Aging with Pride: Innovations in Empowerment and Action

Study Protocol

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1. Overview
    a. Study Title: Aging with Pride: Innovations in Dementia Empowerment and Action
    b. Research Site: University of Washington
    c. Objectives: Healthy People 2020 identified sexual/gender minority older adults as a health disparate population. The lack of efficacious research-based interventions for such vulnerable older adults with Alzheimer's disease and related dementias (AD/RD) and their care partners (CPs) is a significant public health problem. AD/RD will affect up to four million sexual/gender minority older adults with AD/RD and their CPs. These older adults are underserved with significant barriers to healthcare access and the lack of culturally competent care. Caregiving of sexual/gender minority older adults with AD/RD is of concern due to social stigma, marginalization, and isolation, which may be barriers to sustaining caregiving. It is necessary and timely to translate evidence-based culturally adaptable interventions for this underserved and stigmatized population. Reducing Disability in Alzheimer's Disease (RDAD) has been evaluated in a randomized controlled trial and has shown to successfully train community-dwelling CR-CP dyads to increase the physical activity and functioning of individuals with AD/RD, as well as their CPs. It also teaches CPs techniques for managing behavioral symptoms of CRs. RDAD consequently decreases stress of CPs, delays institutionalization of CRs, and increases HRQOL of CRs and CPs. Thus, this study will evaluate the effect of RDAD among CRs with AD/RD and their CPs in the sexual/gender minority population, and this study will test an enhanced RDAD tailored to better respond to distinct sexual/gender minority risks experienced by CPs and CRs with AD/RD, addressing unique sexual/gender minority risk factors (e.g., identity management, stigma-related adverse or traumatic life events, and lack of social support). The enhanced RDAD will be referred to as Aging with Pride: Innovations in Dementia Empowerment and Action (IDEA). We will address the following aims:
        a. Aim 1. Test the translation of RDAD and IDEA programs designed to increase physical activities of older adult care receivers (CRs) with AD/RD and their CPs. Aim 2. Evaluate the short- and long-term effect of RDAD and IDEA on primary *(physical activity for CRs)* and secondary outcomes (*memory-related behavioral disturbances, physical functioning, and QOL for CRs; depressive symptomatology; perceived stress for CRs)*. Aim 3. Test the moderating roles of CR-CP characteristics and severity of CR AD/RD on the treatment effect of RDAD and IDEA.
        b. Study design: This study will utilize a 2-group randomized, single blind with staggered multiple baseline design and three follow-up assessments.

c. Background: Lesbian, gay, bisexual, and transgender (LGBT) older adults are an at-risk, underserved, and rapidly growing population with elevated risk for AD/RD. RDAD, which is grounded in social-learning and gerontological theories, is a present-focused cognitive-behavioral intervention aimed at increasing physical activity and problem-solving while engaging both members of CR-CP dyad. The focus of problem-solving in RDAD is specific to the needs of the CR and CP. The standard RDAD, however, has not been translated to a highly stigmatized and marginalized population, such as LGBT older adults, with unique CR-CP characteristics. Our previous findings indicate that exercise programs for older adults with AD/RD have been found to be more effective for caregiving dyads with a married spouse as caregiver. LGBT older adults, however, are less likely to be married and a significant proportion of caregivers in this population are friends (not family). Moreover, discrimination and stigma across the life course necessitate continual identity management for many LGBT older adults (e.g., nondisclosure of LGBT identity in contexts in which it would be unsafe to disclose or would reduce access to resources and services). These processes may be complicated by cognitive decline in ways that increase stress. For example, with advanced memory decline the CR may inadvertently disclose to an intolerant family member or provider from whom they had previously concealed their identity, resulting in conflict or interpersonal discomfort that the CP must manage and negotiate. Thus, it is essential to address the unique CR-CP characteristics in RDAD to improve treatment effects. This study will extend and test the RDAD intervention with the sexual/gender minority population, and will also develop and test Aging with Pride: Innovations in Dementia Empowerment and Action (IDEA), a modified version of RDAD tailored to better respond to distinct risks experienced by CPs and CRs with AD/RD in the sexual/gender minority population.

