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A Dyadic Approach for a Remote Physical Activity Intervention in Adults with Alzheimer's Disease and their Caregivers: Rationale and Design for an 18-month Randomized Trial

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Abstract

Adults with Alzheimer's disease and related dementia (ADRD) and their caregivers represent a sizeable and underserved segment of the population with low levels of moderate physical activity (MPA). Options for increasing MPA in community dwelling adults with ADRD and their caregivers are limited. A home-based physical activity intervention delivered remotely via video conferencing to groups of adults with ADRD and their caregivers (RGV), represents a potentially effective approach for increasing MPA in this group. We will conduct an 18-month randomized trial (6 mos. active intervention, 6 mos. maintenance, 6 mos. no contact) to compare the effectiveness of the RGV approach with usual care, enhanced with caregiver support (EUC), for increasing MPA in 100 community dwelling adults with ADRD and their caregiver. The primary aim is to compare MPA (min/wk.), assessed by accelerometer, across the 6-mo. active intervention in adults with ADRD randomized to RGV or EUC. Secondly, we will compare adults with ADRD and their caregivers randomized to RGV or ECU on the following outcomes across 18 mos.: MPA (min/wk.), sedentary time (min/wk.), percentage meeting 150 min/wk. MPA goal, functional fitness, activities of daily living, quality of life, residential transitions, cognitive function, and caregiver burden. Additionally, we will evaluate the influence of age, sex, BMI,

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attendance (exercise/support sessions), use of recorded sessions, self-monitoring, peer interactions during group sessions, caregiver support, type and quality of dyadic relationship, and number of caregivers on changes in MPA in adults with ADRD and their caregiver across 18 mos.

Keywords

Alzheimer's disease; caregivers; physical activity; exercise; quality of life; technology

INTRODUCTION

Approximately 5.3 million adults in the U.S. have Alzheimer's disease and related dementias (ADRD). ADRD is associated with the deterioration of brain function resulting in cognitive decline, behavioral and psychiatric symptoms and reductions in functional status including the ability to complete activities of daily living (ADL) and self-care [1]. Physical activity may provide an accessible, practical and economical approach for the management of ADRD. Martin-Ginis et al [2] recently developed an evidence based public health messaging statement for the use of physical activity in the management of ADRD which reads "*Among older adults with Alzheimer's disease and other dementias, regular physical activity can improve performance of activities of daily living and mobility, and may improve general cognition and balance*" [2]. Physical activity may also provide benefits for caregivers of adults with ADRD. Caregiving has also been associated with reduced quality of life [3], musculoskeletal discomfort [4], stroke [5], cardiovascular disease [6], and social isolation which increases risk for depression and anxiety [7]. Data from a limited number of home-based physical activity interventions in caregivers have shown reduced stress, caregiver burden, depression, and improved sleep quality and positive affect [8–11].

Physical activity in adults with ADRD and their caregivers is lower than in healthy older adults [2, 12, 13]. Currently, effective scalable strategies for increasing physical activity in adults with ADRD and their caregivers are unavailable. Exercise trials in adults with ADRD and/or caregivers have primarily assessed the impact of exercise on cognitive and physical function, neuropsychiatric symptoms, or quality of life, and have not evaluated strategies for increasing daily MPA. Participants in these trials were generally required to travel to a medical clinic or community site for supervised exercise [14–19]; however, several interventions have been delivered by home visits from exercise specialists [15, 20–23], or by caregivers who were trained to deliver exercise interventions [24, 25]. Significant barriers associated with these approaches including the time and cost of travel to a clinic or community site, expense of individual home visits, and the additional burden of caregiver directed exercise greatly reduce the potential of these approaches to result in sustained improvements in MPA.

Our group recently completed a 3 mo. single arm pilot trial that demonstrated the feasibility of delivering group-based MPA via video conferencing on a tablet computer to adults with ADRD and a caregiver in their homes [26]. This approach eliminates the need for transportation to a medical clinic or other community facility and provides the potential for peer support and socialization which may be important for the initiation and maintenance of

MPA. However, the effectiveness of the group video approach to increase and maintain MPA over a longer time frame (12–18 mos.) in adults with ADRD and their caregiver is unknown. Thus, we developed the current randomized trial to compare 2 strategies for the delivery of an intervention to increase MPA in adults with ADRD and their caregiver.

