Clinical Interventional Study Protocol

Dementia Caregiver Chronic Grief Management: A Live Online Video Intervention (CGMI-V)

A randomized, longitudinal 144-subject clinical trial of a live online, group-based video intervention addressing dementia caregivers' chronic grief management within the first two years post long-term care placement of a family member with dementia.

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(Any modification to the protocol should be annotated on the coversheet or in an appendix. The annotation should note the exact words that are changed, the location in the protocol, the date the modification was approved by the Executive Committee, and the date it became effective.)

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Dementia Caregiver Chronic Grief Management: A Live Online Video Intervention (CGMI-V)

A randomized, longitudinal 144-subject clinical trial of a live online, group-based video intervention addressing dementia caregivers' chronic grief management within the first two years post long-term care placement of a family member with dementia.

Objectives

The primary objective of this Stage I clinical trial is to determine whether the 8-week CGMI-V has an effect on dementia family caregivers' chronic grief. Secondary objectives are to determine whether the CGMI-V has an effect on dementia family caregivers': (1) symptoms of depression and anxiety, (2) positive states of mind, (3) satisfaction with care provided in the long-term care facility and (4) conflict with staff. In addition, we will explore mechanisms of intervention impact on caregiver outcomes.

Design and Outcomes

The study is a Stage I longitudinal randomized clinical trial to test the effects if the CGMI-V on caregivers' chronic grief, mental health (symptoms of depression and anxiety; positive states of mind) and facility-related (satisfaction with care and conflict with facility staff) outcomes. 144 Alzheimer's disease or a related dementia (ADRD) caregivers whose family members are in long-term care facilities will be randomly assigned to either CGMI-V or a Minimal Treatment (MT) control condition. For both conditions, data will be collected at baseline (pre-intervention), 8 weeks (immediately post-intervention) for intervention effects, and 24 weeks post baseline for maintenance effects.

Interventions and Duration

Caregivers in the CGMI-V condition will participate in eight weekly professionally led, real-time, live-streaming online video group sessions. Those caregivers in the MT control condition will receive written information materials about late-stage ADRD at baseline. For both conditions, caregivers are expected to be in the study for a total of 24 weeks.

Sample Size and Population

A total of 144 ADRD family caregivers will be randomized to either CGMI-V condition (N = 72) or Minimal Treatment (MT) (N = 72). Caregivers will be males and females of any race or ethnic background, 21 years of age and over, whose family members are diagnosed with ADRD and have been residing in long-term care for under one year.

STUDY TEAM ROSTER

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PARTICIPATING STUDY SITES

Rush University College of Nursing in Chicago, Illinois is the only study site.

1 STUDY OBJECTIVES

1.1 Primary Objective

The primary objective of this Stage I clinical trial is to determine whether the 8-week CGMI-V has an effect on dementia family caregivers' chronic grief. We hypothesize that caregivers in the CGMI-V condition compared to those in the MT control condition will report decreased chronic grief levels.

1.2 Secondary Objectives

Secondary objectives are to determine whether the CGMI-V has an effect on dementia family caregivers': (1) symptoms of depression and anxiety, (2) positive states of mind, (3) satisfaction with care provided in the long-term care facility and (4) conflict with staff.

We hypothesize that:

- Caregivers in the CGMI-V compared to those in the MT control condition will report decreased symptoms of depression and anxiety and increased positive states of mind.
- Caregivers in the CGMI-V compared to those in the MT control condition will report increased satisfaction with care provided in the long-term care facility and decreased conflict with facility staff.

In addition, we will explore mechanisms of intervention impact on caregiver outcomes. We hypothesize that CGMI-V works by changing the exacerbators of chronic grief: lack of knowledge about late-stage ADRD, sense of loss, guilt, and caregiver role captivity.

2 BACKGROUND AND RATIONALE

2.1 Background on Condition, Disease, or Other Primary Study Focus

In 2017, an estimated 16 million family caregivers provided approximately 18.4 billion hours of unpaid care to relatives with Alzheimer disease and related dementias (ADRD), valued at US $232.1 billion.[1] As the disease progresses, close to 75% of persons with ADRD are eventually being placed in long-term care facilities (LTCFs), where they reside for on average 2 years prior to death. The caregiving process from home care through long-term placement spans on average 5 to 10 years, which comes with a high price for caregivers' physical and mental health.[1] Compared to age-matched non-caregivers, ADRD family caregivers made twice as many personal emergency room visits and three times as many physician office visits over an 18-month period.[2] In 2017, the prevalence of depression in ADRD family caregivers was up to 40%, a much higher level compared to

age-matched non caregivers. Overall, in 2017, the physical and emotional impact of ADRD caregiving resulted in an estimated US$11 billion in family caregiver health care costs in the United States.[1]

Evidence suggests that, after long-term care placement, ADRD family caregivers experience new feelings of loss, guilt, and role captivity (e.g., feeling trapped in the caregiver role).[3] These feelings can exacerbate caregivers' ongoing symptoms of chronic grief, depression, and anxiety, and place them at increased risk for suicide.[3-10] These symptoms, in turn, may contribute to caregiver conflict with LTCF staff and dissatisfaction with care.[11,12] With the growing number of caregivers who place family members with ADRD in LTCFs, it is imperative to develop interventions that address their mental health needs, including chronic grief.

2.2 Study Rationale

The Stress Process Model[13] has been the predominant paradigm used for interventions with ADRD family caregivers. Interventions based on this model emphasize caregiver knowledge, communication, and conflict resolution, problem-solving, end-of-life care planning, and coping. Accordingly, improvements were found in each of these targeted domains. Overall, though, fewer studies found significant improvement in caregiver mental health outcomes, such as symptoms of depression and anxiety, and burden.[14] We speculate that this may be due to lack of attention to ADRD family caregivers' reactions to loss and grief. In general, grief is considered a normal reaction to loss (i.e., loss of loved one, relationship, role, status). However, in ADRD caregiving, grief often becomes chronic because losses accumulate over time.[10,15-17] Grief intensity reaches high levels during the last two years of caregiving before death, when most persons with ADRD are in long-term care.[18] Further, Givens and colleagues[19] found that caregivers with high grief levels prior to the care recipient's death had even higher levels of grief seven months post death. Thus, it is essential not to wait and to treat grief prior to the care recipient's death. Meuser and colleagues[20,21] proposed that, in ADRD caregiving, chronic grief affects caregivers' depressive symptoms, stress, and burden. These grief-related findings laid the foundation for a paradigmatic shift from the Stress Process model[13] to a grief-centered paradigm and formed the basis for reframing new ADRD caregiving interventions.

Research is increasing that examines caregiver chronic grief as a defining aspect of the ADRD caregiving experience that contributes to caregiver symptoms of depression and anxiety.[22] To date, we know of two studies that tested the effects of grief interventions on ADRD caregiver outcomes; both were conducted by professionals before placement of the care recipient in long-term care. The first study[23] consisted of a brief, 5-week psycho-educational group intervention designed to address loss and grief in ADRD community-based caregivers. In that study, caregiver grief increased from pre to post treatment.[23]

These findings suggest that the 5 weeks may have been too short for caregivers to process their grief. A longer grief intervention (5 months) was used by other investigators.[24] That intervention included community-based ADRD spouse caregivers who received individualized sessions delivered weekly over 5 months with follow-up at 8 months post baseline. At five months, improvements were found in grief, symptoms of depression, and anxiety for all participants. At the eight-month post-baseline follow-up, the positive outcomes were sustained for all except those caregivers whose spouses had been placed in long-term care or had died. These findings suggest that ADRD caregivers needed to continue receiving a grief intervention even after they placed their family member in long-term care to maintain improvements in grief and symptoms of depression and anxiety.[24] Therefore, we created an intervention that targets ADRD caregiver's chronic grief after LTC placement based on a grief-centered paradigm that expands the existing Stress Process Model.