2. Participants
    a. General characteristics: 150 dyads of CRs with AD/RD aged 50 or older and their CPs (N=300) will participate in the study. Either the CR or CP will be sexual/gender minority.
    b. Inclusion Criteria: Inclusion criteria for CR and CP: Either CR or CP is a sexual or gender minority. Inclusion criteria for CR: 1) age at enrollment is 50 years of age or older; 2) living in the community (not in a long-term care facility with nursing home level care); 3) have Alzheimer's disease or other dementia. Based on the definition of dementia suggested by Alzheimer's Association and scientific literature, dementia will be determined 1) by asking CP the current diagnostic

status of CR's AD/RD or 2) by asking CP whether CR has any difficulties in the domains of dementia/memory loss AND needs any help in daily activities. This method has two key aspects: (1) it precludes considerable increased costs that would be necessitated by providing a physical exam and (2) avoids unnecessary delays (and potentially loss of subjects) by scheduling an exam or waiting for receipt of patient charts. Inclusion criteria for CP: 1) willing to spend at least 30 minutes per day for study activities or willing to coordinate with CR's networks to do so; 2) providing care to the CR; 3) living in the community, not in a nursing home or long-term care facility.

c. Exclusion Criteria: Exclusion criteria for CR and CP: 1) having plans to move to a long-term care setting within 6 months of enrollment; 2) having a known terminal illness (with death anticipated within the next 12 months); 3) having been hospitalized for a psychiatric disorder in the 12 months prior to baseline; 4) actively being suicidal and having major hallucinations or delusions (occasional hallucinations or delusions are common symptoms of dementia. CR will be eligible if CR's hallucinations or delusions do not prevent participation in a low impact exercise); and 5) having any physical limitations/chronic conditions preventing participation in a low impact exercise program.
d. Number of Subjects: 150 dyads (N=300)
    i. IDEA Intervention Arm: 75 CR/CP dyads
    ii. RDAD Intervention Arm: 75 CR/CP dyads

3. Recruiting and Screening Participants:
    a. Recruiting and screening: Study announcements will be distributed by aging and health service agencies and Aging with Pride community partners using organizational contact lists via mail and email. In addition, study announcements will be posted at various health, human service and community-based organizations (e.g., health clinics, support groups, buddy programs, community-based churches, social groups) and published in community-based newspapers and newsletters. We will post study announcements on social media platforms. Study announcements include the study website address.

    Using chain referral sampling we will send an email or letter inviting individuals on our contact list to tell their friends about the study. We will ask these individuals to share the flyer provided in the email or letter. We will reimburse individuals $20 for each referred pair that successfully enrolls in the study. We will ask those who call how they learned about the study. The caller will need to name the referring individual for us to send the referring individual $20. Callers won't be required to provide the name of the referring individual if they wish to

keep their participation in the study confidential. If the caller doesn't name a referring individual, the caller may still enroll in the study if eligible. Referring individuals will be paid no more than $60 for 3 pairs that enroll. We will also use the same chain referral sampling to ask participants who have completed the IDEA intervention to tell their friends about the study.

Potential participants may contact the study by phone, email or through an on-line prescreen. Potential participants who learn about the study through the study website and complete a pre-screen are asked if they prefer to be contacted by phone, email or text. Study staff contact potential participants using their preference, following an approved script. Potential participants who email the study receive an email reply asking them to call the study phone number and leave a message if the call is not answered. Study staff return calls from potential participants who leave a message and if the potential participant is not reached leave a brief message reminding them about the study and request that they call back. Study staff will reach CP potential participants by phone so that they can answer CR and CP eligibility screening questions with a staff member to determine eligibility based on the inclusion and exclusion criteria.

We will use Trialfacts to promote, screen and refer eligible participants for the IDEA project. Trialfacts provides patient recruitment services for clinical trials. Ads may run on a combination of platforms including but not limited to: Facebook, Google, Google Display Network, Yahoo, Bing, Instagram, Youtube, Reddit, and Quorra. The ads will be linked to the Trialfacts landing page, which in turn is linked to the online questionnaire. Potential participants who complete the on-line screening will schedule a telephone interview with Aging with Pride: IDEA study staff to confirm their eligibility.

b. Recruitment Materials: Study announcements will be distributed by mail and email using aging and health service agencies' contact lists and will be posted at various health, human service and community-based organizations, and published in community-based newspapers, newsletters, and social media. A short 2-minute video will be on the study webpage and a link will be put in our social media announcements. Upon expressing interest in participating, initial screening of eligibility of CPs and CRs will be conducted by telephone using a script including the purpose and design of the study, a brief review of key elements of the consent form, and an eligibility screen assessment form.

