Technology and Family Thriving Study (Thrive)

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Principal Investigators: Tamara Afifi, Nancy Collins, Kyle Rand
Sponsor: University of California, Santa Barbara and Rendever

Grant Title:
Using Rendever to improve the quality of life of older adults with cognitive impairments in senior living communities and their family members who live at a distance

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Statement of Compliance

The trial will be carried out in accordance with International Council on Harmonisation Good Clinical Practice (ICH GCP) and the following:

- United States (US) Code of Federal Regulations (CFR) applicable to clinical studies (45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56, 21 CFR Part 312, and/or 21 CFR Part 812).

National Institutes of Health (NIH)-funded investigators and clinical trial site staff who are responsible for the conduct, management, or oversight of NIH-funded clinical trials have completed Human Subjects Protection and ICH GCP Training.

The protocol, informed consent form(s), recruitment materials, and all participant materials will be submitted to the IRB for review and approval. Approval of both the protocol and consent form(s) must be obtained before any participant is consented. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. All changes to the consent form(s) will be IRB approved; a determination will be made regarding whether a new consent needs to be obtained from participants who provided consent, using a previously approved consent form.

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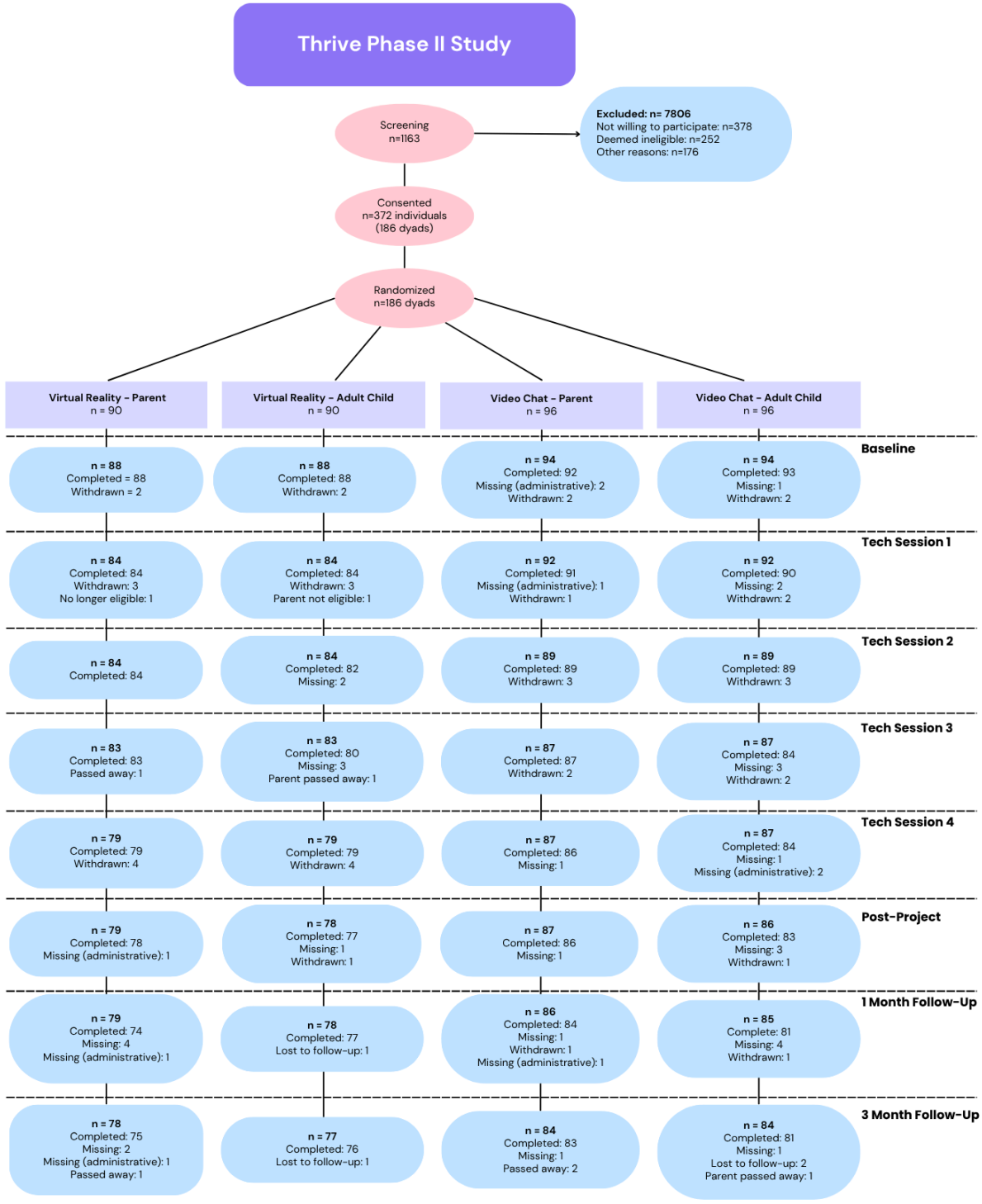
1 Protocol Summary

1.1 Synopsis

Title:	Technology and Family Thriving Study (Thrive)
Grant Number:	2 R42 AG063640-02
Study Description:	
Objectives*:	
Primary Objective:	To test the impact of different forms of technology (virtual reality vs. video chat) on quality of life and family relationships in older adults who reside in senior living communities and an adult child who lives at a distance. The study will also investigate whether responses to the technology and quality of life outcomes depend on older adults' level of cognitive impairment (MCI/ADRD).
Endpoints*:	
Primary Endpoint:	Quality of life, thriving, mental health, loneliness, family relationships, caregiver guilt
Secondary Endpoints:	Social, emotional, physical engagement during technology sessions
Study Population:	Older adults (age 50+) with mild cognitive impairments (MCI) or mild to moderate Alzheimer's Disease or related dementias (ADRD) who reside in senior living communities and an adult child who lives at a distance.
Phase* or Stage:	Phase II
Description of Sites/Facilities Enrolling Participants:	Senior living communities in two regions of the U.S.
Description of Study Intervention/Experimental Manipulation:	Dyads (older adult + adult child) will be randomly assigned to participate together in 4 weekly technology sessions using either (a) Virtual Reality (treatment) or (b) Video Chat (active control).
Study Duration*:	Approximately 4 months
Participant Duration:	Approximately 4 months

1.2 Schema



Note: Because participation in the intervention required both members of the dyad, if one member chose to withdraw during the intervention phase, the entire dyad was discontinued. However, after the

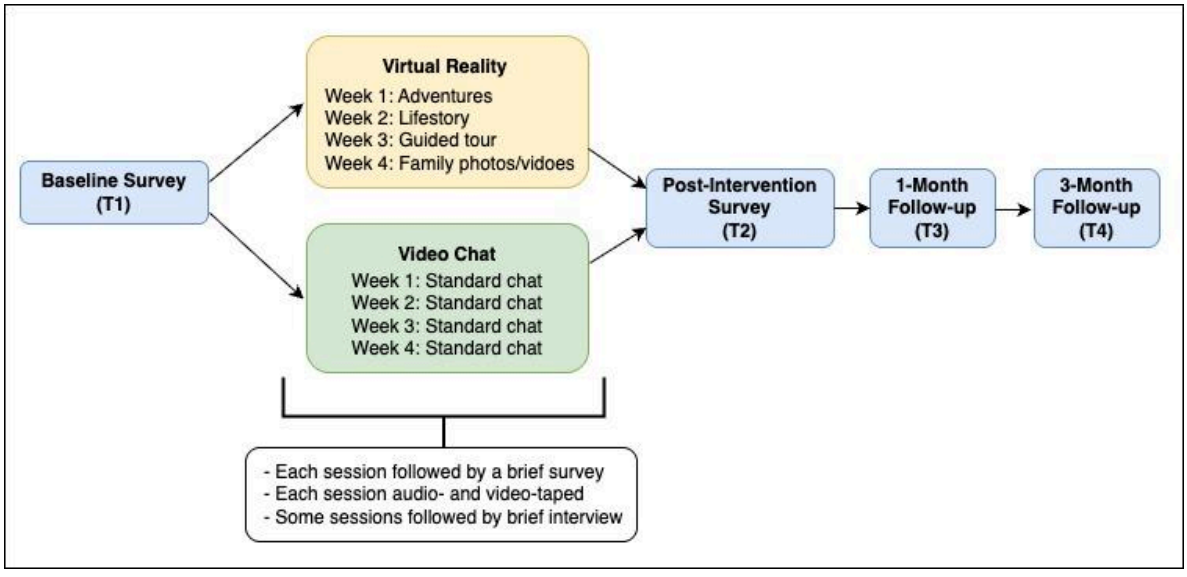
intervention phase was completed, individual members could withdraw independently, allowing the other member to continue participating in post-intervention and follow-up surveys. **Attrition prior to the end of the intervention phase:** 20 dyads + 2 individuals (out of 372 consented) = **42/372**, or **11.3%**. **Total attrition over the course of the trial:** 20 dyads + 12 individuals = **52/372**, or **13.9%**.

Participant retention was monitored throughout the study, and reasons for attrition were recorded. Attrition was categorized into the following predefined groups: (1) **Withdrew consent** (participants voluntarily discontinued for personal reasons, such as time burden or loss of interest); (2) **Adverse events** (participants discontinued due to health or safety reasons – physical or psychological – including withdrawal by the study investigator); (3) **Health-related limitations** unrelated to the intervention that prevented continued participation (e.g., hospitalization, fall, cancer treatment); (4) **Protocol deviations or ineligibility** identified post-randomization (e.g., undisclosed history of seizure); (5) **Partner withdrawal**, where the dyadic nature of the study required discontinuation when a study partner withdrew; (6) **Death** during the study period unrelated to the intervention; and (7) **Lost to follow-up,** where participants became unreachable and did not complete one or more follow-up assessments.

Participants who missed one or more survey assessments but later completed subsequent surveys were classified as having **intermittent missing** data. These cases were not considered lost to follow-up and were retained in all analyses for which valid data were available. Reasons for missed assessments were not always reported but were presumed to reflect temporary nonresponse rather than formal withdrawal or disengagement from the study. In addition, in rare cases, survey data were lost due to administrative or technical errors despite participant completion. These cases were treated as **missing (administrative)** in the relevant analyses.

1.3 Schedule of Activities

Timeline for the Thrive study



Schedule of Assessments for the Thrive Study

	Screen	Consent	Baseline (T1)	Tech 1 (T2)	Tech 2 (T3)	Tech 3 (T4)	Tech 4 (T5)	Post-study (T6)	1 Mo (T7)	3 Mo (T8)
Eligibility	X									
Randomization		X								
Informed Consent		X								
Demographics		X								
Outcome Evaluations*										
Technology sessions - Positive Engagement (self-report)				X	X	X	X			
Technology sessions - Positive engagement (behavioral coding)				X	X	X	X			
Quality of Life			X	X	X	X	X	X	X	X
Mental Health			X	X	X	X	X	X	X	X
Thriving			X					X	X	X
Loneliness and social connection			X	X	X	X	X	X	X	X
Caregiver Guilt			X	X	X	X	X	X	X	X
Family bonding			X	X	X	X	X	X	X	X

* The outcomes listed above refer to general constructs rather than specific measures. Most outcomes will be measured using more than one self-report and/or behavioral assessment.

2 Introduction

2.1 Study Rationale

By 2030, it is estimated that over 20% of U.S. residents will be age 60 or older[1] . Since people are living longer, the number of people with Alzheimer's disease (AD) and Alzheimer's disease-related-dementias (ADRD) is expanding exponentially, affecting approximately 5.4 million Americans.[2] As noted in the strategic directions of the National Institute on Aging (NIA; Goal C), scientists have made remarkable breakthroughs in helping people live longer. But now, we need to ensure quality of life. Until cures for the dementias are discovered, new technologies and interventions that can reduce the stress and emotional burden of AD/ADRD for older adults and their family members (NIA's SBA-Approved SBIR/STTR Priority Topics) are imperative. Virtual reality (VR) is an innovative, noninvasive, drug-free, and increasingly affordable tool that can help older adults and their family members manage the anxiety, stress, and feelings of isolation associated with dementia, as well as promote thriving. In addition, adult children increasingly do not live near their parents and are managing dual career families of their own, making it incredibly difficult to provide care from a distance.[1] Research shows that adult children who

care for an elderly parent from a distance experience distress, anxiety, social impairments, and often feel like their caregiving is inadequate.[3] These experiences are even more difficult when their loved one has dementia because of the relentless, heartbreaking loss of the person they used to know—the loss of memories, ability to learn, and identity. COVID-19 has exacerbated all of these feelings of anxiety, isolation, and desperation on the part of the older adults and their family members. Even if a vaccine for COVID-19 is discovered, the long-term health effects of prolonged social isolation and the crisis of loneliness will persist. Technologies are critically needed to combat these adverse effects.

Rendever, with its innovative virtual reality (VR) platform, provides a solution to the unprecedented challenges of residents' feelings of social isolation, enabling and enhancing social connections with family even when physical contact is not possible. Rendever's advanced communication and networking technology allows multiple people to travel in VR, co-view photos and videos, and engage in novel activities together, all while sharing stories in the process, even if they live in different parts of the world. Our Phase I data indicate that Rendever is safe, easy to use, and transformative for residents and family members. In the pages below, we outline the positive impact Rendever has on residents' *and* family members' mental and relational health. Our pilot data also demonstrate that residents with mild cognitive impairment (MCI) and mild to moderate dementia can safely use the VR and that they loved using it, regardless of their level of cognitive impairment. Given the strong evidence of the feasibility and technological merit of Rendever from Phase I, we are pursuing Phase II with the goal of continuing the research and improving the efficacy of the long-distance features of Rendever with residents with MCI and AD/ADRD and their family members who live at a distance. We will continue to refine and test ease of use and user satisfaction of Rendever (replicating Phase I), while expanding the scientific goals of the project by testing the immediate and longer-term impact of Rendever on the quality of life of residents and their adult children in a rigorous experimental design. We will also continue to investigate whether residents with varying levels of cognitive impairment respond in unique ways to the VR. This will be accomplished by building on the Phase 1 research design in several important ways: (1) expanding the sample to multiple senior living communities to test the impact of Rendever on a larger and more diverse population of residents, (2) adding an active control group (video chat via Zoom) to provide a rigorous experimental test of the impact of Rendever, and to rule out the possibility that any such benefits are simply due to contact with family, (3) adding a 1-month and 3-month follow-up to determine if the potential benefits of Rendever are sustained over time, and (4) expanding our outcome variables to include a broader array of quality of life indices and caregiver guilt so that we can test Rendever's potential to improve the lives of residents in senior living communities, *and* the adult children who are involved in their care.