We designed the **Chronic Grief Management Intervention (CGMI)** for ADRD Caregivers (PI: Paun, O.; Co-Is Farran, C.J., & Fogg, L). Funding: NINR-R21NR010577, 2008-2011.[25,26] as a 12-week group intervention to improve caregivers' (1) knowledge of late-stage ADRD; (2) communication, conflict resolution, and chronic grief management skills; and (3) grief and mental health outcomes. We pilot-tested the effects of CGMI in a pre-test/multiple post-test design with random assignment of 16 long-term care facilities to either the 12-week CGMI or an attention control condition. Data were collected at baseline, 3 months (immediately post-intervention) and 6 months (post-baseline). The content was structured into three major components: (1) knowledge about late-stage ADRD, (2) communication and conflict resolution skills, and (3) chronic-grief-management skills. Those in the attention control condition received two brief minimal-support phone calls at weeks 6 and 18.

Results: Of the total 151 referrals from 16 facilities, 114 ADRD caregivers were screened, and 93 were eligible and enrolled (n = 37 in CGMI; n = 56 in control). The average caregiver age was 60.69 (SD 10.64), while the average age for the care recipient was 83.38 (SD 6.46). The caregivers were predominately Caucasian (87%). Caregivers and care recipients were predominantly female (88%, 74% respectively). Approximately two-thirds of caregivers were adult children. The average time since care recipients' placement in long-term care was 7.10 months (SD 6.80).[26] Overall retention was 89% (n = 34 in CGMI; n = 49 in control). Reasons for dropout were death of the care recipient, caregiver medical problems, and lack of time. A total of 8 distinct groups of caregivers received the CGMI. Attendance averaged 10.44 sessions out of 12 (SD 1.50, R 5-12). At 3 months, we found significant improvement in the intervention group in heartfelt sadness and longing (p = *.027)* and promising effect sizes (ES) in the intervention group scores with a decrease in heartfelt sadness and longing (0.49), loss of relationship (0.33), and guilt (0.29). At the 6-month follow-up, we found a significant drop in guilt (p = .029) in the intervention group

and sustained ES in caregivers' scores on heartfelt sadness and longing (0.38), loss of relationship (0.30), and guilt (0.49). At the 3- and 6-month follow-ups, caregivers reported feeling highly satisfied with the information learned in the group discussions (92%) and with the interventionists' approach (100%). A number of caregivers suggested that there be fewer sessions due to the burden of time. Further, key staff informants (directors of nursing, unit managers, and administrators) at all 16 long-term care facilities (LTCFs) reported back to recruiters that there were caregivers who expressed interest in the intervention but were constrained due to distance and travel to attend weekly meetings at the facilities.

Relevance for the proposed study: CGMI results supported feasibility for recruitment, retention, and attendance. Retention for the CGMI condition was more than 90%. Increase in caregiver knowledge, improvement in heartfelt sadness and longing, and decrease in guilt at 3 months, with sustained effects in further decreased guilt at 6 months, are promising results. The fact that guilt continued to decrease in the intervention group 3 months after intervention completion is significant because guilt is one of the grief-associated feelings that can exacerbate conflict with LTCF staff and reduce satisfaction with care. Based on the established feasibility, effects, and caregiver and key informant feedback, we adapted CGMI in several ways. First, we reduced the 12 weeks of intervention delivery to 8 weeks, maintaining the content in core target areas of the intervention as follows: (1) we condensed the content on knowledge to that most relevant to late-stage ADRD from three to two sessions, (2) we condensed the content on communication/conflict resolution skill and hands-on care to the most relevant LTC situations from three to two sessions, and (3) we maintained the focus on grief processing and grief management skills in a more condensed format from six to four sessions. Second, the intervention was adapted to be delivered via a professionally led, live-streaming video, online group format to accommodate distance participation.

Chronic Grief Management – A Live-Streaming Video Online Intervention (CGMI-V) (PI: Paun, O.; Co-I Cothran, F; Rush University College of Nursing Research Fund, 2016-2017)[27]. The purposes of this study were: (1) to determine the feasibility (recruitment, retention, attendance) of delivering the adapted 8-week CGMI-V in a professionally led, live-streaming video online group format and (2) to explore ADRD caregivers' group experience using online video-based technology. Methods: This was a single-group study with data collection at baseline (caregiver/care recipient demographics) and at 8 weeks (caregiver brief survey and focus group). Prior to intervention implementation, each caregiver received a study-provided iPad with a password-protected link to Adobe Connect. Individual orientation training in the use of the software and equipment was provided by a technology assistant. The manualized intervention was delivered over 8 weeks in 60-minute real-time, online video sessions by the PI. The technology assistant was present either in-person or remotely at each session to provide

assistance to the interventionist and study participants as needed. Recruitment, retention, and attendance were tracked in a Microsoft Access data base. Post intervention, participants completed a 5-item survey and rated on a scale from 0 = *not at all* to 4 = *very much* how much they learned from the intervention content (knowledge, communication and conflict resolution skills, grief management skills) and the extent of their use of the new knowledge and skills. In addition, a post-intervention focus group that was taped and transcribed covered: (1) participants' experience with the technology (ease of use, technical problems, and orientation to online platform and iPad devices) and (2) participants' experience with the live-streaming video online group format (ability to relate to each other emotionally, the group's effect on emotional outcomes).

Results: Five ADRD family caregivers responded to a notice placed in a LTCF newsletter. The four female and one male caregivers were all Caucasian, and so were their care recipients. Only one caregiver was older than 75 years. Three were adult children of the care recipients, one was a spouse, and one was a niece. All caregivers attended at least 5 or more sessions, with 3 of 5 attending all eight sessions. Three caregivers were able to attend and not miss sessions when they were traveling away from home. In the post-intervention focus group, caregivers (n = 5) reported no major problems with navigating the WebEx platform and the iPad technology. They found the individualized orientation and ongoing support by the technology assistant contributed to successful handling of the technology. The most frequent technological problem was an echo, which was addressed at the beginning of each session by fine tuning each caregiver's study-provided headset and iPad volume and microphone levels. Frozen images occasionally became a problem when caregivers were traveling, due to weaker local Wi-Fi capacity. However, those caregivers were able to continue the session without interruption using the audio function. Importantly, caregivers reported that the online environment did not interfere with their ability to relate to each other emotionally, especially because they could see each other via WebEx live-streaming video. Participants indicated that the group size was ideal for the online group interaction and thought that a group larger than 6 would make it more difficult to relate to each other. Consistent with findings in our previous CGMI study, caregivers reported that the intervention helped decrease their sense of guilt and isolation. This was further supported by post-intervention survey results: the highest agreement rate between participants was that the group discussions helped them process their loss and grief associated with long-term care placement 3.6/4 (0.55)[27].

Relevance for the proposed study: this pilot found the use of an online platform and iPad technology feasible for the group-based online delivery of the CGMI-V in a professionally led, synchronous video format. ADRD caregivers reported no major technological difficulties and were able to relate to each other in an online environment.

3 STUDY DESIGN

This study is a Stage I longitudinal randomized clinical trial. ADRD caregivers whose family members are residing in long-term care facilities (LTCFs) will be recruited, screened for inclusion criteria, and randomly assigned to either CGMI-V or a Minimal Treatment (MT) control condition. Caregivers in the CGMI-V will participate in eight weekly, professionally led, real-time, live streaming video online group sessions. Those caregivers in the MT condition will receive written information materials about late stage ADRD at baseline. For both conditions, data will be collected at baseline (pre-intervention), 8 weeks (immediately post-intervention) for intervention effects, and at 24 weeks post-baseline for maintenance effects.