4. Study Procedures:

a. A total of 150 CR/CR dyads will be recruited from all 50 U.S. states and territories and randomly assigned to one of two treatment arms: IDEA (75) or RDAD (75).
b. Pre-Treatment (baseline) assessment: Pre-treatment (baseline) assessments #1 and #2: Upon the random assignment, a research coordinator will contact subjects and schedule two pre-treatment assessments with a 6-week interval via telephone. CP will complete a 40 to 60-minute questionnaire via telephone for each assessment.
c. Interventions: RDAD and IDEA are 9 1-hour sessions, conducted over 6 weeks in the participants' homes or a place of their choice where privacy is ensured. The sessions will be conducted twice a week for the first three weeks; once a week for the next three weeks; in the 12-week maintenance phase 4 15- minute follow-up phone calls will occur once a month for the next 4 months.
    i. RDAD: For the ***RDAD group*** we will use the detailed treatment manual developed and used for earlier translational research (IRB 41906-D, From Evidence-Base to Practice: Implementing RDAD in AAA Community-Based Services, PI: Linda Teri). The manual includes text for the coaches, graphic illustrations of exercises, handouts, and process/treatment fidelity forms. CPs are taught how to encourage and help individuals with dementia with their exercises, and behavioral plans are developed and implemented. The exercise component of RDAD includes aerobic/endurance activities, strength training, and exercises to improve balance and flexibility. Exercises are introduced incrementally and individualized to meet the needs of each person. Each exercise is first demonstrated by the coach, then practiced by the CR and CP. Coaches monitor the exercises closely in order to ensure that they are practiced safely and correctly. In the proposed study, both CRs and CPs will practice and demonstrate the exercises at each session, and both will be encouraged to engage in a minimum of 30 minutes of moderate-intensity exercise every day. In the behavior management component of RDAD, the ABC technique is applied. CPs are taught to identify the antecedent (A) to a CR behavioral issue or problem (B) as well as the consequences (C) of the behavior. CPs are instructed to identify and modify CR behavioral problems that can impair day-to-day function, adversely affect CP-CR interactions, and interfere with exercise participation. They are given specific training in how to identify precipitants of CR problem behaviors, and how to modulate their own responses to these problems. CPs are also encouraged to identify pleasant activities that can be incorporated into the exercise program for both persons in the dyad. Finally, CP issues, such

as depression, burden, and stress, are assessed and sources of support are identified.

ii. IDEA: For the ***IDEA group*** we will use the existing detailed treatment manual, incorporating three specific risk factors that have been empirically derived and are LGBT-specific, into the behavioral component of the intervention. These include: 1) identity management; 2) stigma-related adverse or traumatic life events; and 3) lack of social support. The three LGBT-specific components are integrated into the existing training and exercises so that the time and exposure to intervention training are equivalent across RDAD and IDEA. As part of the behavior management component using ABC technique, CPs are taught how to assess and respond to CR's LGBT identity management challenges and the impact of adverse or traumatic life events, as well as how to build and sustain social support to support exercise adherence for CRs and CPs. To further increase exercise adherence and support from peers and family members, an AD/RD education DVD will be provided; the educational component includes topics such as symptoms, progression, and treatment of dementia; the effect of exercise and support on AD/RD. IDEA coaches will be trained to use motivational interviewing techniques focused on person-centered engagement, development of participant self-efficacy, and support mobilization to address barriers and facilitators to positive change in primary outcomes. For LGBT populations these may include lack of empowerment due to historical trauma, stigma, non-disclosure of stigmatized identities, and social isolation.

d. Covid-19 adaptation: During the COVID-19 outbreak the intervention delivery procedures described above will be conducted virtually by a video-conferencing platform. We will ask participants if they have a computer, iPad or cell phone capable of using any of these video conferencing platforms. For those participants who do not have video conferencing capability or prefer not to use video conferencing we will resume in-home sessions when it is deemed safe to do so according to the CDC.

e. Post-treatment assessments: Research staff will conduct, via telephone, post-treatment assessment #1 after the in-person sessions, post-treatment assessment #2 after the phone sessions, and a follow-up assessment at 13th month with CP participants to evaluate treatment effectiveness on outcomes for CR and CP participants. Participants will receive $25 for each assessment, described as reimbursement for time and expertise in research topics. Change of

address pre-stamped and addressed postcards will be given to all participants to be used to notify project staff for change of address and contact information.

