participant not discuss other group members' personal information with anyone outside of the walking group. This helps us to know that anything shared will not go beyond the walking group. These meetings are held in the participants' homes.

The second component is a group walk, led by a CHW for 45 minutes, 3 times a week, for 16 weeks. The group walk protocol uses the concept of interval training. The program starts slowly and gradually increases in workload by manipulating three factors: (a) intensity: governed by speed; (b) volume: duration and/or distance; and (c) work/recovery cycle: how long work phase lasts compared to the recovery phase. Walks will be conducted with a group of 6 participants. Each walk will begin with 10 minutes of stretching and warm up. Then, participants will walk for 30 minutes. The walk will conclude with 5 minutes of cool down. The groups will include bilingual and monolingual Spanish speaking participants.

The third component consists of scheduling pleasant events. During the cool down phase of each walking session, the CHW will ask each participant to identify a pleasant event that they intend to do with another person before the next

meeting. Individuals may choose to do this activity with another member of the group, with family, or with friends outside the group. Subsequent sessions will start with participants reporting on how effectively they implemented their pleasant event plan while the CHW and the group provide positive reinforcement and feedback. This component provides a means to generalize the intervention into the participants' everyday lives and relationships. Participants will walk at a centrally located public park, which is owned and operated by the Miami-Dade County Parks and Recreation Department.

A fidelity measure has been developed to assess the consistency with which different CHWs deliver the HOLA intervention. This is an anchored rating scale characterizing core components of HOLA. Mental health specialists will be supervised and give one-on-one feedback to the CHWs. If there is drift, adjustments will be made to make sure that what is being delivered is fully consistent with the intervention as designed. In addition, Dr. Jimenez will attend five walking sessions for every group to supervise and provide corrective feedback as needed. There will also be a detailed manual of operations.

Endpoints
Primary Outcome Measure Title: Feasibility and acceptability of HOLA
Primary Outcome Measure Description: As measured by meeting 100% of targeted sample (N = 30), with 20% or less of eligible subjects refusing to participate, 85% or more of participants completing the post-intervention assessment, and 80% or more of sessions attended by participants.
Primary Outcome Timeframe: Baseline to follow-up assessment (16 weeks).

Secondary Outcome Measure Title: Changes in neurocognitive impairment
Secondary Outcome Measure Description: As measured by the WAIS-IV Digit Span Processing and Trails Making Test A and B. The WAIS-IV Digit Span Processing is a summary score with the lower scores indicating increased cognitive impairment. For Trails Making Test A and B the primary score is the time to complete the task with higher times indicating increased cognitive impairment.
Secondary Outcome Timeframe: Baseline to follow-up assessment (16 weeks).

Secondary Outcome Measure Title: Changes in changes in activity, psychosocial functioning, or biomarkers of cognition.
Secondary Outcome Measure Description: As measured by GPAQ (activity); PHQ-9, GAD-7, Multidimensional Scale of Perceived Social Support (psychosocial functioning); and interleukin-15, irisin, adiponectin, BDNF, IGF-1, and VEGF (biomarkers of cognition). The GPAQ is a summary score with higher scores indicating increased activity levels. PHQ-9 is a summary score with higher scores indicating increased depression levels. The GAD-7 is a summary score with higher scores indicating increased anxiety levels. The Multidimensional Scale of Perceived Social Support is a summary score with higher scores indicating increased levels of perceived social support. Levels of interleukin-15,

irisin, adiponectin, BDNF, IGF-1, and VEGF are calculated from blood draws with well-defined average ranges.
Secondary Outcome Timeframe: Baseline to follow-up assessment (16 weeks).

9) Data and Specimen Banking*

Data will be collected with pre-programmed questionnaires. Data will be exported to SPSS for analysis. All electronic data will be stripped of identifiers and will be stored in password-protected files. For each data file, a code number will be assigned, and the master list, linking code numbers with names, will be stored separately. The data will be stored on password protected, network computer hard drives in the Department of Psychiatry and Behavioral Sciences, which will only be accessible to the PI.