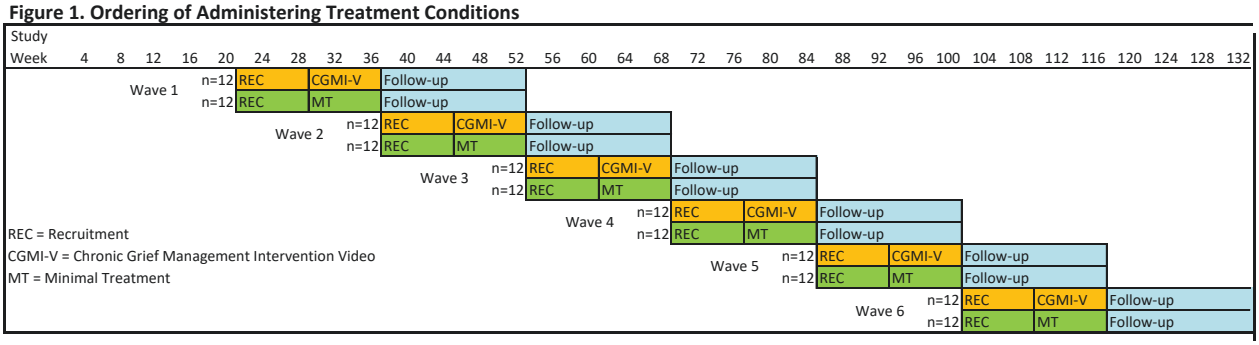
Primary Outcome: Controlling for background variables, establish effect sizes of the CGMI-V condition and Minimal Treatment (MT) control condition on changes in caregiver chronic grief. We hypothesize that caregivers in the CGMI-V condition compared to those in the MT control condition, will report decreased chronic grief levels.
Secondary Mental Health Outcomes: Controlling for background variables, establish effect sizes of the CGMI-V and Minimal Treatment (MT) control condition on changes in caregiver symptoms of depression and anxiety and on positive states of mind. We hypothesize that caregivers in the CGMI-V condition compared to those in the MT control group will report (2.1) decreased symptoms of depression and anxiety and (2.2) increased positive mental states.
Secondary Facility-related Outcomes: Controlling for background variables, establish effect sizes of the CGMI-V condition and the Minimal Treatment (MT) control condition on changes in caregiver satisfaction with care provided in the facility and conflict with staff. We hypothesize that caregivers in the CGMI-V condition compared to those in the MT control condition will report (3.1) increased satisfaction with care provided in the facility and (3.2) decreased conflict with staff.
Mechanism of Intervention Outcome: Explore mechanisms of intervention impact on caregiver outcomes. We hypothesize that CGMI-V works by changing the exacerbators of chronic grief: lack of knowledge, sense of loss, guilt, and role captivity.

Study population and location: We will recruit a sample of 144 ADRD caregivers who have a family member residing in dementia care or memory care units in long-term care facilities located in the Chicago metropolitan area. We have well-established collaborating relationships with 35 long-term care facilities that will give us access to a diverse pool of approximately 1,000 ADRD family caregivers. Caregivers will be randomly assigned to either the CGMI-V condition (n=72) or the MT control condition (n=72). Caregivers will receive the CGMI-V intervention at home or another location of their choosing, using iPads with an online platform (WebEx). Caregivers in the MT condition will receive written

information about late stage ADRD at baseline. Each individual caregiver is expected to be in the study for a total of 24 weeks from enrollment to follow-up.

Study implementation: The study will be implemented in six waves. Beginning in Month 5 of the study, we will start recruiting and enrolling 24 caregivers for Wave 1, who will be randomly assigned to either the CGMI-V condition (n = 12; 6/group) or MT control condition (n = 12). After these 24 caregivers have been enrolled, the study team will start recruiting and enrolling an additional 24 caregivers for Wave 2. There will be a total of six waves. Each wave will have 8 weeks to recruit, screen, enroll, randomize to condition, and complete baseline data collection, followed by 8 weeks to implement the intervention condition, and data collection immediately post-intervention and 24 weeks from baseline follow-up. Once enrollment is completed for a wave, recruitment will start for the following wave. This pattern will be the same for all six waves. This will result in 144 caregivers being enrolled, 72 for the CGMI-V condition, and 72 for the MT control condition. Figure 1 illustrates the progression of the study waves through the study timeline.

Figure 1. Ordering of Administering Treatment Conditions



Intervention: For the CGMI-V intervention condition, study materials (participant manual, technology instructions) will be sent to participants electronically. We will mail hard copies of the manual and technology instructions to those caregivers who prefer to have them printed out. The iPad tablet and the earbuds with microphone will be mailed to participants prior to the first session. As needed, caregivers will receive an individualized over-the-phone orientation (20-30 minutes) in the operation of the equipment from the technology assistant. Each session will start with a brief technology check-up and review of ground rules including maintaining confidentiality.

Each CGMI-V group session will be conducted by one interventionist who has therapeutic group leading experience. For treatment fidelity purposes, the study interventionists will be trained in the delivery of the group intervention and the iPad and online technology. Each group will have not more than six participants. The intervention consists of approximately 60-minute sessions delivered weekly for eight consecutive weeks and will follow the standardized CGMI-V intervention manual (Appendix A).

The purpose of the CGMI-V is to improve ADRD caregivers' (1) knowledge about late-stage ADRD; (2) communication and conflict resolution skills, and (3) skills managing their loss and chronic grief. Sessions 1-2 address caregiver knowledge about late-stage ADRD, and the resources available to dementia families in the LTCF and the community at large.[3,28] Sessions 3-4 address caregiver skill in communication and conflict resolution and hands-on care in the context of LTCF.[3,15-17,28-30] Sessions 5-8 address caregiver loss and grief management skills using discussion guides tailored to specific grief management topics.[31-37] The participant manual outlines each session's content and includes questions to facilitate discussion. Additional materials are provided for knowledge and skill topics. These are fact sheets about late-stage ADRD that are published by the Alzheimer's Association, a guide with resources for ADRD family caregivers published by the Family Caregiver Alliance, and a chapter on hospice services (Appendix A).

Control condition. Caregivers in the control condition will receive Minimal Treatment (MT) consisting of written information about late-stage ADRD (Alzheimer's Association) at baseline. The Project Director will mail caregivers in the MT control condition all written information materials.

4 SELECTION AND ENROLLMENT OF PARTICIPANTS

We will recruit a sample of 144 ADRD caregivers who have a family member residing in dementia care or memory care units in long-term care facilities located in the Chicago metropolitan area. We have well-established collaborating relationships with 35 long-term care facilities that will give us access to a diverse pool of approximately 1,000 ADRD family caregivers.

4.1 Inclusion Criteria

Participants must meet all inclusion criteria listed below in order to participate in this study.

- 21 years of age or older
- Identified as family member, fictive kin (self-identified family member) or partner of care recipient at any time post permanent placement of care in LTCF
- Care recipient has a documented ADRD diagnosis and resides in any type of unit in a long-term care facility
- Possessing self-reported basic computer literacy and in-home internet access
- Able to speak, read, and write English
- Not currently attending another ADRD caregiver grief management group

- Experiencing high to moderate levels of grief per screening with the Marwit-Meuser Caregiver Grief Inventory-Short Form (scores 25 or above), and/or experiencing high levels of depressive symptoms per screening with PHQ9 (scores 10 or above)
- Caregivers whose care recipients die during the course of the intervention will remain in the study

4.2 Exclusion Criteria

All candidates meeting any of the exclusion criteria listed below will be excluded from study participation.

- Younger than 21 years of age
- Care recipient does not have a documented diagnosis of ADRD;
- Self-reports a lack of basic computer skills and no internet access.
- Unable to speak, read, and write English
- Currently attending an ADRD caregiver grief management group
- Experiencing low levels of grief per screening with the Marwit-Meuser Caregiver Grief Inventory-Short Form (scores below 25), and/or experiencing low levels of depressive symptoms per screening with PHQ9 (scores below 10)

4.3 Study Enrollment Procedures

Recruitment. Successful recruitment strategies used in our prior studies[25-27] will be used. These include: (1) a notice describing the study placed in the providers' monthly newsletters distributed to family caregivers at each facility; (2) study flyers and interest forms posted around the LTCFs (e.g., front desk, family lounge); (3) individualized letters mailed by the facilities' business office introducing the project to family caregivers of ADRD residents; and (4) oral presentations about the project to staff and family caregivers during "family night" events. All written and oral communication will use lay language to describe study purpose, eligibility criteria, intervention, and data collection methods. All written materials will include information about participants' time commitment and study contact information (e-mail address and phone number) that caregivers may use if interested. Interested participants will call or e-mail the study office or fill out the interest form, agreeing to be contacted by study staff. Completed interest forms will be left in the facility's front office or e-mailed directly to the study e-mail address.

Consenting. After they contact the study office, caregivers will be scheduled to undergo eligibility screening. The Project Director will describe the screening process and the instruments used to screen and will ask and document caregivers' verbal consent to be screened for eligibility. Once eligibility is determined, participant caregivers will be

informed of the next steps for enrollment in the study. Study staff will use a Web-based tracking system, Microsoft Access, to document individual reasons for ineligibility and reasons for declining participation in caregivers who met eligibility criteria. Caregivers who meet the inclusion criteria will be sent paper or electronic copies of the study informed consent form for examination. Within the next 24-48 hours, a telephone appointment with the PI or the Project Director will be scheduled to answer any questions caregivers may have about the study prior to obtaining informed consent. If agreeable to join the study and depending on how they preferred to receive the informed consent forms, caregivers will return the signed documents either electronically (e-signature) or in paid, study self-addressed envelopes.