METHODS

Intervention overview

We propose to compare 2 strategies for the delivery of an intervention to increase MPA in community dwelling adults with ADRD and their caregiver (dyads): real-time group video conferencing (RGV) vs. enhanced usual care (EUC- caregiver participation plus support). Adults (age 55 yrs.) with mild to moderate ADRD (n=100) and their caregiver (n=100) will be randomized (1:1) to one of the 2 intervention arms for an 18-mo. trial (6 mos. active intervention, 6 mos. maintenance, 6 mos. no contact). Participants in both arms will be provided with an iPad® for intervention delivery, Fitbit (Fitbit Inc., San Francisco, CA) for self-monitoring MPA, and will be asked to complete 150 min of MPA/wk. Dyads in the RGV arm will be asked to complete three 45 min sessions (5 min warm-up, 30 min aerobic MPA (3–5 METs), 5 min resistance, balance & coordination, 5 min cool-down/stretching) led by a trained health coach and delivered via Zoom® software (Zoom® Video Conferencing Inc., San Jose, CA) on an iPad® during mos. 0–6, and 1 session/wk. during mos. 7–12, to groups of 5–8 dyads in their home. Dyads in the EUC arm will be asked to complete a self-directed structured exercise plan which includes 150 min/wk. of MPA plus resistance, balance, and flexibility activities (2 d/wk.). Dyads in both arms will be provided with written materials regarding exercise and physical activity from the National Institute on Aging and will be asked to complete brief (15–20 min) FaceTime® meetings (0–6 mos.= 2/ mo.; 7–12 mos.= 1/mo.) with the health coach to discuss progress, provide support and receive additional guidance on strategies for increasing MPA. The primary aim is to compare MPA (min/wk.) across the 6-mo. active intervention in adults with ADRD randomized to RGV or EUC. MPA will be assessed by accelerometer. We expect greater MPA in the RGV compared to the EUC arm. Our secondary aims are to compare adults with ADRD and their caregivers randomized to RGV or ECU on the following outcomes across 18 mos.: MPA (min/wk.), sedentary time (min/wk.), percentage meeting 150 min/wk. goal, functional fitness, activities of daily living (adults with ADRD), quality of life, residential transitions (adults with ADRD), cognitive function (adults with ADRD), and caregiver burden (caregivers). We expect more favorable changes for all secondary outcomes for both adults with ADRD and caregivers in the RGV compared with the EUC arm. Additionally, we will evaluate the influence of process variables/participant characteristics on MPA in adults with ADRD and their caregiver across 18 mos.: age, sex, BMI, attendance (exercise/support sessions), use of recorded sessions, MPA self-monitoring, peer interactions during group sessions, caregiver support, type and quality of dyadic relationship, and number of caregivers.

Intervention-theoretical model

The proposed intervention is based on Social Cognitive Theory [27] and will focus on the social cognitive techniques shown to be most effective for changing physical activity

including intention formation, goal setting (weekly MPA goals), self-monitoring (Fitbit) and feedback (monthly support sessions) [28, 29]. These techniques will be enhanced by employing behavior shaping (gradually modifying physical activity), prompts (iPad® calendar reminders), scheduling time for MPA, environmental cues, modeling by caregivers and other adults with ADRD (RGV only), positive reinforcement/social support during group sessions (group session leader, caregivers, other adults with ADRD), and other self-regulatory techniques. The intervention is also informed by both social ecologic model [30] and social network theory [31] as content will be tailored to both the physical and social environment of participants utilizing group support, peer support, caregiver support, creating a safe space for physical activity in the household, providing resources for physical activity in the community, and working with community agencies to disseminate findings.

Participant Eligibility

Primary care physician (PCP) clearance will be required of participants with ADRD and their caregiver. To enhance generalizability, individuals taking ADRD or other medications, receiving treatment for other chronic diseases, or with risk factors such as hypertension, tobacco use, lipid abnormalities, T2DM, etc., will be allowed to participate with PCP clearance.

Adults with ADRD.—Inclusion: 1) Very mild to moderate dementia (Mini Mental State Exam ≥ 11 , Short Test of Mental Status ≥ 11 , or Telephone Interview for Cognitive Status (TICS) ≥ 6). [32, 33]. 2) Age ≥ 55 yrs. 3) Low-risk of falls, assessed by PCP consent 4) Ability to participate in MPA, e.g., walk including with an assistive device, as verified PCP clearance. 5) Ability to communicate verbally. 6) Vision and hearing sufficient to safely comply with the intervention program as verified by PCP clearance. 7) Reside at home and receive support from a caregiver. 8) Internet access in the home. **Exclusion:** 1) Current exercise, i.e., > 3 , 30-min bouts of planned exercise/wk. 2) Clinically significant psychiatric disorder; systemic illness or infection likely to affect safety; clinically-evident stroke; myocardial infarction or coronary artery disease in the last 2 yrs.; cancer in the last 5 yrs.; or significant pain or musculoskeletal symptoms that would prohibit exercise. 3) Unwilling to be randomized.

Caregivers.—Inclusion: 1) Age ≥ 18 yrs. 2) Spends at least 20 hrs./wk. with the adult with ADRD. **Exclusion:** 1) Unable to participate in MPA. 2) Unwilling to be randomized. 3) Serious medical risk, such as cancer within the last 5 yrs. or cardiac event, e.g., heart attack, stroke, angioplasty within the last 2 yrs.

Recruitment

The University of Kansas Alzheimer's Disease Center (KU-ADC) will supervise the recruitment effort. The KU-ADC data base, which currently contains ~2,500 adults with ADRD who have agreed to be contacted about future research trials, will be the primary recruitment source for this trial. The KU-ADC will identify individuals in their database who appear to be eligible based on patient records and will provide names and contact information to study staff. Study staff will contact the patient/caregiver to describe the study, answer questions and to assess initial patient and caregiver eligibility. Home visits to obtain

informed consent will be scheduled with those remaining interested following the initial contact. Separate informed consent will be obtained for the patient and caregiver. If the patient with ADRD has a surrogate decision maker, we will obtain consent from that individual and assent from the patient. Project staff will fax/email a form to the PCP of both the patient and caregiver, which describes the eligibility criteria, study requirements, and requests clearance for participation. Those found to be ineligible will be provided with written materials describing available resources for increasing their MPA.

Randomization

Dyads will be stratified by sex and computer randomized by the study statistician with equal allocation to the RGV or EUC arms. Intervention assignments will be concealed in envelopes and delivered to the study coordinator. Assignments will be revealed to adult/caregiver dyads at the orientation session described below.