Blood samples will be stored at the University of Miami Center for AIDS Research Laboratory Sciences Core (D) at -80 ºC until analysis. The labels on the blood sample tubes will not contain *participant ID numbers*. The blood samples will be stored in locked freezers in locked rooms within access-limited sections of the building.

All the data will be stored and secured using the procedures outlined above. Access to records and participant data will be allowed only to the study personnel.

Study data request goes through a web-based check-in and check-out procedure implemented by CLaRO. The Data Manager or designee monitors the logs. Upon granting of the approval, the requester will either get the hard copy of the data or link to access the electronic data. All the data will not contain any identifying information.

10) Data Management*

As a pilot study, we will evaluate the feasibility of recruitment, assessment procedures, retention, acceptability, and implementation of HOLA in a sample of midlife and older Latinos LWH (**Aim 1**). Consistent with recommendations from biostatistical workgroups funded by NIH, this pilot study is not powered to test a hypothesis. This approach to analysis of feasibility data mirrors the structure of the first HOLA trial and other pilot trials conducted at the CNSA. Successful recruitment will be defined as meeting 100% of targeted sample (N = 30), with 20% or less of eligible subjects refusing to participate. Adequate retention will be defined as 85% or more of randomized subjects completing the post-intervention assessment. Acceptability is defined as 80% or more of sessions attended by subjects. To identify modifications needed in the design of a larger, confirmatory randomized controlled trial (**Aim 2**), we will use a project evaluation questionnaire developed by investigators at the CNSA and used in previous studies. The items are a mix of rating scales, yes/no questions, and open-ended questions that allow participants to give feedback in short

answer format with specific interest in understanding the participants' opinions regarding the specific components of the intervention. To explore changes in cognitive decline risk factors (waist circumference, dyslipidemia, hypertension, and glucose), psychosocial functioning (depression and anxiety severity, social support), and health-related quality of life (**Aim 3**), a one-way ANOVA will be used to illustrate the change in scores from baseline to post-intervention in all the outcome measures used.

A repeated measures ANOVA, as we have proposed, is appropriate to explore the intervention effects on cardiometabolic risk factors, psychosocial functioning, and health-related quality of life given that this type of analysis is often used in studies that investigate either changes in mean scores over three or more time points. In the exploratory analyses, we will use age, SES, and years of education as covariates. In addition, a list of current medications will also be collected at baseline. Should the participants' medications be dose-adjusted, changed altogether, or if they are started on new medications such as statins, then we will adjust for them in them in the exploratory analysis as well. Covariates will be tested as moderators of treatment response.

Maintenance of Confidentiality:

Our staff is CITI certified and trained with maintenance of confidentiality. The information provided by study participants will be held as personal and confidential to the extent permitted by law. In addition to the safeguards included as part of the recruitment and screening process by assigning a patient a study ID to de-identify participants, all study participants will be given the contact information for the Principal Investigators to answer any questions that may arise. Participants will be informed that they may end their participation at any time without affecting access to any other services they are currently receiving. All study procedures will be conducted according to good clinical practice and all other relevant regulatory guidelines.

All electronic data will be stripped of identifiers and stored in password-protected files on servers at the Department of Psychiatry and Behavioral Sciences. These data are password secured for minimal access to authorized personnel associated with the study. For each data file, a code number will be assigned, and the master list, linking code numbers with names, will be stored separately. At the conclusion of the project, the record linking the assigned research number and participant identity will be destroyed. Data will be entered into password secured databases by staff authorized by the principal investigator to do this, and they will abide by confidentiality regulations of the HSRO. No subject will be identified by any published report.

11) Provisions to Monitor the Data to Ensure the Safety of Subjects*

The Principal Investigator, Dr. Daniel E. Jimenez, assumes responsibility for developing and implementing a data and safety monitoring plan to assure minimal risk and data integrity in this study. The plan assures that all data collected concur with all local, state and federal guidelines. The PI will work closely with his collaborators and will follow any data monitoring and safety requirements set forth by NIH.

The PI will examine accumulating data to assure protection of participants' safety while the study's scientific goals are being met and will conduct periodic reviews of accumulating safety and efficacy data. Along with his collaborators at the University of Miami Miller School of Medicine, he will determine whether there is support for continuation of the study, or evidence that study procedures should be changed, or if the study should be halted, for reasons relating to the safety of the study participants, the feasibility of the intervention under study, or inadequate study procedures (e.g., poor recruitment).