Randomization. The study will be implemented in six waves. Beginning in Month 5 of the study, we will start recruiting and enrolling 24 eligible caregivers for Wave 1, who will be randomly assigned to either the CGMI-V condition (n = 12; 6/group) or MT control condition (n = 12) using a randomization software for clinical trials. After these 24 caregivers have been enrolled, the study team will start recruiting an additional 24 caregivers for Wave 2. There will be a total of six waves. Each wave will have 8 weeks to recruit, screen, and complete baseline data collection, followed by 8 weeks to implement the intervention condition, and 24 weeks from baseline follow-up. Once enrollment is completed for a wave, recruitment and randomization will start for the following wave. This pattern will be the same for all six waves. This will result in 144 caregivers being enrolled, 72 for the CGMI-V condition, and 72 for the MT control condition (Figure 1).

5 STUDY INTERVENTIONS

5.1 Interventions, Administration, and Duration

The intervention consists of approximately 60-minute sessions delivered weekly for eight consecutive weeks and will follow the standardized CGMI-V intervention manual (Appendix A). The purpose of the CGMI-V is to improve ADRD caregivers' (1) knowledge about late-stage ADRD; (2) communication and conflict resolution skills, and (3) skills managing their loss and chronic grief. Sessions 1-2 address caregiver knowledge about late-stage ADRD, and the resources available to dementia families in the LTCF and the community at large.[3,28] Sessions 3-4 address caregiver skill in communication and conflict resolution and hands-on care in the context of LTCF.[3,15-17,28-30] Sessions 5-8 address caregiver loss and grief management skills using discussion guides tailored to specific grief management topics.[31-37] The participant manual outlines each session's content and includes questions to facilitate discussion. Additional materials are provided for knowledge and skill topics. These are fact sheets about late-stage ADRD that are published by the Alzheimer's Association, a guide with resources for ADRD family caregivers published by the Family Caregiver Alliance, and a chapter on hospice services (Appendix A). Table 1 illustrates target areas, session title and content, and resources used in each session.

Table 1. CGMI-V Sessions, Target Areas, Content, and Resources				
Session/ Week	Session Title	Target Areas	Content	Resources
1	Getting Started	Knowledge	Address ADRD late and end-stage changes: physical, cognitive, behavioral, emotional	Signs and symptoms of late-stage ADRD Fact Sheet (Alzheimer's Association)
2	What Do You Know About This Place and the Community?	Knowledge	Discuss LTCF philosophy of care, structure, regulations, policies, and personnel roles. Resources for the CG and the CR post placement in the facility and the community at large.	Resources for Persons with Alzheimer Disease; When to Seek Hospice Care (Reynolds, S.)
3	How Do I Get My Message Through?	Communication/Conflict-Resolution Skills	Practice conflict-resolution techniques with LTCF staff, CR, other residents, and their family members	Communication (Alzheimer's Association)
4	Doing for and Working with My Loved One	Hands-on Care Skills	Discuss hands-on care for CR and participation in LTCF activities	Resources and Information Kit-Caregiver Tips (Family Caregiver Alliance)
5	Losses and Separation	Grief Management Skills	Recognize losses and process reaction to separation	Discussion guide in participant manual
6	What Defined Our Relationship?	Grief Management Skills	Recollect and re-experience the relationship with the CR	Discussion guide in participant manual
7	How Do I Let Go and Readjust?	Grief Management Skills	Process relinquishing old attachments and assumptions; process readjusting to the new without forgetting the old	Discussion guide in participant manual
8	Life Goes On	Grief Management Skills	Discuss reinvesting in new attachments, goals; process group closure	Discussion guide in participant manual
ADRD = Alzheimer and related diseases; CG = caregiver; CR = care recipient; LTCF = LTCF facility				

Control condition. Caregivers in the control condition will receive Minimal Treatment (MT) consisting of written information about late-stage ADRD (Alzheimer's Association) at baseline. The Project Director will mail caregivers in the MT control condition all written information materials.

5.2 Handling of Study Interventions

CGMI-V is a behavioral group-based intervention delivered by trained interventionists who have group leading experience. The interventionists will receive an eight-hour training on

intervention delivery and technology use (Appendix B).

5.3 Concomitant Interventions

5.3.1 Allowed Interventions

Participants in this group-based study may attend other informal ADRD caregiver support groups.

5.3.2 Required Interventions

There are no concomitant required interventions for this study.

5.3.3 Prohibited Interventions

Participants will be excluded if already attending an ADRD caregiver chronic grief management support group.

5.4 Adherence Assessment:

We will use a Web-based tracking system, Microsoft Access, to assess the receipt of the dose consisting of eight group sessions. We will calculate attendance rates for each participant and record reasons for missing sessions. We will assess enactment of the CGMI-V intervention with specific items in an anonymous participant survey administered at 8 and 24 weeks (e.g., "Since our last assessment meeting, how often have you used: communication skills and conflict resolution techniques learned in the program when interacting with facility staff?")

6 STUDY PROCEDURES

Study procedures are outlined on the following pages.

6.1 Schedule of Evaluations

Assessment	Eligibility Screening (phone/online interview)	Enrollment /Randomization	Baseline (phone/online interview)	8-weeks post baseline (phone/on line interview	24-weeks post baseline (phone/on line interview
Eligibility Screening Verbal Consent	X				
Inclusion/Exclusion Criteria	X				
Study Informed Consent Signed		X			
Caregiver/Care Recipient Socio-demographics			X		
Caregiver/Care Recipient Situational Characteristics			X		
Caregiver Chronic Grief			X	X	X
Caregiver Depressive Symptoms			X	X	X
Caregiver Anxiety Symptoms			X	X	X
Caregiver Positive States of Mind			X	X	X
Conflict with Facility Staff			X	X	X
Satisfaction with Care			X	X	X
Caregiver Knowledge of ADRD			X	X	X
Caregiver Sense of Loss			X	X	X
Caregiver Guilt			X	X	X
Caregiver Role Captivity			X	X	X
Caregiver Adherence to CGMI-V Survey (Satisfaction Survey)				X	X
Change in status survey (CG/CR)				X	X

6.2 Description of Evaluations

Study evaluations consist of: (1) eligibility screening for inclusion criteria, (2) Baseline assessment immediately after enrollment, (3) 8-weeks post-baseline, for intervention effects, and (4) 24-weeks post-baseline for maintenance effects.

6.2.1 Screening Evaluation

Consenting Procedure

The Project Director will schedule a phone or online screening interview with caregivers expressing an interest in the study. The Project Director will explain the screening process and the questionnaires used to ascertain participant eligibility and invite any caregiver questions. After all questions are addressed, verbal consent to screening will be documented after the screener explicitly asks the caregivers if they consent.

Screening

Caregivers who verbally consent will be screened using computer-assisted telephone interviewing (CATI) for the following inclusion criteria:

- 21 years of age or older
- Identified as family member, fictive kin (self-identified family member) or partner of care recipient
- Within the first two years of care recipient's permanent placement in a long-term care facility (LTCF)
- Care recipient is a resident in a dementia or memory care unit in the LTCF, where a diagnosis of ADRD is mandatory
- Possessing self-reported basic computer literacy and in-home internet access
- Able to speak, read, and write English
- Not currently attending another ADRD caregiver grief management group
- Experiencing high to moderate levels of grief per screening with the Marwit-Meuser Caregiver Grief Inventory-Short Form[38] (scores 25 or above), and/or experiencing high levels of depressive symptoms per screening with PHQ9[39] (scores 10 or above)

Caregivers meeting all eligibility criteria will be sent a consent form including detailed information about the study. A phone or online meeting will be scheduled with the PI or the Project Director within the next 24-48 hours for discussion of study,

content of consent form, and to respond to any other questions.

Enrollment

Participants will be enrolled into the study once their signed study informed consents are being returned to study office. A baseline appointment will be scheduled within the next 24-48 hours.

