Feasibility of a Dyadic Life Review Intervention for Older Patients with Advanced Cancer and Mild Cognitive Impairment (MCI) and their Caregivers

Study Protocol and Statistical Analysis

NCT05200572

Date: 1/20/2022

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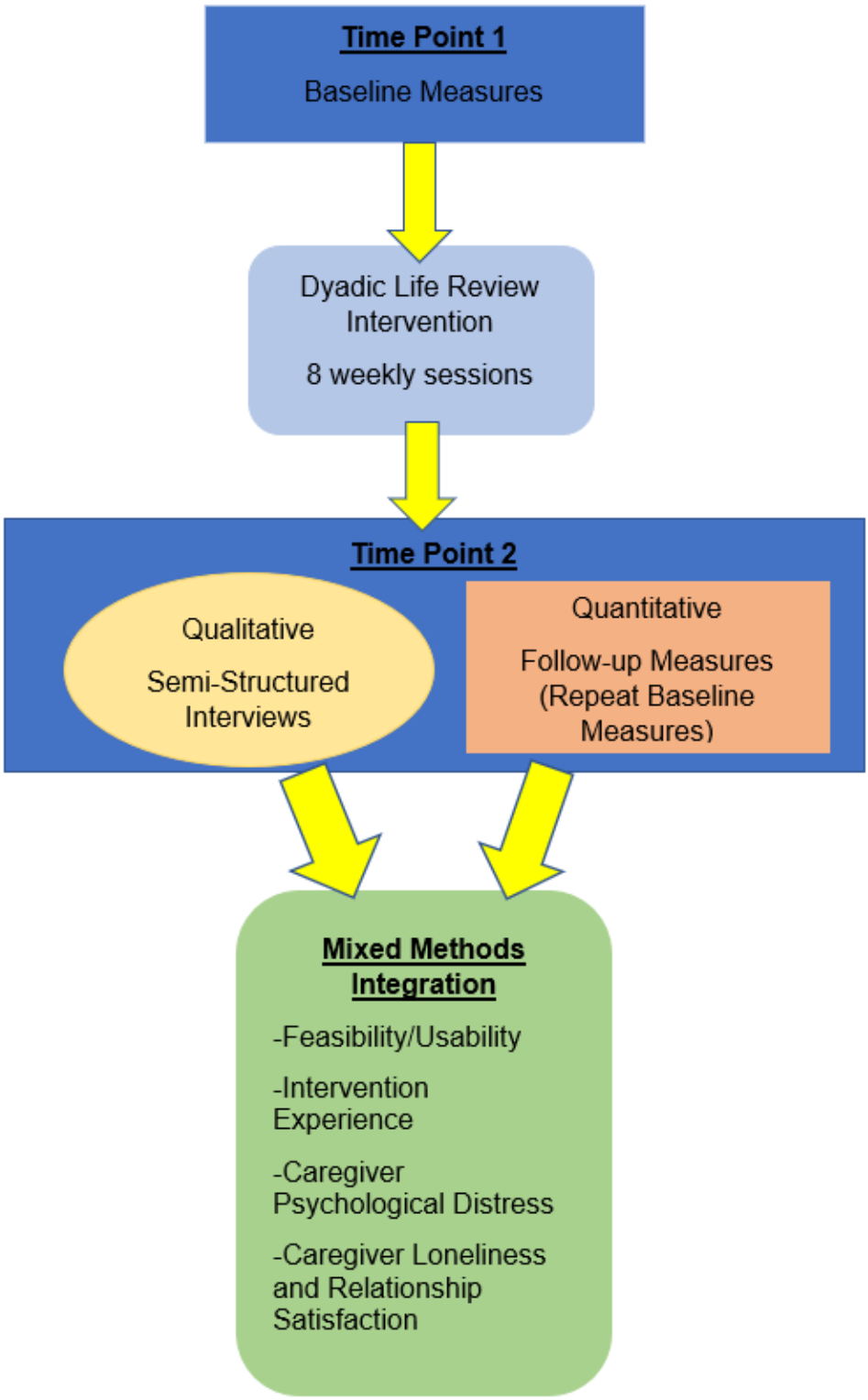
Study Schema:



1. PURPOSE OF STUDY

The purpose of this study is to test the feasibility of a telehealth Dyadic Life Review (DLR), adapted from individual Life Review Therapy, with caregivers of older adults with advanced cancer, including those with Mild Cognitive Impairment (MCI). The study will enroll dyads of caregivers and older patients with advanced cancer and dyads of caregivers and patients with advanced cancer and Mild Cognitive Impairment (MCI). Life Review Therapy has only been delivered individually and there are no dyadic mental health interventions designed to target the mechanism of communal coping and reduce distress and emotional health outcomes in both older patients with advanced cancer and their caregivers. This innovative pilot study will gather data to test the feasibility of adapting Life Review Therapy to be delivered as a dyadic life review (DLR) and examine pre-post intervention changes in caregiver psychological distress.

1.1. Objective and Specific Aims (40 patient/caregiver dyads):

Objective: The research team will adapt and refine a dyadic life review intervention for older patients with advanced cancer, older patients with advanced cancer and MCI, and their caregivers. A mixed methods (i.e., integration of qualitative and quantitative data) approach will be used to gain understanding of the usability and feasibility of a telehealth DLR intervention with older adults with advanced cancer and their caregivers and examine effects on distress and emotional health in both the patient and caregiver.

1.2 Primary Aim:

1.2.1 To evaluate the feasibility of the dyadic life review intervention in older patients advanced cancer, with or without MCI, and their caregivers by determining consent rate, intervention adherence rate, and patient/caregiver acceptability. Hypothesis: We will achieve a dyad consent rate of 70%, dyad intervention adherence rate of 70%, and the intervention will be generally acceptable by dyads (determined from semi-structured interviews).

1.3 Secondary Aims:

1.3.1 To examine the pre-post change in the primary outcome of caregiver self-reported psychological distress, and secondary outcomes of caregiver loneliness, relationship satisfaction, and mental health outcomes, and changes in the associations between patient and caregiver distress.

1.4 Mixed Method Aim:

1.4.1 To enhance understanding of the usability of a telehealth based DLR intervention for older patients with advanced cancer and MCI, older patients with advanced cancer and MCI, and their caregivers and gain feedback on the intervention from separate semi-structured interviews of patients and caregivers. Integration will occur by using the qualitative data from semi-structured interviews to explain changes in the caregiver outcomes. The interviews will provide explanation for changes or lack of changes in the quantitative measures seen.

1.5 Exploratory Aims:

1.5.1 To explore the feasibility of collecting heart rate variability (HRV) from older patients with incurable cancer, MCI, and feasibility of collecting HRV from their caregivers.

1.5.2 To explore relationships between measures associated with the target mechanism model of communal coping to inform future development of a single communal coping measure in older patients with advanced cancer and their caregivers.

2. BACKGROUND AND RATIONALE

Older patients with cancer will make up 60% of all cancer diagnoses by 2035.[1] The increase in older patients with cancer places more burden on caregivers.[2] Advanced cancer brings multiple challenges in each area of life for both older patients and caregivers. Cancer caregivers take on multiple domains of care, contributing to loneliness and relationship distress, with caregivers older than 50 experiencing more adverse mental and physical health outcomes.[3] Supportive care interventions should involve caregivers.

Older adults with cognitive impairment and advanced cancer and their caregivers experience a vicious cycle of reciprocal distress, depression, and anxiety.[4] It is estimated that 67% of patients over 65 will make up the new cases of cancer between 2010 and 2030.[1] Older patients with cancer also present with comorbidities and other age-related conditions, such as Mild Cognitive Impairment (MCI) or dementia. These conditions place an immense burden on cancer caregivers.[5] Cancer caregivers support multiple areas of life for patients with cancer, including but not limited to medication management, treatment appointments, activities of daily living (ADLs) and instrumental activities of daily living (iADLs), financial needs, and emotional support.[6] Considering the reciprocal distress and emotional health between patients and caregivers, and compounded needs of older patients with advanced cancer who have cognitive impairment, interventions targeting both the patient and caregiver dyad are needed. However, few mental health interventions have been adapted to this growing but vulnerable dyad that considers the trajectories of relationship satisfaction and loneliness in patient/caregiver dyads in this context where needs are immensely high.

2.1 *MCI and Cancer:*

MCI is prevalent in older patients with advanced cancer. This unique population of older patients with both advanced cancer and MCI and their caregivers have very high needs that are currently unmet. In a large nationwide study of older patients with advanced cancer, 33.5% met criteria for cognitive impairment.[7] Studies suggest caregivers of older adults with cognitive impairments experience burden,[8] relationship distress,[9] and loneliness. Considering the combination of MCI and advanced cancer, the responsibilities of caregivers are compounded, potentially leading to more significant distress and worsening loneliness.