Phase II: VR as a Relationship Maintenance Tool with Residents with Cognitive Impairments

Largely due to the lack of disease-changing treatments for AD/ADRD, there has been growing interest in nonpharmacological interventions that can reduce the burden of dementia.[4] Some of these interventions have been shown in meta-analyses to be quite effective. Interventions that rely on music therapies, exercise, reminiscence therapies, sensory stimulation, cognitive/emotional stimulation, behavior management, and person-centered care have been associated with a reduction in agitation, enhanced mood, and improved quality of life for residents with MCI and dementia.[5] [6] [7] [8] A key question is: what does VR offer beyond what is already available in these existing approaches?

In this project, VR is viewed as a relationship maintenance mechanism that promotes positive engagement. We conceptualize positive engagement as emotional connections between the resident and adult child, engagement in conversations with each other while in the VR, engagement in the technology itself, and positive affect (e.g., joy, excitement).[9] We rely on some of the tenants of the

theory of resilience and relational load (TRRL) to explain why VR, as a relationship maintenance tool, fosters positive engagement. As the TRRL and other theories (e.g., attachment theory) suggest, people want to feel loved, secure, and valued.[10] [11] These feelings occur across the lifespan, but are especially salient at the end of life when one's social networks shrink and health is more easily compromised than at other points in adulthood.[12] The TRRL builds on the theory of emotional capital[13] and argues that investing in one's relationships over time through positive relationship maintenance builds emotional reserves that people can draw from when they are stressed, promoting resilience and potential thriving. Positive relationship maintenance involves the "prosocial, strategic, and routine or habituated experiences, behaviors and actions people use" to sustain their relationships. Shared experiences in VR are prosocial maintenance activities that could help strengthen resident-adult child bonds and feelings of unification against life's challenges. When family members actively maintain their relationships, they also tend to communicate in more secure, engaged, supportive, and empathetic ways.19 Ultimately, these security-oriented stress appraisals, emotional connections, and communication are important because research has linked bonds with family and leisure activities to better mental and physical health in older adulthood.[14] .

Virtual reality, however, is more than a pleasurable activity for residents with cognitive impairments. It has the potential to alter the way they feel about their relationships and the world around them. VR "is an experiential interface in which the components of perception (visual, tactile, and kinesthetic) are the bases for interactivity, encouraging a sense of 'being there'—that is, the sensation of being actually inside the virtual environment."[15] Residents in senior living communities are often separated from the rest of society socially and spatially. There is a consistent body of literature on telepresence and the use of an array of technologies (e.g., robots, video chat, smart homes, multi-sensory interactive windows) to combat older adults' loneliness.[16] However, VR is different than these methods because of the immersion into a virtual world; rather than simply chatting with family via a large video screen, rich sensory stimuli can make residents feel as if they are actually inside the virtual world engaging in real activities with them.[17] . The shared, novel experiences allow residents and family members to reduce boredom, break out of their routine, and savor shared adventures and meaningful moments in real time, regardless of geographical separation.[18]

Virtual worlds can also create a feeling of security for residents with dementia, who are anxious without their family, and for their adult children, who long for an emotional connection with the parent they used to know. Social presence is a "sense of being with another" in a virtual environment.[19] It allows people to transcend their location in space and feel as if they are with each other psychologically. Virtual reality activates the psychological processes in the brain that become stimulated when people are focused on each other. A component of social presence is co-presence or "the degree to which the observer believes he/she is not alone and secluded, their level of peripheral or focal awareness of the other, and their sense that the other is peripherally or focally aware of them."[18] Taking residents with dementia back in time through VR allows them to experience the joy of their past and allows the adult children to experience their parent's true presence.[20] .

The positive engagement that shared VR creates should, in turn, improve the quality of life of residents and their adult children. **For residents with and without cognitive impairments, quality of life means being able to maintain important family connections, have control over their lives, and feel as if their lives still have meaning**.[21] . We are conceptualizing quality of life as general happiness with one's life and also low levels of social isolation/loneliness, positive mental health, and the ability to thrive. Rendever could be a crucial way to connect residents with their adult children, reducing social isolation and

improving the mental and relational health of everyone involved. Virtual reality allows older adults to continue to grow, experience new sensations, travel, and live life outside senior living communities. This may be especially true if VR allows residents with varying levels of cognitive impairment to connect to their past and do things they can no longer do because of cognitive and/or physical limitations. Because of the immersive nature of VR, Rendever should be more effective at promoting these processes compared to other means, such as video chat. In Phase II, we also want to show that using Rendever has a longer-term impact beyond the moments right after its use. Importantly, adult children who live in another state might not have as many opportunities to engage in activities with their parents compared to a sibling who lives nearby. Shared VR experiences can create common ground and give the dyad something exciting to talk about that is unique to that relationship, fostering a social bond in ways that last beyond the VR sessions. Therefore, our first aim and hypotheses are:

AIM1: Determine whether Rendever (vs. control) improves **quality of life** for residents and their adult children who live at a distance.

- **H1a**: Residents and adult children in the VR condition (vs. control) will show significantly **greater improvements in quality of life** (reductions in loneliness, improvements in mental health and thriving) both concurrently and over time (relative to baseline).
- **H1b:** The positive effects of the VR condition (vs. control) on residents' and adult children's **quality of life** will be **mediated** by (explained by) increases in **positive engagement** (positive affect, engagement with the technology and with the adult child while using it, emotional closeness with the adult child).

A second aim of Phase II is to continue to determine the level of cognitive impairment for which Rendever is most beneficial. Virtual reality has been used successfully with older adults with MCI and mild to moderate AD/ADRD to enhance cognition, navigation, spatial orientation, attention, spatial memory, mobility, and balance. Research with residents with and without dementia suggests that VR is enjoyable and can induce positive affect. For instance, virtual environments have been found to increase joy and relaxation in residents and reduce anxiety and sadness.[16] Researchers have also tested sustained attention while using VR, versus a paper version of the task, among residents with MCI and dementia. Residents, regardless of the level of cognitive impairment, found the VR enjoyable, reported high feelings of security and low levels of discomfort and anxiety, and preferred the VR over the paper condition. Interestingly, residents with greater apathy preferred the VR condition the most and reaped the greatest benefits. Virtual reality has also been used with older adults without cognitive impairments for reminiscence therapy and shown that the number of memories generated is greater with familiar than unfamiliar settings.[22] Other researchers have found that VR can enhance autobiographical memory in older adults with MCI[23] and that VR can improve memory in older adults with MCI more than music therapy. **Little research, however, has examined the impact of VR on older adults' social well-being, particularly among residents with dementia. What has been missing from VR is sophisticated networking and livestreaming functions, which Rendever provides.** The ability for residents to travel back in time to their childhood home and other memorable places with their adult child while sharing stories together should facilitate positive engagement for both of them.

We already demonstrated in Phase I that Rendever can be used safely with residents with MCI and mild to moderate AD/ADRD and that residents loved the experience, regardless of their level of cognitive impairment. Our Phase I results suggest that Rendever is beneficial for residents with MCI and mild to moderate dementia, especially if it involves reminiscence therapy. We also found in our automated and human coding that the higher the MMSE-2 score (or the less dementia), the more engaged the resident

was in the LifeStory VR session. However, residents with dementia reported being more immersed in the VR sessions than residents with MCI. It could be that as the dementia becomes increasingly severe, it is more likely to restrict residents' bodily movements. However, dementia might enable residents to become more immersed in another world than if they have MCI. These speculations need to be tested with a larger sample in Phase II. We also did not have a large enough sample to test for differences between the two groups for quality of life indices. Therefore, research questions are posed instead of hypotheses. Phase II extends the literature by examining whether the impact of VR on residents' quality of life depends on their level of cognitive impairment, primarily because of the level of engagement. Likewise, the adult child's quality of life might also improve because of jointly benefiting from engagement in the VR with one's parent. Finally, Rendever should produce greater engagement than video chat because of the shared immersion into an altered reality. Therefore, our second aim and research questions are:

AIM2: *Determine whether the positive effects of Rendever (vs. control) on residents' and their adult children's quality of life depends upon* ***residents' level of cognitive impairment*** *(MCI vs. mild to moderate AD/ADRD).*

- **RQ1:** Are the effects of the VR condition (vs. control) on **quality of life moderated** by residents' level of cognitive impairment (MCI vs. mild to moderate AD/ADRD) both concurrently and over time (relative to baseline)?

- **RQ2:** If the effects of the VR condition (vs. control) on **quality of life** are moderated by residents' level of cognitive impairment, are these differences **mediated** by (explained by) group differences in **positive engagement**?

Finally, having parents move into a senior living community can be stressful and anxiety-producing for adult children. We focus on residents of senior living communities and their adult children living at a distance because the distance can make it challenging to maintain their relationship and difficult for the adult children to feel like they have control over the quality of care provided for their parents. Adult children who cannot easily visit their parents and monitor their care often experience care-giver guilt. They feel guilty and anxious that their parent is in a senior living community and report dissatisfaction with information they receive about their parent's care.[24] Adult children's guilt, worry, and stress about their parent's safety and care has been exacerbated with COVID-19 because the disease can spread rapidly in these communities and put its entire population at risk. Adult children have also been unable to physically visit their parents because of the pandemic, further contributing to their existing anxiety and guilt. To improve the quality of life of the resident and ease the concerns of the adult child, it is essential that the senior living community involve the adult child in the parent's care and provide programming that allows residents to experience a high quality of life. The synergy that is created through the shared VR experiences should reduce caregiver guilt for the adult child not only because the child is engaged in the VR with their parent, but also because they see first-hand the positive effects that it has on their parent's engagement over time. Thus, our final aim and hypotheses are posed:

AIM3: *Determine whether Rendever (vs. control) reduces* **caregiver guilt** *for adult children who live at a distance, and whether these effects depend on the adult child's own response to the VR and their parent's response to the VR (a dyadic effect).*

- **H2a**: Adult children in the VR condition (vs. control) will show significantly **greater reductions in caregiver guilt** both concurrently and over time (relative to baseline).

H2b: The effects of the VR condition (vs. control) on **adult children' caregiver guilt** will be **moderated** by the adult child's own **positive engagement** and the parent's positive engagement, such that the beneficial effects of the VR condition will be amplified when positive engagement is higher (vs. lower) for self and parent (a dyadic effect)

2.2 Background

Cognitive decline in older adults is a public health crisis, with high costs to society and few preventative measures or solutions. Alzheimer's disease affects approximately 5.4 million Americans and it is estimated that by 2050, this number will more than double to 13.8 million. The cost of caring for adults with Alzheimer's disease (AD) and Alzheimer's disease-related dementias (ADRD) in health care, long-term care, and hospice in 2019 was $244 billion. What is equally pressing, however, are the emotional and relational costs of dementia for older adults and the family members who love and care for them. New technologies are essential that can reduce the caregiver burden of AD/ADRD (NIA's strategic plan). Before COVID-19, family members were already concerned about the quality of care provided for their loved one with dementia in senior living communities and these concerns have been amplified by the pandemic. The virtual reality (VR) program, Rendever, provides an innovative and affordable solution to these challenges by enabling older adults in senior living communities to maintain important family relationships, engage fully with life, and reconnect with their past, regardless of physical location, through its advanced networking and live streaming capabilities. There is neurological, behavioral, and physiological evidence that virtual environments allow people to feel the emotional presence of others in ways that surpass their location in space. Unfortunately, little research has examined VR's impact on older adults' social relationships, primarily due to the lack of networking and communication capabilities of other VR programs.

In our Phase I study, we tested the feasibility of Rendever with residents with mild cognitive impairments (MCI) or mild to moderate dementia and their family members who lived at a distance. Our metrics for both Aims were exceeded. Data collected with 21 family dyads showed Rendever to be safe, easy to use, and transformative for the families. Residents and their family members reported extremely high user satisfaction, enjoyment, and immersion. Rendever also significantly reduced residents' feelings of isolation, increased positive affect, decreased negative affect, increased quality of life, and improved emotional closeness with family members over time compared to baseline. In addition, it significantly improved mental health and reduced negative affect and caregiver guilt for the family member over time compared to baseline. Residents with MCI and mild to moderate dementia also equally enjoyed the VR. In Phase II (the current project described), we continue to refine the long-distance features of Rendever, while expanding the scientific goals of the project by testing the immediate and longer-term impact of Rendever on the quality of life of residents and their adult children in an experimental design. We also continue to investigate whether residents' responses to the VR depend upon their level of cognitive impairment. Resident-adult child dyads (N=200) will participate. Half of the residents will have MCI and half will have mild to moderate dementia. The dyads will be randomly assigned to a VR group or an active control group of video chat (Zoom).

2.3 Risk/Benefit Assessment

2.3.1 Known Potential Risks

Risks to psychological well-being: Although the VR activities are designed to be pleasant and enjoyable, there is a chance that participants will experience emotional distress (sadness, regret) when participating in some of them. For example, some residents who participate in the "Life Story" activity might feel distressed if the activity makes them think about past memories that are painful or negative. Looking at family photos through the VR could also make residents think about their mortality, the passing of a spouse, missed opportunities with their family, and conflicted aspects about their relationships. They might also feel frustrated if they cannot remember the names of people or things in photos. In addition, family members may feel sad when thinking about how their relationship with their loved one has changed as a result of dementia or the passage of time. In addition, although the Rendever platform is designed to increase social engagement and connection, difficult family dynamics may take place if residents and their family members behave in a distant or unsupportive manner during the VR activities. Based on previous pilot work using Rendever in similar residential communities and the Phase 1 pilot data, these experiences will likely be rare and mild in severity.