Baseline Assessments

Participants who are enrolled into the study, will be assessed at baseline using CATI, for the following outcomes:

- Caregiver and care recipient socio demographics
- Caregiver and care recipient situational characteristics
- Caregiver grief
- Caregiver depressive symptoms
- Caregiver anxiety symptoms
- Caregiver positive states of mind
- Caregiver conflict with facility staff
- Caregiver satisfaction with care in the facility
- Caregiver knowledge of ADRD
- Caregiver sense of loss
- Caregiver guilt
- Caregiver role captivity

Randomization

The study will be implemented in six waves. Beginning in Month 5 of the study, we will start recruiting and enrolling 24 caregivers for Wave 1, who will be randomly assigned to either the CGMI-V condition (n = 12; 6/group) or MT control condition (n = 12). After these 24 caregivers have been enrolled, the study team will start recruiting and enrolling an additional 24 caregivers for Wave 2. There will be a total of six waves. Each wave will have 8 weeks to recruit, screen, enroll, randomize to condition, and complete baseline data collection, followed by CGMI-V implementation over 8 consecutive weeks (Figure 1).

6.2.2 Follow-up Assessment: Immediately Post-intervention (8 weeks from baseline)

This study will not use follow-up visits. All follow-up evaluations will be performed using computer-assisted telephone interviewing (CATI). The following study outcomes will be measured within 24-48 hours from intervention completion for

intervention effects:

- Caregiver grief
- Caregiver depressive symptoms
- Caregiver anxiety symptoms
- Caregiver positive states of mind
- Caregiver conflict with facility staff
- Caregiver satisfaction with care in the facility
- Caregiver knowledge of ADRD
- Caregiver sense of loss
- Caregiver guilt
- Caregiver role captivity
- Caregiver adherence to CGMI-V/Satisfaction Survey (intervention condition)
- Changes in caregiver and care recipient status

6.2.3 Completion/Final Evaluation (24 weeks from baseline)

This study will not use a final visit. All Completion/Final evaluations will be performed using computer-assisted telephone interviewing (CATI). The following study outcomes will be measured at 24 weeks from baseline for maintenance effects:

- Caregiver grief
- Caregiver depressive symptoms
- Caregiver anxiety symptoms
- Caregiver positive states of mind
- Caregiver conflict with facility staff
- Caregiver satisfaction with care in the facility
- Caregiver knowledge of ADRD
- Caregiver sense of loss
- Caregiver guilt
- Caregiver role captivity
- Caregiver adherence to CGMI-V /Satisfaction Survey (intervention condition)
- Changes in caregiver and care recipient status

Based on our previous pilot studies[25-27], we do not anticipate early termination of the CGMI-V study. We will document reasons for participant voluntary drop-out and will ask participants who may have dropped out prior to completing the 8 group-based CGMI-V sessions to participate in the 8 and 24-week follow-up assessments.

7 SAFETY ASSESSMENTS

Participant safety will be monitored once each individual is screened and enrolled in the study. CGMI-V is a low risk behavioral intervention designed to support ADRD

caregivers emotionally in the context of placement of a family member with ADRD in a long-term care facility. The proposed intervention poses minimal risk to participants.

During screening and data collection for both conditions, there is potential risk for caregivers to disclose:

- Depressive symptoms (high levels indicative of clinical depression)
- Suicidal ideation

During the Chronic Grief Management Intervention-Video (CGMI-V) intervention implementation, emotional upset may occur especially during the last four sessions, when grief processing becomes the focus of the intervention. Caregivers may disclose high levels of:

- Depressive symptoms (high levels indicative of clinical depression)
- Suicidal ideation

7.1 Specification of Safety Parameters

- A score greater than16 points (indicative of risk for clinical depression) on the Center for Epidemiological Studies-Depression Scale (CES-D)[40]
- A score >1 on the PHQ 9 suicidal assessment item: "Thoughts that you would be better off dead or of hurting yourself"
- Verbalizing suicidal ideation during CGMI-V group session intervention implementation

7.2 Methods and Timing for Assessing, Recording, *and* Analyzing Safety Parameters

CGMI-V is a low risk behavioral intervention designed to support ADRD caregivers emotionally within the first two years of placement of a family member with ADRD in a long-term care facility. The proposed intervention poses minimal risk to participants. Identified safety parameters identified above in 7.1 will be assessed at: pre-enrollment screening, and the three data collection points (baseline and 8 and 24-weeks). Interventionists will implement suicide protocol in the event of reported suicidal ideation during group sessions.

7.3 Adverse Events and Serious Adverse Events

An **adverse event (AE)** is generally defined as any unfavorable and unintended diagnosis, symptom, sign (including an abnormal laboratory finding), syndrome or disease which either occurs during the study, having been absent at baseline, or if present at baseline, appears to worsen. An example of an Adverse Event (AE) anticipated for this study would be, during data collection, a Center for Epidemiological Studies-Depression Scale (CES-D) score greater than16 points, indicative of risk for clinical depression. Whether or not this high

score is associated with study participation, we will monitor and report it as an AE, per protocol.

A **serious adverse event (SAE)** is generally defined as any untoward medical occurrence that results in death, is life threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital anomaly. An example of a Serious Adverse Event (SAE) anticipated for this study would be a participant's endorsement of suicidal ideation when screened with the PHQ-9 or disclosing suicidal ideation in a group session. Whether or not associated with study participation, we will monitor and report suicidal ideation or intention as a SAE, per protocol adopted from the Office of the Human Research Protection Program's *Research Protocols and Risk of Suicide Guidelines* (2012).

An Unanticipated Problem (UP) for this study would be any study participant incident, experience or outcomes that are unexpected in severity or frequency suggesting that participants are at greater risk of harm than anticipated. An example of an Unanticipated Problem (UP) for this study would be a participant becoming extremely upset with intervention content, to the point of dropping off from the study as a consequence. Whether or not associated with study participation, we will monitor and report per protocol.

7.4 Reporting Procedures

The PI will use standardized NIA forms to report all adverse effects (AEs) and serious adverse effects (SAEs) (except death) in writing to the NIA Program Officer (PO), Safety Officer (SO) and Rush University IRB on a **quarterly** basis.
Any Unanticipated SAEs not listed in the Data Safety Monitoring Plan related to the intervention will be reported by the PI on an expedited basis within **48 hours** from determination of occurrence to the NIA PO, SO, and IRB, following–up with a written corrective plan with measures to prevent reoccurrence.
The PI will report any participant death whether or not related to study participation and regardless of intervention condition to NIA PO, SO, and IRB on an expedited basis within **24 hours** from determination of occurrence.
Unanticipated problems including other incidents, outcomes, or experiences that are not SAEs (e.g. data breach, confidentiality threat) will be reported by the PI using standardized forms to NIA PO, SO, and IRB within **48 hours**, including a corrective plan and measures to prevent reoccurrence. .

7.5 Follow-up for Adverse Events

Participants experiencing AEs will be referred for outpatient or inpatient treatment (depending on severity). Follow-up will span the 24-week duration of the study participation.

7.6 Safety Monitoring

The Principal Investigator (PI) will be responsible for ensuring participant and data safety on a daily basis. As a Stage I, single site, and minimal risk study, we will establish an internal committee to assist with data safety monitoring (DSM). In addition, an NIA-approved Safety Officer (SO) will oversee the DSM, and will review data and adverse events twice per year and more frequently if necessary. The SO will act in an advisory capacity to the NIA Director and PO to monitor participant safety, evaluate the progress of the study, and to review procedures for maintaining the confidentiality of data, the quality of data collection, management, and analyses.

8 INTERVENTION DISCONTINUATION

CGMI-V is a Stage I, single site, minimal risk behavioral intervention study. There is no anticipated intervention discontinuation for this study. Study participants may withdraw voluntarily from participation in the study at any time and for any reason. We will continue to follow these participants, with their permission, at the 8 and 24 week assessment points. Participants in the CGMI-V condition who discontinue early will not be replaced, as this is a group-based intervention where "the dose" consists of eight consecutive weekly group sessions.