Procedures for the study will follow quality assurance (QA) procedures established by CLaRO for data management and safety, to ensure quality and consistency in the implementation of the protocol and data quality, to adhere to regulatory requirements and, most importantly, to protect the safety of study participants. The study will be monitored by the CLaRO Study Monitoring Unit, which is based at the School of Nursing and Health Studies. The Study Monitoring Unit will (1) verify compliance with regulatory requirements, (2) ensure that the PI and engaged study team members are fully informed of regulatory requirements and properly trained to perform the duties assigned, and (3) monitor procedures to prevent errors and minimize protocol deviations that can negatively affect quality of the data collected and compromise human subjects' protection. The project will have a quality assurance (QA) review: prior to initiation, upon conducting baseline procedures with the first wave of study participants; and bi-annually for interim reviews. For the initiation review the Study Monitoring team reviews protocol procedures and their manualization, documentation of staff training, evaluates that the study site is prepared to conduct the study, and ensures that the Regulatory Binder is complete. Interim monitoring visits will verify that study screening, consent, and data storage procedures are being conducted as stated in protocol. After each QA visit the Study Monitoring team prepares a written report that is sent to the study PI and to the CLaRO Executive Committee. These reports include deficiencies noted and plans for corrective action. The Study Monitoring team follows up with the study team to ensure that the corrective plan and any required reports to the IRB are filed in a timely manner. Protocol violations that are recurrent or

serious will be brought to the attention of the CLaRO Executive Committee for determinations regarding corrective action.

Adverse Event Reporting

In the event that an adverse event or otherwise untoward incident occurs as a direct result or in the context of the project, we will closely follow IRB directives and reporting policies. Specifically, we will report to the University of Miami IRB within 10 working days, in writing, all serious adverse or otherwise untoward events associated with procedures. To ensure monitoring of other study-related participant safety events or incidents, procedures regarding confidentiality and data integrity will be continually monitored and regularly audited.

In our experience, serious, unexpected adverse events related to study participation are rare. In addition, screening for adverse events potentially related to the study intervention will occur during the routine administration of study assessment measures. These interview-based indicators will augment required Serious Adverse Event (SAE) reports by the CHWs and study personnel, including specific items in the assessment interviews evaluating episodes of muscle or fall-related injuries, unexpected medical events, medical emergency room admissions, medical hospitalizations, or unplanned medical clinic visits. Should an adverse event occur, Dr. Jimenez (PI) will report it to the University of Miami Institutional Review Board (IRB) using the IRB SAE form. Dr. Jimenez, in collaboration with co-investigators, will review the adverse event report and gather other information as needed to investigate it and determine the need for subsequent action. Dr. Jimenez will ensure that all adverse events are reported to the IRB in accordance with the University of Miami policies and in a timely manner. Any subsequent action will be documented and reported to the IRB.

Identifying Events: As noted, we will operationalize adverse/safety events for the study and protocols for their resolution. All interventionists and assessors will be trained on these protocols. Initially we will base these protocols on those developed for the HOLA pilot trial. For that trial, there were two categories of events: adverse events and safety alerts. These events may be identified during the baseline interview or the intervention period. Baseline adverse events are items that are identified and recorded by the interviewer during the baseline interview and are unrelated to the study or intervention. Adverse events are situations that occurred during the intervention period and are identified by the interventionist or by the interviewer during the 16-week assessment or any off-protocol interaction with a participant. All off-protocol contacts will be recorded. Adverse events occur anytime following randomization until study completion. Safety alerts are identified by the interviewer during the baseline interview or occur anytime following randomization until study completion. Below are the specific events that trigger a formal response:

Acute Baseline Alerts/Adverse Events

- Hospitalization of Participant
- Institutionalization of Participant

- Emergency Room Visit of Participant
- Death of Participant

Safety Alerts/Adverse Events

- Severe Medical Problem of Participant
- Participant has PHQ-9 score 10 or higher
- Participant Abuse
- Participant threatens to harm him or herself or others

The baseline adverse events and adverse events that occur during the study period are events that fall within the standard definition of adverse events within a clinical intervention study. Safety alerts are those events that do not fall within the standard definition of adverse events but are specific to the participant population.