5. Outcome Measures:
    a. Change in physical activity (CR) [Time Frame: Baseline (pre-treatment) to 13, 30, and 52 weeks post-treatment]
        i. Measured by the number of days of exercise for at least 30 minutes in the past week. Higher scores indicate more days of activity.
    b. Change in physical functioning (CR) [Time Frame: Baseline (pre-treatment) to 13, 30, and 52 weeks post-treatment]
        i. Assessed using mean score on physical functioning subscale of SF-36 (Medical Outcomes Study [MOS] 36-Item Short Form), consisting of 10 items assessing if participants' health limit them in activities such as walking, climbing, lifting, etc. on a 3-point scale ranging from 'yes, limited a lot' to 'no, not limited at all.' Higher scores indicate higher physical functioning.
    c. QOL (CR) [Time Frame: Baseline (pre-treatment) to 13, 30, and 52 weeks post-treatment]
        i. Quality of life was evaluated using summed scores on the Quality of Life in Alzheimer's Disease (QOL-AD), a 13-item measure widely for quality of life in interventions with persons with AD/RD. Range of scores 13-52 with higher scores indicating better quality of life.
    d. Memory-related behavioral disturbances (CR) [Time Frame: Baseline (pre-treatment) to 13, 30, and 52 weeks post-treatment]
        i. Assessed using mean scores on the memory-related subscale (7 items) of the 24-item Revised Memory and Behavior Problem Checklist (RMBPC). Higher scores indicate higher memory-related behavioral disturbances.
    a. Depressive symptomology (CP) [Time Frame: Baseline (pre-treatment) to 13, 30, and 52 weeks post-treatment]
        ii. Depressive symptomology was assessed by summed score on the 10-item Center for Epidemiological Studies-Depression Scale (CESD-10), validated among older adults and commonly used with caregiver populations. Range of scores 0-27 with higher scores indicating higher levels of depression.
    b. Perceived stress (CP) [Time Frame: Baseline (pre-treatment) to 13, 30, and 52 weeks post-treatment]
        iii. Assessed with mean scores on the Perceived Stress Scale (PSS) is a 14-item self-report measure designed to measure nonspecific, appraised stress during the past month. Higher scores indicate more stress.

6. Identifiability of data:
    a. Each and every subject will be assigned a unique identification number. This number serves as an indirect link between the assessment data collected and any identifying information gathered as a part of the study. Only the PIs and authorized research staff will have access to the link between data and the direct identifiers.
    b. Participants' name and their contact information (home address, email address, phone numbers) will be accessed by research staffs to make contacts for interventions and follow-up tests with participants. Participants will also provide contact information of CR's designated LAR, if applicable.
    c. The direct subject identifiers will be stored in a password-protected computer in an encrypted file. Any physical copies of direct identifiers (such as consent forms) will be stored in a secured and locked cabinet. Only the PIs and authorized research staff will have access to the link between data and the direct identifiers. Only the PIs and authorized research staff will have keys to the cabinet.
7. Consent
    a. In-Person Consent Process: 1) The study office will mail two copies of the consent form to the CP-CR dyad prior to the visit. The coach will visit the participants' in their home or a place of their choice where privacy is ensured. When the coach arrives, the participants will be asked if they have read their forms. If they have not, the coach will ask them to read the forms. The CR will be asked if they would like the coach to read their consent form out loud. The coach will answer any questions the CP-CR dyad has about the study. The coach will ask the dyad if they want to participate in the study. If they do not, the coach will politely end the visit. If they want to participate, the coach will ask them each to sign and date two copies of the consent form. If the CR is incapable of making informed decisions, the coach will obtain their verbal "assent" or agreement to participate in a study. After the consent forms have been signed, the coach will give each participant one copy and keep the other copy for the study's records in a secured cabinet at the UW research office.
    b. Tele-Consent Process: Once eligible CP-CR dyads have been identified, eligibility criteria met, and interest in the study established, they will be scheduled for a tele-conference consent visit. The UW office will mail the consent forms to each member of the dyad and ask them to review them prior to a consent visit. The study office will also send electronic consent forms to the CP and CR with instructions for signing electronically during the consent visit. During the tele-conference consent visit the coach will ask the participants if they have read their forms. If they have not, the coach will ask them to read the forms. CR will be asked if they would like Coach to read their consent form out loud. The coach will answer any questions the CP-CR dyad have about the study. The coach will ask the dyad if they want to participate in the study. If they do not, the coach will politely end the visit. If they want to participate, the coach will ask them each to