In the **Phase 1 pilot data**, which included 21 resident-family dyads (42 individuals) and 63 VR sessions, there were minimal reports of psychological discomfort. There were no instances of negative emotional distress, anger, or negative interpersonal dynamics between family members. When residents were asked if the VR session made them anxious, 57 out of the 63 times they said "not at all". When asked if the VR session made them tired, 56 out of 63 times they said "not at all," and when asked to rate how "secure" they felt during the VR session, their mean rating was 9.1 on a 10-point scale (10 indicating "completely secure"). In no case did a session have to be interrupted or suspended due to emotional or social distress, and in no case did a resident (or family member) request to end a session. Residents and family members greatly enjoyed the VR sessions, and many wanted to continue the sessions beyond the 15 minutes scheduled. They also wished there were more sessions and many residents asked if they could do the study over again with another family member. Sessions where residents traveled back to their childhood home and other memorable locations ("Life Story") lasted anywhere from 30 minutes to over 60 minutes and brought an abundance of positive, shared memories. In addition, results from the Phase 1 pilot study indicate that residents with MCI and residents with dementia did not differ in how much they enjoyed the VR and found it easy to use. Finally, the survey data indicated that the shared VR experiences significantly reduced feelings of isolation, increased positive emotions, decreased negative emotions, improved quality of life, and improved emotional closeness with family members over time. Based on the findings thus far, risks to psychological well-being are projected to be minimal in the Phase II project. Nevertheless, because this is a vulnerable population, careful safeguards (described below) will be in place to minimize and mitigate these risks, and any adverse psychological responses will be managed with the utmost care and respect for residents and family members.

Risks to confidentiality: Participants may be uncomfortable sharing personal information with researchers or being videotaped for research purposes. In addition, although all research data will be carefully safeguarded (and identified only by a random family code), there is a small risk (as with any digitally stored data) that data security will be breached and personally identifiable information could be obtained by non-research personnel.

Risks to autonomy: Participants may feel pressured to join the study (or remain in the study) so that they do not disappoint the researchers or their family members. In addition, although the consent process will take place with very careful safeguards, there is a small risk that participants with cognitive impairment may not fully understand the study procedures or associated risks. Careful safeguards will be in place to minimize these risks.

Risks to physical safety: The VR activities pose some mild risk to the participants' physical safety, particularly the older adults. One potential risk is experiencing dizziness and nausea as a result of the VR experiences. Because some participants have dementia, they could be at risk of experiencing hallucinations or becoming aggressive as a result of the VR. There is also a risk of mild skin irritation around the eyes and nose caused by the VR headset. Finally, due to the current COVID-19 pandemic, there is increased risk that the VR headsets could transmit bacteria and germs. Careful safeguards will be in place to minimize and mitigate these risks. In the **Phase I pilot data**, which included 63 VR sessions, there were no instances of hallucinations or aggression, and no instances of physical instability following the VR sessions. Of the 63 sessions, 57 reported "no nausea at all," and the remaining cases reported only mild nausea (mostly during the first session when the VR experience was new). In addition, of the 63 sessions, "no discomfort at all" was reported in 54 of them, and "no eye irritation at all" was reported in 51 of the sessions. Finally, across 63 sessions, in no case did the resident or family member request to remove the headset or to stop the session. Based on the Phase 1 findings, risks to physical safety will likely be minimal in the Phase II project in 12 new, but similar, communities. Nevertheless, because the population is vulnerable, careful safeguards will be in place to minimize potential physical risks.

2.3.2 Known Potential Benefits

This study is designed to test the feasibility and impact of the Rendever platform (vs. video chat). We hope that participants will experience personal and relational benefits as a result of their participation.

Personal benefits: Senior residents in this study may experience improvements in emotional well-being, including increases in positive emotion, subjective vitality, and meaning in life. Residents often lack opportunities for exploration and novelty, especially for those with limited mobility and cognitive impairments. By participating in this study, residents will have an opportunity to engage in novel and emotionally meaningful activities that are socially shared, even while they are physically separated from loved ones. Family members may also benefit in numerous ways. By participating in enjoyable activities with their loved one, they may experience reductions in stress and worry about them, or guilt about not being able to see them in person. The VR activities will enable family members to interact with their loved ones remotely, but in a positive and emotionally meaningful way. Finally, participants may experience feelings of satisfaction associated with their contribution to scientific research on healthy aging, and as a function of building a familiar and caring relationship with research staff.

Relational benefits: Residents and family members may experience improvements in their relationships with each other, including increases in intimacy, emotional closeness, social support, and healthy communication. Participants will have structured opportunities for social connection for 4 consecutive weeks. This may allow residents and family members to engage in positive activities that build emotional capital and strengthen emotional bonds. The VR/Zoom activities are designed to be positive and emotionally meaningful, and the Rendever/Zoom platforms allow them to be socially shared. These activities will be guided by research staff, which should minimize stress and burden for residents and

family members. This should enable residents and family members to enjoy the shared VR/Zoom activities, and to build closeness in ways that might not otherwise be available to them.

Preliminary data from 21 resident-family dyads provides encouraging evidence that residents and family members are benefiting from their participation in this project. Residents and family members reported loving the VR experiences, with extraordinarily high levels of satisfaction (means ratings of 9 on a 0-10 scale). Numerous residents asked if they could do the study again with a different family member, and no dyads withdrew from the study. Strong bonds also developed between participants and members of the research team, and many social connections were built and strengthened. Statistical analysis of survey data shows that residents experienced significant decreases in feelings of isolation and negative emotion across the study, and significant increases in positive emotion and feelings of closeness to their family members. Family members experienced significant decreases in caregiver guilt and depression, and increases in positive well-being.

2.3.3 Assessment of Potential Risks and Benefits

Until cures for the dementias are discovered, new technologies are needed to help reduce the emotional burden on individuals and families. Virtual reality is an innovative, noninvasive, drug-free, and increasingly affordable tool that can assist older adults in residential care communities and their family members thrive personally and relationally. The crisis of loneliness that predated the COVID-19 pandemic, and the current pandemic, highlight the urgent need for innovative tools and methods for fostering social connection at a time when older adults are isolated from family. Preliminary testing of Rendever shows that it improves positive emotions, energy, and mental health in older adults without cognitive impairments. However, the feasibility of Rendever for residents with dementia, *as well as its remote capabilities with family members*, has not been scientifically tested. Results from the Phase 1 pilot study provide encouraging preliminary evidence of Rendever's efficacy, but this Phase II intervention project will provide an essential, rigorous scientific test of the usability, technological merit, and impact of Rendever in this population.

The knowledge gained from this Phase II study will be a vital step toward determining if Rendever can be used effectively with residents with dementia and remotely with both residents and family members, and showing that VR technology provides significant benefits compared to standard technology currently available (i.e., video chat via Zoom). It will also provide a much-needed test of Rendever's software and remote networking capabilities. Finally, because little research has implemented VR with residents with MCI and dementia in the same study, this study will provide critical information about the level of cognitive impairment for which VR/Rendever might be best suited. If Phase II is successful, it will provide evidence for a validated and more marketable product that residential care communities can confidently adopt and incorporate into their activities for residents with cognitive impairments to improve quality of life, facilitate thriving, reduce caregiver burden for family members, and challenge existing thoughts on aging.

Protection against risk to psychological well-being. Residents will be carefully selected for inclusion in the study by the research team, in consultation with the Director and staff of each residential community and adult children, based upon their known medical history (e.g., cognitive impairments, MMSE scores, AD8 scores, and history of hallucinations or aggression). No resident will participate in the project unless they are approved to participate by the Director and key staff (as was the policy for the Phase 1 pilot study). The sample will include a spectrum from MCI to mild and moderate AD/ADRD (with MMSE-2

scores ranging from 13 to 26). Residents with later stage AD/ADRD (or MMSE-2 scores below 13), who may be at higher risk of adverse psychological reactions, will be *excluded*. During all study activities, members of the research team will be physically present with participants, and will carefully monitor their verbal communication and emotional responses. If at any point during the study a participant indicates discomfort or distress, the researcher will recommend that they take off their headset (or pause their VR/Zoom session) and will check in with them to decide on further action. One of the PIs will be on call at all times during the study to ensure the safety of the residents. If further action is needed, the PI will inform the Director at the senior living community. Any hallucinations the residents may experience will be monitored. Because residents with severe dementia are not eligible for the study, and because 63 sessions have been run with no instances of hallucinations, the adverse outcome of hallucinations is highly unlikely.

Following the success of Phase 1, the safeguards currently in place will be continued to ensure that the ***reminiscence activities*** (the virtual/Zoom Lifestory and Family Photos activities) are meaningful and positive. Research shows that using pictures to reflect on one's relationships enhances the mental health of residents and is particularly useful for residents with AD/ADRD because they often recall their past even if their short-term memory is tenuous.14 Individualizing the VR/Zoom experience and focusing on the residents' past and on nostalgic experiences should increase the likelihood that VR/Zoom will induce positive emotions and be enjoyable. However, because reminiscing about one's past can sometimes produce negative emotions, the recommendations of other researchers will be followed and only pictures and travel locations that the adult child believes are associated with positive emotions will be used.14 For example, if the family member believes that photos of a deceased loved one will evoke negative emotions, those photos will be avoided. Nevertheless, one can never fully predict whether a resident will respond negatively in a particular moment. If a study participant experiences emotional distress, researchers will suggest skipping to the next photo or travel location. If the participant remains distressed and wishes to conclude the session, researchers will pause the activity, help the resident remove the headset, and provide reassurance and comfort.

In the unlikely event that a participant experiences moderate or strong psychological distress that is attributable to the study, the PIs will discuss with the resident (and family member) the possibility of discontinuing the study. Such conversations would take place with the utmost sensitivity and care. In the 21 resident-family member dyads completed in the **Phase 1 pilot study**, no instances of emotional distress were experienced during the reminiscence activities. On the contrary, residents and family members almost uniformly loved these activities and typically stayed in their VR sessions long beyond the planned 15-minute activity, with an abundance of positive emotion and shared memories. Moreover, preventative safeguards worked effectively. For example, there was one instance where an adult child and researcher decided not to include photos or videos of a particular relative with whom the resident had a strained relationship. In another instance, the resident was a Vietnam veteran and the adult child and researcher decided not to show any VR videos of war memorials to prevent possible PTSD. During the initial contacts with the resident and adult child, the researchers will conduct an oral history interview where they find out about the resident's hobbies, interests, history, and relationships with family members. This information will be used as a guide to help create positive, meaningful experiences and avoid potential adverse reactions.

Based on previous research on reminiscence therapy with residents with dementia, family members will be provided with careful guidance on how to respond to the resident during their VR/Zoom sessions. For example, they will be encouraged to simply let the resident enjoy the family photos and travel

experiences naturally (and let the photos and travel experiences be the prompts), to listen to the resident, allow the resident to share his/her feelings and memories, and to not force memories the resident might not have or attempt to change their memories. Some residents with dementia might get upset if they fail to recognize themselves, others, or their family home in a photo. In such cases, the family member will be asked to avoid asking the resident to recall specific people or names, to guide them toward more positive emotions, and try to refrain from telling the resident that he/she is wrong about a memory of an event. The family member will also be encouraged to pause and take off their headset (or take a break from the Zoom session) if they are experiencing negative feelings or potential physical side effects. Each week, the researcher will briefly check in with the adult child and resident separately about their experiences, which will include assessing how they are feeling and answering any questions or concerns they might have as a result of the session. In the Phase 1 pilot study, *no such concerns were raised*.

The researcher conducting each VR session will also carefully monitor how the adult child is communicating with the resident. If a resident becomes uneasy, the researcher will check in with them, redirect the conversation if needed, or stop the conversation if it becomes problematic. Most older adults have satisfying relationships with their friends and family, but some do not.32 Dementia can also strain those relationships. Harmful family relationships will be screened for and deemed ineligible to participate ahead of time, but family dyads with a range of relational experiences will be allowed to participate. Research shows that shared activities can bring residents and family members emotionally closer to each other and improve their communication.24, 25 The VR/Zoom activities should induce positive emotions and feelings of connection over time because of the novel, shared experiences. There is also likely a selection bias in that family members who already have a good relationship are more likely to participate in the study than those who do not. Nevertheless, if a research assistant observes unpleasant interpersonal dynamics, the assistant will contact the PIs, who will check in with participants and decide whether the study needs to stop.

As indicated above, 63 virtual reality sessions were conducted in one community (Maravilla) for the **Phase 1 pilot study.** During these sessions, there were no instances of problematic family dynamics, and no instances in which participants withdrew from the session, or in which the research team suspended a session. In addition, all 21 dyads completed all research sessions with no families withdrawing from the project. Most importantly, residents and family members thoroughly enjoyed the VR sessions and preliminary analyses of the survey data shows that residents and family members experienced significant improvements in emotional well-being and family closeness. Thus, although careful safeguards will be put in place, there is a low risk of adverse psychological outcomes from this study.

Protection against risks to confidentiality. *Safeguards during data collection:* Residents will complete surveys and interviews in a private room and will be reminded that they can skip any questions they are uncomfortable answering. Verbal consent for audiotaping will be gathered at the start of each VR/Zoom session, and permission to keep these recordings for research purposes will be obtained from both members of the dyad. In addition, verbal consent for videotaping will be obtained at the start of each VR/Zoom session from residents. *Safeguards for data storage:* All survey data will be identified by a random family code number. The master list with participants' names and family codes will be stored on a password-protected computer in the PI's locked office and destroyed at the end of the study. Online data will be collected on a secure online platform (Qualtrics). Digital audio and video recordings will be kept indefinitely (with permission) and stored on a secure online server (UCSB Box) that is HIPAA compliant.

Protection against risks to autonomy. Participants will be carefully screened for inclusion in the study based upon their records, MMSE-2 scores and AD8 scores, and other relevant information. Participants with severe cognitive impairment, who might not be capable of understanding study procedures and risks (i.e., not capable of providing informed consent/assent) will be excluded. Following ethical guidelines recommended for research on Alzheimer's patients (and developed with IRB approval in the Phase 1 pilot study), consent procedures and forms/scripts will be carefully prepared to meet the needs of residents and family members. Consent materials will be written in language that is easy to understand, and potential risks and safeguards of the study will be clearly described. Research assistants will be carefully trained to conduct the consent process with sensitivity (and without pressure) and to view the rights and welfare of study participants as their top priority. Residents will be encouraged to ask questions and, if desired, to have a residential community care provider (or other trusted person) present during the consent process. Consent forms and scripts will emphasize that participation is completely voluntary and that participants can withdraw from the study at any time without any repercussions and also receive compensation for each part of the study they have already completed. Consent will be an ongoing process that will take place at all stages of participation. Participants will receive modest compensation to thank them for their time and effort, but compensation is not intended to cause undue influence. The total compensation rate ($150 per person) is approximately $18 per hour, which is respectful of participants' time but not coercive. If participants decide to withdraw from the study, they will receive compensation for the time they already invested.