9 STATISTICAL CONSIDERATIONS

9.1 General Design Issues

CGMI-V is a Stage I longitudinal randomized clinical trial. ADRD caregivers whose family members are in long-term care facilities (LTCFs) will be recruited, screened for inclusion criteria, and randomly assigned to either CGMI-V or a Minimal Treatment (MT) control condition. Caregivers in the CGMI-V condition will participate in eight weekly professionally led, real-time, live-streaming video online group sessions. Those caregivers in the MT control condition will receive written information materials about late-stage ADRD at baseline. For both conditions, data will be collected at baseline (pre-intervention), 8 weeks (immediately post-intervention) for intervention effects, and 24 weeks post baseline for maintenance effects. The design for this study was chosen to avoid the type of group clustering or contamination that would be engendered by the use of a randomized cluster design. The study hypotheses are outlined below:

Primary Hypothesis

Hypothesis 1: We hypothesize that caregivers in the CGMI-V condition compared to those in the MT control condition, will report decreased chronic grief levels.

Secondary Hypotheses

Hypothesis 2: We hypothesize that caregivers in the CGMI-V condition compared to those in the MT control group will report (2.1) decreased symptoms of depression and anxiety and (2.2) increased positive mental states.

Hypothesis 3.1 and 3.2: We hypothesize that caregivers in the CGMI-V condition compared to those in the MT control condition will report (3.1) increased satisfaction with care provided in the facility and (3.2) decreased conflict with staff.

Mechanism of Intervention Hypothesis

Hypothesis 4: We hypothesize that CGMI-V works by changing the exacerbators of chronic grief: lack of knowledge, sense of loss, guilt, and role captivity.

Primary Outcome Measures

Caregiver Chronic Grief will be measured with the 50-item Marwit-Meuser Caregiver Grief Inventory (MM-CGI).[6] This inventory has three subscales: (1) *Personal Sacrifice Burden:* 18 items measuring individual losses experienced as a result of caregiving, (2) *Heartfelt Sadness and Longing:* 15 items measuring interpersonal emotional reactions in response to caregiving, and (3) *Worry and Felt Isolation:* 17 items measuring feelings of losing connections with, and support from, others. Items are rated on a 5-point scale (1 = *strongly disagree* to 5 = *strongly agree*), with a possible range of 50 to 250 points. Grief scores may be calculated by subscale and then added to formulate a total grief score. Total grief scores above 175 indicate high levels of caregiver grief, requiring formal intervention and support. Cronbach's alpha subscale scores range from .90 to .96, indicating high internal consistency reliability for each subscale and for their combined total grief score. Test-retest Cronbach's alpha scores range from .71 to .75, indicating stability of the measure over time in all three subscales.[15]

Secondary Outcomes Measures

Depressive symptoms will be measured with the 20-item version of The Center for Epidemiological Studies Depression Scale (CES-D).[40] Responses are based on a four-point frequency rating (0 = *rarely or none of the time* to 3 = *all of the time*), with a possible range of 0 to 60. A score above 16 indicates existence of depressive symptoms. Internal consistency reliability range r =.85 to .90, and test-retest reliability r = .45 to .70.[40]

Anxiety symptoms will be measured with the 20-item State-Anxiety subscale of the State-Trait Anxiety Inventory (STAI).[41] Responses are based on a scale of 1 to 4 (1 = *almost never* to 4 = *almost always*), with a possible range of 20-80, where higher scores indicate greater anxiety. Alpha coefficients for older adults range .90-.92, indicating high internal consistency reliability.[41]

Positive States of Mind will be measured with the Positive States of Mind Scale (PSOMS)[42] to assess the extent to which caregivers were able to achieve six positive states of mind in the previous seven days. Other studies[21] found that caregivers who scored high on the PSOMS also scored lower on the grief scale. The scale comprises six items that capture: (1) focused attention, (2) productivity, (3) responsible caregiving, (4) restful repose, (5) sensuous nonsexual pleasure, and (6) sharing. The responses range from 0 = *unable to achieve* to 3 = *easy to achieve*. Cronbach's alpha coefficient was .77, indicating high internal consistency reliability.

Conflict with facility staff will be measured with a subscale of the Family Perception of Caregiving Role (FPCR). The 61-item FPCR[3,30] contains four subscales to measure dimensions of role stress: (1) loss of relationship aspects with care recipient, (2) guilt from perceived failure in caregiving, (3) captivity resulting from obligations of caregiving, and (4) conflict with facility staff related to caregiving. Responses are rated on a 7-point Likert scale (1 = *strongly disagree* to 7 = *strongly agree*), with a possible range of 61 to 427. Items are summed to form subscale scores and a total FPCR score. Cronbach's alpha coefficients ranging from .70 to .84 indicate high internal consistency reliability for each subscale and for the total FPCR score. Test-retest reliability was .79 for FPCR total score.[3,30] We will score the 10-item Conflict with Facility Staff subscale; its Cronbach's alpha coefficient is .84.

Satisfaction with care will be measured with the Family Perceptions of Care Tool (FPCT).[3.30] The 51-item FPCT contains four subscales that reflect caregivers' perceived satisfaction with: (1) physical care provided to their family member in the facility, (2) activities for facility residents, (3) unit management, and (4) staff consideration for resident and family member. Responses are rated on a 7-point Likert scale (1 = *strongly disagree* to 7 = *strongly agree*), with a possible range of 51 to 357. Items are summed to form subscale scores and a total FPCT score. Cronbach's alpha coefficients ranging from .85 to .97 indicate high internal consistency reliability for each subscale and for the total FPCT score. We will use all 51 items to assess caregiver satisfaction with care received in the LTCF.[3.30]

Exacerbators of Chronic Grief

We will measure four exacerbators of ADRD caregiver chronic grief: (1) caregiver lack of knowledge about dementia, (2) caregiver perception of loss, (3) guilt, and (4) role captivity.

Knowledge of dementia/AD will be measured with the 22-item Family Knowledge of Alzheimer's Test (FKAT).[30] This instrument captures what a family caregiver knows about the disease process, how the care recipient is behaving, and how the LCTF is caring for him or her. Responses are based on a true/false scale, with a maximum score of 22 correct answers. Test-retest reliability was .82 ($p < .05$), KR 21 ($n = 50$) = .61.

Loss will be measured with the 7-item Loss subscale of the FPCR[3,30] (full description above). Cronbach's alpha for this subscale was 0.73.

Guilt will be measured with the 5-item Guilt subscale of the FPCR[3,30] (full description above). Cronbach's alpha for this subscale was 0.70.

Role captivity will be measured with the 7-item Captivity subscale of the FPCR[3,30] (full description above). Cronbach's alpha for this subscale was 0.81.

Background Measures

Caregiver and care recipient socio-demographics. To describe caregiver and care recipient baseline background data, we will collect standardized information. These survey questions are drawn from the initial population survey used by the East Boston site for the Established Populations for Epidemiologic Studies of the Elderly project (EPES).[43] Situational characteristics. Three direct questions will be asked at baseline to assess: (1) number of years since the care recipient was diagnosed with ADRD, (2) time since placement in the LTCF, and (3) visiting pattern in the LTCF (times per week and number of hours per visit).

9.2 Sample Size and Randomization

Precision analysis. Because we are estimating an effect size, rather than a *p* value, we are primarily concerned with precision of estimation rather than power. The standard deviation associated with total grief as measured with the MM-CGI is around 35.78 raw units. Thus, a change of one SD represents a two-thirds of a unit change in the MM-CGI Likert Scale. If we obtain a sample of 64 participants per condition, our standard error of measurement (SEM) around this effect size estimate will be about 4.47 units, producing confidence intervals between -8.77 and +8.77 units. This will allow us to estimate a Cohen's *d* within .25 SD units of the actual value, a reasonably robust estimate, 95% of the time. Adjusting for a 10% attrition rate, we will collect a total sample of 72 participants per condition (a total of 144 participants).[57]

9.2.1 Treatment Assignment Procedures

The study is a Stage I longitudinal randomized clinical trial. ADRD caregivers whose family members are in LCTFs will be recruited, screened for inclusion criteria, and randomly assigned to either CGMI-V or a Minimal Treatment (MT) control condition. Randomization will be stratified in six Waves of 24 participants each, to insure that there are exactly 12 participants in each condition. In Wave 1, we will randomly assign the first 24 enrolled participants to either the CGMI-V condition (n = 12; 6/group) or MT control condition (n = 12). The same process will continue for the next five Waves. Recruiters and data collectors will be blinded as to the random assignment of each participant. Once caregivers sign the consent to enroll in the study, the Project Director will use randomization software to assign each enrolled participant to CGMI-V or the MT condition. The Project Director will then inform the participants directly of their assignments and ask them to maintain confidentiality about their assignment at data collection points.