Caregiver role

A caregiver will be asked to participate in the intervention with the adult with ADRD. Caregivers who for any reason are unable to provide care at any time during the trial will be replaced by another caregiver selected in consultation with the adult with ADRD. The new caregiver will also be asked to provide consent, complete baseline outcomes, and be oriented to the appropriate intervention arm. We will evaluate the impact of change in caregivers on change in MPA in our exploratory analysis. We do not feel that the person with ADRD can safely participate in the unsupervised physical activity. Thus, if an alternative caregiver cannot be identified the individual with ADRD will be censored from the study from that time forward and will be referred to the University's Alzheimer's Disease Center for alternative physical activity programs.

Intervention components common to both arms

MPA recommendations.—The U.S. Centers for Disease Control and Prevention physical activity guidelines for Americans [34] and the American College of Sports Medicine exercise recommendations for older adults (> 65 yrs.) [35] both recommend at least 150 min/wk. of moderate intensity physical activity (3.2–4.7 METs) to achieve health benefits. [36] Recommendations for older adults also include muscle-strengthening, flexibility, and balance exercise [35]. Considerable evidence suggests that regular physical activity at this level in both older and younger adults (18–64 yrs.) reduces the risk and/or has therapeutic benefits for numerous diseases and conditions including cardiovascular disease, hypertension, stroke, type 2 diabetes, osteoporosis, some cancers, etc. [34, 35]. The prevention and management of ADRD is not listed as a potential benefit of current physical activity recommendations, as the level of activity required to achieve such benefits is currently unknown [37]. We will recommend 150 min/wk. of MPA for both adults with ADRD and their caregivers in the proposed trial based on the documented health benefits for numerous chronic conditions in non-demented adults [35] and the accumulating evidence suggesting a positive impact on the health and function of both adults with ADRD [2] and their caregivers [8, 9, 22].

Self-monitoring-physical activity.—Adults with ADRD and caregivers in both arms will be asked to wear a Fitbit Versa Lite activity tracker on their non-dominant wrist over the duration of the 18-mo. trial. This request may appear onerous; however, wearing the Fitbit is akin to wearing a wristwatch. Real-time data from the Fitbit is automatically transferred, via the web, to cloud storage (Fitabase, Small Steps Labs LLC, San Diego, CA), thus, participant burden is minimal. Fitbit data is available to both participants and the health coach via the Fitbit app. Immediate participant feedback of daily steps, minutes of sedentary time, and time spent in light, moderate and vigorous physical activity will be available via a graphic display on the device and the Fitbit app. The health coach will log into each participant account once per week to verify they are wearing and charging the device and to monitor participant activity solely for use in providing motivation and feedback during the individual support sessions. Outcome data for MPA and sedentary time will be assessed by accelerometer as described subsequently. Dyads will be reminded to wear and charge the Fitbit during group exercise (RGV only) and individual support sessions, and will receive automatic reminder messages every 3 days via the iPad® using the iCal app.

Orientation.—One week prior to initiating the intervention, health coaches will conduct a home visit (~ 60 min) with each adult with ADRD/caregiver dyad in both intervention arms. Health coaches will deliver all necessary equipment and orient participants to the use of all equipment/software, answer questions regarding the general requirements of the trial, and demonstrate/practice the basic aerobic and resistance exercises with participants. Each dyad will be provided with the following: iPad®, iPod® touch, 2- Fitbit Versa Lites ® (one for the adult with ADRD and one for the caregiver) and resistance bands (TheraBand, Akron, OH). The iPad® will be used to deliver either the real time exercise sessions (RGV only), individual support sessions, and for syncing the Fitbit of adults with ADRD. The iPod® will be used to sync the Fitbit of caregivers, as the iPad® is capable of syncing only one Fitbit. The iPod® will also allow for communication between the caregiver and the health coach via iMessage. Dyads in the RGV arm will be provided with an iPad®/HDMI adaptor, which allows video conference sessions to be displayed on a larger TV screen, if desired. All software/apps (i.e., Zoom, DropBox, Fitbit app) for each intervention arm will be loaded on the iPad / iPod to provide access to recorded videos, written materials, and activity tracking. Reminders regarding upcoming group video and/or health educator/dyad support sessions will be programed using the iCalendar app on the iPad®. Access to non-study related materials, e.g., web browsing, app store etc. will be blocked on all iPads®/ iPods® until completion of the maintenance intervention (12 mos.).

Individual support sessions.—Dyads will be asked to attend 15–20-min education/support sessions (2 sessions/mo. during the active intervention (0–6 mos.) and 1 session/mo. during maintenance (7–12 mos.) delivered remotely on the iPad® using FaceTime®. No individual support sessions will be scheduled during the no-contact period (13–18 mos.). Sessions will be designed to educate and support the adult with ADRD and caregivers with meeting their 150 min/wk. goal for MPA. Each session will include a review of physical activity self-monitoring data, goal setting, strategies to increase and support MPA, and discussion of a topic relevant to MPA. During the active intervention (0–6 mos.) topics will include the importance of MPA for health and function, how to include MPA in the daily

schedule, reduce barriers to physical activity, appropriate types of activity, creating a safe environment for physical activity, alternative activities for inclement weather, importance of hydration, etc. During maintenance (7–12 mos.) the discussion will focus on strategies to ensure continued participation in MPA, opportunities for physical activity in the community, and continued encouragement of dyadic activity. Topic outlines and information relative to support sessions will be pre-loaded on the iPad® where they can be accessed at any time across the 18-mo. trial.