Protection against risks to physical health/safety. Participants will be carefully screened for inclusion in the study. Residents will be excluded if they have a history of vertigo, hallucinations, or aggression. The Samsung VR headsets are only moderately immersive (compared to other headsets, which are more strongly immersive), which should reduce the chances of dizziness or nausea. Participants will always be seated while using the VR/Zoom, further reducing the chance of vertigo and the risk of them falling, tripping, or running into something. There are no cords for them to get tangled in and the headsets will fit nicely around their eyes and glasses. If the resident has dementia, the research assistant (or the resident's caregiver if present) will help the resident with all parts of the study. To reduce risk of skin irritation, participants will be wearing the VR headsets for a limited amount of time for each session, approximately 20 minutes (but longer if they choose to extend the session, which they often did in the Phase I pilot study). Participants will be invited to take breaks whenever needed, or to quit if they would like to. After the VR/Zoom activity is completed, residents will be asked to remain seated while completing surveys or interviews. Once completed, research assistants will encourage the resident to monitor their status and stand when they feel comfortable doing so. Residents with dementia will have a research assistant (or personal caregiver, if present) to assist them.

With respect to the risk of potential exposure to germs and bacteria, dyads in the VR condition will use personally-assigned headsets for the duration of the study (4 weeks). At the end of 4 weeks of VR, headsets will be collected (adult children will return them by pre-paid mail) and carefully cleaned before being distributed to the next group of dyads. The headsets and control tablets will also be cleaned after every use. Headsets will be cleaned with an approved solution and then sanitized using Cleanbox®, a premium and eco-friendly hygiene solution for the decontamination of VR headsets (https://www.cleanboxtech.com). Cleanbox primarily uses a medical grade Ultraviolet C directional lighting to destroy viruses, with 99.99% efficacy within a single 1-minute cleaning cycle. Importantly, UVC light has been proven effective in destroying MERS and SARS, which are both also coronaviruses. If COVID-19 restrictions are still in place when the data are collected, the researchers will also wear face

coverings, gloves, and maintain social distance when possible. They will also encourage the resident to put on their own headset if they are able. The researchers will also take their temperature each day before coming to the community and monitor their health and not enter a community if they are experiencing COVID-19 symptoms or have traveled on an airplane recently.

General safeguards. The following general steps will be taken to help minimize any additional risks: (1) ensure the screening requirements for inclusion in the study are closely followed, (2) ensure that HIPAA rules are enforced with regard to access to any private medical information, (3) ensure that research assistants are trained to follow the strict guidelines set forth in the Human Subjects Protocol, and (4) ensure that all research assistants complete the mandatory human subjects training as part of the IRB application. Metrics for success will be met when (1) the technology works smoothly after numerous implementations with the residents and family members, (2) the residents and family members enjoy using the technology and report primarily positive emotions and relational feelings after using the VR, (3) any negative experiences with the VR are minimal and have been resolved and prevented in sustained uses with the residents, (4) the screening procedures (e.g., MMSE-2) for cognitive impairment are adequate and we determine the level of cognitive impairment best suited for the ethical use of Rendever, and (5) the residents are able to successfully complete the survey measures and interview questions.

3 Objectives and Endpoints

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS
To test the impact of different forms of technology (virtual reality (VR) vs. video chat (VC)) on quality of life and family relationships in older adults who reside in senior living communities and an adult child who lives at a distance.	● Quality of life ● Thriving ● Mental health ● Loneliness and social connection ● Family relationships ● Caregiver guilt	Each measure is an outcome variable to test the primary objectives.
Determine whether the effects of the technology intervention (VR vs. VC) on residents' and their adult children's outcomes depend upon residents' level of cognitive impairment (MCI vs. mild to moderate AD/ADRD).	● Quality of life ● Thriving ● Mental health ● Loneliness and social connection ● Family relationships ● Caregiver guilt	Each measure is an outcome variable to test the primary objectives.
Determine whether the different forms of technology (VR vs. VCt) have different immediate impacts on positive engagement and family bonding during the technology sessions, and whether these immediate responses mediate any impacts of the intervention on parent and adult child outcomes.	● Self-reported emotional and social engagement during the intervention sessions ● Observational and computer coding of social and behavioral (kinesic) engagement during the interventions sessions	Each measure is an outcome variable to test the secondary objectives.

4 Study Design

4.1 Overall Design

Purpose of the clinical trial: The virtual reality (VR) program, Rendever, enables older adults in senior living communities to maintain important family relationships, engage fully with life, and reconnect with their past, regardless of physical location, through its advanced networking and live streaming capabilities. This Phase II project will continue to refine the long-distance features of Rendever, while expanding the scientific goals of the project by testing the immediate and longer-term impact of Rendever on the quality of life of residents and their adult children in an experimental design. The study will also continue to investigate whether residents' responses to the VR depend upon their level of cognitive impairment.

Study Design: The design of this study is a 2 (Intervention Group: Virtual Reality vs. Active Control) x 2 (Level of Cognitive Impairment: MCI vs. AD/ADRD) x Time (7 time points) design. Participants will be older adults (age 50+) with mild cognitive impairments (MCI) or mild to moderate Alzheimer's Disease or related dementias (AD/ADRD) who reside in senior living communities, and an adult child who lives at a distance. Residents will participate from a private room located in their senior living community. Adult children (age 18+) will participate from their own home, at least 45 minutes driving distance away. Resident-adult child dyads will be randomly assigned to an intervention group (Virtual Reality vs. Control) using a random number generator. Dependent variables will include measures of quality of life (quality of life, thriving, depression, mental health, positive and negative affectivity, loneliness, and social connection), family bonding (closeness, satisfaction, communal coping), and caregiver guilt (guilt, stress, and burden) assessed through surveys and interviews over the 4-month study period. Secondary outcome measures will include positive engagement *during the technology sessions* (positive affect, engagement with the technology and with the adult child while using it, emotional closeness) measured through surveys, interviews, and observational methods during the intervention phase of the study.

The experimental intervention will be implemented in a between-group design. Resident-adult child dyads will be randomly assigned to either the (a) Rendever Virtual Reality Condition or the (b) active Control Condition involving video chat (via Zoom). Participants will complete a baseline survey (T1), followed by four activity sessions, once a week for 4 consecutive weeks (T2-T5). Following the intervention period will be a 1-month and 3- month follow-up survey to determine if potential benefits of the intervention are sustained over time (T6, T7). Residents and adult children will also be interviewed briefly after the final VR/Zoom sessions. In addition, all VR/Zoom sessions will be video- and audiotaped. Computerized coding and human coding will examine residents' positive engagement while using the technology. In addition, audiotapes will be transcribed and subjected to linguistic analysis to assess emotional responses and interpersonal features of the resident-adult child's conversations.

In VR Session 1 (virtual adventures), the dyad will choose 5 travel adventures (e.g., a safari, riding in a hot air balloon, boat ride in Thailand) among 25 possible pre-programmed adventures. In Session 2 (virtual Life Story), the research assistants will take residents and their adult child back to 8-10 favorite addresses or destinations from the past (e.g., childhood homes, family vacation sites). For Session 3 (guided experience), the dyad will choose 1 virtual tour experience guided by a research assistant (e.g., hiking Machu Picchu, tour of Rome). In Session 4 (virtual photos and videos), adult children will upload

15 family photos and 1 video with a simple "drag and drop" interface to Rendever's password-protected, online portal.

Sample size, recruitment, and statistical power: The resident-adult child dyads (N = 192) will participate from 12 senior living communities (16 dyads per community). Half the communities (n = 6) will be located in central California where the research team from the University of California, Santa Barbara resides. The other half (n = 6) will be in Boston, where the Rendever team resides. A power analysis using simulation methods (for multilevel regression models and structural equation models) was used to determine the sample size. Whenever possible, effect sizes were estimated from the Phase I pilot study data. The attrition rate was assumed to be approximately 15% across the 4- month longitudinal study. The results of the simulation study reveal that a sample size of 192 dyads (96 in VR condition, 96 in control) evenly split between cognitive impairment groups (MCI vs. dementia) will achieve a high level of power (.85) for detecting the minimal expected effect size (conceptualized as effect size of d=.2) across the different analytic approaches considered. This sample size will provide high power (85%) for detecting even relatively small effects of the VR condition over control, and excellent power for detecting even larger effects, which are anticipated.

Statistical analysis: Because data from resident-adult child dyads is dependent, and because the dyad is the unit of analysis for assignment to experimental conditions, the analysis of quantitative data will utilize linear models designed for nested (clustered) data. Hypothesis testing will be conducted with multi-level, random effects regression models and multilevel structural equation modeling.

4.2 Scientific Rationale for Study Design

A key question we aim to address in this study is what unique benefits VR– specifically, Rendever's VR– provides beyond existing methods for enhancing connection across distances, reducing loneliness, and improving well-being. Given the widespread adoption of video conferences, particularly during the COVID-19 lockdowns, we selected Zoom as an active control condition. Video calls represent a commonly used, accessible intervention for combating loneliness, making Zoom an appropriate benchmark for comparison. THis allows us to isolate the specific contributions of VR –such as increased immersion, presence, and engagement–while ensuring that all participants receive some form of social interaction. However, we acknowledge potential limitations of this control, including differences in ease of use for the family member, technological familiarity, and the extent to which each method fosters meaningful social experiences.

4.3 Justification for Intervention

The selected mode of intervention delivery–weekly ~20-minute VR sessions– was informed by the success and findings of our Phase I study, which demonstrated feasibility and positive engagements with this schedule. Limiting sessions to approximately 20 minutes helps mitigate potential adverse effects of extended VR exposure, such as eye fatigue, while ensuring participants have sufficient time to meaningfully engage with the experience.

This intervention schedule strikes a balance between collecting valuable data and minimizing participant burden, ensuring that study participation remains accessible and manageable. The structured weekly sessions, each featuring a different activity showcasing Rendever's VR product offerings, allow us to

assess the impact of VR on resident-adult child connection, well-being, and loneliness in a comprehensive manner.

To obtain evaluable data, minimum participation is defined as attending at least 3 of the 4 sessions, ensuring adequate exposure to the intervention for meaningful analysis. This threshold accounts for expected variability in participation, such as participant travel, hospitalizations, or changes to health, while maintaining the study's ability to detect potential effects.

4.4 End-of-Study Definition

A participant is considered to have completed the study if he or she has completed the baseline (T1), four technology sessions (T2-T5), post-study survey (T6), and follow-ups at 1-month (T7) and 3-month (T8).

5 Study Population

5.1 Inclusion Criteria

Older Adult:

1. Be at least 50 years old
2. Fluent in English or Spanish
3. Score between 13 and 27 on the mini-mental state examination (MMSE-2), reflecting mild cognitive impairment or mild to moderate dementia
4. Have an adult child living at least 45 minutes driving distance who is willing to participate with them - if the older adult did not have an adult child, they could nominate another family member who served in a caregiving role (e.g., niece or nephew)
5. Relationship with the adult child must be free of extreme negativity, aggression, or abuse

Adult Child:

1. Be at least 18 years old
2. Fluent in English or Spanish
3. Live at least 45 minutes driving distance from parent's senior living community
4. Relationship with the parent must be free of extreme negativity, aggression, or abuse

5.2 Exclusion Criteria

Older Adult:

1. history of severe vertigo, seizures, or dementia-related hallucinations, paranoia, or aggression
2. Unable to view images in virtual reality or Zoom due to visual impairments

Adult Child:

1. History of severe vertigo, seizures, hallucinations, or aggression
2. Unable to view images in virtual reality or Zoom due to visual impairments

5.3 Lifestyle Considerations

N/A

5.4 Screen Failures

Screen failures are defined as participants who indicated interest in participating but are ineligible or those who verbally consent to participate in this study but are not subsequently entered into the study. Individuals who do not meet the criteria for participation in this trial (screen failure) because of meeting one or more exclusion criteria will not be rescreened.

5.5 Strategies for Recruitment and Retention

Planned distribution of subjects by sex/gender, race, and ethnicity:
Participants will be **192** resident-adult child dyads recruited from 12 senior living communities (approximately 16 dyads per community). Half of the residents (age 50+) will have mild cognitive impairment (MCI) and half will have mild to moderate Alzheimer's disease and Alzheimer's disease related dementias (AD/ADRD). Half of the residents will be recruited in California by the research team at UCSB and half will be recruited in Boston by the Rendever research team. Residents will be recruited from 6 communities in or within 30 minutes of Santa Barbara and 6 communities near Boston. Recruitment efforts will be extended to additional communities if additional participants are needed, or if doing so would increase sample diversity. Adult children (age 18+) will participate remotely, and may reside anywhere in the world. The average age of residents across the 12 communities is 87. Most communities include independent living, assisted living, and memory care programs. Residents from all three programs will be recruited for the study if they meet eligibility requirements. The communities do not have precise data on residents' levels of cognitive impairment, but it is estimated that 29% of residents have MCI and 40% have AD/ADRD.

The demographic makeup of the participating communities is majority female (approximately 70%) and majority white (approximately 85%), with small percentages of Hispanic (5.3%), Black (2.2%), and Non-Hispanic Other (6%) groups. Based on the demographic features of the participating communities, the planned distribution of subjects by sex, race, and ethnicity will be a function of these underlying features and efforts to increase the diversity of our sample by oversampling residents who are male and/or members of under-represented racial and ethnic groups.

With respect to gender, because female residents outnumber male residents by approximately two to one in senior living communities nationally, and in the communities participating in the study, we anticipate that our sample will include more female than male residents. We plan to over-sample male residents, resulting in a planned enrollment of 80 percent female, 20 percent male residents in the sample.

With respect to race and ethnicity, the overwhelming majority of residents in senior living communities are White, both in national statistics (84%) and in the communities participating in the study (85%). Thus, we anticipate that our sample will include more White than non-White residents. Increasing the ethnic and socioeconomic diversity of the sample is a high priority for this study. Through outreach efforts (described below) we plan to over-sample residents who identify as members of minority groups,

resulting in a planned enrollment of 80 percent White, 20 percent (combined) Hispanic, Black, Asian, and other non-Hispanic White residents. The participating communities in California have slightly higher percentages of Hispanic residents, whereas those in Boston have slightly higher percentages of Black and Asian residents. Together, these East and West Coast communities will allow us to increase the overall diversity of our sample and improve the generalizability of our findings.