electronically sign, date and submit the consent forms. If the CR is incapable of making informed decisions, the coach will obtain their verbal "assent" or agreement to participate in a study.

c. Comprehension: After the forms have been read, the coach will ask the participants if they have any questions and answer all their questions. Before signing the consent forms, the coach will ask the participants: 1) whether they understand the consent form; 2) whether they have asked all of their questions and have had enough time to discuss the study; 3) whether they have received satisfactory answers to all their questions; 4) whether they have received enough information about the study to decide if they want to participate; 5) whether they understand that they are free to leave the study at any time without having to give a reason and without affecting their medical care.
d. Ongoing Process: Each session of the interventions and the assessments will be preceded by a brief review of the participants' rights, including their right to withdraw from the study and the right to refuse to answer any questions. Coaches will be carefully trained to discontinue any assessment, interview, or treatment procedures if the participant indicates either verbally or nonverbally an unwillingness to participate.
e. Documentation of consent will be obtained for all research procedures.
f. Cognitively impaired adults and other adults unable to consent: If the subject is determined to be incompetent and unable to provide consent for themselves based on the results of the decision making capacity assessment, the assent of the subject will be obtained, and consent will be obtained from a legally authorized representative (LAR). The subject will be asked to designate an individual to serve as a LAR who is authorized under the laws of the jurisdiction in which the research is conducted. For example, in Washington State, individuals who are considered to be LARs (RCW 7.70.065) are the appointed guardian; the person to whom the subject has given a durable power of attorney, which must include the authority to make health care decisions; the subject's spouse or state-registered domestic partner; the adult children of the subject; the parents of the subject; and the adult siblings of the subject. The designated LAR will be contacted by the project coordinator, and the study will be explained to the designated LAR, including risks and benefits, and that participation is completely voluntary, and can be discontinued at any time without affecting the receipt of any other services. The consent form will be mailed (including a postage-paid return envelope) to the designated LAR. The LAR will then mail the signed consent form in the postage paid envelope to the project coordinator.

Alternatives to LARs: According to previous studies, it is likely that LGBT older adults with Alzheimer's disease and related dementias (AD/RD) will not have an LAR. LGBT older adults are less likely to be married or partnered and less likely to have children. They tend to have limited contact with relatives, and many of them are reluctant to disclose their sexual and gender identity to their family. Many LGBT people form "families of choice" as a way of coping with rejection by biological family and relatives. Families of choice often include non-legally-recognized partners and close friends, who are not recognized as LARs. Thus, a "family of choice" CP participating in the study with their CR will serve as an alternative to an LAR if there is no LAR or if the LAR's relationship with the CR is negative or estranged.