9.3 Interim analyses and Stopping Rules

There are no planned interim analyses, as this is a low risk, Stage 1 clinical trial. Interim analyses will only occur if there is a requirement from the Safety Officer in response to specific participant safety issues surrounding the study.

9.4 Outcomes

Multilevel modeling will be used to examine effect sizes associated with both the primary and secondary outcomes. All primary and secondary outcomes will be measured at Baseline, 8 weeks, and 24 weeks.

9.4.1 Primary outcome: Chronic Grief

Caregiver Chronic Grief will be measured with the 50-item Marwit-Meuser Caregiver Grief Inventory (MM-CGI).

9.4.2 Secondary outcomes:

Depressive Symptoms will be measured with the 20-item Center for Epidemiological Studies Depression Scale (CES-D).

Anxiety Symptoms will be measured with the 20-item State-Anxiety subscale of the State-Trait Anxiety Inventory (STAI).

Positive States of Mind will be measured with the 6-item Positive States of Mind Scale (PSOMS).

Conflict with Facility Staff will be measured with the 10-item Conflict with Facility Staff subscale of the Family Perception of Caregiving Role (FPCR).

Satisfaction with Care will be measured with the 51-item Family Perceptions of Care Tool (FPCT).

9.5 Data Analyses

We will track all study participants following CONSORT guidelines and enter all data into a REDCap database. SPSS for Windows (Version 22) and R (Version 3.1.1) will be used for data management and statistical analysis. A two-tailed 0.05 significance level will be used for all statistical tests except where noted below. All analyses will be performed on an intent-to-treat basis. Missing data will be imputed using the R mi package, a multiple imputation computer program based on the work of Rubin. Histograms will be obtained for these variables, and skew and kurtosis will be assessed to assess statistical normality. From previous research, we expect the error rates to have statistically normal distributions or distributions that can be transformed to normality using logarithmic and square root transformations. We will perform any necessary transformations using Tukey's ladder of transformation before conducting statistical analysis. Because these trials are designed to estimate precise effect sizes rather than probability values, the results of each trial will be the effect size (comparing treatment and control groups) and confidence intervals around this estimate.

Aim 1. Controlling for background variables, establish effect sizes of the CGMI-V condition and Minimal Treatment (MT) control condition on changes in a primary caregiver chronic grief outcome.
Multilevel linear models will be run for the CGMI-V and MT control conditions. Multilevel models are used to estimate autocorrelation across the three time points. We hypothesize that chronic grief will decrease more in the CGMI-V condition relative to the MT control condition. Caregiver sex, age, relationship to the care-receiver, as well as care recipient death or discharge from the facility, will be controlled for as covariates in the analysis. Sex and caregiver/care recipient relationship, as well as care recipient death or discharge from the facility, will be entered into the model as dummy-coded variables. We will examine the interaction effects (δ) to make certain that they are large

enough to justify a more robust clinical trial. While there is some likelihood of obtaining significant findings in this study, the primary purpose of this analysis is to estimate effect sizes.

Aim 2. Controlling for background variables, compare the effect sizes of the CGMI-V condition and MT control condition on changes in secondary caregiver mental health outcomes: depression symptoms and anxiety symptoms and positive states of mind. We hypothesize that one dependent measure (positive states of mind) will increase more and the other two (depression symptoms and anxiety symptoms) will decrease more in the CGMI-V group relative to the MT control condition.

Apart from the dependent measures examined, this analysis will parallel that described in Aim 1. As in Aim 1, the primary goal of this analysis is to estimate effect sizes associated with the CGMI-V.

Aim 3. Controlling for background variables, compare the effect sizes of the CGMI-V condition and MT control condition on secondary facility-related outcomes: caregiver satisfaction with care and conflict with staff in the LTCF. We hypothesize that caregiver satisfaction with care will increase and that conflict with staff in the LTCF will decrease in the CGMI-V condition relative to the MT control condition.

Apart from the dependent measures examined, this analysis will also parallel that described in Aim 1. As in Aim 1, the primary goal of this analysis is to estimate effect sizes associated with the CGMI-V.

Aim 4. Examine the mediating effects of chronic grief exacerbators on chronic grief, mental health, and facility-related outcomes. We hypothesize that improvement in chronic grief exacerbators will mediate the improvements in caregiver chronic grief, mental health, and facility-related outcomes.

The focus of the proposed study is on change in chronic grief, mental health, and facility-related outcomes between measurement points and change in chronic grief exacerbators as a mediating variable. Thus, we propose to use residualized change scores (i.e., the difference between the observed score of a variable and the predicted score based on the baseline measure of that variable) throughout the analyses. These scores have the advantage of evaluating change between measurement points without concerns about regression toward the mean that are associated with standard change scores and have the advantage of reducing the number of variables in the model. In general, the analytic model will include covariates to control for background characteristics of the participants and time since baseline. The mediation effects of changes in chronic grief exacerbators (lack of knowledge, sense of loss, guilt, and role captivity) on three outcome measures (chronic grief, mental health, and facility-related outcomes) will be examined in three separate models. The regression mediation models described in MacKinnon[76] will be used to estimate these effects. The null hypothesis is that changes in chronic grief exacerbators will not mediate any of the three outcome

measures. As mentioned in the first three aims, the primary goal of this analysis is to estimate the size of these mediation effects, rather than to obtain statistically significant differences.

In accordance with NIH policy we will perform an analysis to estimate effect sizes associated with CGMI-V intervention between gender and racial/ethnic subgroups.

10 DATA COLLECTION AND QUALITY ASSURANCE

10.1 Data Collection Forms

Trained Research Assistants (RAs) blinded to treatment condition will use Computer-assisted Telephone Interviewing (CATI) to complete all initial screening and data collection interviews. Study RAs will read each question and enter the response directly into the secure, web-based Research Electronic Data Capture (REDCap).

10.2 Data Management

The Project Director will coordinate and closely monitor all day-to-day operations related to data collection and management. The Project Director will schedule and track all data collection appointments, monitor, and document missed appointments.

The study Data Manager will set up and manage data using CONSORT and the Microsoft Access tracking program, will set up data collection forms in REDCap, and will clean data.

The study Statistician will develop a coding manual, will oversee quality of data coding and computer entry, will track subject attrition, and will program for specific statistical procedures.

All outcomes measurement instruments will be set up as data collection forms in REDCap.

10.3 Quality Assurance

10.3.1 Training

The PI and one co-I or the project Director will provide Research Assistants (RAs) who will collect data for this study with an initial manualized 8-hour training consisting of an overview of the study, a thorough review of the measurement instruments including role playing data collection using study instruments, and orientation to inputting data using REDCap (Appendix C).

RAs will be trained in being sensitive to participants' needs during data collection and how to respond to participants who score high on the depression scale and/or indicate risk of suicide using a safety protocol.

The PI and/or co-I/Project Director will hold regular monthly meetings with all RAs to address any issues related to data collection.

10.3.2 Metrics

To verify accuracy of test administration, the Project Director will compare three randomly selected samples of baseline assessments from each treatment condition, will discuss inconsistencies/missed items with the data collectors and will correct any potential differences in test administration.

The study Data Manager will ensure that data is correctly inputted into REDCap and will provide immediate feedback to the PI if any irregularities are noticed.

10.3.3 Protocol Deviations

RAs will be trained to report any protocol deviations as they occur. The Project Director will document the protocol deviation and a meeting with the PI and the RA in question will be scheduled within 24-48 hours from occurrence to review the deviation and determine a plan of action for remediation.