With respect to adult children who will be recruited in tandem with their parents (residents), we assume that their racial and ethnic makeup will be similar to their parents. However, in terms of gender, our Phase 1 pilot study revealed that male and female family members were equally likely to participate (57% male, 43% female) with their (mostly female) parents. Thus we estimate that roughly 50% of the adult children in this Phase II study will be male, and that their racial and ethnic identity will match that of residents. We will work hard to recruit a diverse set of families through special outreach efforts to adult children as well as their parents.

Rationale for selection of sex/gender and racial/ethnic group members:
Targeted enrollment estimates are based on a joint consideration of the gender/racial/ethnic characteristics of the communities participating in the study, and the significant recruitment efforts that will be undertaken to over-sample male residents and members of under-represented minority groups. With these efforts, and the large sample size for this study (192 dyads, 384 individuals), the resulting data will permit us to explore potentially important racial/ethnic differences in the effectiveness (ease of use and satisfaction) of Rendever, and its impact on quality of life and caregiver guilt.

Proposed outreach programs for recruiting sex/gender and racial/ethnic group members as subjects:
Increasing the diversity of our sample will be a high priority. The following efforts will be made to increase diversity: (a) the research team will work closely with Directors at each community to identify eligible residents from under-represented groups so that we can enhance our personal outreach efforts; (b) we will recruit an ethnically diverse research team, including Spanish speaking staff and research assistants who will build rapport and comfort among Spanish-speaking families. Likewise, we will engage in special outreach efforts for Black and Asian residents, with diverse members of our research team, to create meaningful and authentic social connections; (c) we will plan special meet-and-greet sessions at Grace Village, the affordable housing community where 40% of residents use Spanish as their primary language, and 10% use other primary languages (including Chinese and Russian). We will have recruitment materials translated into Spanish (including flyers, letters to family members, and consent materials) and, if needed, other languages. (d) We will host culturally sensitive recruitment events and prepare culturally sensitive research materials, activities (in VR/Zoom), and tokens of appreciation. (e) Finally, to increase the socio-economic diversity of the sample, we will provide resources to facilitate the participation of lower-income families (e.g., Wi-Fi hotspots for family members).

In addition to these steps, we will broaden recruitment efforts to additional communities if doing so would increase the diversity of the sample. As noted above, we already have permission to recruit residents from 4 additional communities in the greater Boston area. We will continually monitor the status of our outreach efforts and will expand to these communities if necessary.

Finally, the recruitment plan will include residents who have physical disabilities or visual impairments. Residents with physical limitations (who need the assistance of wheelchairs, walkers, or staff to move) will be included in the study (and, if needed, assisted by a personal caregiver or staff member). Residents with visual impairments will be screened to determine their ability to see images in the VR headset or on

the Zoom screen. In the Phase I pilot study, 3 of the participating residents were legally blind but were able to see the VR images (which are large and designed for seniors) and successfully participate in the study.

Rationale for proposed exclusion sex/gender or racial/ethnic groups:
No participants will be excluded based upon sexual identity, sexual orientation, gender, or racial/ethnic identification.

Recruitment Plan: Following successful recruitment procedures developed in the Phase 1 pilot study, the recruitment process will be conducted in several steps.

Step 1: Letters to the families of the residents will be emailed, describing the study and letting them know that, if they qualify, their family might be invited to participate in the study in the near future. The letter will also give them contact information for the researchers so that they can opt out of the study if they prefer not to be contacted.

Step 2: The Director at each community will announce the study to residents via email, flyers, and community newsletters. Directors will also announce the study at large gatherings (e.g., monthly community meetings, movie nights), where researchers will be present to introduce themselves and answer questions. Residents will be invited to contact the researchers (in person, via phone, or email) if they are interested in learning more. THe research team will also hold community meet-and-greet events, where they will pass out flyers (in English and Spanish, where relevant) and gather names of interested residents.

Step 3: Directors and key staff of the communities will assist in identifying eligible residents (screening for eligibility).

Step 4: Once identified, potentially eligible residents will be invited to talk with the researchers (in the resident's room or apartment, or in another private space if preferred) to determine if they are interested in participating, and verify that they are eligible to participate. The researchers will explain the purpose and procedures of the study and gather initial verbal consent to participate. At this time, researchers will administer the MMSE to verify eligibility. If a resident's ability to consent is uncertain, the researcher will complete an IRB-approved screener assessing their decision-making capacity to consent, and consent will be obtained from the resident's legal guardian as needed.

Step 5: Contact information for an adult child with whom they would like to participate will be requested from eligible residents. If the resident has more than one eligible adult child, the researcher will randomly select from the list of eligible children. Researchers will call the adult child, explain the study, and gather initial verbal consent. If the adult child declines to participate, then the researcher will consult with that child (and the resident if needed) and will contact another eligible adult child, if available. If no child is willing and able to participate in the study, the resident will be offered an opportunity to engage in a virtual reality activity just for their enjoyment. In our Phase 1 pilot study, there were only a couple of instances in which one or more adult children were unable or unwilling to participate with an interested resident.

Step 6: Once all initial verbal consents are received from the resident and adult child, the family dyad will be enrolled in the study.

Step 7: Residents and adult children will next complete the formal consent process. Residents will be given written consent forms to sign. In addition, a consent script will be read out loud to residents with mild to moderate dementia (and any other residents who request it) to ensure they understand the study procedures and associated risks and safeguards. Adult children will be emailed an online link to a digital consent form. If applicable, the resident's legal guardian will be emailed a link to an online, digital consent form.

Step 8: Continuing consent will be obtained from residents with mild to moderate dementia before beginning each of the VR/Zoom sessions using a verbal consent "check-list" (created and approved by the UCSB IRB) whereby the researcher states the purpose of the study, what will happen, the risks, and the benefits in very plain language and asks the resident if they understand each question. If the resident is capable and competent at answering the questions, and is alert and oriented to their surroundings, or if the resident reports they do not want to participate, then the sessions will not proceed that day. The researchers will speak with the Director of the senior living community, adult child, and later with the resident to make a determination whether or not the family should continue the study. If a resident or adult child wants to stop the study, they may do so at any time.

Retention:
Participants will be asked to complete 5 weeks of study activities (T1 to T5), followed by 1-month and 3-month follow-up surveys (T6-T7). The first week (T1) will consist of consent and a baseline survey. Next, participants will engage in virtual reality (VR) or Zoom activities once a week for 4 consecutive weeks. After each VR/Zoom session, participants will complete a brief survey. After Session 4 (T5) and 1-month later (T6) they will also complete a brief interview. Each VR/Zoom session will last approximately 1 hour (including set-up, 20 minute VR/Zoom activity, break, and survey/interview). Some sessions may last longer (up to 1.5 hours) if residents and adult children want to stay longer, as they often did in the Phase 1 pilot study (especially for the Life Story and Virtual Photos/Videos sessions). Residents will complete their VR/Zoom activities in a private room in their senior living community; adult children will complete their activities remotely from their own homes. Follow-up surveys will be conducted in person for residents and via online surveys for adult children.

Retention of study participants will be a high priority. Building on successful procedures developed in the Phase 1 pilot study, a number of steps will be taken to foster retention. First and foremost, the research team will work hard to build strong rapport with participants by interacting in a warm and welcoming manner, by explaining all research activities in a clear and respectful manner, and by being responsive to all questions and concerns. Second, at all stages in the research process the research team will be sensitive to the physical and emotional needs of participants. In particular, research assistants will make sure that participants are comfortable with the VR/Zoom equipment, that any physical limitations and challenges are approached in a sensitive and caring manner, that emotional responses are carefully monitored and responded to as needed (e.g., allowing participants to share their emotional experiences in both unstructured as well as structured ways), and that VR/Zoom activities are pleasant and enjoyable. For example, when preparing reminiscence activities (Life Story and photos/videos), the research team will work with family members to ensure that these activities are pleasant and meaningful (e.g., selecting photographs and locations that are associated with positive memories such as the resident's childhood home and locations they loved to visit from their past).

In order to make the project easier for older adults to participate in and to promote their comfort and safety, participants will be instructed to remain seated when using the VR/Zoom equipment. If the residents have MCI, they will have the option of completing their surveys on their own (with some assistance) or having a research assistant read the surveys to them and record their responses. If the resident has AD/ADRD, the survey will be read to them and the responses will be recorded. In addition, participants with AD/ADRD (and any other residents who request it) will be picked up in their room and escorted to and from the study room. If a resident is unable (or unwilling) to come to the study room, they will have the option to participate in VR/Zoom sessions from their own room. All of the equipment is portable.

Another important tool for fostering retention will be to provide clear and effective study materials that guide participants through the study and reduce burden. Residents will receive clear, visually appealing, and simple study reminder sheet listing dates and times of their scheduled study sessions, and contact information for the research team. It will also include photographs of the researchers' faces to enhance visual recognition. The residents will be encouraged to keep the schedule on their refrigerator or somewhere they can see it. Adult children will receive a carefully constructed packet guiding them through each VR/Zoom session and providing tips and reminders for each week. Rendever will also assist family members in uploading photos, including those from the resident's childhood, with a simple "drag and drop" interface to Rendever's secure, online portal. For adult children who will be operating the equipment remotely, the research team will ensure that the VR equipment runs smoothly, that a research team member responds quickly and effectively to questions and troubleshooting requests, and that the research teams are mindful and appreciative of family members' time and schedule.

Another way that retention will be fostered is through flexible scheduling. VR/Zoom sessions will be offered at a variety of times throughout the day and on weekends in order to accommodate the schedules of busy residents and families. If the resident has AD/ADRD, however, we will not schedule them later in the afternoon or evening to prevent Sundowning. The research team will call (and email, if preferred) residents and adult family member reminders a few days before and then again, the day before their VR/Zoom appointments or surveys/interviews. Research assistants will also confirm with the adult family member that he/she is able to take part in the VR/Zoom session that day (and reschedule if needed). Reminders and flexible scheduling are essential to retaining participants.

Continued participation will be encouraged by providing authentic expressions of appreciation at all stages in the study, and by emphasizing each participant's important contribution to scientific research on successful aging. In addition to verbal expressions of gratitude, residents and family members will be given small tokens of appreciation at key points in the study. For example, after the final VR/Zoom session, residents will receive a handwritten thank you note from the research team. After each VR/Zoom session, residents will be provided with juice and a snack, and an opportunity to rest and chat with the researchers. These gifts and snacks will follow the COVID-19 restrictions of each community, if they are still in place. Small measures such as these increase participants' enjoyment, sense of purpose, and commitment to the project. It is also hoped that these measures will lead participants to leave the study feeling that their participation was worthwhile and meaningful.

Finally, although the research team will work hard to retain participants in the study, researchers will be very mindful of the vulnerable population and careful to avoid any sense of coercion. The research team will be respectful and considerate to any participants who would like to withdraw from the study and will refrain from any efforts to pressure them to continue.

Participant Incentives:
Both the participating family members and residents will receive a total compensation rate of $150 per person. This is approximately $18 per hour, which is respectful of participants' time but not coercive. If participants decide to withdraw from the study, they will receive compensation for the time they already invested. The first financial incentive ($100 per person) will be given to subjects in person (resident participant) or mailed (family member participant) after completing the last VR/Zoom session. The last payment will be given to subjects after they complete the final follow-up survey at 3-months.

6 Study Intervention(s) or Experimental Manipulation(s)

6.1 Study Intervention(s) or Experimental Manipulation(s) Administration

6.1.1 Study Intervention or Experimental Manipulation Description

Until cures for the dementias are discovered, new technologies are needed to help reduce the emotional burden on individuals and families. Virtual reality is an innovative, noninvasive, drug-free, and increasingly affordable tool that can assist older adults in residential care communities and their family members thrive personally and relationally. Research shows that using pictures to reflect on one's relationships enhance the mental health of residents and is particularly useful for residents with AD/ADRD because they often recall their past even if their short-term memory is tenuous. Individualizing the VR experience and focusing on the residents' past and on nostalgic experiences should increase the likelihood that it will induce positive emotions and be enjoyable. However, because some research shows that reminiscing about one's past life can sometimes produce negative emotions, we follow the recommendations of other researchers and will only use pictures and travel locations that the family members believe are associated with *positive* emotions.

Preliminary testing of Rendever shows that it improves positive emotions, energy, and physical/mental health in older adults without cognitive impairments. However, the feasibility of Rendever for residents with dementia, as well as its remote capabilities with family members, has not been tested until our Phase I pilot study. This is the next step in the process of testing the technology where we can show that VR has a positive and longer-term impact on quality of life for the residents and their adult children.

Residents with dementia long to maintain connections to family, have control over their lives, and feel as if their lives still have meaning. VR, through the Rendever platform, could provide an important means through which they maintain their relationships with their children and reclaim their past. The Rendever platform could also benefit adult children by helping them feel emotionally connected to their parents while reducing their caregiver's guilt about their parent's quality of life. This study is an important next step toward determining if Rendever can improve the quality of life of residents with dementia and their adult children living at a distance. If this Phase II study is successful, it will provide evidence for a validated and more marketable product that residential care communities can confidently adopt and incorporate into their activities for residents with cognitive impairments to improve quality of life, facilitate thriving, and challenge existing thoughts on aging. In this study, Rendever's VR is used as the study intervention and the video conferencing platform, Zoom, is used as the active control.

VR Sessions: Dyads assigned to the VR condition will engage in four VR activities: **(1) virtual adventures, (2) virtual travel to one's childhood homes and other memorable destinations ("Life Story"), (3) virtual guided travel experiences, and (4) virtual family photos and videos**. In VR Session 1 (**virtual adventures**), the dyad will choose 5 travel adventures (e.g., a safari, riding in a hot air balloon, boat ride in Thailand) among 25 possible pre-programmed adventures. In Session 2 (**virtual Life Story**), research assistants will take the residents and their adult child back to 8-10 favorite addresses or destinations from the past (e.g., childhood homes, family vacation sites, schools they attended, where they were married). The adult child will input the addresses into the Rendever portal. For Session 3 (**virtual guided experiences**), the researchers will take the dyad on a narrated tour of a chosen destination. They will be provided a list of approximately 20 travel destinations and will be allowed to choose one to explore. The researcher will read fun facts about the destination while they are seeing it inside the VR. For Session 4 (**virtual photos and videos**), the adult children will upload 20-25 family photos and 2 videos with a simple "drag and drop" interface to Rendever's password-protected, online portal. The order of the sessions is designed so that the first session does not require any extra effort of the part of the adult child; it allows the adult child enough time to upload photos, videos, and addresses before sessions #2 and #4.