8. Privacy and Confidentiality:
    a. Privacy Protections: Only UW research staff members will contact study subjects. All intervention sessions will be conducted by trained research staff in a place where privacy is ensured. Coaches will ensure that sessions remain confidential and that they are in a place where others cannot observe. Sessions will be audio recorded only for the purpose of monitoring treatment fidelity. Assessment data collected will be available only to the project staff and investigators directly involved with this study. No others will have access to the data. Collected data are confidential. Each subject will be assigned a unique identification number. Direct identifiers including contact information will be stored separately from the data collected through questionnaires, interviews, and assessments. The data cannot identify a subject without having access to the link between the identification number and the direct identifiers. A study subject cannot be identified by anyone except the UW lead researchers and authorized research staff members who have legitimate access to the single record identifying subjects by their research ID number. This record will be stored and maintained separate from all data and other information gathered. All data will be stored in encrypted computer files and records will be identified by a unique identification number that are assigned by the study. The data files will not contain any identifying information.
    b. All members of the research team will complete required training in human subjects and HIPAA, including training in data management and confidentiality.
    c. Retention of identifiers and data: We will not destroy any identifiers (or links between identifiers and data/specimens) and data that are part of research records until after the end of the applicable records retention requirements.
9. Risk/Benefit Assessment:

a. Anticipated Risks: Subjects in the study may be inconvenienced or experience psychological discomfort related to assessment questions including previous experiences of LGBT-specific adverse experiences and everyday discrimination. Subjects may also experience mild physical discomfort related to engaging in new physical exercise activities. These problems have not previously occurred in Drs. Teri or Fredriksen-Goldsen's studies, and we estimate the risks to be minimal. Subjects are informed that they are free to not answer any question and not to participate in any exercises.

b. Protections against psychological discomfort: To minimize the risk of distress or emotional upset, the following steps will be taken: 1) The PIs are experienced in conducting interviews and assessments by phone and in-person with subjects experiencing cognitive impairment and mood or behavioral disturbance; they are also experienced with research involving LGBT older adult health. Throughout the study they will respond in a sensitive and respectful manner, in-person or by phone, to individuals who are distressed. 2) The coaches will receive training from the PIs to monitor for distress and will be advised to immediately contact the PIs with any concerns related to the intervention or assessments resulting in psychological discomfort to the subjects. All concerns will be addressed in collaboration with the PIs. Subjects will be advised of their right to not answer any question(s) and/or to withdraw from the study at any time. No adverse emotional responses have been reported in our prior experience with training staff to deliver behavioral strategies. All sensitive questions in the proposed study are worded respectfully and have been used in previous studies with no adverse consequences. 3) The CPs will receive training from the coaches on how to monitor for distress and how to identify and monitor potential triggers and redirect CRs to other activities with more pleasant memories. 4) If psychological distress is identified, for example severe depression or anxiety, referral to a primary care provider or mental health provider will be initiated. Resources (e.g. contact information of CR's primary doctor or mental health provider) will be identified at the beginning of the intervention. Distress requiring referral has never occurred in previous studies of the RDAD intervention.

c. Protections against physical discomfort: If subjects experience mild physical discomfort related to engaging in new physical exercise activities, they will be informed that they do not need to participate in any exercises. We estimate physical discomfort to be minimal in the proposed study.

d. A potential breach of confidentiality regarding subjects' sexual/gender identity and/or medical condition may cause psychological or social harm. All team members signed a confidentiality agreement prior to being involved in the study. All participant information is to be kept strictly confidential with the only

exception being incidents of abuse of a dependent adult or minor child and risks of imminent harm to others or to the subject. All researchers have completed training in research with human subjects.

10. Analysis Plan: All participant data will be included in the study, according to the intent-to-treat principle, after excluding participants who withdrew prior to completing their baseline assessment. Analysis will be completed using Stata/MP 16.1 (StataCorp, 2019). To assess whether randomization of patients was successful, the two treatment groups will be compared by baseline demographics and clinical characteristics using two-sample *t*-tests, Chi-Square tests of independence, or Fisher's exact tests as appropriate. To test efficacy of the interventions, we will use linear mixed models to test the short- and long-term intervention effects on outcomes, with time treated as a categorical variable. The models included random intercepts and slopes for each participant to account for individual variability at baseline and change over time of the outcome variables and included baseline scores of the outcomes as fixed effects. Mixed-effects logistic regression models were estimated for binary outcomes, and continuous outcomes were estimated with mixed-effects linear regression models. Moderation effects were evaluated using interaction terms in the linear mixed models. The proposed sample size with a two-sided significance of 5% and a statistical power of 80% is sufficient to detect a small effect (d= 0.25), which is greater than a minimal clinically important difference level. The statistical significance of all hypothesis tests were set at two-sided level of p = .05.