10.3.4 Monitoring

The data will be examined yearly. The items to be monitored are: adverse events, attrition rate, reasons for dropping out of the study, and group session attendance rates. Ongoing attention will be given to participant recruitment, accrual and retention, follow-up, flow of data forms, protocol adherence, and quality of data. Special attention will be given to participant safety, including ongoing assessment of potential adverse effects and the magnitude of their impact on participants. The PI will assume major responsibility to perform the data and safety monitoring function on an ongoing basis. Data collectors (RAs) will be required to meet every month with the Project Director and the PI throughout the duration of the research project to address any ongoing instrument use and data collection issues. The Project Director will be present with each RA to the first assessment and will randomly select 3 baseline assessments from each treatment condition to check for missed items and/or inconsistencies. The Data Safety Monitoring Committee will report to the PI within 10 days of the meeting. If the DSMC recommends suspension of the study, the Rush IRB will be notified within 5 days from the determination. All data collection procedures will be reviewed every 4-6 months. All revisions/changes will be documented in the meeting minutes.

11 PARTICIPANT RIGHTS AND CONFIDENTIALITY

11.1 Institutional Review Board (IRB) Review

This protocol and the informed consent document (Appendix D) and any subsequent modifications will be reviewed and approved by the Rush University IRB committee responsible for oversight of the study.

11.2 Informed Consent Forms

All written and oral communication will use lay language to describe study purpose, eligibility criteria, intervention, and data collection methods. All written materials will include information about participants' time commitment and study contact information (e-mail address and phone number) that caregivers may use if interested. Interested participants will call or e-mail the study office or fill out the interest form, agreeing to be contacted by study staff. These forms will be left in the facility's front office or e-mailed directly to the study e-mail address. After they contact the study office, caregivers who meet the inclusion criteria will be sent paper or electronic copies of the informed consent and HIPAA forms for examination. Within the next 24-48 hour, a telephone appointment with the PI or the Project Director will be scheduled to answer any questions caregivers may have about the study prior to obtaining informed consent. If agreeable to join the study, and depending on how they preferred to receive the forms, caregivers will return the signed documents either electronically (e-signature) or in paid, study self-addressed envelopes. Recruitment will be overseen by the PI and the Project Director. In facilities with African American residents, recruitment will be overseen by Dr. Inventor (Co-I), who has expertise in recruitment of participants of diverse backgrounds.

A signed consent form will be obtained from each participant. The consent form will describe the purpose of the study, the procedures to be followed, and the risks and benefits of participation. A copy will be given to each participant and this fact will be documented in the participant's record.

11.3 Participant Confidentiality

To protect against privacy risks associated with the use of WebEx live streaming video to deliver the interventions we will take the following measures: 1) each caregiver will use a unique password-protected iPad to access WebEx, 2) each group of caregivers will use a unique password-protected link to access the online sessions for their individual group, 3) caregivers will be strongly encouraged to use the iPads strictly for study purposes and not share their passwords with anyone else, 4) iPads will be checked and reset with a new password when passed to a new set of caregivers, and 5) the recorded audio and video

sessions will remain password protected and only relevant study personnel (PI, Co-Is, interventionists) will have access to them for fidelity and quality control purposes.

Any data, forms, reports, recordings, and other records that leave the site will be identified only by a participant identification number (Participant ID/PID) to maintain confidentiality. All written records will be kept in a locked file cabinet. All computer entry and networking programs will be done using PIDs only. Information will not be released without written permission of the participant, except as necessary for monitoring by IRB, the NIA, and the OHRP.

11.4 Study Discontinuation

The study may be discontinued at any time by the IRB, the NIA, the OHRP or other government agencies as part of their duties to ensure that research participants are protected.

12 ETHICAL CONSIDERATIONS

The following NIH ethical principles guide the CGMI-V study: (1) social and clinical value, (2) scientific validity, (3) fair subject selection, (4) favorable risk-benefit ratio, (5) independent review, (6) informed consent, and (7) respect for potential and enrolled subjects. In practice, we enact these principles in the following ways:

1) We seek to establish effect sizes for the CGMI-video intervention on chronic grief in caregivers of persons diagnosed with ADRD who were placed in long-term care facilities LTCFs). Chronic grief can contribute to mental health problems in family caregivers, such as anxiety, depression, and suicidality.[5-8,22] Moreover, family caregiver grief and its exacerbators (lack of knowledge, sense of loss and guilt, and caregiver role captivity) can provoke dissatisfaction with care provided in the LTCFs and increase conflict with staff.[3,11,12] Although placement exacerbates family caregivers' grief, LTCF do not provide families with grief-focused support specific to this transition.[12,24] Thus, there is a critical need for post-LTCF-placement grief interventions for ADRD caregivers whose family members are in LTCF.
2) We were unable to find any existing post-placement, online group interventions for ADRD caregivers. Therefore, we pilot-tested a professionally led, post-placement, live-streaming video, online group intervention: the CGMI-Video. For the CGMI-V pilot, retention was high (100%), and caregivers expressed satisfaction with the method of delivery, leading us to develop CGMI-V in a Stage I randomized clinical trial.
3) We will recruit participants who have a family member residing in one of 35 facilities located in the Chicago metropolitan area that have dementia care and/or memory care units owned by two for-profit LTCF providers. We have access to a pool of family caregivers of more than 1,000 residents diagnosed with ADRD. We have well-established collaborating relationships with these facilities, as we have recruited from them for our preliminary studies.
4) The intervention poses minimal risks to participants. The benefits of acquiring new knowledge about late-stage dementia and AD, practicing communication and conflict

resolution skills, along with processing loss and chronic grief, are very likely to outweigh potential risks. Risks during data collection are mitigated by enacting our study safety protocol, and risks related to the online video platform are mitigated by multiple layers of password protection.

5) This protocol and the informed consent document and any subsequent modifications will be reviewed and approved by the Rush University IRB committee responsible for oversight of the study. The PI will use standardized NIA forms to report all adverse effects (AEs) and serious adverse effects (SAEs) (except death) in writing to the NIA Program Officer (PO), Safety Officer (SO) and Rush University IRB on a **quarterly** basis. The PI will report any participant death whether or not related to study participation and regardless of intervention condition to NIA PO, SO, and IRB on an expedited basis within **24 hours** from determination of occurrence. Unanticipated problems including other incidents, outcomes, or experiences that are not SAEs (e.g. data breach, confidentiality threat) will be reported by the PI using standardized forms to NIA PO, SO, and IRB within **48 hours**, including a corrective plan and measures to prevent reoccurrence.

6) The study informed consent outlines the purpose of the study, provides information regarding rights of study participants, outlines study procedures, and communicates information concerning confidentiality and the voluntary nature of study participation. Participants will be informed that they may withdraw from the study at any time without jeopardizing theirs' or their family members' access to care in the facility where the study is being conducted.

7) We ensure respect for participants and potential participants by adhering to our informed consent outlines, following all data safety monitoring protocol, and protecting the confidentiality of participants and potential participants.

13 COMMITTEES

As a Stage I, single site, and minimal risk study, we will establish an internal committee to assist with data safety monitoring (DSM). Drs. Susan Buchholz and Lisa Barnes will serve as members independent of the study team. Dr. Buchholz is a Professor in the Department of Adult Health and Gerontological Nursing and has extensive clinical (Advanced Nurse Practitioner) and research experience with geriatric populations. Dr. Barnes is a Professor and Cognitive Neuropsychologist at the Rush University Medical College. Dr. Barnes has served on the DSM Internal Committee for our NIH-funded pilot study (R21NR010577) and is familiar with the PI's work with ADRD caregiver grief. In addition, the following members of the research team will serve on the committee: Carol Farran, DNSc, FAAN, Louis Fogg, PhD (statistician), Arlene Miller, PhD, RN, Sarah Ailey, PhD, RN, and Olimpia Paun, PhD, PMHCNS-BC.

14 PUBLICATION OF RESEARCH FINDINGS

We will disseminate the findings from this study in scholarly oral presentations and written manuscripts and in the Long Term Care Facility community newsletters and oral presentations to family caregivers, administrators, and key stakeholders. If effective, this intervention will be translated into practice by training staff (i.e. social workers) to deliver the CGMI-V in their LTCF.

Any presentation, abstract, or manuscript will be made available for review by the sponsor and the NIA prior to submission.

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16 SUPPLEMENTS/APPENDICES

APPENDIX A: INTERVENTION (CAREGIVER) MANUAL

APPENDIX B: INTERVENTIONIST MANUAL

APPENDIX C: RESEARCH ASSISTANT MANUAL

APPENDIX D: ICF