2.2 *Life Review Therapy and Outcomes for Older Adults*:

Older patients with MCI and advanced cancer present a compounded burden on caregivers, with reciprocal distress worsening emotional health and quality of life for both patients and caregivers. Studies suggest a major gap in interventions for older patients with MCI and advanced cancer.[10] Intervention studies to date have focused on prevention of cognitive decline or early identification of

cognitive impairments.[11,12] However, no studies focus on loneliness and distress of caregivers in this clinical context. Life Review was developed in 1968 and has been repeatedly shown to improve multiple emotional outcomes.[13] Life Review therapy has been used in older adults in community settings, improving quality of life and reducing depression.[14] In older adults with cognitive impairment, Life Review improved cognitive functioning.[15] Additionally, Life Review therapy has been combined with memory specificity training demonstrating the Life Review is feasible in older patients with memory decline.[16] A patient/caregiver DLR intervention could promote a communal coping mechanism and result in improved emotional health for both caregivers and patients.

2.3 ***Dyadic Life Review Intervention:***

The traditional Life Review Therapy[17] uses an 8-week, structured approach, with each session focused on a period of the life span, such as, childhood, adolescence, and so on. The intervention is often applied chronologically, but with flexibility for clinical judgements to explore other time periods that may arise for patients. For this proposal, Life Review Therapy will be adapted to be delivered dyadically, by the PI, a licensed mental health counselor and other trained clinicians with expertise in care of older adults, specifically for the older patient with advanced cancer and cognitive impairment and caregivers at risk or experiencing loneliness. The Dyadic Life Review (DLR) intervention will be delivered by one of three licensed mental health clinicians via videoconferencing over eight sessions. The goal of DLR is to enhance the dyad's communal coping and thereby reduce the loneliness and relationship distress experienced by both the older patient and caregiver. Communal coping is a process that enhances the dyad's joint resilience in supporting and managing the illness.6 Life review therapy has been found to reduce depression in older adults[14] and promote emotional health and quality of life in patients with cancer in palliative care.[18] Life review therapy combined with memory training has shown improved emotional health and cognitive functioning in older patients with cancer.[16] Reminiscence therapies, which have similar processes and mechanisms to life review therapy improves cognitive functioning, anxiety, and depression in older adults with cognitive impairments.[19] The vulnerable population of older patients with cancer and cognitive impairment may benefit from a DLR intervention as the intervention supports the patient/caregiver dyad in promoting communal coping, reducing loneliness and distress in both patients and caregivers, and supporting cognitive functioning in patients.

2.4 ***Heart Rate Variability and Psychosocial Assessments:***

Studies have demonstrated a link between heart rate variability as a physical measure that correlates with the response to stressful life events.[20] Additionally, heart rate variability has been shown as an effective measure for a person's stress resilience.[21] Recent studies have measured HRV in patients with cancer as a marker of distress,[22] and utilized HRV as a mechanism for a biofeedback intervention to support patients with cancer in regulating stress and emotions.[23] However, no studies have explored HRV in older patients with cancer and their caregivers. This exploratory aim could support the further adaptation of patient and caregiver (dyadic) interventions and results could help power future studies.

The proposed study adapts and refines a well-established Life Review intervention to be used in a telehealth dyadic format to test the feasibility of using a telehealth dyadic life review intervention. Caregivers are an integral part to the management and navigation of advanced cancer in older patients. Additionally, when older patients with advanced cancer have MCI, caregivers take on even more roles to support the older patient's everyday life and long-term care. Intervention studies have examined preventative interventions to stall

cognitive decline, as well as interventions for identifying cognitive decline in patients with cancer. There are no studies that have engaged the caregivers of older patients with advanced cancer and MCI in the intervention design. Further, the use of a video-conferencing technology allows the intervention to be scalable. Many older patients with cancer and caregivers receive care and treatment from community clinics. Additionally, with the current state of the COVID-19 pandemic, delivering the DLR intervention provides an opportunity to test the feasibility of a telehealth intervention to promote safety as well as accessibility to older patients and caregivers in community settings.

3. ADMINISTRATIVE ORGANIZATION

Research locations:

3.1 The setting of this study will be Wilmot Cancer Institute (WCI) and Highland hospital. The WCI and Highland hospital site is the largest provider of cancer care across 16 counties in upstate New York. The WCI has an established infrastructure for conducting clinical research. WCI provides sources of collaboration, research training programs, weekly grand round presentations, and highly productive special interest research groups.

3.2 Rochester Roybal Center for Social Ties and Aging Research: The Rochester Roybal Center for Social Ties and Aging is funded through an NIH P30 grant and National Institute of Aging with the mission to support the development of behavioral interventions targeting the improvement of social connectedness for caregivers of family members with dementia. The Roybal Center will provide STAR resources to support caregiver assessments.

3.3 DLR participation will take place through video-conferencing. Participants will be encouraged to participate from their home or other private location. Wherever the location may be, the PI or other trained licensed mental health clinicians who are conducting the DLR intervention will ensure privacy in a private room with a closed door. Participants will be provided with a HIPAA compliant tablet to use for participation in the intervention activities and the intervention will be delivered using HIPAA compliant video-conferencing technology provided by the University of Rochester. The coordinator will be in touch with patients by phone throughout the length of the study. The study coordinator will help organize the scheduling/rescheduling of baseline assessments, DLR session, and follow-up assessments and interviews, and will be available for any patient or caregiver questions.

4. STUDY DESIGN

Forty dyads will be enrolled in a single-arm mixed methods intervention trial in order to evaluate the feasibility of enrolling older patients with advanced cancer, older patients with advanced cancer and MCI, and their caregivers. This single-arm feasibility study will allow the PI and the team to develop and examine the feasibility of a telehealth-based DLR intervention that has not previously been adapted or tested in these populations. A pre-post test design will be used to measure effects of the DLR intervention on the primary outcome of psychological distress in caregivers. Patients and caregivers will undergo separate semi-structured interviews.

4.1 SUBJECT POPULATION

4.1.1 Subject Characteristics

a) **Number of Subjects:** We propose to enroll a total of 40 dyads. We will recruit at least 20 dyads of older patients with both advanced cancer and MCI and their caregivers.

All dyads will be recruited via cancer clinics in the University of Rochester/Wilmot Cancer Institute (URWCI) catchment area.

b) **Gender and Age of Subjects:** We intend to recruit across the gender spectrum, including females and males. Patients will be ≥ 65, with no upper age limit. Caregivers of all older patients with will be ≥ 50, also with no upper age limit. Based on a previous study by our team[5] we anticipate more female caregivers to enroll, as general caregivers within the population caring for older adults with cancer and/or MCI are predominantly female. Using these previous demographics, we anticipate the following breakdown of caregiver/patient dyads:

Dyad Gender Combinations	Percentage of sample
Male Patient/Male Caregiver	10%
Male Patient/Female Caregiver	40%
Female Patient/Female Caregiver	20%
Female Patient/Male Caregiver	30%

c) **Racial and Ethnic Origin:** There are no exclusion criteria based on racial and ethnic origin. We expect the sample to be representative of the population of older patients with advanced cancer and their caregivers seen at URWCI and living in the WCI catchment area.

4.2 STUDY INTERVENTIONS

DLR will consist of 8 sessions delivered by a trained licensed clinician (i.e, the PI or other trained clinician) via video-conferencing in weekly sessions of 60 minutes. Each session will facilitate a recall of each phase of life (Table 1). The patient and caregiver will each be asked structured questions to prompt reminiscence of memories from that phase of life. The DLR intervention guide attached to this protocol provides a framework of questions for each session, which follow the current standardized Life Review Handbook.[20] The guide acts as a framework, interventionist are able to use clinical judgment to prompt further or ask follow the patient and caregiver if pertinent events are being recalled outside of that time period. This will provide data to examine the feasibility of the DLR intervention and adapt and refine the intervention to the study's target population. Additionally, the patient and caregiver will be asked to recall if either the patient's or caregiver's recalled memory parallels the other's experiences (e.g. To Caregiver: "Does any aspects of [patient's] experience make you think of your own experiences around that time period?"). The fourth session will review recalled memories and focus on promoting communal coping in the present by drawing parallels of strength and resilience to managing MCI and cancer. The final session will review shared memories, from time periods the dyad was together, to enhance communal coping through connecting

shared memories. Each session will have flexibility for clinical judgement.

Table 1: Intervention Overview	
Week	Session Life Period
1	Childhood
2	Adolescence
3	Young Adulthood (20-35 years)
4	Mid-Intervention review and dyadic processing
5	Mid-life (35-50 years)
6	Earlier later life (50-65 years)
7	Later life (65 years +)
8	Final review of shared memories and dyadic processing

5. INCLUSION AND EXCLUSION CRITERIA

The eligibility criteria are aimed at identifying older patients with advanced cancer and older patients with advanced cancer and MCI. Patients will be asked to identify a caregiver, caregivers will also be consented to participate in study processes.

5.1 Patient Inclusion Criteria:

- Age ≥ 65
- Able to provide informed consent. All patients will be assessed using the University of California, San Diego Brief Assessment of Capacity to Consent (UBACC)56 – a score >14.5 will define ability to independently provide informed consent. Eligible patients have Stage III or IV cancer of any type
- Additionally, at least 20 patients will have a will have a high likelihood of MCI based on screening score of <26 on the Montreal Cognitive Assessment (MoCA) within their eRecord chart
- Able to read and understand English

5.2 Exclusion Criteria for all patients:

- Patients scoring <14.5 on the UBACC
- Unable to identify caregiver to participate in study

We anticipate enrolling at least 20 patients with advanced cancer and MCI and up to 20 patients with advanced cancer without MCI.