Reviewing and Reporting Adverse Events: When an alert or adverse event is identified by a member of the research team the event must be reported to the PIs or designee within 24 hours and recorded on the Alert/Adverse Event Form. The event must be resolved using the approved protocol within 3 days of learning of the event. For example, any uncovering of incidental findings by the research staff will immediately be reported to Dr. Jimenez who will a) review the information; b) meet with participants to make appropriate referrals and to c) take any actions that are required by state law to insure the safety of participants. As noted, the informed consent will make clear to participants that any incidental findings that suggest that there is imminent danger may engender certain reporting requirements by state and federal law. For example, if participant abuse is suspected during a participant contact, the assessor/interventionist will report the event to the PIs or designee (e.g., clinical supervisor, project manager) will contact the participant to determine the nature of the situation and to devise a plan of action. The participant will be advised to contact their primary care physician. If the participant refuses or is not able to able to control the situation Adult Protective Services may be contacted. In the event that an unclassified or emergency situation does arise, personnel are advised to consult with the PI, or if circumstances do not allow for such consultation to use their best judgment (e.g., call 911 if necessary). Documentation of all adverse/safety events will be maintained in locked files in the Department of Psychiatry and Behavioral Sciences.

Dr. Jimenez will promptly inform other collaborators of any proposed changes in recruitment or in the protocol that are relevant to safety, as well as any actions taken by the IRB as a result of their continuing review of the project. In the event of any major changes in the status of an ongoing protocol, which will occur only with IRB approval, the PI will inform CLaRO staff immediately. Such changes would include, but are not limited to:

- Amendments to the protocol
- Temporary suspension of participant accrual, or of the protocol

- Any change in informed consent or IRB approval status
- Termination of participant accrual, or of the protocol
- Other problems or issues that could affect the human subjects in the study

12) Withdrawal of Subjects*

If a subject finds the research procedures to be upsetting or aversive, they will have the option to withdraw from the study. Participation will be completely voluntary and will not affect the treatment they are receiving. Participants will be told that they may choose not to answer any questions and may decide to terminate the interview at any time. Research staff will be instructed to terminate interview sessions if participants appear to be stressed by the process. Additionally, the research staff will know how to link participants immediately with treatment personnel including case managers or therapists if participants appear to be stressed.

13) Risks to Subjects*

Recruitment and Informed Consent:
Written informed consent will be obtained at the visit prior to any research activities. All questions will be answered prior to obtaining their signature on the consent form.

Participants retain the right to have their questions answered by an investigator via telephone or an appointment for an in-person meeting. Because we believe that consent is an ongoing process in any study, we will continue to educate participants about the nature of the research and address any questions that may arise throughout the course of the study.

Participants will not receive their genetic results. Genetic testing is performed for research-only purposes and is not nor should it be considered usual medical care. The purpose of conducting the genetic testing and the fact that they will not be informed of results will be explained to participants as part of the informed consent process.

Potential Risks

If participants feel uncomfortable during the research interview, they will be encouraged to take a break and to continue again later or will be asked if they want to stop the interview. The research assistant (RA) may also offer to call a case manager, another staff member, or concerned others (such as a close friend) to make sure the participant has someone to talk with about the interview. Some questions or tasks may cause some individuals to become uncomfortable. This has happened rarely with similar interview sessions. In fact, most participants experience the interview process in a positive way and enjoy the opportunity to be heard by an interested listener. Individuals with depression and anxiety typically

feel enhanced rather than diminished by these interviews. Nevertheless, several precautions will be taken to prevent stress from developing during the interview.

Overall, study personnel and collecting outcomes data are all experienced in conducting clinical research and are able to engage subjects without causing them distress. If a subject finds the research procedures to be upsetting or aversive, they will have the option to withdraw from the study. Participation will be completely voluntary and will not affect the treatment they are receiving at the UM/JMMC Adult HIV Outpatient Clinic. Participants will be told that they may choose not to answer any questions and may decide to terminate the interview at any time. Research staff will be instructed to terminate interview sessions if participants appear to be stressed by the process. Additionally, the research staff will know how to link participants immediately with treatment personnel including case managers or therapists if participants appear to be stressed.