RGV arm

Schedule.—Group exercise sessions will be scheduled on 3 days/wk. during the active intervention (0 to 6 mos.) and 1 day/wk. during maintenance (mos. 7–12). Group sessions will not be scheduled during the no-contact period (13–18 mos.). During orientation sessions, dyads will be asked to provide times of the day, between 10 a.m. and 7 p.m., that would be most convenient to complete the group sessions. Based on this information we will offer dyads in each cohort the choice between 2 potential session times each day. Prompts reminding adults with ADRD/caregivers of upcoming sessions will be sent using iMessage on the iPad® (adult with ADRD)/iPod® (caregiver) and iCalendar.

Session delivery.—Real-time exercise sessions will be delivered to adults with ADRD/caregiver dyads in their home by a trained health coach experienced in working with adults with ADRD using Zoom® video conferencing software. This software allows multiple users to see and interact with each other and the health coach via the iPad®. Tutorials describing trouble shooting for common technical problems with the Zoom® software, e.g., internet connectivity etc., will be loaded on the iPad®. Dyads with technical issues during the intervention may also contact research staff by phone or email.

MPA session content.—Each session will include a warm-up (~5 min), moderate intensity aerobic activity (~30 mins; 3–5 METs), resistance and balance/coordination exercise (~5 min), and cool-down/stretching (~5 min). Each session will include MPA, e.g., walking/jogging standing in place or sitting in a chair, sit to stand, dance movements; resistance exercise, e.g., TheraBand®-arm curls, leg extensions, side leg raises, and seated rows; and balance exercise, e.g. heel to toe walks, balance walk, and standing on one foot with/without support of a chair. We will provide modifications for participants having difficulty with any specific exercises. Health coaches will encourage interactions between participants during group sessions and ensure interactions between participants do not focus on dementia [38], but rather on issues relative to supporting their peer's efforts to increase MPA.

Outside session MPA.—Group sessions will provide the potential to accumulate 90 min/wk. (3 sessions × 30 min/session) during the active intervention (0–6 mos.) and 30 min/wk. (1 session) during maintenance (7–12 mos.). Thus, MPA in addition to that accumulated in group sessions will be required to meet the MPA goal of 150 min/wk. To provide a transition from a sedentary to a more physically active lifestyle we will recommend goal of 45 min of MPA/wk. at wk. 1 and increase the goal by 15 min/wk. to reach the 150 min/wk. goal at wk. 8. At the completion of each group session health coaches

will provide a “weekly challenge” for participants to try a new activity or create and perform a new exercise routine etc. in order to reach the 150 min/wk. goal. Additionally, the National Institute on Aging (NIA) pamphlet “Exercise and Physical Activity: Your Everyday Guide” will be loaded on the iPad® to assist participants in meeting the 150 min/wk. goal.

Video recordings.—Video recordings of all group exercise sessions will be uploaded to Dropbox®. Participants/caregivers will be encouraged to access video recordings using their iPads®/iPods® to assist with meeting the 150 min/wk. goal. Frequency and duration of participant/caregiver video access will be tracked using Dropbox® analytics.

No contact follow up (13–18 mos.).—Group video and individual support sessions will be discontinued. Participants will be asked to continue to obtain 150 min/wk. of MPA and self-monitor their MPA via Fitbit. Access to the video recorded sessions will be maintained; however, new content will not be added.

EUC arm

Intervention.—Individuals with ADRD and caregivers will be provided information regarding increasing MPA available from the “Exercise and Physical Activity: Your Everyday Guide from the National Institute on Aging”, provided with a Fitbit for self-monitoring, and encouraged to achieve 150 min/wk. of MPA. The NIA guide reviews the importance of endurance, strength, balance and flexibility exercise, provides suggestions for incorporating physical activity into daily life, describes how to properly perform different types of exercises, and includes examples of daily exercise schedules. Protocols for individual support sessions and self-monitoring have been described previously (see Intervention components common to both arms).

No contact follow-up (13–18 mos.).—Individual support sessions will be discontinued. Participants will be asked to continue to obtain 150 min/wk. of MPA and self-monitor their MPA via Fitbit. To provide a transition from a sedentary to a more physically active lifestyle we will recommend goal of 45 min of MPA/wk. at wk. 1 and increase the goal by 15 min/wk. to reach the 150 min/wk. goal at wk. 8.

Health coach training—Health coaches will be trained by study staff and will shadow an experienced health coach for a minimum of 3 mos. prior to delivering the intervention on their own. All health coaches will be trained on how to perform each exercise, the order of presentation of the exercises, and provide guidance on how to recognize and correct common mistakes in performing specific exercises. Health coaches will also be trained regarding strategies for effective communication with adults with ADRD, e.g., speaking clearly and slowly, providing/repeating simple specific instructions [39], focusing on reassurance and empathy for each participant [40], and fostering interaction between participants with strategies to ensure the focus of the interactions is not on dementia [38].

Intervention fidelity

Recordings from all group MPA (RGV only) and individual support sessions will be reviewed by study staff who will compare recordings with a check list of exercises/topics

scheduled to be included in each session. Health educators covering <80% of scheduled content, or failing to deliver physical activity as prescribed, will receive additional training, and will be dismissed if the problem recurs.