5.3 Caregiver Inclusion Criteria:

- One caregiver for each patient will be eligible and must be chosen by the patient. For the purposes of this study, a caregiver is defined as a valued and trusted person in a patient's life who is supportive in health care matters by providing valuable social support and/or direct assistive care.
- Caregivers will be selected by the patient when asked if there is a "family member, partner, friend or caregiver with whom you discuss or who can be helpful in health-related matters;" patients who cannot identify such a person ("caregiver") will remain eligible for the study.

- Age 50 or older
- Ability to provide consent
- Proficient in English

5.4 Caregiver Exclusion Criteria:

- Caregivers unable to understand the consent form due to cognitive, health or sensory impairment will be excluded

We anticipate enrolling at least 20 caregivers of patients with advanced cancer and MCI and at most 20 caregivers of patients with advanced cancer.

5.5 Vulnerable Subjects: Recruitment will exclude vulnerable populations such as fetuses, neonates, children, pregnant woman, prisoners, and institutionalized individuals. We will also exclude adults who are deemed to not have decisional capacity and those who lost their consent capacity during the study period, as per their treating oncologist.

6. RECRUITMENT METHODS

Subjects will be enrolled at University of Rochester Wilmot Cancer Institute and Highland Hospital. The clinic schedules of oncologists will be screened for eligible patients and caregivers.

6.1 Patient and Caregiver Identification and Recruitment:

Potential patients will be identified in multiple ways. First study participants will be identified by their treating physician, the nurses that work with the physicians, members of the research team, and the study coordinator. The PI and study coordinator will utilize eRecord to screen eligible patients with Stage III or IV cancer, of any type. With permission from oncology providers, the PI and study coordinator will screen clinic schedules for eligible patients with Stage III or IV cancer, of any type. The study coordinator contacts the physician (or their designee) and lets them know that a patient may be eligible for the study. The physician (or their designee) then confirms if the patient meets study eligibility criteria. If there is a question about eligibility, the PI will be contacted and will meet with the patient and/or health care proxies, review the medical records, and perform an assessment of eligibility if necessary. After meeting with the physician (or their designee), the study coordinator will meet with the patient, and explain the details of the study. Study staff will introduce the study to the patients and provide adequate time to read the consent. Consent will not be obtained until a caregiver is identified.

Recruitment of caregivers: If patients are agreeable to participating in the study, patients will be asked if there is a "family member, partner, friend or caregiver, age 50 or older, with whom you discuss or who can be helpful in health-related matters;" to participate as a caregiver. If patients are unable to identify a caregiver, they will not be enrolled as the dyad involvement is central to the primary aim of the study. If patients are able to identify a caregiver, the study coordinator will give the patient a study information sheet that summarizes the purpose of the study, what the study entails, and study staff contact information. If the caregiver is interested in participating, s/he will contact the study staff using the contact information provided on the study information sheet. The study coordinator will then introduce the study to the caregiver and provide adequate time to read the consent. In order to align with the NIA funder for including

caregivers of older patients with both advanced cancer and caregivers, recruitment will aim to reach maximum variation of caregiver loneliness.

Identification and recruitment via advertisements in cancer clinics and related sites: Our RSRB-approved advertisements will be displayed in cancer clinics, local sites of interest, and social media (e.g., Clinical Translational Science Institute, University of Rochester) and distributed by clinicians and clinical staff. The advertisements contain information about the study duration, assessments, and eligibility criteria. If the patient is interested, they can contact the study team (e.g., the study coordinator or principal investigator (PI) via phone or email) to discuss the study, determine likelihood of eligibility, ask for permission to contact the patient's physician for their approval, and set up a time to conduct the informed consent discussion in a private location.

Identification and recruitment via direct referral from nurses and physicians: We are working with several oncologists (including, but not limited to our co-investigators Drs. Mohile, Mangussen) and their medical team (e.g., nurses, nurse practitioners) to identify potential patients at the Wilmot Cancer Institute and Highland Hospital who are likely eligible for our study. If the patient is eligible based on information in the medical records and from the physician and medical team, we will request that the physician refer the patient to us or obtain the physician's permission to contact the patient to discuss our study and to conduct the informed consent discussion if the patient is interested in the study.

7. CONSENT PROCESS

7.1 Informed Consent: Informed consent will be obtained from the patient and caregiver by the PI or study coordinator in person during a clinic visit. The study coordinator uses the informed consent document as a written aid and goes over every detail of the study with the patient in person and recruits them to the study. The study coordinator, the oncologist and the nurses are available to answer any questions the patient or caregiver may have about any aspect of the study prior to consenting and throughout the entire study period. Patients and caregivers may choose to sign the informed consent immediately on the day the study information is presented to them or they may choose to take the informational consent form home and discuss it with others. If they want to participate in the study, they can sign it the next time they meet with the study coordinator or investigators. If the patient is participating in a telehealth visit and expresses interest, the member of the study team will ask patient for his/her permission to be mailed an informational consent for their review. Immediately after review of the informed consent or verbal consent script, an IRB-approved adapted version of the San Diego Brief Assessment of Capacity to Consent (UBACC0 will be administered to determine capacity to consent.

7.2 Verbal Informed Consent: If the patient or caregiver cannot meet in person with the study coordinator to sign the informed consent, the study coordinator will verbally consent the subject. The study coordinator will use the verbal consent script, then sign and date it to confirm that s/he followed the script and the subject agreed to participate in the study. Following the completion of verbal consent with the subject, the coordinator will mail or email the subject an information sheet that summarizes what the study entails and the subject's involvement in it.

Waiver of documentation of consent:

We are requesting for waiver of documentation of consent as the research involves no more than minimal

risk to the subjects (patient or caregiver) and involves procedures for which written consent is normally not required outside the research context. The only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality.

7.3 During informed consent procedures, individuals will be told about possible risks and benefits of participation. This will include information that questions asked may cause them to feel uncomfortable or upset. They will be informed that: they may withdraw from an assessment at any time for any reason and receive full reimbursement for that assessment; and, they may withdraw from the research study at any time without negative consequences. Subjects are further informed that we will perform an immediate evaluation of their dangerousness towards self or others should safety concerns arise during assessments or treatment sessions. As well, they will be informed that we may contact their primary care physicians should concerns arise about medical or psychological risk. The staff will assess the participant's understanding of the study using an IRB-approved adapted version of the San Diego Brief Assessment of Capacity to Consent (UBACC), that we have implemented successfully in past URMC studies involving older adults. If a participant fails to answer all questions correctly, the staff will re-explain the study and then test the participant again. The consent will be an ongoing process during the study. Explanations of the study and verbal consent will be conducted at each data collection. Participants will be reminded that their participation is voluntary and that they can withdraw at any time for any reasons.

7.4 Baseline Measures and Study Procedures: The baseline measures will then be performed via REDcap survey links or mailed baseline measures with return addressed envelope, if patient and caregiver are unable to complete via REDcap or mailing, the study coordinator or PI will collect baseline measures via telephone, and study procedures will then occur. The patient must be determined to have decision-making capacity to provide informed consent by their treating oncologist and by the San Diego Brief Assessment for Capacity to Consent questions within the informed consent process. If patients are determined to not have decision-making capacity or they require a healthcare proxy to provide consent, they will not be enrolled.

7.5 Human Subject Protection: Ethical standards for human subjects will be strictly followed in accordance with the University of Rochester Research Subject Review Board Investigator Guidance policy and the University of Rochester Policy on Enrollment of Adult Decisionally Incapacitated Research Subjects and Permission of Authorized Representatives.

Patients with MCI may be considered a vulnerable population but are necessary to answering our research questions. For all patients, we will formally assess capacity to consent using the University of California San Diego Brief Assessment of Capacity to Consent (UBACC), adapted for our study. Following the informed consent process, decisional capacity for clinical research participation will be confirmed with the UBACC. The UBACC is a 10-item scale that can be administered by a Bachelor Degree-level research coordinator. The UBACC determines patient's understanding of key aspects of the consent process (e.g. purpose of study, risks of study). A UBACC total score >14.5 will be considered confirmed for decisional capacity for clinical research. For patients scoring <14.5, on the UBACC, they will be unable to participate.

7.6 Participation: Current, state, federal, and institutional regulations concerning informed consent will be followed. Participation in this study is voluntary. Participants are free not to take part or to withdraw at any

time, for whatever reason, without risking loss of present or future care they would otherwise expect to receive. In the event that a patient does withdraw from the study, the information they have already provided will be kept in a confidential manner. Participants may discontinue participation in the study at any time if they decide they do not wish to take part any longer. Participants may be withdrawn from the study by research personnel if it is deemed in their best interest to no longer participate.

7.7 Duration: Patients who consent to the study will be in this study for 14 weeks. Patients will be consented to actively participate, receive phone calls or meet with the research study team for up to 14 weeks after their initial visit. The research team may contact patients in the future to gain further information first hand regarding patients' overall health and treatment. Dr. Kehoe may decide to take patients off the study without their consent if the study is stopped. Additionally, patient data will be kept indefinitely at URMC, even after the study is closed or a patient passes away. It will be maintained in a locked database with password access only (See Section 14).

8. STUDY PROCEDURES

8.1 Measures:

Patient measures will include demographics, cognitive, psychological, and functional independence measures.