The resident will experience the VR sessions in a private room at the senior living community, accompanied by the researcher who will help them put on the headset and operate the VR using a control tablet. When written consent is gathered, the adult children and older adults will complete three brief background measures that assess their physical health (Promis-29 measure, a chronic health conditions checklist, and the Lubben social isolation index) right afterward (this will be done the week before the baseline survey and is a way to break-up the baseline survey in two, to reduce the amount of time spent on any one survey). The baseline survey will be completed the week prior to the first VR session. A research assistant (or senior personnel if the older adult has dementia) will administer the surveys verbally and record the responses. If the residents have MCI, they should be able to complete their own paper and pencil survey with assistance. The adult child will be emailed a link to a Qualtrics survey to complete immediately after each VR session. We will briefly (15 min) interview residents and adult children separately after the last technology session and at the 1-month follow-up. Instead of interviews at the follow-ups. Interviews with the adult children will be conducted via the telephone. Participants will be asked what they liked and did not like about the technology sessions and how they felt doing it with their family members.

The adult children will participate in the VR sessions from their own home. They will be mailed the VR headset, along with a pamphlet containing a timeline, an outline of what will happen, how to operate the equipment, and tips for having a successful experience. Rendever will contact the adult children to set up the WiFi and explain the VR. A research assistant will also call the adult child before the first session and go over the procedures. The adult child will be encouraged to talk with their parents about what they are experiencing while in the VR together. Based upon previous research on reminiscence therapy, the adult children will be encouraged to simply let their parents enjoy the photos and travel experiences naturally, to listen to them share their memories, and not to force memories they might not have or attempt to change them.

Zoom Sessions: Dyads assigned to the active control condition will follow the same weekly procedures and survey/interview assessments as those in the VR condition, except that they will be engaging in video chat conversations instead of VR. During the COVID-19, Zoom became residents' new, standard

mode of communicating with family in the communities in this study. The researchers will be operating Zoom for the residents with laptop computers. Similar to the VR condition, the researchers will email the adult children instructions and a schedule, contact them to make sure they have access to Zoom, know how to use it, have access to a computer, and pilot test it before their first session. During each Zoom session, the resident and adult child will be encouraged to talk with each other like they normally would.

6.1.2 Administration and/or Dosing

All residents will participate in their study sessions and surveys from a private room in their senior living community. All adult children will complete their study sessions and all surveys virtually. Resident-adult child dyads will complete a consent form and three brief background measures (on physical health and social isolation), a baseline survey the week before the technology sessions, followed by 4 virtual reality (VR) or Zoom experiences (described below) once a week for four consecutive weeks, a post-study survey, and then a 1- and 3-month follow-up survey. Each VR/Zoom session will last approximately 30 minutes, but could be longer if participants desire. Surveys will occur immediately after each VR/Zoom session, as well as an interview after the last VR/Zoom session (see the table below). All residents will receive the same surveys and all of the adult children will receive the same surveys (the adult children have slightly different measures, such as caregiver guilt, which residents do not complete). All primary outcome measures will be asked at four key time points (baseline, 1-week post-intervention, 1-month post-intervention, and 3-months post-intervention). The surveys after each technology session will be much briefer, focusing on secondary outcomes including experiences with the technology, affective states, and how they felt about their relationship with their family member while using the technology and during the past week. After the study is completely over, the adult children will be emailed a brief, three-minute commercialization survey that asks them the extent to which they would use the product at home if it were available and how much they would pay for it.

All of the VR/Zoom sessions with the residents will occur in person. All interviews will be audio-taped and the VR/Zoom sessions with the residents will be audio and video-taped. The videotapes will be coded later with human and automated coding to assess residents' bodily and conversational engagement while using the VR. All of the audiotapes will be transcribed. The follow-up interviews will be collected face-to-face with the residents and via the telephone for the adult children. The surveys will be conducted in person with the older adult residents. The adult children will complete all of their surveys online through clicking on a Qualtrics link sent to their email.

6.2 Fidelity

6.2.1 INTERVENTIONIST TRAINING AND TRACKING

To ensure consistent administration of the intervention, fidelity will be monitored through structured observation of the sessions (VR and Zoom) and standardized procedures for survey administration. For VR sessions, we will collect information to confirm adherence to the session protocol, including session duration, participant engagement, and any technological challenges encountered (such as WiFi outages in the community or adult child's home). Resident and adult child surveys will be monitored for completeness, response rates, and all research assistants will be carefully trained in survey administration to ensure accurate data collection.

6.3 Measures to Minimize Bias: Randomization and Blinding

Stratified Block Randomization Schedule (created with R "randomizeR" package):

- Strata = 4 (UCSB/Rendever x MCI/Dementia)
- Groups (VR/Zoom) = 2 | Block size = 4 (resulting in 6 possible combinations to draw from)
- Iterations (sequences) = 12 | 12 sequences of 4 = 48 subjects
- Results = 48 subjects per strata (equal allocation to conditions)
- Total N = 48 subjects x 4 strata = **192 dyads**

"A" = VR "B" = Zoom

UCSB – MCI

```
 [1] "A"  "B"  "B"  "A"
 [2] "A"  "B"  "A"  "B"
 [3] "B"  "A"  "A"  "B"
 [4] "B"  "A"  "A"  "B"
 [5] "B"  "A"  "A"  "B"
 [6] "B"  "A"  "B"  "A"
 [7] "B"  "A"  "B"  "A"
 [8] "A"  "B"  "A"  "B"
 [9] "B"  "B"  "A"  "A"
[10] "B"  "A"  "A"  "B"
[11] "A"  "A"  "B"  "B"
[12] "B"  "B"  "A"  "A"
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UCSB – DEMENTIA

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 [1] "B"  "A"  "B"  "A"
 [2] "B"  "A"  "A"  "B"
 [3] "B"  "A"  "B"  "A"
 [4] "B"  "A"  "B"  "A"
 [5] "B"  "B"  "A"  "A"
 [6] "B"  "A"  "B"  "A"
 [7] "B"  "A"  "A"  "B"
 [8] "A"  "A"  "B"  "B"
 [9] "B"  "A"  "B"  "A"
[10] "B"  "A"  "B"  "A"
[11] "A"  "B"  "A"  "B"
[12] "A"  "A"  "B"  "B"
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RENDEVER – MCI

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 [1] "B"  "B"  "A"  "A"
 [2] "B"  "A"  "B"  "A"
 [3] "B"  "A"  "A"  "B"
 [4] "A"  "B"  "A"  "B"
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 [7] "B"  "A"  "B"  "A"
 [8] "A"  "B"  "A"  "B"
 [9] "B"  "B"  "A"  "A"
[10] "B"  "B"  "A"  "A"
[11] "B"  "A"  "A"  "B"
[12] "B"  "B"  "A"  "A"
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RENDEVER – DEMENTIA

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 [1] "A"  "A"  "B"  "B"
 [2] "A"  "B"  "B"  "A"
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 [5] "B"  "A"  "B"  "A"
 [6] "A"  "A"  "B"  "B"
 [7] "B"  "A"  "B"  "A"
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 [9] "B"  "A"  "A"  "B"
[10] "B"  "A"  "B"  "A"
[11] "B"  "A"  "A"  "B"
[12] "A"  "A"  "B"  "B"
```

6.4 Study Intervention/Experimental Manipulation Adherence

Participant adherence to the intervention will be tracked through weekly monitoring of technology session attendance. While sessions are expected to follow the intended schedule, flexibility is allowed for health-related absences or travel, with sessions rescheduled as needed to maintain engagement.

Survey completion is a required component of adherence monitoring. Residents will complete surveys with researchers to ensure data accuracy. Adult children will be verbally reminded at the end of each session to complete their surveys. Researchers will monitor survey completeness and provide up to three reminders via text, call, and/or email to encourage adult child participants to complete their surveys.

Study adherence records, including session attendance and survey completion tracking, will be maintained to assess participant engagement and intervention adherence throughout the study.

6.5 Concomitant Therapy

N/A

6.5.1 Rescue Therapy

N/A

7 Study Intervention/Experimental Manipulation Discontinuation and Participant Discontinuation/Withdrawal

7.1 Discontinuation of Study Intervention/Experimental Manipulation

If a participant experiences an adverse reaction while using VR, they will be given the option to continue the session viewing the same experiences on a tablet instead. In this case, all remaining study procedures will be completed as indicated by the study protocol.

If a clinically significant finding is identified after enrollment, the investigator or a qualified designee will determine if any change in participant management is needed. Any new clinically relevant finding will be reported as an adverse event (AE).

The data to be collected at the time of study intervention discontinuation will include:

- The reason(s) for discontinuing the participant from the intervention, including documentation of adverse events or tense interpersonal dynamics.

7.2 Participant Discontinuation/Withdrawal from the Study

Participants are free to withdraw from participation in the study at any time upon request.

An investigator may discontinue a participant from the study for the following reasons:

- Significant study intervention non-compliance
- Lost-to-follow up; unable to contact subject
- Any event or medical condition or situation occurs such that continued collection of study data would not be in the best interest of the participant
- The participant meets an exclusion criterion (either newly developed or not previously recognized) that precludes further study participation.

The reason for participant discontinuation or withdrawal from the study will be recorded on the Case Report Form (CRF). Subjects who sign the informed consent form and are randomized but do not receive the study intervention may be replaced. Subjects who sign the informed consent form, and are randomized and receive the study intervention, and subsequently withdraw, or discontinued from the study will not be replaced.

7.3 Lost to Follow-Up

A participant will be considered lost to follow-up if he or she fails to return for 1 scheduled visit and study staff are unable to contact the participant after at least 3 attempts.

The following actions must be taken if a participant fails to attend their required virtual study visit:

- The investigator or research assistant will attempt to contact the participant, reschedule the missed visit within the next week, and emphasize the importance of maintaining the assigned visit schedule and ascertain if the participant wishes to and/or can continue in the study.
- Before a participant is deemed lost to follow-up, the investigator or research assistant will make every effort to regain contact with the participant (3 telephone calls or texts and emails).
- Should the participant continue to be unreachable, he or she will be considered to have withdrawn from the study with a primary reason of lost to follow-up.

8 Study Assessments and Procedures

8.1 Endpoint and Other Non-Safety Assessments

Screening and Eligibility Assessment
Screening procedures will be conducted prior to enrollment to determine participant eligibility. The screening process will include:

- A review of inclusion and exclusion criteria to ensure eligibility
- A cognitive assessment using a validated tool (e.g., Mini-Mental State Examination 2 and AD8)
- Informed consent obtained from participants and, if applicable, their legally authorized representative
- A baseline assessment of demographic information and chronic health conditions, Promis-29 measure of physical health, and Lubben social isolation index
- Participants who meet the eligibility criteria will be enrolled in the study.

Baseline Assessments
Prior to the intervention, the following baseline assessments will be completed:

- **Questionnaires:** self-report measures assessing quality of life, mental health, thriving, loneliness, relationship quality, and caregiver guilt (for the adult child only) will be administered.

Intervention Data Collection
Participants will engage in technology sessions, once a week, for four weeks with the following procedures:

- Sessions will be facilitated by trained study personnel between the resident and adult child
- Participants will complete weekly self-reported measures on their session experiences, mood, their study partner's behavior, and perceived benefits
- Study personnel will monitor for potential adverse reactions (e.g., dizziness, discomfort) and document participant responses to the session

Post-Study and Follow-Up Assessments
After the intervention phase is complete, the following assessments will be completed:

- **Interviews**: Interviews will be conducted between the participants and trained study personnel to gather additional information about the participants' experiences and attitude towards the technology. A post-study interview will be conducted with both the resident and adult child participant. A second interview will be conducted with the resident participant at 1-month post intervention.

Questionnaires: self-report measures assessing quality of life, mental health, thriving, loneliness, relationship quality, and caregiver guilt (for the adult child only) will be administered.

8.2 Safety Assessments

SAFETY PLAN

1. Complete Screening Document (Staff at community)
2. MMSE-2 (UCSB/Rendever senior personnel) & AD8 (adult child completes)
3. All proper levels of consent are gathered—consent is also gathered again every time before VR begins if resident has mild or moderate dementia
4. Ask staff to identify three things that might trigger a resident (if he/she has dementia) and three things that typically calm him/her.
5. Train staff on what the VR is like (try on headsets)
6. Who is the clinician/staff member on location that day in the event that there is an adverse reaction? Gather name and phone number/schedules.
7. Senior personnel (grad student, post doc, faculty) will always be operating the VR with the resident if they have dementia.
8. Training with the adult child on VR and how to communicate with parents ahead of time.
9. Trial run with the VR right before it begins to assess how it feels
10. Check in with the resident and adult child throughout the VR sessions.
11. We will also carefully monitor any hallucinations, seizures, or dizzy spells that residents experience by asking staff members if there are any concerns and on what day. If we believe the VR is connected to any hallucinations or seizures, we can discuss the possibility with the family of removing them from the study.

Safety Plan if there is an adverse reaction:

1. Ask to take off their headset and remove it for them.
2. Turn off the sound on the headset and listen to the resident. Try not to persuade them that their feelings aren't real/or are incorrect.
3. Ask how they are feeling and provide comfort.
4. If they are okay, ask if they would still like to continue by viewing the experience from the tablet with their adult child instead of the VR.
5. If they are feeling dizzy, confused, beginning to feel ill, ask if they would like a drink of water or like to lie down.
6. If they are still agitated, remembering the list of things that tend to calm the resident (e.g., taking a walk, a picture, a specific staff member, a specific area that provides comfort)
7. If the researcher is not able to calm the resident, the researcher will ask the staff member on site that day to come over and help calm them.
8. If the adult child is also distressed, the researcher will ask the dementia expert on the grant (Dr. Joan Monin) to follow-up with the adult child (if the adult child would like additional information on coping strategies).

8.3 Adverse Events and Serious Adverse Events

8.3.1 Definition of Adverse Events

Any untoward or unfavorable medical occurrence in a human study participant, including any abnormal sign (e.g. abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the participants' involvement in the research, whether or not considered related to participation in the research.