Protection of Risk of Physical Discomfort: Because the HOLA intervention involves physical exercise, to which some participants may be unaccustomed, we will put several safeguards in place to avoid injury or harm. These safeguards have been used successfully in other studies involving exercise done by Dr. Signorile (co-investigator). First, the 10-meter walk test will be used to evaluate walking ability. The use of this test is recommended in order to obtain the most valid clinical assessment of walking speed when using it as a 1-time indicator of health status. In addition, all participants will be evaluated with a set of screening questions to identify individuals who may be at risk of harm from engaging in exercise. We will require these individuals to additionally obtain written recommendations for physical exertion from their physicians specifically responding to the identified health concern before engaging in HOLA. Third, CHWs will work with participants to set exercise goals that are safe and reasonable in relation to their exercise capacity. Furthermore, exercise plans and instructions to participants will be within the accepted range recommended by the American College of Sports Medicine guidelines. Fourth, CHWs will supervise all walks to observe participants' ability to tolerate exercise. CHWs will maintain a list of the phone numbers of the participants' physicians to contact with health concerns about participants. CHWs will be certified in CPR and will have cell phone capacity in the unusual event of a medical emergency. In the case of minor effects of exercise such as muscle soreness, CHWs will be trained to provide advice regarding stretching or other remedies to ameliorate symptoms. If symptoms worsen, the exercise protocol will be modified after discussion with Dr. Signorile.

Protection of Risks During Venipuncture: Blood draws will be performed by certified phlebotomists who routinely perform venipuncture; steps will be taken to diminish the risk of minimal discomfort, bruising, excessive bleeding, clotting, and/or fainting. If subjects have unusual symptoms, pain, or any other problems arising due to venipuncture, they can also contact the CHW or PI directly.

Breach of Confidentiality Risk: The study also involves talking in a group setting during the walking sessions. Participants will be asked not to discuss other group members' personal information with anyone outside of the walking group. They will be asked to not share the names of fellow group members with anyone. Participants will also be reminded that they do not have to share information that they are not comfortable discussing. Although the CHW will remind all participants to keep the walk discussions private, this cannot be guaranteed.

Our staff is CITI certified and trained in the maintenance of confidentiality. The information provided by study participants will be held as personal and confidential to the extent permitted by law. In addition to the safeguards included as part of the recruitment and screening process by assigning a patient a study ID to de-identify participants, all study participants will be given the contact information for the Principal Investigators to answer any questions that may arise. Participants will be informed that they may end their participation at any time without affecting access to any services they are receiving. All study procedures will be conducted according to good clinical practice and all other relevant regulatory guidelines.

All electronic data will be stripped of identifiers and stored in password-protected files on servers at the Department of Psychiatry and Behavioral Sciences. These data are password secured for minimal access to authorized personnel associated with the study. For each data file, a code number will be assigned, and the master list, linking code numbers with names, will be stored separately. At the conclusion of the project, the record linking the assigned research number and participant identity will be destroyed. Data will be entered into password secured databases by staff authorized by the principal investigator to do this, and they will abide by confidentiality regulations of the HSRO. No subject will be identified by any published report.

14) Potential Benefits to Subjects*

The potential benefits of the project to the participant is that the participant may acquire and practice health behaviors that lead to improved wellbeing. The benefit to society is that the project may help demonstrate the potential the HOLA health promotion intervention in improving cognition in HIV-infected patients.

In relation to the anticipated benefits, the risks to the subjects are reasonable in relation to the benefit of improved wellbeing. Participant information is de-identified to minimize loss of confidentiality; psychological stress or discomfort can be addressed by trained mental health professionals; discomfort during venipuncture is mitigated by trained phlebotomists.

15) Vulnerable Populations*

N/A

16) Multi-Site Research*

This is not a multi-site study.

17) Community-Based Participatory Research*

N/A

18) Sharing of Results with Subjects*

Study results will be published in scientific journals. Individual subject results will not be shared unless the safety of the participant is at risk.