Demographics: Patient and caregiver demographics will be collected, including age, gender, race, ethnicity, marital status, education and socio-economic status will be captured. Cancer and treatment variables, comorbidities, and medications list will be collected from the medical record by study staff.

Questionnaires: Psychosocial, survey-style questionnaire assessments will be conducted at baseline and post-intervention, will take less than 1 hour, will consist primarily of quantitative (closed-ended) questions, and will employ the REDCap online survey system, licensed to the University of Rochester, for patients and caregivers to complete on their own. The REDCap questionnaires will be coded by a member of the study team who has experience coding and creating questionnaires and with the methodology of REDCap questionnaire entry.

Patient Measures	Target Aim	Information
UCLA Loneliness Scale, short-form	Secondary Aim: support recruitment to reach maximum variation of caregiver loneliness scores	Score of 6 or greater indicates loneliness
Unidimensional Relationship Closeness Scale	Secondary Aim: relationship domain	Quality of relationship with care-receiver: assesses quality of relationship between participant and family member and has demonstrated valid

		scores across several relationship types, including spouses and other family members
PROMIS29	Secondary Aim: mental health and physical health domains	Assesses for seven domains of depression, anxiety, physical function, pain interference, fatigue, sleep disturbance, and ability to participate in social roles.
Perceived Stress Scale	Secondary Aim: mental health domain	Measure the degree to which situations are appraised as stressful
Geriatric Depression Scale (GDS)	Secondary Aim: mental health domain	Identify clinical threshold of depression in older adults
Distress Thermometer and Problem List	Secondary Aim: primary outcome	10-point self-report measure to capture distress and identify a list of sources of that distress
Dyadic Adjustment Scale-7 (DAS-7)	Secondary Aim: relationship domain	7-item measure to assess relationship quality
Dyadic Support Questionnaire (DSQ)	Secondary Aim: relationship domain	18-item measure to assess individual's perceptions of received and provided support.
Peace, Equanimity, and Acceptance in the Cancer Experience (PEACE)	Exploratory Aim 1.5.2: communal coping domain	Measure of an individual's acceptance and/or struggle in coping with an illness
Control Preference Scale	Exploratory Aim 1.5.2: communal coping domain	Measurement of perceived control in how people make treatment decisions with life-threatening disease
Inclusion of Other in Self	Exploratory Aim 1.5.2: communal coping domain	Perceived closeness the respondent feels with another person
Interpersonal Needs Questionnaire	Exploratory Aim 1.5.2: communal coping domain	Relationship belonging and perceived burden

Caregiver Measures	Target Aim	Information
UCLA Loneliness Scale, short-form	Secondary Aim: support recruitment to reach maximum variation of caregiver loneliness scores	Score of 6 or greater indicates loneliness
Unidimensional Relationship Closeness Scale	Secondary Aim: relationship domain	Quality of relationship with care-receiver: assesses quality of relationship between participant and family member and has demonstrated valid scores across several relationship types, including spouses and other family members
PROMIS29	Secondary Aim: mental health and physical health domains	Assesses for seven domains of depression, anxiety, physical function, pain interference, fatigue, sleep disturbance, and ability to participate in social roles.
Perceived Stress Scale	Secondary Aim: mental health domain	Measure the degree to which situations are appraised as stressful
Caregiver Reaction Scale	Secondary Aim	Items assess both positive and negative aspects of caregiving, have been shown to be responsive to intervention. Subscales: role captivity, overload, relational deprivation, competence, personal gain, family beliefs, family conflict, job conflict.
Geriatric Depression Scale (GDS)	Secondary Aim: mental health domain	Identify clinical threshold of depression in older adults
Distress Thermometer and Problem List	Secondary Aim: primary outcome	10-point self-report measure to capture distress and identify a list of sources of that distress
Dyadic Adjustment Scale-7 (DAS-7)	Secondary Aim: relationship domain	7-item measure to assess relationship quality
Dyadic Support Questionnaire (DSQ)	Secondary Aim: relationship domain	18-item measure to assess individual's perceptions of received and provided support.
Peace, Equanimity, and Acceptance in the Cancer	Exploratory Aim 1.5.2: communal coping domain	Measure of an individual's acceptance and/or struggle in

Experience (PEACE)		coping with an illness
Control Preference Scale	Exploratory Aim 1.5.2: communal coping domain	Measurement of perceived control in how people make treatment decisions with life-threatening disease
Inclusion of Other in Self	Exploratory Aim 1.5.2: communal coping domain	Perceived closeness the respondent feels with another person
Interpersonal Needs Questionnaire	Exploratory Aim 1.5.2: communal coping domain	Relationship belonging and perceived burden

Heart Rate Variability (HRV) will be calculated with the ambulatory monitoring heart-rate device Firstbeat Bodyguard 2® that measures RR intervals with a rating sample of 1 ms. The device utilizes a valid and reliable method for sampling RR intervals and provides software to analyze the raw data. We will calculate two time and frequency domain measures of HRV: SDNN (the standard deviation of all normal RR intervals measured between consecutive sinus beats), and RMSSD (the root mean square of successive differences between adjacent normal R-R intervals). In addition, we will measure frequency domain measures, natural log of high frequency (HF, total spectrum power of all NN intervals between 0.15 to 0.4 Hz) for vagal tone/RSA, natural log of low frequency (LF, total spectrum power of all NN intervals between 0.04 to 0.15 Hz), and LF/HF ratio. The use of HRV in this study will be to explore the feasibility of collecting HRV data via telehealth in this method and with this included dyad population. Additionally, there are links between HRV and stress management and emotional regulation.[20] This exploratory measure will provide information about HRV, stress management, and emotions in older patients with cancer and their caregivers to improve the intervention and power future studies.

Time Point 1 Measures: Patients and Caregivers will complete the baselines, time point 1 measures within two weeks of beginning their DLR intervention.

Time Point 2 Measures: The same measures provided at baseline, will be repeated within two weeks after the conclusion of the DLR intervention.

Semi-Structured Interviews: The in-depth interviews with the patients and caregivers (interviewed separately) will focus on patient and caregiver experiences before, during, and after the telehealth DLR intervention. Patients and caregivers will be interviewed separately to ensure that each partner has a chance to disclose feelings and experiences without being censored by the other partner. Interview transcripts for a dyad will be compared later to establish common themes.

8.2 Study Procedures:

• After Informed Consent: Immediately after informed consent, the UBACC will be administered to determine capacity to consent. the study coordinator or PI will provide patients and caregivers with a HRV device to bring home. If patients are unable to bring the HRV device home, study staff will mail HRV device to patient/caregiver with return address envelope. This is an exploratory aim to explore the feasibility of collecting HRV with older patients and caregivers in this way. Patients and caregivers will then return the

HRV device at their next clinic visit or mail back in provided return address mailer.

• Heart Rate Variability Collection (HRV): Study staff will coordinate a zoom call with the patient and caregiver to demonstrate how to use the HRV device. Patient and caregivers will each take turns using the HRV device. Patients and caregivers will separately follow the following procedures when wearing the HRV device:

- set timer for 20 minutes
- sit in comfortable position
- quiet space with no distractions
- dimly lit room
- no use of phone or any devices
- maintain normal breathing

• Baseline: Following informed consent, patients and caregivers will undergo Time Point (TP) 1 measures. Patients will be provided a data-enabled tablet with HIPAA-compliant video-conferencing application and instructed on its use, along with tablet instructions. The study coordinator will assign each dyad a unique meeting ID number within the table instruction manual. This ID number will allow the dyad to log in to the video-conferencing application for each session. The study coordinator will train and support participating dyads on how to use the tablet and video-conferencing application. If patients and caregivers consent to have sessions and interviews recorded, this will be done through a HIPAA-compliant zoom software. If participating dyads do not have access to internet, a data plan will be provided for purpose of the study. No data will be stored on the tablet. At completion of the study, participants will return the tablets to the study coordinator. If tablets are lost or stolen, no PHI will be stored on the tablet, so this will not be accessible. The participants will contact the study coordinator with any concerns about the tablets. If a tablet is broken during the course of the study, another tablet will be provided.

• Intervention Period: The intervention period is 8 weeks; eight weekly 60 minute sessions will be delivered through video-conferencing. The sessions will be audio-recorded to ensure fidelity. Interventionist may use their clinical judgement to modify session lengths or shift session topics based on patient and caregiver expressed needs during sessions.

• Follow-up: Within 2 weeks of intervention completion (weeks 9-10), patients will be administered the UBACC to determine the patients maintained capacity to consent through the duration of the study; patients and caregivers will undergo TP 2.

• Patient and Caregiver measures will be performed by the PI or a trained study coordinator. TP1 and TP2 measures can be completed either in person or through videoconferencing. Study staff will score assessments and enter into a REDCap database.

• Semi-structured interviews: 80 separate patient and caregiver interviews (from 40 dyads) will be conducted by the PI or a trained study coordinator within 2 weeks after completion of the intervention. Interviews will be audio-recorded, in a private space, by telephone with the patient and caregiver separately.

• Follow-up HRV measurement: Within 2 weeks of completing the intervention, study staff will mail the HRV device (Firstbeat Bodyguard 2) to patients and caregivers along with return address mailer. This will be exploratory to understand the feasibility of collecting HRV in this way. Patients and caregivers will follow the same steps they completed before the DLR intervention (second bullet described above).