8.3.2 Definition of Serious Adverse Events

Any adverse event that: (a) results in death, (b) is life threatening, or places the participant at immediate risk of death from the event as it occurred, (c) requires or prolongs hospitalization, (d) causes persistent or significant disability or incapacity, (e) results in congenital anomalies or birth defects, (f) is another condition which investigators judge to represent significant hazards.

8.3.3 Classification of an Adverse Event

8.3.3.1 Severity of Event

Events will be rated as either **mild** (symptoms are easily tolerated and are of minor type causing no loss of time from normal activities; symptoms do not require medical or therapeutic intervention; 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; may cause some interference with functioning), or **severe** (events interrupt the participant's normal daily activities and require systemic psychological or medical treatment; usually incapacitating)

8.3.3.2 Relationship to Study Intervention/Experimental Manipulation

All events will be assessed as to the likelihood that they are related to the study intervention and/or participation. Categories are: **definitely related** (the adverse event is clearly related to the investigational procedure), **possibly related** (the adverse event follows a reasonable temporal sequence from administration of the intervention but could readily have been produced by a number of other factors), **not related** (the adverse event is clearly not related to the intervention, another cause is most plausible; and/or a plausible temporal sequence is inconsistent with the onset of the event and the intervention and/or a causal relationship is considered biologically or psychologically implausible).

8.3.3.3 Expectedness

All AEs will be assessed as to whether they were expected to occur or unexpected, meaning not anticipated based on current knowledge found in the protocol and described in study related forms and scripts. 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 recruitment material, or **expected** - event is known to be associated with the intervention or condition under study.

8.3.4 Time Period and Frequency for Event Assessment and Follow-Up

The occurrence of an adverse event (AE) or serious adverse event (SAE) may come to the attention of study personnel during study visits and post-study interviews.

Strict procedures will be followed for collecting and reporting of adverse events and unanticipated problems. All AEs, SAEs, and unanticipated problems (UPs) will be collected on an **Adverse Event Form** in both paper and electronic format. Paper forms will be completed by researchers on site immediately

following the study session in which the event occurred, or immediately after the adverse event comes to their attention (through personal communication from a study participant, family member, or residential community staff). Information on the paper forms will then be transferred to the digital form within 24 hours. PIs (Afifi and Collins) will receive an immediate alert whenever an electronic Adverse Event Form is submitted. Afifi and Collins will be responsible for classifying adverse events in terms of ***severity, expectedness,*** and ***potential relatedness*** to the study, which will be recorded on the Adverse Event Form.

PIs will record events with start dates occurring any time after informed consent is obtained until the last day of study participation. At each study visit, researchers will carefully monitor for any AEs. AEs will be followed for outcome information until resolution or stabilization.

8.3.5 Adverse Event Reporting

AEs will be reported to PIs within 24 hours. Mild AEs will be reported to the IRB and NIH PO in interim and annual reports. However, moderate or severe AEs will be reported to the IRB and NIH PO within 24 hours of the adverse event occurring or within 24 hours after the adverse event comes to attention via phone or email. Due to the low-risk nature of this project (and safeguards that will be implemented), we anticipate that AEs will be rare and mild. However, if we discover that AEs occur with greater frequency than expected, or are more severe than expected, then we will classify them as UPs, which will trigger expedited reporting and collaboration with IRB and NIH staff. All AEs and UPs will be reported to the NIH PO in quarterly interim reports and in the annual Data and Safety Monitoring Report. The PIs will also report all adverse events and unexpected problems to the IRB in the annual progress report (unless more frequent reporting is requested by the UCSB IRB).

8.3.6 Serious Adverse Event Reporting

SAEs are not anticipated in this study; but, if such an event does occur, it will be reported immediately to the PIs via telephone or email. The PIs will then transmit this information via phone or email to the IRB and the NIH PO within 24 hours. The PIs, along with the IRB and NIH PO, will determine whether the SAE is related to the intervention and which steps (if any) should be taken as a result of the event. The expedited report will be followed by a detailed, written SAE Report as soon as possible, which will be submitted to the IRB and the NIH PO.

8.3.7 Reporting Events to Participants

N/A

8.3.8 Events of Special Interest

N/A

8.3.9 Reporting of Pregnancy

N/A

8.4 Unanticipated Problems

8.4.1 Definition of Unanticipated Problems

This protocol uses the definition of Unanticipated Problems as defined by the Office for Human Research Protections (OHRP). Any incident, experience, or outcome that meets all of the following criteria: (a) unexpected, in terms of the nature, severity, or frequency, given (1) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (2) the characteristics of the study population; (b) 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); and (c) suggests that the research places participants or other at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

8.4.2 Unanticipated Problems Reporting

UPs will be reported to PIs within 24 hours. The PIs will then evaluate the severity of the UP and its potential relatedness to the study intervention. They will then transmit this information to the IRB and the NIH PO within 48 hours (via phone or email) to discuss corrective action, if needed. If the UP is classified as related to the study intervention, then the study protocol, and consent procedures and forms, will be modified to incorporate the unanticipated problem and any new safeguards that will be implemented. The expedited report will be followed by a detailed, written UP report as soon as possible. This report will increase a corrective plan and measures to prevent reoccurrence of the UP.

8.4.3 Reporting Unanticipated Problems to Participants

N/A

9 Statistical Considerations

9.1 Statistical Hypotheses

STUDY AIMS:

- **AIM 1:** Determine whether virtual reality (vs. control) improves quality of life for residents and their adult children who live at a distance.
- **AIM 2:** Determine whether the positive effects of virtual reality (vs. control) on quality of life depend upon residents' level of cognitive impairment (MCI vs. mild to moderate AD/ADRD).
- **AIM 3:** Determine whether virtual reality (vs. control) reduces caregiver guilt for adult children and whether these effects depend on the adult child's own responses to the technology and their parent's responses to the technology.

- Primary Efficacy Endpoint(s):
    - Older adults
        - Quality of Life
        - Thriving
        - Positive and negative affectivity
        - Depression
        - Mental health symptoms
        - Loneliness and social connection
        - Relationship quality with adult child
    - Adult Children
        - Thriving
        - Positive and negative affectivity
        - Depression
        - Mental health symptoms
        - Caregiver guilt and perceived stress
        - Relationship quality with parent
- Secondary Efficacy Endpoint(s):
    - Older adults and adult children
        - Conversational, social, and emotional engagement during technology sessions
        - Kinesic (physical) engagement during technology sessions (older adult only)
        - Relationship connection and bonding during technology sessions

9.2 Sample Size Determination

Power analysis approach: The approach to estimating power was to use simulation methods. Using this approach, the hypothesized population model and its associated model parameters are used to randomly generate data for the study, including sampling variability. Data are generated thousands of times, simulating thousands of hypothetical studies, and then summarized to explore how many of the simulated studies contain the parameter of interest. The proportion of time each individual effect is significant across all of the simulations is the power of that effect or the expected number of times one would observe that effect to be significant if an alternative hypothesis was true in the population. This approach is the only way to estimate power in this study because of the complexity of the statistical models needed to estimate the treatment effects, that account for the dyadic relationship (resident-adult child) and the longitudinal repeated measures of the outcomes of interest (7 time points). We used the simulation facilities in Mplus (version 8.3) to estimate the models.

To address the proposed aims, which involve dyadic longitudinal models, some with mediation, the power analysis relied heavily on the Phase 1 pilot data as estimates for effects of interest (including within-group changes in well-being over time, baseline to VR). This helps provide a starting point for the simulated datasets. These models, however, are quite complex and involve model parameters for which the pilot data cannot provide reasonable estimates. For example, the pilot study did not collect data on a control group. To be conservative, the power analysis used conservative estimates of effect sizes for models that included differences between VR and the control group (e.g., d = 0.2). To determine power, the analysis focused on power of the treatment impact for a given aim (e.g., the hypothesized increase in

quality of life for those in the VR condition for Aim 1, both concurrently and over time), while varying other model parameters that affect power (e.g., standard error of random intercepts and error variance) and exploring the impact of sample size. That is, simulations considered different sample sizes, variances, and standard errors, to ensure that the planned sample size was a large enough sample to provide sufficient power across all study aims. It is important to note that there are many parameters for which there was no pilot data, so conservative parameter estimates (e.g., moderately large standard errors and small betas) were used for simulation purposes to ensure sufficient power. In many aims, the effect of the treatment includes both concurrent comparisons across VR and the control (Zoom) and longitudinal differences, which were computed using random effects.

Power analysis results: Sample size was determined by a joint consideration of the (a) expected range of effect sizes across the outcome variables, (b) the planned data analytic strategy, and © the expected attrition rate. Because of the complexity of the research design and range of hypotheses to be tested, initial sample size estimates were focused on ensuring a high level of power for detecting effects of the experimental manipulation of VR versus control (Zoom) on the outcomes. Based on pilot data that studied the impact of VR on changes over time in the emotional well-being of resident-adult child dyads (similar to the procedure in the current study), we estimated the range of the parameters from that sample when possible.

The planned sample size needed to detect an effect size corresponds to the smallest of these effect sizes as our minimal detectable effect of interest – a conservative strategy that would give us adequate power. Various simulation studies were run, varying sample size, effect size of concurrent differences and longitudinal differences, and other model characteristics related to power (e.g., error variance and variance of the random effects). While the models for each aim vary in their specific effects, there are similarities across them. The moderating effects of cognitive impairment are the most specific effects, which would lend itself to lower power. Thus, these models were used as a lower bound for power in this grant and guided the decision on sample size, because if these ML-SEM models with moderation had sufficient power, we can be confident that our other proposed analyses would be sufficiently powered.

We specified a ML-SEM model that included a random effects regression model. We modeled the moderation by including an interaction term (4 conditions: treatment group x cognitive impairment) on its prediction of the fixed effect of quality of life for the Resident in T2-T5 and T6-T7. Additionally, we estimated concurrent differences across the four conditions, conservatively estimating that the effect was small across time (d = .2). Using parameter constraints, power was studied for concurrent differences between VR and control (e.g., at a given time point) as well as sustained gains over time between VR and Control.

We computed that a sample size of **192 dyads (96 in VR condition, 96 in control)** evenly split between cognitive impairment (**MCI vs. dementia**) will achieve a high level of power (.85) for detecting the minimal expected effect size across the different analytic approaches considered. Assuming an attrition rate of approximately 15% across the 4-month longitudinal study, we calculated a required initial sample size of no less than 181 dyads. Based on this analysis, along with the additional considerations noted above, we selected a slightly higher **initial sample size of 192**. Because data from family dyads is dependent, for most analyses the dyad will be treated as the unit of analysis for assignment to experimental conditions and will be modeled accordingly in all statistical analyses. The results of the simulation study reveal that an effective sample size of 192 dyads will provide high power (85%) for detecting even relatively small effects of the VR condition over control (Zoom), which we conceptualized

to be an effect size of d=.2, which affords excellent power for detecting even larger effects, which we anticipate will occur.

9.3 Populations for Analyses

Participants will be older adults with mild cognitive impairments (MCI) or mild to moderate Alzheimer's Disease or related dementias (ADRD) who reside in senior living communities and an adult child who lives at a distance. Dyads will be randomly assigned to one of two treatment conditions (video chat vs. virtual reality). All participants who are enrolled in the study and complete the baseline assessment will be included in the primary analyses regardless of whether they complete all components of the intervention.

9.4 Statistical Analyses

9.4.1 General Approach

Primary analyses will be based on an **Intent-to-Treat (ITT)** approach in which all randomized participants will be analyzed according to their assigned treatment group, regardless of completion of the intervention. Primary analyses will be performed on the ITT population using appropriate statistical models to compare treatment groups. Secondary analyses will evaluate additional outcomes and mediation models to explore potential explanatory pathways. Missing data will be handled using appropriate statistical techniques including linear models with maximum likelihood estimation. Additional exploratory analyses may be conducted to explore trends, identify potential moderator variables, and generate hypotheses for future research. These results will be interpreted cautiously. All analyses will be performed using validated statistical software (SPSS, R, and Mplus), and findings will be reported in accordance with CONSORT guidelines and relevant best practices in the field. Where appropriate, adjustments for multiple comparisons will be applied to control for Type I error inflation.

9.4.2 Analysis of the Primary Endpoint(s)

The longitudinal dataset including survey and observational data will enable both between and within participant tests of the hypotheses outlined. The data collected will have three levels of nestedness: repeated measures over time (Level 1), nested within person (either older adult or adult child; Level 2), nested within intervention group (VR vs. Control; Level 3). For some analyses (e.g., Aim 1 and 2), we would not estimate the dyad together since, for example, we do not have specific hypotheses about how the resident and the adult child will differ from each other over time and because the parent and adult child will complete somewhat different measures. Outcomes related to Aim 1 and Aim2 will be assessed with linear mixed-models and, where appropriate, with multilevel structural equation modeling (ML-SEM). ML-SEM merges traditional multilevel modeling, which can accommodate hierarchical data, with structural equation modeling (SEM) techniques, which can accommodate multiple outcomes and mediators, as well as latent variables. Therefore, the analytic approach for some hypotheses tests (e.g., tests of mediation and tests of dyadic models) will be multilevel structural equation modeling (ML-SEM) in Mplus (or R) to simultaneously estimate a within- and between-person model, accounting for individual change over time and the treatment effect at the between-person level. Using parameter constraints, analyses will examine concurrent differences between VR and control (e.g., at a given time point) as well as sustained gains across VR and control using an approach similar to contrast coding.

9.4.3 Analysis of the Secondary Endpoint(s)

Secondary outcomes will be assessed with linear mixed-models and, where appropriate, with multilevel structural equation modeling (ML-SEM) and dyadic modeling of parent-child interactions during the technology sessions.

9.4.4 Exploratory Analyses

Exploratory analyses will be conducted to gain additional insights into the treatment effect, identify potential subgroup differences, and evaluate additional or novel treatment outcomes. These analyses will be hypothesis-generating and may include assessments of trends over time, additional efficacy outcomes, qualitative or linguistic analyses of open-ended data and conversation/session transcripts and video-taped data, and potential dyadic associations. As exploratory analyses are not pre-specified in the statistical analysis plan, results will be interpreted with caution and considered for informing future research and trial design.