Participant Incentives

Both adults with ADRD and caregivers will be provided \$50 for data collection at baseline, 6, 12, and 18 mos. and \$25 for the assessment of MPA via ActiGraph at 3 mos. to compensate for time required to complete testing. As an additional incentive, adults with ADRD and caregivers will be allowed to keep the iPad®/iPod® and the Fitbit on completion of the active intervention (12 mos.).

Assessments—Our primary outcome MPA will be assessed at baseline (1 wk. prior to starting the intervention), 3, 6, 12, and 18 mos. Secondary/exploratory outcomes will be assessed at baseline (1–2 wks. before starting the intervention), 6, 12 and 18 mos. in the adult with ADRD or caregiver's home. Our experience suggests these assessments, which will be completed by trained staff blinded to condition, will require ~75 min to complete. Staff will receive refresher training and complete reliability assessments for all physical measures 2–3 times/yr.

Adult with ADRD and Caregiver

Moderate Intensity Physical Activity (MPA) and Sedentary Time.—MPA and sedentary time will be assessed using an ActiGraph model wGT3x-BT tri-axial accelerometer (3.3 × 4.6 × 3.5 cm, wt. = 19 g., dynamic range ± 8 g). The ActiGraph provides valid and reliable assessments of MPA in adults [41, 42]. There is a lack of consensus on the best protocols to collect, process, and score ActiGraph data [43]. Thus, our decisions regarding ActiGraph location, monitoring period, data processing etc. were based on current practice, as described below. Participants will be asked to wear the ActiGraph on a belt over the non-dominant hip at the anterior axillary line during waking hours for 7 consecutive days, except for bathing and swimming. A 7-day monitoring period provides a reliable estimate of MPA [44, 45]. The hip, rather than the wrist location, will be used due to the lack of comparable data and established protocols for assessment of MPA using wrist-worn ActiGraphs [46]. Research staff will distribute and demonstrate proper placement of the ActiGraphs at home visits scheduled at 0, 6, 12 and 18 mos. ActiGraphs will be distributed by mail for the 3-mo. assessment. Daily reminders to comply with the ActiGraph protocol will be sent to participant's iPad® each morning during the 7-day monitoring period. ActiGraphs will be initialized and downloaded using ActiLife Software version 6.13.3 or higher (ActiGraph Corp, Pensacola, FL) and set to collect in the raw data mode from all 3 axes at 60 Hz. Although the wGT3x-BT collects raw data from 3 axes, the widely used cut-points for determining activity intensity in adults proposed for this trial use acceleration data from the ActiGraph vertical axis [47]. However, raw data from all 3 axes will be downloaded and stored, and will be available should algorithms for processing this data become available during this trial. Accelerometer data will be processed using the protocol for adults used in the 2003–2004 and 2005–2006 cycles of NHANES [47, 48]. Data will be aggregated over 60-sec epochs. The following intensity cut-points will be used: sedentary (< 1.0 MET; 100 counts/min), light (1.1–2.99 METs; 101–2019 counts/min),

moderate (3.0–5.99 METs; 2020–5988 counts/min) and vigorous ≥ 6 METs; ≥ 5999 counts/min) [47, 48]. Non-wear time will be defined as at least 60 consecutive minutes of zero counts, with allowance for 1–2 min of counts between 0 and 100. Counts ≥ 20,000/min will be considered spurious [49]. All accelerometer data processing will be completed using custom SAS/R programs developed by the project statisticians, in collaboration with our research group.

Functional fitness.—Functional fitness will be measured using Functional Fitness Test (FFT) previously called the Senior Fitness Test [50]. The individual fitness test items involve common activities such as getting up from a chair, walking, lifting, bending, and stretching. Reliability of the FFT in older adults with cognitive impairment is high in all of the test items (ICC = 0.93) [51].

BMI.—Weight will be measured in duplicate in light clothing on a calibrated scale (Model #PS6600, Belfour, Saukville, WI) to the nearest 0.1 kg. Standing height will be measured in duplicate with a portable stadiometer (Model #IP0955, Invicta Plastics Limited, Leicester, UK). BMI will be calculated as weight (kg)/height (m²).

Quality of the dyadic relationship.—Quality of the dyadic relationship will be assessed at baseline, 6, 12, and 18 mos. using the dyadic relationship scale (DRS) which measures negative and positive dyadic interactions from the perspective of both the patient and the caregiver. The DRS has acceptable construct, discriminant, and concurrent validity, as well as reliability for both patients and caregivers[52].

Adults with ADRD only

Activities of daily living.—Activities of daily living will be assessed using the Disabilities Assessment for Dementia (DAD)[53]. The DAD includes 40 items: 17 related to basic self-care and 23 to instrumental activities of daily living. DAD demonstrated a high degree of internal consistency (Cronbach's alpha = .96) and excellent inter-rater (n = 31, ICC = .95) and test-retest (n = 45, ICC = .96) reliability with no gender bias.

Quality of life.—Quality of life will be assessed using the QOL-ADRD[54], a brief, 13-item self-report and 15-item caregiver-report. The QOL-ADRD has shown acceptable validity and reliability when completed by adults with ADRD or a caregiver proxy (ICC = .76 and .92 respectively) [54].