9. RISKS TO SUBJECTS

The potential risks to study participants are minimal for all procedures. For research assessments (self-report questionnaires and semi-structured interviews), the primary risks are invasion of privacy, breach of confidentiality (if safety issues are detected), or mild reactions of distress or fatigue. All assessment measures and procedures have been safely used previous research with older adults; no sustained negative effects from assessments are expected, but negative outcomes cannot be ruled out. For the DLR intervention, the primary risks are emotional distress or fatigue and potential loss of privacy. Regarding distress and fatigue, subjects may think about stressors, negative life events, and caregiving burden/distress; they will receive support from the interventionist for such experiences. No sustained negative effects are expected, but negative outcomes from behavioral interventions cannot be ruled out. Regarding privacy, given the videoconferencing modality, participants will be given information upfront about risks to privacy and instructed on actions they can take to protect their privacy.

10. POTENTIAL BENEFITS TO SUBJECTS

Subjects may benefit from participating in research interviews and completing the questionnaire measures, as these assessments provide them with the opportunity to be carefully listened to and comprehensively evaluated. They may further benefit from feelings of altruism connected with participation in research designed to better understand the mental health needs and experiences of community-residing older adults. Study subjects who receive DLR may benefit as this intervention targets loneliness, which is a significant risk factor for reduced well-being, morbidity and mortality.

11. COSTS FOR PARTICIPATION

There are no costs to the participants for participating in this study.

12. PAYMENT FOR PARTICIPATION

The patient and caregiver will each receive $80 ($80 for patients and $80 for caregivers; $160 total for dyad/pair) total for their participation in the study. Patients and caregivers will each receive $40 for their time during informed consent and baseline measures. Patients and caregivers will then each receive $40 for completion of the post-intervention measures and interview. Patients and caregivers will be paid using the Advarra/OnCore Clinical Trial Management System (CTMS). If patients and caregiver choose to enroll, they will be provided instructions during informed consent to enroll in the Advarra/OnCore CTMS.

13. SUBJECT WITHDRAWALS

Current, state, federal, and institutional regulations concerning informed consent will be followed. Participation in this study is voluntary. Participants are free not to take part or to withdraw at any time, for whatever reason, without risking loss of present or future care they would otherwise expect to receive. In the event that a patient does withdraw from the study, the information they have already provided will be kept in a confidential manner. Participants may discontinue participation in the study at any time if they decide they do not wish to take part any longer. Participants may be withdrawn from the study by research personnel if it is deemed in their best interest to no longer participate.

14. PRIVACY AND CONFIDENTIALITY OF SUBJECTS AND RESEARCH DATA

All intervention sessions and follow-up interviews will be recorded using digital audio recorders. Following systematic transfer from the digital recorders to a password-protected computer and backup on secure drives

hosted at URMC, the digital files will be erased. All audio recorders and transcripts will be kept in locked file cabinets in locked research offices of the study coordinator at URMC.

The study team will assign a numerical Study ID to each participant once they have signed the consent form. Study forms and questionnaires will use this number and the participant's first and last initials as identifiers to ensure data integrity. Other identifying information will not exist on these forms. A complete list of study participants with study ID, name, and contact information will be maintained separately for the purpose of contacting participants for research or study-related updates; this database will be maintained until the study is closed. This linkage information will only be accessible to the PI, study investigators, and the individual responsible for maintaining the database.

Additionally, the data can be collected and managed by the research teams at University of Rochester Medical Center using REDCap electronic data capture tools hosted at URMC.
URMC provides the following information on the REDCap program: "Vanderbilt University, in collaboration with a consortium of institutional partners, has developed a software toolset and workflow methodology for electronic collection and management of research and clinical trial data, called REDCap (Research Electronic Data Capture). The REDCap system is a secure, web- based application that is flexible enough to be used for a variety of types of research. It provides an intuitive interface for users to enter data and real time validation rules (with automated data type and range checks) at the time of data entry. REDCap offers easy data manipulation with audit trails and functionality for reporting, monitoring and querying patient records, as well as an automated export mechanism to common statistical packages (SPSS, SAS, Stata, R/S-Plus). Through the REDCap Consortium, Vanderbilt has disseminated REDCap for use around the world

All data collected for the current study will be used in post hoc analyses as appropriate. Overall study results will be presented to participants, faculty and staff at the University of Rochester Medical Center after completion of the study. Study results will be presented at professional meetings and published.

15. DATA AND SAFETY MONITORING PLAN

15.1 AE/SAE Definitions

- The following definitions are used in this DSMP and are consistent with the NIA's Adverse Event and Serious Adverse Event Guidelines and the University of Rochester's Research Study Review Board (RSRB) policies:
- An adverse event (AE) is any untoward or unfavorable medical occurrence (both physical and psychological) in a human subject, including any abnormal sign (for example, suicide ideation), symptom, or disease, temporally associated with the subject's participation in the research, whether or not the AE is considered related to the subject's participation in the research.
- A serious adverse event (SAE) is an event that (per OHRP guidelines) that:
    1. results in death;
    2. is life-threatening (places the subject at immediate risk of death from the event as it occurred);
    3. results in inpatient hospitalization or prolongation of existing

hospitalization;

4. results in a persistent or significant disability/incapacity; or
5. Is another condition that investigators judge to represent significant hazards.

- An unanticipated problem (UP) is any incident, experience, or outcome that meets all of the following criteria:

1. unexpected, in terms of nature, severity, or frequency, given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the study population;
2. related or possibly related to participation in the research (possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research);
3. suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

Note: The vast majority of adverse events occurring in human subjects are not unanticipated problems. A small proportion of adverse events are unanticipated problems. Unanticipated problems include other incidents, experiences, and outcomes that are not adverse events.

16.2 Classification of Severity and Study Relatedness

Adequate review, assessment, and monitoring of adverse events requires they be classified as to severity, expectedness, and potential relatedness to the study intervention. This section includes descriptions of how adverse events will be classified in these domains, as these classifications determine the reporting requirements.

Severity classifications are as follows:

- Mild: Awareness of signs or symptoms, but easily tolerated and are of minor irritant type causing no loss of time from normal activities. Symptoms do not require therapy or a medical evaluation; signs and symptoms are transient.
- Moderate: Events introduce a low level of inconvenience or concern to the participant and may interfere with daily activities, but are usually improved by simple therapeutic measures; moderate experiences may cause some interference with functioning.
- Severe: Events interrupt the participant's normal daily activities and generally require systemic drug therapy or other treatment; they are usually incapacitating.

Note: Severity is not synonymous with seriousness. Severe anxiety is not likely to be an SAE, for example. Likewise, a severe headache is not necessarily an SAE. However, mild chest pain may result in a day's hospitalization and thus is an SAE.

Expectedness is a key dimension in classifying adverse events. AEs must be assessed as to whether they were expected to occur or unexpected, meaning not anticipated based on current knowledge found in the protocol, investigator brochure, and informed consent document. Categories are:

- Unexpected - nature or severity of the event is not consistent with information about the condition under study or intervention in the protocol, consent form, or investigator brochure.

- Expected - event is known to be associated with the intervention or condition under study.

For the current study, the following are expected AEs and SAEs based on the study population and behavioral intervention under investigation. The study population is characterized by older age, caregiver stress, and social disconnectedness. The intervention is a six-session group behavioral intervention delivered via video conferencing that involves learning behavioral skills to promote positive social experiences in one's life in the context of caregiving demands.

- Expected AEs are:
  - Increased stress, anxiety, worry, depressive symptoms, and other forms of emotional distress (including suicide ideation) may occur in some participants due to the nature of thinking about stressors in one's life;

- Expected SAEs are:
  - Hospitalization due to physical and/or psychological factors;
  - Suicide attempts;
  - Deaths due to natural causes

Relatedness is another key dimension in classifying adverse events. The potential event relationship to the study intervention and/or participation will be assessed by the PI and Co-I's. Categorizations are as follows:

- Definitely Related: The adverse event is clearly related to the behavioral intervention or assessment procedures – i.e. an event that follows a reasonable temporal sequence from administration of the study intervention, follows a known or expected response pattern to the suspected intervention, that is confirmed by improvement on stopping and reappearance of the event on repeated exposure and that could not be reasonably explained by the known characteristics of the subject's clinical state.
- Possibly Related: An adverse event that follows a reasonable temporal sequence from administration of the study intervention follows a known or expected response pattern to the suspected intervention, but that could readily have been produced by a number of other factors.
- Not Related: The adverse event is clearly not related to the investigational intervention/procedure - i.e. another cause of the event is most plausible; and/or a clinically plausible temporal sequence is inconsistent with the onset of the event and the study intervention and/or a causal relationship is considered biologically implausible.

16.3 AE/SAE Reporting

This study is a minimal risk study adapting and refining a behavioral intervention. This section describes the study team's process for identifying AEs and SAEs, collecting information regarding the events, and reporting procedures. All AEs will be documented on an Adverse Event Form (electronic format) and stored in the regulatory file. An Adverse Event log may also be kept. Study staff will notify the study PI of an adverse event as soon as possible—at the latest by the end of the day in which the event was discovered. The PI has the final decision regarding what is to be reported on the adverse event form and has the option to reclassify an AE as a serious adverse event (SAE). All AEs experienced by the participant during the time frame specified in the protocol (e.g., from the start of intervention through the end of the study) are to be reported.