10 Supporting Documentation and Operational Considerations

10.1 Regulatory, Ethical, and Study Oversight Considerations

10.1.1 Informed Consent Process

10.1.1.1 Consent/assent and Other Informational Documents Provided to participants

Consent forms describing in detail the study intervention, study procedures, and risks are given to the participant and written documentation of informed consent is required prior to starting intervention/administering study intervention. The following consent materials are submitted with this protocol: (1) Consent form for Parent, (2) Consent form for Adult Child, and (3) Consent forms for Legal Representative.

10.1.1.2 Consent Procedures and Documentation

1: Once identified, potentially eligible residents will be invited to talk with the researchers (in person) to determine if they are interested in participating, and verify that they are eligible to participate. The researchers will explain the purpose and procedures of the study and gather initial verbal consent to participate. At this time, researchers will administer the MMSE-2 to verify eligibility. If a resident's ability to consent is uncertain, the researcher will complete an IRB-approved screener assessing their decision making capacity to consent (see Evaluation of Decision-Making Capacity for Consent to Act as a Research Subject below), and consent will be obtained from the resident's legal guardian as needed. If the resident has dementia, the researcher will collect verbal consent, and consent will also be obtained from the resident's adult child (who would be participating) and legal guardian (if different from the adult child).

2: Contact information for an adult child with whom they would like to participate will be requested from eligible residents. If the resident does not have the contact information, the researchers will attempt to get this information from the Director of the senior living community. If the resident has more than one

eligible adult child, the researcher will randomly select from the list of eligible adult children. Researchers will call the adult child, explain the study, and gather initial verbal consent. The adult child will also complete the 8-item Informant Interview to Differentiate Aging and Dementia measure (AD8) to provide additional verification of the resident's (their parent's) dementia status. This additional information will be valuable because seniors can become accustomed to cognitive tests, making their MMSE-2 scores unreliable indicators of their level of dementia.

3: Once all initial verbal consents are received, the resident-adult child dyad will be enrolled in the study. Participants will then be scheduled to complete the baseline survey. Prior to the survey, residents and adult children will complete the formal consent process. Residents will be given written consent forms to sign. In addition, a consent script will be read out loud to residents with mild to moderate dementia (and any other residents who request it) to ensure they understand the study procedures and associated risks and safeguards. Adult children will be emailed an online link to a digital consent form and a baseline survey the week before the first VR/Zoom session. If applicable, the resident's legal guardian will be emailed a link to an online, digital consent form.

4: Continuing consent will be obtained from residents with mild to moderate dementia before beginning each of the VR/Zoom sessions using a verbal consent "check-list" (created and approved by the IRB for the Phase 1 pilot study) whereby the researcher states the purpose of the study, what will happen, the risks, and the benefits in very plain language and asks the resident if they understand each question (see Evaluation of Decision-Making Capacity for Consent to Act as a Research Subject below). If the resident is capable and competent at answering the questions, and is alert and oriented to their surroundings and what will happen during the VR/Zoom session, the resident may participate in the session. If the resident is unable to answer the questions and/or is not alert and oriented to their surroundings, or if the resident reports they do not want to participate, then the session will not proceed that day. The researchers will speak with the Director of the senior living community, adult child, and later with the resident to make a determination whether or not the family should continue in the study. If the resident or adult child wants to stop the study, they may do so at any time.

Consent forms and scripts: Participants will be informed (via written consent forms and verbal scripts), of the purpose of the study, all study procedures, and known risks and benefits. They will be informed that their participation is completely voluntary, that they can withdraw from the study at any time without negative consequences, that they will receive compensation for the time they invested in the study if they decide to withdraw, and that their information will be safeguarded and kept strictly confidential. Following procedures developed in Phase 1, consent forms/scripts will be written in language that is easy to understand, and participants will be encouraged to ask questions. Researchers will refrain from placing pressure on residents or family members to enroll or remain in the study.

EVALUATION OF DECISION-MAKING CAPACITY for CONSENT TO ACT AS A RESEARCH SUBJECT

Rendever Study, UCSB, 2019-2020
Participant ID _____

Is the resident alert and able to communicate with the examiner? ___ Yes ___ No

Cue #1: In summary, this is a study where you and your son/daughter will test a new virtual reality program together
Question 1: What is the purpose of this study?

Cue #2: To summarize, during the study you will participate in three VR sessions with your son/daughter and be asked a series of questions about it.
Question 2: Tell me something that will happen to you during the study.

Cue #3: In summary, some of the risks of this study are that you could feel mildly ill or dizzy from the technology.
Question 3: Tell me a possible risk to you of being in this study.

Cue #4: Remember, you can drop out of the study at any time.
Question 4: If you want to drop out of the study, when can you do this?

Question 5: Considering what we have discussed, what have you decided about participating in this study?
____to participate ___not to participate ___other:

I hereby certify that the above participant is alert, able to communicate and able to give acceptable answers to the above items.

Evaluator _____ Date _____

Witness _____ Date _____

10.1.2 Study Discontinuation and Closure

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating part to study participants, investigators, and the funding agency. If the study is prematurely terminated or suspended, the Principal Investigators (PIs) will promptly inform study participants, the Institutional Review Board (IRB), and funding agency and will

provide the reason(s) for the termination or suspension. Study participants will be contacted, as applicable, and be informed of changes to study visit schedules.

Circumstances that may warrant termination or suspension include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to participants
- Insufficient compliance of study staff to the protocol (i.e., significant protocol violations)
- Determination that the primary endpoint has been met
- Data that are not sufficiently complete and/or evaluable

The study may resume once concerns about safety, protocol compliance, and data quality are addressed, and satisfy the funding agency, sponsor, IRB, or relevant regulatory or oversight bodies (OHRP, DSMB).

10.1.3 Confidentiality and Privacy

Participant confidentiality and privacy is strictly held in trust by the participating investigators, their staff, the safety and oversight monitor(s), and the funding agency. This confidentiality is extended to the data being collected as part of this study. Data that could be used to identify a specific study participant will be held in strict confidence within the research team. No personally-identifiable information from the study will be released to any unauthorized third party without prior written approval of the funding agency.

All research activities will be conducted in as private a setting as possible. For older adult participants, this will take place in a private room in their senior living community. For the adult children participants, this will take place from the comfort of their own home.

The study monitor, other authorized representatives of the funding agency, representatives of the Institutional Review Board (IRB), or regulatory agencies, may inspect all documents and records required to be maintained by the investigator, including consent forms and study participant information.

The study participant's contact information will be stored on a password-protected computer in a locked office for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for as long a period as directed by the reviewing IRB and funding agency requirements.

At the end of the study, participants' quantitative research data, which is for purposes of statistical analysis and scientific reporting, will be stored at a registered data depository. This will not include the participant's contact information or any other information that could directly or indirectly identify them. Rather, individual participants and their quantitative research data will be identified by a unique study identification number. The study data entry and study management systems used will be secure and only registered users will be able to access the de-identified data.

Measures Taken to Ensure Confidentiality of Data Shared per the NIH Data Sharing Policies
It is NIH policy that the results and accomplishments of the activities that it funds should be made available to the public. The PI will ensure all mechanisms used to share data will include proper plans and safeguards for the protection of privacy, confidentiality, and security for data dissemination and reuse (e.g., all data will be thoroughly de-identified and will not be traceable to a specific study participant). Plans for archiving and long-term preservation of the data will be implemented, as appropriate.

Certificate of Confidentiality - To further protect the privacy of study participants, the Secretary, Health and Human Services (HHS), has issued a Certificate of Confidentiality (CoC) to all researchers engaged in biomedical, behavioral, clinical or other human subjects research funded wholly or in part by the federal government. Recipients of NIH funding for human subjects research are required to protect identifiable research information from forced disclosure per the terms of the NIH Policy (see https://humansubjects.nih.gov/coc/index). As set forth in 45 CFR Part 75.303(a) and NIHGPS Chapter 8.3, recipients conducting NIH-supported research covered by this Policy are required to establish and maintain effective internal controls (e.g., policies and procedures) that provide reasonable assurance that the award is managed in compliance with Federal statutes, regulations, and the terms and conditions of award. It is the NIH policy that investigators and others who have access to research records will not disclose identifying information except when the participant consents or in certain instances when federal, state, or local law or regulation requires disclosure. NIH expects investigators to inform research participants of the protections and the limits to protections provided by a Certificate issued by this Policy.

10.1.4 Future Use of Stored Specimens and Data

Data collected for this study will be stored on secure servers, in locked cabinets that can only be accessed by the research team, and analyzed and stored on the PI's password-protected computer in a locked office. After the study is completed, the de-identified, archived quantitative data will be transmitted and stored at a registered repository for use by other researchers including those outside of the study. Permission to retain *identifiable* video and audio recordings indefinitely will be included in the informed consent. (Identifiable recordings will never be stored publicly.) In addition, permission to retain *de-identified* survey data and transcriptions indefinitely and share with other researchers in the future for research purposes will be included in the informed consent.

10.1.5 Key Roles and Study Governance

Principal Investigator	**Medical Monitor or Independent Safety Monitor**
Kyle Rand, BS, CEO Rendever, Inc. PO Box 3383, Saratoga Springs, NY kyle@rendever.com	Dr. Scott Grafton University of California, Santa Barbara, Santa Barbara, CA 93106 grafton@ucsb.edu
Tamara Afifi, PhD, Professor and Chair University of California, Santa Barbara, Santa Barbara, CA 93106 tafifi@ucsb.edu	
Nancy Collins, PhD, Professor University of California, Santa Barbara Santa Barbara, CA 93106 ncollins@ucsb.edu	

10.1.6 Safety Oversight

An independent safety monitor will review all data safety and monitoring reports, and will be informed of all adverse outcomes in accordance with the data safety and monitoring plan.

10.1.7 Clinical Monitoring

N/A

10.1.8 Quality Assurance and Quality Control

Each research site will perform internal quality management of study conduct, data collection, documentation and completion. Both research sites will meet weekly to update on site progress.

Quality control (QC) procedures will be implemented as follows:

Informed consent --- Study staff will review both the documentation of the consenting process as well as a percentage of the completed consent documents. This review will evaluate compliance with GCP, accuracy, and completeness. Feedback will be provided to the study team to ensure proper consenting procedures are followed.

Paper surveys and the electronic data --- Data initially captured on paper surveys (see Section 10.1.9, Data Handling and Record Keeping) and will ultimately be entered into the study database.

Intervention Fidelity — Consistent delivery of the study interventions will be monitored throughout the intervention phase of the study. Procedures for ensuring fidelity of intervention delivery are described in Section 6.2.1, Interventionist Training and Tracking.

Protocol Deviations – The study team will review protocol deviations on an ongoing basis and will implement corrective actions when the quantity or nature of deviations are deemed to be at a level of concern.

Should independent monitoring become necessary, the PI will provide direct access to all trial related sites, source data/documents, and reports for the purpose of monitoring and auditing by the sponsor/funding agency, and inspection by local and regulatory authorities

10.1.9 Data Handling and Record Keeping

10.1.9.1 Data Collection and Management Responsibilities

Data collection will be the responsibility of the clinical trial researchers at each site (Boston and Santa Barbara) under the supervision of the site investigators. The investigator will be responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported. All source documents will be completed in a neat, legible manner to ensure accurate interpretation of data.

Hardcopies of the resident/older adults' surveys will be stored in a locked cabinet, in a locked office at each site (Boston and Santa Barbara). Survey responses from the hardcopies will be entered into Qualtrics by research staff. Data recorded in the electronic case report form (eCRF) derived from source

documents will be consistent with the data recorded on the source documents. Adult child surveys will be completed online in Qualtrics.

Clinical data (including adverse events (AEs) and expected adverse reactions data) will be entered into a 21 CFR part 11-compliant data capture system. The data system includes password protection and internal quality checks, such as automatic range checks, to identify data that appear inconsistent, incomplete, or inaccurate. Clinical data will be entered directly from the source documents.

10.1.9.2 Study Records Retention

Study documents (both paper and electronic) will be retained for a minimum of 3 years from the date of Federal Financial Report (FFR) submission.

10.1.10 Protocol Deviations

This protocol defines a protocol deviation as any noncompliance with the clinical trial protocol or International Council on Harmonisation Good Clinical Practice (ICH GCP) requirements. The noncompliance may be either on the part of the participant, the investigator, or the study site staff. As a result of deviations, corrective actions will be developed by the site and implemented promptly. These practices are consistent with ICH GCP:

- Section 4.5 Compliance with Protocol, subsections 4.5.1, 4.5.2, and 4.5.3
- Section 5.1 Quality Assurance and Quality Control, subsection 5.1.1
- Section 5.20 Noncompliance, subsections 5.20.1 and 5.20.2.

It will be the responsibility of the site investigator to use continuous vigilance to identify and report deviations. All deviations will be addressed in study source documents, reported to the National Institute on Aging and the Program Officer. Protocol deviations will be sent to the reviewing Institutional Review Board (IRB) per their policies. The site investigator will be responsible for knowing and adhering to the reviewing IRB requirements.

10.1.11 Publication and Data Sharing Policy

This study will be conducted in accordance with the following publication and data sharing policies and regulations:

National Institutes of Health (NIH) Public Access Policy, which ensures that the public has access to the published results of NIH funded research. It requires scientists to submit final peer-reviewed journal manuscripts that arise from NIH funds to the digital archive PubMed Central upon acceptance for publication.

This study will comply with the NIH Data Sharing Policy and Policy on the Dissemination of NIH-Funded Clinical Trial Information and the Clinical Trials Registration and Results Information Submission rule. As such, this trial will be registered at ClinicalTrials.gov, and results information from this trial will be submitted to ClinicalTrials.gov. In addition, every attempt will be made to publish results in peer-reviewed journals. Considerations for ensuring confidentiality of these shared data are described in Section 10.1.3.

10.1.12 Conflict of Interest Policy

The independence of this study from any actual or perceived influence, is critical. Therefore, any actual conflict of interest of persons who have a role in the design, conduct, analysis, publication, or any aspect of this trial will be disclosed and managed. Furthermore, persons who have a perceived conflict of interest will be required to have such conflicts managed in a way that is appropriate to their participation in the design and conduct of this trial. The study leadership in conjunction with the NIA has established policies and procedures for all study group members to disclose all conflicts of interest and will establish a mechanism for the management of all reported dualities of interest.

10.2 Additional Considerations

NA

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