Residential transitions.—Residential transitions from home to institutional care, will be tracked by health coaches. We will also assess caregiver desire to institutionalize the adult with ADRD using the 6-item Morycz's Desire-to-Institutionalize Scale [55]. This scale demonstrated moderate reliability with KR-20 alpha of .694 for Whites, .742 for African Americans, and .767 for Hispanics [56].

Cognitive function.—Cognitive function will be assessed using the Cognitive Function 4a and Applied Cognition Abilities 4a instruments from the Patient-Reported Outcomes Measurement Information System (PROMIS) Cognitive Function Battery [57–59]. The PROMIS Cognitive Function and Cognitive Function Abilities Subset item banks assess

patient-perceived cognitive deficits. Facets include mental acuity, concentration, verbal and nonverbal memory, verbal fluency, and perceived changes in these cognitive functions. The extent to which cognitive impairments interfere with daily functioning, whether other people observe cognitive impairments, and the impact of cognitive dysfunction on quality of life are also assessed. These relatively short scales were derived from an intensive item analysis using Item Response Theory and qualitative analysis to produce short but reliable measures [59].

Caregiver Outcomes

Quality of Life.—Quality of Life will be assessed using the SF-36[60] which has acceptable reliability and validity in the general population [61].

Caregiver Burden.—Caregiver Burden will be assessed using the Zarit Burden Interview-short version, a 12-item self-report questionnaire in which the caregiver is asked to answer using a 5-point scale. The short version [62] has shown acceptable correlations (0.92 to 0.97) with the full 22-item version in caregivers of adults with ADRD.[63].

Semi-structured interview.—At 6 and 18 mos. study staff will conduct semi-structured interviews by phone with a 20% random sample of caregivers from both intervention arms to gather information that might be useful for improving the intervention and/or implementing the intervention in settings serving adults with ADRD. At 6 mos. topics will include, enjoyment of the remote video sessions and individual education sessions, difficulties with compliance, suggestions for improvements and overall satisfaction with the intervention, caregiver's enjoyment of the exercise and educational sessions, performance of health coaches, physical activity recommendations etc. At 18 mos. topics will include long term satisfaction with the program, perceived ability to continue physical activity after intervention completion, and perceived benefits of the intervention. Qualitative content analysis (Atlas, ti 6.2) will be conducted to search for broad themes across interviews [64].

Exploratory outcomes

Session attendance.—Group MPA (RGV only) and support sessions attendance will be obtained from records maintained by the health coach and expressed as the percent of possible sessions from 0–6 mos. and 7–12 mos. Attendance for adults with ADRD, enrolled caregivers, and alternative caregivers will be recorded separately.

Use of recorded videos.

Use of recorded videos (frequency and duration of access, RGV only) will be assessed using Dropbox® analytics.

Self-monitoring of physical activity.

Self-monitoring of physical activity will be assessed across the 18 months as the percentage of days with Fitbit data over a minimum of 8 hrs., between 6 am and midnight.

Caregiver support.

Caregiver support will be assessed using the percentage of group MPA (RGV) and/or individual support sessions completed by both the person with ADRD and their caregiver.

Type of dyadic relationship.—We will document the type of caregiver, e.g., spouse, adult child, paid staff, and evaluate the impact of caregiver on our primary and secondary outcomes.

Number of caregivers.—We will document the number of different caregivers for adults with ADRD and evaluate the impact of change in caregivers on our primary and secondary outcomes.

Sample size/power

One hundred adults with ADRD and their caregiver (100 dyads) will be randomized to achieve adequate power to test short-term (0–6 mos.) and long-term (0–18 mos.) effects of the intervention. Statistical power for detecting a significant effect on the primary outcome (MPA of the adult with ADRD) depends on the following parameters: the number of participants in each arm (50/arm), the number of measurements (7 days at 0, 3, and 6 mos.=21 for primary aim; 7 days at 0, 3, 6, 12, and 18 mos.=35 for secondary and exploratory aims), correlations among repeated measures, attrition, and effect size. This trial is powered to detect a between-arm difference (RGV vs. EUC) of 10 min/d. in MPA. This difference represents additional 70 mins. of MPA/wk. in the RGV arm. An increase in MPA of this magnitude is associated with improved performance of activities of daily living and mobility in older adults with ADRD [2]. Conservatively assuming a large variability for change in MPA ($SD=30$ min/d.), a 10-min/d. difference in MPA corresponds to a small to moderate size of short-term effect ($f=0.17$). Also, if we reasonably assume a smaller between-arm difference (6 min/d. = 42 min/wk.) during maintenance (7–12 mos.) and no contact (13–18 mos.), this yields a long-term effect size of $f=0.15$. The average correlation between repeated measures of MPA in our 3-mo. pilot trial was 0.22. We considered a relatively high attrition rate of ~20% for our power calculation, i.e., final $n = 84$ with attrition up to ~20%. Power analysis using this information and G*Power 3.1.9.2 indicated that our sample of 100 adults with ADRD (42 participants/arm after attrition) would produce 80% power to test an overall between-arm difference in the short term (0–6 mos.) and 81% power in the long term (0–18 mos. This sample size would also provide 80% power to detect a between-arm difference in change as small as $f=0.10$ (small) over 0–6 mos., and $f=0.10$ (small) over 0–18 mos. In summary, our proposed sample size of 100 dyads will provide sufficient statistical power to address all our proposed aims.