19) Setting

Group walks will be conducted at a public park that is centrally located to the participants. All assessments and blood draws will be conducted in private rooms at the at the UM/JMMC Adult HIV Outpatient Clinic.

20) Resources Available

Department of Psychiatry and Behavioral Sciences
The Department of Psychiatry and Behavioral Sciences offers clinical evaluation and treatment services for a broad range of emotional, cognitive, and behavioral disorders in patients of all ages, socioeconomic levels, and cultural backgrounds. Services are available on an outpatient, inpatient, or partial hospitalization basis and include individual, family, and group approaches. Specialty areas include geriatric psychiatry, anxiety and mood disorders, stress and psychobiologic dysfunction; biofeedback; behavioral medicine; memory disorders; psychopharmacology; alcohol and substance abuse; and women's mental health, among others. The Center on Aging, among others, link other organizations in research, education, and treatment for special populations at risk. The Department's outpatient programs are located in the Jackson Mental Health Hospital Center. Inpatient facilities for children, adolescents, and adults are located at the Jackson Mental Health Hospital Center and the Highland Park Pavilion, as well as the University of Miami Hospital and Miami VA Medical Center. Through its Division of Consultation Psychiatry and Psychosomatic Medicine, the Department provides consultation to all clinical departments as well as programs of illness prevention and long-term care management. The Department provides educational and consultative services to the Dade County Jail, the South Florida Evaluation and Treatment Center, and various courts and governmental agencies through its Forensic Psychiatry Program.

Center for Latino Health Research Opportunities (CLaRO)
The NIMHD has renewed support of health disparities research at the SONHS through the Center for Latino Health Research Opportunities (CLaRO; U54MD002266-11). CLaRO, an interdisciplinary center led in collaboration with Florida International University, is funded from 2017-2022. CLaRO's unifying theme is conducting and promoting multi-level community-based participatory research to prevent substance use, violence/trauma and HIV/AIDS syndemic conditions and reduce their adverse health and mental health outcomes. CLaRO's focus is on tailored interventions for Latino subgroups who represent pockets of vulnerability and require precise and specialized interventions that optimize access to and impact of interventions. CLaRO contains two community-based randomized trials of culturally-tailored behavioral interventions: (1) HoMBRES de Familia, which is testing an intervention to prevent HIV, substance abuse and violence among Latino seasonal farmworker fathers and their sons; and (2) Computer Assisted Family Intervention to Treat Self-Harm Disparities in Latinas and Sexual/Gender Minority Youth (CA CIFFTA), which tests a family intervention for Latinas and sexual/gender minority youth. CLARO also sponsors a Pilot Projects Program, scientific resources, training and mentorship to serve as an engine for the advancement of early-stage investigators and for diversifying the workforce of successful health disparities investigators. The CLaRO theme, agenda and priorities were developed in collaboration with a network of community partners who will play an ongoing role as a Community Advisory Board, in guiding and disseminating CLaRO science and advancing neighborhood capacity building and multilevel interventions to promote health in Latino communities.

21) Prior Approvals

N/A

22) Confidentiality

This is not a multicenter study. Please see above for information how we will maintain confidentiality.

23) Provisions to Protect the Privacy Interests of Subjects

Participants will sign a statement attesting to their understanding that their information will be kept private and confidential to the extent permitted by law. Participants know that they will be assigned unique case numbers (and their names will not be used) to protect their identity. Participants will be encouraged to ask questions throughout the consent process and will be provided contact information for Dr. Jimenez (PI) and the University of Miami's Human Subjects Research Office. Data will only be available to researchers approved by the IRB and to the study monitoring

unit. Participants will be reminded of their ability to stop the interview or refuse to answer questions that make them uncomfortable. During all study procedures (e.g., recruitment, consent process), participants will be assured that their information is confidential and will sign a statement attesting to their understanding that their information will be kept private and confidential to the extent permitted by law.