All adverse events, regardless of their seriousness, severity or relatedness to the intervention are reportable to NIA PO and STAR Center Pilot Core Directors, and the University of Rochester Institutional Review Board.

The following reporting schedule will be adhered to:

- Adverse events and serious adverse events that are not deemed "related and unexpected" will be reported to: the STAR Center MPIs (Drs. Heffner & Van Orden) at the next regularly scheduled meeting (held monthly at a minimum); the STAR Center Pilot Core Directors quarterly; the IRB per IRB policies, at a minimum, annually at the time of continuing review; the NIA Program Officer quarterly (or more often as deemed necessary by the STAR Center Pilot Core Directors).
- If SAEs occur that are unexpected (i.e., not listed in the Data and Safety Monitoring Plan), they will be reported to the STAR Center MPI's, the NIA Program Officer, the IRB, and to the STAR Center Pilot Core Directors within 48 hours of study's knowledge of SAE. The expedited report will be followed by a detailed, written SAE report as soon as possible. Note that follow up information may be required and asked for by the independent safety monitoring body directly, or through the NIA or its representative.
- Unexpected deaths, that is, deaths not due to natural causes will be reported to the STAR Center MPI's, the NIA Program Officer, the IRB, and to the STAR Center Pilot Core Directors within 24 hours of study's knowledge of death.
- Unanticipated problems that do not indicate increased risk to participants, will be reported to the IRB and NIA within 10 calendar days of identifying the problem. Unanticipated problems that may cause increased risk to participants will be reported to the STAR Center Pilot Core Directors, the IRB, and NIA within 48 hours of identifying the problem. The Unanticipated Problems report must include a corrective plan and measures to prevent reoccurrence. Reports of Unanticipated Problems, as defined above, will be forwarded to OHRP using ohrp@osophs.dhhs.gov, within two weeks of the event.

16.4 Protection Against Study Risks

This section provides information on how adverse events and other risks to participants in the study will be mediated and specifies events that would preclude a participant from continuing with the intervention. This section also includes the informed consent procedures and measures to protect participants against risk during the study.

Informed Consent Process. This section explains the informed consent process and how it is used to protect participants.

- The consent process informs a volunteer about the study, indicates the participation is voluntary and he/she has the right to stop at any time. Risks are enumerated in the informed consent form and described orally during the consent process.
- Individuals will provide written or verbal informed consent prior to start of the baseline interview. Consent forms will only be used if they have a current IRB approval stamp. The informed consent process will be conducted in a manner to facilitate questions from potential study subjects. If a study team member is unable to answer a question, an investigator will be contacted. All questions from potential subjects should be answered prior to signature. The PI, a co-investigator, or an IRB-approved consent designee must be present when a subject signs the informed consent form. That

member of the study team must sign the informed consent form at the same time and in the presence of the subject. The consent form must be signed and dated by the subject and the consent designee. No subjects will be involved in research activities unless an investigator or a designated study staff has obtained documentation of legally effective informed consent of the subject. The collection of protected health information (PHI) and questionnaires are considered to be research activities requiring prior documentation of informed consent.

- Consent will only be sought under circumstances that provide the prospective subject sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The information that is given to the subject or the representative shall be in language understandable to the subject. Potential study subjects will be given ample time to read and consider the consent form. All subjects will be reminded of the voluntary nature of study participation. Using the consent form to structure discussion, research personnel will explain the study, its potential benefits and risks, and alternatives, and document the consent process by signature of the subject and the person obtaining consent. During informed consent procedures, individuals will be told about possible risks and benefits of participation. This will include information that questions asked may cause them to feel uncomfortable or upset. They will be informed that: they may withdraw from an assessment at any time for any reason and receive full reimbursement for that assessment; and, they may withdraw from the research study at any time without negative consequences. Subjects are further informed that we will perform an immediate evaluation of their dangerousness towards self or others should safety concerns arise during assessments or intervention sessions. As well, they will be informed that we will contact their primary care physicians should concerns arise about medical or psychological risk. The staff will assess the participant's understanding of the study using an IRB-approved adapted version of the San Diego Brief Assessment of Capacity to Consent (UBACC), that we have implemented successfully in all of our studies with older adults. If a participant fails to answer all questions correctly, the staff will re-explain the study and then test the participant again. The consent will be an ongoing process during the study. Explanations of the study and verbal consent will be conducted at each data collection. Participants will be reminded that their participation is voluntary and that they can withdraw at any time for any reasons.

Protection Against Risks. This section describes measures to protect participants against study specific risks, as well as plans for notifying participants of trial results during and after the conclusion of the trial and providing the participants' health providers with the appropriate information from the trial, as needed, concerning individual participants. Study procedures, both assessments and interventions, pose minimal risk to participants. Below, we describe potential risks and study procedures to protect against these risks.

- In order to protect the confidentiality of subject information, we will take a number of precautions. These include training research interviewers in confidentiality procedures; entry and storage of data using coded identification labels; maintenance of project computers in secure locations with restricted access by enforced password protection; use of HIPAA compliant data management software (REDCAP). Back-ups of all study files will be made daily to allow for recovery of data due to disk failure. All data, including assessment measures, will be obtained with the written consent of the patient. Information pertaining to individual participants will be released with the patient's informed and written consent only, except in unusual cases where withholding the information might pose a serious risk or danger to the participant or others. All data will be identified by a uniquely

coded study number assigned to each participant. Access to the master list of study numbers will be restricted to the PI and the CRC. Confidentiality will be further maintained by the storage of "hard copy" data (if applicable) in locked files in a locked office. Access to computerized data is restricted and subject to review by the PI. Publications or presentations will report only cumulative data or descriptions certain to maintain participants' anonymity. All data collection involving human subjects will be HIPAA compliant. All data involving human subjects will be stripped of any identifiers; the data will be stored in a secure HIPAA compliant program called REDCAP, which manages protected health information in a HIPAA compliant manner. Audio recordings of semi-structured interviews will be transcribed and then destroyed to protect the security and confidentiality of identifiable information.

- In order to protect subjects' privacy, audio recordings of semi-structured interviews will only be made with subjects' written consent; subjects will be free to refuse to answer any questions they would prefer to not answer; interviews will be conducted in private settings. Participants will be given information in the consent form before joining the DLR intervention about the fact that the program is provided via Zoom and privacy limitations associated with videoconferencing software (which will be URMC HIPAA compliant).
- Risks associated with emotional distress or fatigue will be minimized by employment of research personnel with appropriate backgrounds and experience and work with psychological factors and elderly subjects. The baseline research interview will last approximately two hours in total. Given the length of time involved for this assessment, and concerns regarding subject health and well-being, subjects will be reminded that if they become fatigued, they may terminate the interview at any time, and that the interview can be conducted over multiple sessions as needed. Research personnel will further be trained to recognize potential signs of fatigue among elderly subjects, and to actively suggest alternative data collection strategies (including telephone-based and mail-in interviews), in order to reduce the possibility of overwhelming study subjects and to ensure completeness of data collection. These strategies have been employed effectively in the PI and Co-I's past research involving older adult populations.
    - During the course of assessment interviews, the CRC will monitor subjects' reactions for signs of distress or fatigue. If necessary, subjects may take breaks from the interview, or complete the interview over several sessions if fatigue becomes a concern.
    - If a subject's safety becomes a concern, the researcher will evaluate the subject's emotional state and safety. If the subject appears distressed, the CRC will briefly attempt to de-escalate the patient's distress. If these measures do not effectively reduce the patient's distress within 10-15 minutes and depending on the severity of the patient's distress, the CRC will call Dr. Kehoe (or the person covering for her), who will maintain a cell phone for this purpose. If neither is available, or if otherwise necessary, intervention will be provided by a clinician with Strong Behavioral Health's Older Adults Clinic, or by an on-call clinician in the University of Rochester Medical Center Community Mental Health Clinic (CMHC) or Psychiatric Emergency Department.
    - Given that we will be assessing depressive symptoms and subjects may report suicide ideation, the CRC's will be trained in the STAR Center's safety protocol for mental distress, suicide risk, and elder abuse, which involves items from the Columbia Suicide Severity Rating Scale and clinical interview. Subjects will be informed that study staff will perform an immediate evaluation of their dangerousness towards self or others should safety concerns

arise during assessments or treatment sessions. Subjects will also be informed that their confidentiality may be breached should concerns arise about their dangerousness to self or others. Finally, they will be informed that suspected child abuse will be reported, as mandated by law. Any subject who endorses death or suicidal ideation will be asked additional questions to assess his/her safety. Any endorsements of active suicidal ideation will involve notifying Dr. Kehoe for review of risk and protective factors and consideration of emergency psychiatric services. While it is expected (based on prior research) that only a small minority of subjects for the current study will report significant distress (and even fewer suicide ideation or elder abuse), CRC's will be trained in the study's safety protocol. A small minority of participants may experience elder abuse. In the case of suspected elder abuse, subjects will be given an immediate referral to the Elder Abuse Prevention Program provided in their region (this program is available nationally, typically through Area Agencies on Aging in all states). A phone call will be made to the primary care provider. Any suspected cases of elder abuse will be immediately reviewed with the PI before the CRC ends the assessment. Situations involving potential imminent dangerousness may involve the use of emergency services and law enforcement authorities. This safety protocol has been used successfully in STAR Center prior and on-ongoing studies.