Analysis plan

Baseline equivalence.—The distributional properties of baseline demographic characteristics (MPA, BMI, age, sex, race/ethnicity, level of dementia, etc.) and dyadic relationship between adults with ADRD and their caregiver (quality, type, number of caregivers) will be inspected within the sample and between the RGV and EUC arms. Variables that demonstrate a significant nonequivalence between RGV and EUC arms will be statistically controlled in the hypothesis testing to improve accuracy of our inferences on

intervention effects. Additionally, variables that significantly differ between dyads that dropped out and those that did not will be controlled to minimize any systematic bias stemming from attrition.

Analysis-primary aim.—Our primary aim is to compare MPA (min/wk.) across the 6-mo. active intervention in adults with ADRD randomized to RGV and EUC. Our analysis will account for/evaluate the clustering of observations (repeated measurements; level 1) within participants (level 2) and dyads (level 3; if multiple caregivers) by estimating intra-class correlations and variances/covariances of regression coefficients at, and across different levels in random-effects multilevel models (mixed models). To address the aim, models will examine overall between-arm difference in MPV across time (group effect), linear/non-linear change in MPV over time (time effect), and, if appropriate, between-arm difference in this change (group-by-time interaction), while controlling for (i) the number of contacts with research staff and (ii) the baseline characteristics imbalances between participant subgroups (RGV vs. EUC, dropouts vs. completers). For example, a significant interaction would indicate that adults with ADRD in the RGV arm achieve more minutes of MPA compared to those in the EUC arm and this difference becomes greater as intervention participation increases.

Analysis-secondary aims.—Our secondary aims are to compare adults with ADRD and their caregivers randomized to RGV or ECU on the following outcomes across 18 mos.: MPA (min/wk.), sedentary time (min/wk.), percentage meeting 150 min/wk. goal, functional fitness, activities of daily living (adults with ADRD), quality of life, residential transitions (adults with ADRD), cognitive function (adults with ADRD), and caregiver burden (Caregivers). Similar mixed models will be fitted separately for these outcome variables to examine group effect, time effect, and group-by-time interaction while controlling for the number of contacts with research staff and the baseline characteristics imbalanced between participant subgroups.

Exploratory aim.—Our exploratory aims will evaluate the influence of process variables/participant characteristics on MPA in adults with ADRD and their caregiver across 18 mos.: age, sex, BMI, attendance (MPA/support sessions), use of recorded sessions, MPA self-monitoring, peer interactions during group sessions, caregiver support, type and quality of the dyadic relationship, and number of caregivers. If MPA is not significantly different between RGV and EUC across 18 mos., i.e., no significant group effect or group-by-time interaction, we will combine the two arms and examine associations of the process variables/characteristics with MPA in mixed modeling. However, if a significant between-arm difference in MPA is identified, we will determine whether the process variables/characteristics enhance or attenuate the treatment effects, i.e., moderation, by testing a 2-way interaction with the group effect and/or a 3-way interaction with the group-by-time interaction term. In addition, we will examine how caregiver MPA influences the MPA of adults with ADRD over the 6-mo. active intervention, 6 mos. maintenance, and 6 mos. no contact. Some variables will be measured only at baseline, some will be summarized across the trial, while others will be assessed at specific time points. Thus, we will carefully design our models to assure the appropriateness of the analysis.

Missing data.—Missing data is anticipated due to either attrition, participant dropout, or nonresponse, e.g., ActiGraph non-wear or malfunction. Our intent-to-treat approach will employ full information maximum likelihood (FIML) estimation in the modeling, which does not discard participants who dropped out but utilizes all available data from their partial measurements, thereby producing unbiased parameter estimates and smallest possible standard errors. Missing observations due to nonresponse will be handled by Monte Carlo Markov Chain (MCMC) multiple imputation (MI) [65]. A sufficient number of imputed datasets will be created to ensure accurate recovery of missing data and analysis results from each imputed dataset will be combined to make valid statistical inferences. Our imputation process will incorporate a number of auxiliary variables, thereby increasing the likelihood of meeting the missing a random (MAR) assumption [66]. The state-of-the-science on missing data indicates that FIML and MI are extremely robust and leads to unbiased generalizability [67].

DISCUSSION

Aging is the prominent risk factor for the development of ADRD. Thus, the prevalence of ADRD is expected to increase to 13.8 million by 2050 as the number of adults age 65 and over increases [68]. Individuals who survive with ADRD will eventually become completely dependent on others for assistance with basic ADLs, including eating [1]. Adults with ADRD and their family members, who provide the majority of unpaid care for adults with ADRD living in the community, suffer significant emotional, financial and physical stress [7]. Thus, interventions targeting the promotion of physical activity which may improve functional status in adults with ADRD and the quality of life and level of burden of caregivers, are warranted.

The majority of adults with dementia are cared for at home by a caregiver with the goal of maintaining this living situation as long as possible [69]. Increased MPA may improve the health and physical function of both adults with ADRD and their caregiver. As outlined in the National Plan to Address Alzheimer's Disease "enabling caregivers to continue to provide care while maintaining their own health and well-being" is a primary need for communities and the nation (Strategy 3B) [70]. Thus, including adults with ADRD and their caregiver represents an efficient approach to increasing MPA in both groups. The time constraints associated with caring for an adult with ADRD represent a significant barrier to caregiver participation in community-based exercise programs [71]. Participation in MPA with the patient, as we have proposed, provides a dedicated time for caregiver exercise and an opportunity for interaction between the adult with ADRD and caregiver that is different from the usual daily routine interactions such as personal care tasks etc. [25]. Caregiver participation and social support may also improve adherence to physical activity programs [14, 20, 22].