Participants will be assigned unique case numbers (and that their names will not be used) to protect their identity

24) Compensation for Research-Related Injury

Although risks are unlikely, an injury may occur. If an injury should occur, treatment will in most cases be available. If participants have insurance, their insurance company may or may not pay for these costs. If they do not have insurance, or if their insurance company refuses to pay, they will be expected to pay. Funds to compensate for pain, expenses, lost wages and other damages caused by injury are not routinely available.

25) Economic Burden to Subjects

There are no costs associated with your participation in this study.

26) Consent Process

For individuals that are interested in the participating in the research study, the study will obtain an informed consent form from the participant. The initial screening will be conducted over the phone and verbal consent (waiver of documentation of consent) is requested for this portion only. The study will provide the participant a copy of the consent form, and, because the participant may have a low level of literacy, will then read the consent form out loud.

Upon the completion of the telephone screening and if the participant appears eligible for the study, a baseline visit will be conducted. In light of COVID-19, investigators have decided to conduct the informed consent process through one of the following modalities: 1) in-person (when The University of Miami allows following and guidelines for safety), 2) via a HIPAA compliant telehealth platform (REDCap, HIPAA compliant zoom license) or 3) over the phone. For the new enrollments, participants who have expressed interest in our research studies and have completed the screening process will be contacted by phone. During the call, an appointment will be scheduled to conduct the informed consent process and an E-signature will be collected upon completing the consent process through the telehealth platform. The Informed Consent Form will be either mailed or emailed to the participants who prefer to be consented over the phone or are unable to be consented using the telehealth platform. An impartial witness will be required for the participants that are consented over the phone. The witness could be a staff member from the University of Miami who is not part of this study, or a participant's friend or relative.

The signatures for the participant and his/her witness will be collected. Signed consent could be either emailed or mailed by the participant to the University of Miami team member who is conducting the consent process. The team member consenting will thoroughly document the informed consent process on the research participant's chart. Documentation will include purpose for the remote consent (COVID-19), and the steps involving the process. The note will also address the specific reason why the research team doesn't have the signed and dated document.

Once the entire consent form has been read and explained, the assessor will give the participant a chance to ask any additional questions. If the participant agrees to participate, they will be asked to sign the informed consent form and will be given a copy of the signed form.

The consent form for participation in the study are submitted within this protocol for approval to the University of Miami Institutional Review Board (IRB) Behavioral Subcommittee for the Protection of Human Subjects.

The person obtaining consent should document how s/he confirmed that the participant consented and signed the consent form. The note should include a statement indicating why the informed consent document signed by the participant was not retained, (e.g., COVID-19 remote consent). If the participant cannot send a picture of the signed document, the person obtaining consent should document why a copy of the signed document is not available. See example below:

"Informed consent was obtained on Date at Time. The participant could not come to the site for the consent process due to COVID-19 social distancing requirements. A copy of the consent document was emailed/mailed to the prospective participant before the consent discussion. The consent process was performed by phone/ZOOM and REDCap. The individuals attending the discussion were: (list the names of the individuals). The person obtaining consent explained the research to the participant and answered the participant's questions. The person obtaining consent asked the participant questions to ascertain whether s/he understood the study, and the participant was able to answer the questions. The participant voluntarily agreed to participate. The subject signed and dated the consent document. The research was not able to obtain a copy of the signed original consent document because consent was obtained remotely due to COVID-19. After signing the consent document, the participant took a picture and sent it to the research team/ OR the participant was unable to send a picture of the document. If consent process was delivered by phone and no e-signature was collected. A witness observed and listened the entire process."

Non-English Speaking Subjects

We will translate and back-translate the informed consent forms and submit them to the IRB for approval.

Waiver or Alteration of Consent Process (consent will not be obtained, required information will not be disclosed, or the research involves deception)

N/A

Subjects who are not yet adults (infants, children, teenagers)

N/A

Cognitively Impaired Adults

Cognitively impaired adults will be excluded from this study.

Adults Unable to Consent

Adults who are unable to consent will be excluded from this study.

27) Process to Document Consent in Writing

Signed consent will be collected. After the study is explained and the study participant verbally indicates that he or she understands study procedures, the participant will sign and date the consent form. The participant will be given a copy of the signed consent form for his/her records, and the second copy will be stored in a locked office.

28) Drugs or Devices

N/A