- The study PI (Dr. Kehoe) will provide regular supervision to research staff.

16.5 Data and Safety monitoring

This section describes who is responsible for data and safety monitoring, including type of information that will be reviewed and frequency of such reviews.

The purpose of the Data and Safety Monitoring Plan (DSMP) is to specify the procedures and rationales of the current study to ensure the safety of participants and the validity and integrity of the data. This specifies who will look at the data and review any adverse events, how often, and what they are authorized to do. The use of Data and Safety Monitoring Boards (DSMBs) may be indicated if studies have multiple clinical sites, are blinded (masked), and/or employ particularly high-risk interventions or vulnerable populations. This study on the other hand will be conducted utilizing a low risk intervention in a population of older adults residing independently in the community. Therefore, STAR Center Pilot Core leadership will be responsible for data and safety monitoring, including oversight of the DSMP and systematizing monitoring safety issues.

The Principal Investigator (PI) will be responsible for ensuring participants' safety on a daily basis. The STAR Center Pilot Core Director will act in an advisory capacity to the NIA Director and to evaluate the progress of the study, including periodic assessments of data quality and timeliness, participant recruitment, accrual and retention, participant risk versus benefit, performance of trial sites, and other factors that can affect study outcome. The committee will make recommendations to NIA's Director concerning the continuation, modification, or conclusion of the trial.

The STAR Center Pilot Core leadership will also provide a data processing, analysis and coordination function. This will be accomplished, in part, at the meetings of Pilot Core leadership with administrative reports by the PI that describe participants screened, enrolled, completed, and discontinued, as well as baseline characteristics of the study population. Given that this is a pilot study, further plans for data processing, analysis, and coordination are not warranted for this study. Interim analyses are not planned given the nature of this study.

16.5.1 Frequency of Data and Safety Monitoring

The STAR Center Pilot Core leadership will meet twice annually, either in-person or by teleconference call to review study progress, data quality, and participants safety. Safety reports are sent to the committee at least twice a year and will include a detailed analysis of study progress, data and safety issues.

16.5.2 Confidentiality

All materials, discussions and proceedings of the data safety monitoring meetings are completely confidential. Members and other participants in such meetings are expected to maintain confidentiality.

16. DATA ANALYSIS PLAN

16.1 Sample Size Considerations: In order to assess feasibility, using a reference of 0.5 for consent and adherence rate, 40 dyads would achieve 83% power using a one-tailed test at significance of 0.05. The quantitative data will be used to guide sample size calculations for a future randomized pilot. Therefore, a sample of 40 patient/caregiver dyads will support the assessment of feasibility of the telehealth DLR with older patients and caregivers and allow for thematic saturation through qualitative semi-structured interviews.

16.2. Analysis of Aims:

16.2.1 ***Primary aim:*** To evaluate the feasibility of enrolling and delivering the telehealth DLR intervention, we will calculate proportion of: 1) approached patient/caregiver dyads who enrolled (70%); 2) enrolled dyads who completed all 8 DLR sessions (70%); and 3) general acceptability of the DLR intervention by patients and caregivers. General acceptability will be examined through coding of transcribed semi-structured interviews from the 40 dyads (separate interviews for patients and caregivers; 40 patient interviews and 40 caregiver interviews). A sub-group analysis will examine any differences between older patients with only advanced cancer and their caregivers and older patients with both advanced cancer and MCI and their caregivers in enrollment, adherence, and acceptability.

16.2.2 ***Secondary and Exploratory Aims:*** To examine the pre-post change in caregiver psychological distress, we will utilize a regression analysis that will include the pre-measurement of caregiver distress as a covariate. We will also include gender and income as covariates in this model. A regression analysis will also be used to examine changes in the exploratory measures using the same covariates. A sub-group analysis will compare the difference in changes from pre to post intervention between dyads that include older patients with only advanced cancer and dyads with older patients with both advanced cancer and MCI.

16.2.3 ***Mixed Methods Aim:***

Qualitative Data Analysis: Semi-structured interviews will be audio-recorded and transcribed into MAXQDA software for coding and analysis. Abductive analysis will be used to code transcribed interviews and extract themes. Two independent coders will code the data until thematic saturation is achieved. Coding will be compared and discrepancies resolved through an iterative process and achieving consensus. Semi-structured interviews will gather information about the acceptability of the intervention, perceptions of the dyadic approach to the interventions, and evaluate patient and caregiver perceptions of communal coping. A sub-group coding analysis will be performed to examine any differences in responses between older patients with only advanced cancer and their caregivers and older patients with both advanced cancer and MCI and their caregivers.

Integration: Qualitative and quantitative data, including baseline and follow up measures and

transcribed semi-structured interviews, will be integrated to develop a more complete understanding of the feasibility of a telehealth DLR intervention in this unique population and to gain understanding of the patient and caregiver experiences and gather thick descriptions about barriers and facilitators for the intervention. The qualitative data can provide explanatory data for any changes in the quantitative measures from pre to post intervention for both patients and caregivers.

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Interview Script for Patients/Caregivers:

Interviews will cover several broad topics; interviewers will probe participants' responses for more detail as needed.

The same questions will be asked of both patients and caregivers, who will be interviewed separately. Names will be used wherever possible in place of bracketed terms.

1. "What are some strengths you see in this type of intervention?"
   a. "What did you like most about the intervention?"
2. "What are some limitations you see in the current intervention you were provided information about?"
   b. "What did you dislike about the intervention?"
3. "How do you feel about the length of the total intervention?"
4. "How do you feel about the length of each session?"
5. "How suitable is this intervention give your current demands and daily responsibilities?"
6. "What, if any, are memories or experiences you feel you would not want to share with [caregiver/patient]?"
7. "What, if any, are some memories or experiences you feel are most important to share with your caregiver?"
8. "What were your impression of the first half of the intervention (weeks 1-4), how did you feel about sharing about your childhood, adolescents, and young adulthood?"
9. "What were your impression of the second half of the intervention (weeks 4-8), how did you feel about sharing about middle age and more recent memories and experiences?"
10. "What would you have changed about this dyadic life review intervention?"
11. How did this intervention help your relationship with your partner?
12. "How do you cope with this illness?"
    a. "Have [repeat identified coping strategies] changed since doing this dyadic life review?"
    b. "If so, how have they changed?"
13. "What does coping look like between you and your partner?"
    a. "Can you give examples of what that looks like?"
14. "If you experienced loneliness or a sense of isolation before this, how did that change during the intervention?"
    a. "If these experiences did change for you, what helped this to change?"
15. "If you're willing, what were some things you and [caregiver/patient] talked about on the way home from the session or the night after that session?"
16. "Is there any other feedback about the intervention you would like to provide?"

Dyadic Life Review Intervention Guide:

Session 1: Childhood

Welcome and thank you for your time today. Today we will be focusing on each of your childhood experiences. I will have some questions to help us get started with our conversation. There is no right or wrong response. You are free to move through memories as they come and I [the interventionist] may prompt for more detail or information as you recall these events.

[Direct questions to first patient then the caregiver, when possible use patient and caregivers' names to support building rapport through this process]

1. How are you feeling today?

2. Let's take a minute and have your minds take you back to your childhood, birth through 13. Tell me a memory that first comes to your mind?

    2a. [Caregiver] What did this memory [Patient] just share make you feel or think about?

        What was the first memory that came to mind for you [caregiver]?

    2b. [Patient] What did this memory [Caregiver] just share make you feel or think about?

3. Who was most influential in your life during this period?

    3a. [Caregiver] What did this memory [Patient] just share make you feel or think about?

        Who was most influential for you in your childhood [caregiver]?

    3b. [Patient] What did this memory [Caregiver] just share make you feel or think about?

4. Tell me about your favorite place during childhood?

    4a. [Caregiver] What did this memory [Patient] just share make you feel or think about?

        Tell me, [Caregiver] about your favorite place during childhood?

    4b. [Patient] What did this memory [Caregiver] just share make you feel or think about?

Session 2: Adolescence

Welcome and thank you for your time today. Today we will be focusing on each of your adolescent experiences. I will have some questions to help us get started with our conversation. There is no right or wrong response. You are free to move through memories as they come and I [the interventionist] may prompt for more detail or information as you recall these events.

[Direct questions to first patient then the caregiver, when possible use patient and caregivers' names to support building rapport through this process]

1. How are you feeling today?

2. Let's take a minute and have your minds take you back to your adolescence. Tell me a memory that first comes to your mind from this period of your life?

    2a. [Caregiver] What did this memory [Patient] just share make you feel or think about?

        What was the first memory that came to mind for you [caregiver]?

    2b. [Patient] What did this memory [Caregiver] just share make you feel or think about?

3. Who was most influential in your life during this period?

    3a. [Caregiver] What did this memory [Patient] just share make you feel or think about?

        Who was most influential for you in your adolescence[caregiver]?

    3b. [Patient] What did this memory [Caregiver] just share make you feel or think about?

4. What were your most pleasant memories about your adolescence?

    4a. [Caregiver] What did this memory [Patient] just share make you feel or think about?