Remote delivery of MPA eliminates the need to travel to an exercise facility which can be a significant barrier to exercise for both adults with ADRD and their caregivers [72, 73]. Survey results from our pilot trial [26] and published focus group data from other research groups [73] suggests that adults with dementia express a clear preference for group over individual exercise. Adults with ADRD and their caregivers are often socially isolated [7,

74]; thus, the group format provides an opportunity for social interaction which may be associated with improved exercise adherence in both adults with dementia [75] and their caregiver [28]. It may also be easier for adults with ADRD to focus on the intervention in the familiar home environment as opposed to an unfamiliar community environment with its associated distractions [73].

Increased MPA is associated with significant health and functional benefits in both adults with ADRD [2] and older adults without dementia [35]. Therefore, we consider randomization of participants to a non-exercise control arm to be unethical. Our EUC arm provides written materials, plus individual education and support from a trained health coach; thus, participants in both intervention arms have the potential for success. We are aware of the inherent differences between the intervention arms in the frequency of contact, and potential level of peer and health coach support/interaction. This trial was not designed to isolate the effect of specific intervention components but was designed to evaluate our two interventions as “packages,” as they would be delivered by agencies serving this population. However, our exploratory analyses will evaluate the influence of process variables/participant characteristics on MPA in adults with ADRD and their caregiver in both the RGV and EUC arms.

The duration of exercise interventions in apparently healthy older adults [17, 76] and in adults with ADRD [77, 78] is typically 6 mos., as this time period evokes changes in cardiorespiratory fitness [79, 80] which has been associated with improvements in performance of ADLs, and reductions in cognitive decline, brain atrophy, and dementia progression [81, 82] in adults with ADRD, and increased quality of life, physical function, and cognition in apparently healthy older adults [8, 9, 83, 84]. Additionally, a 6 mos. intervention allows 2 mos. for the progression of the intensity and duration of weekly MPA and still provides 4 months of MPA at the recommended target of 150 min/wk. The inclusion of assessments of MPA at 12 and 18-mos. allows evaluation for the sustainability of any increases in MPA following a maintenance intervention and a 6 mo. no-contact follow-up, and both short and long-term changes in secondary outcomes.

The following design attributes ensure the scientific rigor of the proposed trial: 1) Randomized design with equal allocation to groups with concealed allocation of group assignments. 2) Adequate statistical power to address the primary aim. 3) Strategies to ensure the recruitment of sufficient participants to achieve our desired sample size. 4) Retention/incentive strategies to reduce loss to follow-up. 5) Secondary and exploratory aims to maximize the use of data; e.g., functional fitness, activities of daily living (basic/instrumental), quality of life, residential transitions, neuropsychiatric symptoms, cognitive function and analysis to examine the impact of process variables/participant characteristics on change in MPA. 6) The use of a theory-based intervention delivered by trained health coaches. 7) Delivery of both intervention arms by the same health coach to cohorts of participants to minimize health educator effects. 8) Review of recordings of all scheduled exercise and parent/participant meetings to ensure intervention fidelity. 9) Assessments completed by trained staff blind to intervention arm. 10) Evaluation of staff inter-rater reliability for all physical assessments (2–3 times/yr.). 11) Structured participant interviews at 6 and 18 mos. to obtain information for improving and/or implementing the intervention.

In summary, this two-arm randomized trial will compare 2 strategies for the delivery of an intervention to increase MPA in adults with ADRD and their caregiver; real-time group video conferencing (RGV) vs. enhanced usual care (EUC). If effective, RGV is a scalable and sustainable format, which could be used by community agencies, or others to efficiently deliver MPA to adults with ADRD and caregivers in their homes.

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Table 1.

Design Overview for an 18-month Physical Activity Intervention for Adults with Alzheimer's Disease and Related Dementias and their Caregivers

	INTERVENTION ARMS	
	Real time group video (RGV)	Enhanced usual care (EUC)
Intervention target	Adult with ADRD/caregiver dyad	Adult with ADRD/caregiver dyad
MPA recommendation	150 min/wk.	150 min/wk.
Intervention components		
Written materials	NIA-Exercise and Physical Activity: Your Everyday Guide	NIA-Exercise and Physical Activity: Your Everyday Guide
MPA sessions	Group real-time, delivered by trained health coach via video conferencing	N/A
<i>Session frequency</i>		
<i>0–6 mos.</i>	3 /wk.-scheduled	N/A
<i>7–12 mos.</i>	1 /wk.-scheduled	N/A
<i>13–18 mos.</i>	0/wk.	N/A
<i>Session Content</i>	30 min aerobic MPA, 15 min RE, balance/coordination	N/A
<i>Session Intensity</i>	3–5 METs	N/A
Individual education, support, feedback sessions		
<i>Delivery</i>	FaceTime®	FaceTime®
<i>Duration</i>	20 min	20 min
<i>Frequency</i>		
<i>0–6 mos.</i>	2/mo.	2/mo.
<i>7–12 mos.</i>	1 /mo.	1 /mo.
<i>13–18 mos.</i>	0/mo.	0/mo.
Self-monitoring MPA	Fitbit	Fitbit

Note: NIA=National Institute on Aging, MPA= moderate physical activity, RE= resistance exercise