        Tell me, [Caregiver] what were your most pleasant memories from your adolescence?

    4b. [Patient] What did this memory [Caregiver] just share make you feel or think about?

Session 3: Young Adulthood (20-35 years)

Welcome and thank you for your time today. Today we will be focusing on each of your young adulthood experiences. I will have some questions to help us get started with our conversation. There is no right or wrong response. You are free to move through memories as they come and I [the interventionist] may prompt for more detail or information as you recall these events.

[Direct questions to first patient then the caregiver, when possible use patient and caregivers' names to support building rapport through this process]

1. How are you feeling today?

2. Let's take a minute and have your minds take you back to your young adulthood, 19-35. Tell me a memory that first comes to your mind?

    2a. [Caregiver] What did this memory [Patient] just share make you feel or think about?

        What was the first memory that came to mind for you [caregiver]?

    2b. [Patient] What did this memory [Caregiver] just share make you feel or think about?

3. What was life like for you in your 20's and early 20's?

    3a. [Caregiver] What did this memory [Patient] just share make you feel or think about?

        What was life like for you during this period [caregiver]?

    3b. [Patient] What did this memory [Caregiver] just share make you feel or think about?

4. Tell me about your work? If you did not work, tell me about the activities or roles you spent the most time in?

    4a. [Caregiver] What did this memory [Patient] just share make you feel or think about?

        Tell me, [Caregiver] about your work, or if you did not work, your primary activities or roles during this time in your life?

    4b. [Patient] What did this memory [Caregiver] just share make you feel or think about?

5. ***If applicable to patient/caregiver:***

    For romantically involved dyads: Did you two meet during this time period? If so, tell me about this time and what your felt? What you thought about?

    5a. [Caregiver] What did this memory [Patient] just share make you feel or think about?

    For parent/adult child dyads: What was it like becoming a parent during this time?

    5b. [Caregiver] What did this memory [Patient] just shared about becoming a parent make you feel or think about?

*Note: these question from 5 can be shifted to whichever time period session the patient met their significant other caregiver, friend caregiver, or to the period they became a parent if it does not fall within this period.

Session 4: Dyadic Processing and Review of Session 1-3

Welcome and thank you for your time today. Today we will be focusing on reviewing what you have each shared up to this point. I will have some questions to help us get started with our conversation. There is no right or wrong response. You are free to move through memories as they come and I [the interventionist] may prompt for more detail or information as you recall these events.

[Direct questions to first patient then the caregiver, when possible use patient and caregivers' names to support building rapport through this process]

1. How are you feeling today?

2. Let's take a minute and recall some of the memories both [Patient] and [Caregiver] shared over the first three sessions.

    2a. [Patient] what has stood out to your up to this point about what [Caregiver] has shared thus far?

        [Caregiver] what about you? What has stood out?

    2b. [Patient] Is there are memory you haven't shared so far that you are particular proud to share with [Caregiver]?

        [Caregiver] what about you? Is there a particular memory you have shared or still would like to share that you a particularly proud of?

3. [Patient] how would you describe your perception of [Caregiver] after recalling periods of your life together?

    3a. [Caregiver] how would you describe your perception of [Patient] after recalling these periods of life together?

4. We have talked about a large portion of your lives so far, share with me your overall feelings about these memories and periods of your life.

    4a. [Caregiver] What did what [Patient] just share make you feel or think about?

        Tell me, [Caregiver] about your overall feelings about these memories or period of your life.

    4b. [Patient] What did what [Caregiver] just share make you feel or think about?

Session 5: Mid-Life (35-50 years)

Welcome and thank you for your time today. Today we will be focusing on each of your mid-life experiences. I will have some questions to help us get started with our conversation. There is no right or wrong response. You are free to move through memories as they come and I [the interventionist] may prompt for more detail or information as you recall these events.

[Direct questions to first patient then the caregiver, when possible use patient and caregivers' names to support building rapport through this process]

1. How are you feeling today?

2. Let's take a minute and have your minds take you back to your mid-life, 35-50 years of age. Tell me a memory that first comes to your mind?

    2a. [Caregiver] What did this memory [Patient] just share make you feel or think about?

        What was the first memory that came to mind for you [caregiver]?

    2b. [Patient] What did this memory [Caregiver] just share make you feel or think about?

3. Who was most influential in your life during this period?

    3a. [Caregiver] What did this memory [Patient] just share make you feel or think about?

        Who was most influential for you in your mid-life [caregiver]?

    3b. [Patient] What did this memory [Caregiver] just share make you feel or think about?

4. How do you feel you have changed from the earlier periods of life to this time period?

    4a. [Caregiver] What did what [Patient] just share make you feel or think about?

        [Caregiver] How do you feel you have changed from the earlier periods of life to this time period?

    4b. [Patient] What did what [Caregiver] just share make you feel or think about?

Session 6: Early late life (50-65 years)

Welcome and thank you for your time today. Today we will be focusing on each of your early late life experiences. I will have some questions to help us get started with our conversation. There is no right or wrong response. You are free to move through memories as they come and I [the interventionist] may prompt for more detail or information as you recall these events.

[Direct questions to first patient then the caregiver, when possible use patient and caregivers' names to support building rapport through this process]

1. How are you feeling today?

2. Now we are going to reflect on early late life, ages 50-65 years. Tell me a memory that first comes to your mind?

    2a. [Caregiver] What did this memory [Patient] just share make you feel or think about?

        What was the first memory that came to mind for you [caregiver]?

    2b. [Patient] What did this memory [Caregiver] just share make you feel or think about?

3. Who was most influential in your life during this period?

    3a. [Caregiver] What did this memory [Patient] just share make you feel or think about?

        Who was most influential for you in your childhood [caregiver]?

    3b. [Patient] What did this memory [Caregiver] just share make you feel or think about?

4. Tell me about your friendships or relationships during this period?

    4a. [Caregiver] How did this what [Patient] just share make you feel or think about?

        Tell me, [Caregiver] about your friendships or relationships during this period?

    4b. [Patient] How did what [Caregiver] just share make you feel or think about?

For some caregiver enrolled, this may be the present age period for them. If so the questions are still relevant, but also consider adding:

5. [Caregiver] are there any other really important memories that come to mind from the periods we discussed so far?

    5a. [Caregiver] Why do you think these came to mind for you today?

    5b. [Patient] How did what [Caregiver] just share make you feel?

    5c. [Caregiver] What pieces of wisdom would you like to hand down to younger generations?

Session 7: Later Life (65+ years)

Welcome and thank you for your time today. Today we will be focusing on each of your late life experiences. I will have some questions to help us get started with our conversation. There is no right or wrong response. You are free to move through memories as they come and I [the interventionist] may prompt for more detail or information as you recall these events.

[Direct questions to first patient then the caregiver, when possible use patient and caregivers' names to support building rapport through this process]

1. How are you feeling today?
2. Today we will discuss the present time period of life. What was the most influential event from this period?
    2a. [Caregiver] What did this memory [Patient] just share make you feel or think about?
        What was the first memory that came to mind for you [caregiver]?
    2b. [Patient] What did this memory [Caregiver] just share make you feel or think about?
3. Tell me about your friendships and relationships during this period of life?
    3a. [Caregiver] What did what [Patient] just share make you feel or think about?
        [Caregiver] Tell me about your friendships and relationship during this period of life?
    3b. [Patient] What did this memory [Caregiver] just share make you feel or think about?
4. In your entire life, what relationship stands out as most influential?
    4a. [Caregiver] What did this memory [Patient] just share make you feel or think about?
    4b. [Caregiver], in your entire life, what relationship stands out as most influential?
        [Patient] What did this that [Caregiver] just shared make you feel?
5. [Patient] What pieces of wisdom would you like to hand down to younger generations?
    Note: If caregiver's age falls within this period:
    5a. [Caregiver] What pieces of wisdom would you like to hand down to younger generations?

Session 8: Final Session Dyadic Processing and Review

Welcome and thank you for your time today. Today we will be focusing on a review of our 8 weeks together and the memories you have each shared. I will have some questions to help us get started with our conversation. There is no right or wrong response. You are free to move through memories as they come and I [the interventionist] may prompt for more detail or information as you recall these events.

[Direct questions to first patient then the caregiver, when possible use patient and caregivers' names to support building rapport through this process]

1. How are you feeling today?
2. [Patient] What was the most meaningful memory to you that [Caregiver] shared during this time together?
    2a. [Caregiver] What did what [Patient] just share make you feel or think about?
        [Caregiver] What was the most meaningful memory to you that [Patient] shared during this time together?
    2b. [Patient] What did what [Caregiver] just share make you feel or think about?
3. Do you feel you have lived your life as you hoped to live it?
    3a. [Caregiver] What did what [Patient] just share make you feel or think about?
        [Caregiver] do you feel you have lived your life as you hoped to live it?
    3b. [Patient] What did what[Caregiver] just share make you feel or think about?
4. [Patient] What is one thing you want to tell [Caregiver] after hearing about these periods of their life?
    4a. [Caregiver] What did what [Patient] just share make you feel or think about?
        [Caregiver] What is one thing you want to tell [Patient] after hearing about these periods of their life?
    4b. [Patient] What did what [Caregiver] just share make you feel or think about?