Study Protocol and Statistical Analysis Plan

for

FitMi AD: a safe and motivating computer-guided exercise system for individuals with MCI or mild dementia due to Alzheimer's disease

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Background

Alzheimer's disease (AD) is a leading cause of cognitive decline in older adults, affecting over 5 million individuals in the US with an estimated annual cost of over $200 billion. There is no known cure for AD, and it is associated with accelerated decline in physical function, higher risk of falls, and increased rates of comorbidities including diabetes, congestive heart failure, and cerebrovascular disease. Regular exercise can improve overall health and physical function as well as reduce the incidence of comorbidities for individuals with AD. Further, there is preliminary evidence that exercise may delay the onset of AD in individuals with mild cognitive impairment (MCI). However, individuals with MCI or mild dementia due to AD tend to be older, have unique needs, and exhibit memory and other cognitive impairments that make it difficult to participate in regular exercise. Caregiver support can help, but caregivers often lack sufficient training in how to care for these individuals and have limited tools for holding them accountable to exercise over the long-term. Existing home-based exercise technologies are also not optimized to promote activity in older individuals. This project seeks to address this gap by evaluating a novel at-home guided exercise system designed specifically for individuals with MCI or mild dementia that could increase the amount of exercise they perform, improving independence and promoting a healthier lifestyle.

Trial Design

This study will be a multi-site randomized controlled trial comparing home-based exercise with FitMi AD to home-based exercise with the standard of care (i.e. a booklet of exercises) for individuals with MCI or mild dementia due to Alzheimer's disease (AD). The trial will be carried out at two separate study sites: Rancho Los Amigos National Rehabilitation Center and Havana Research Institute. Participants who qualify for the study will be randomly assigned to either the FitMi AD therapy group or the control group (booklet of exercises). Participants in both groups will be instructed to perform self-guided therapy for at least 30 minutes per day for 3 months. After 6-weeks, participants will return for a mid-way assessment. Participants will return again after the 3-month exercise period for a follow-up assessment. At this assessment, participants will return the FitMi AD system and the booklet of exercises. The trial will be approved by the Rancho Research Institute, Inc. Institutional Review Board at Rancho Los Amigos National Rehabilitation Center and WCG Institutional Review Board.

Participants

Inclusion criteria:

1. have MCI or mild dementia due to AD (i.e. Clinical Dementia Rating (CDR) score 1 for mild dementia or 0.5 for MCI)
2. ability to clearly see the screen and hear the audio instructions from the tablet
3. have a family member or friend who can answer questions about the participant's daily living skills
4. willing to participate in a research study.

Exclusion criteria:

1. age < 50 years old
2. use of a wheelchair as a primary mobility device (use of a cane or walker is permitted)
3. presence of other neurologic conditions such as movement disorders or history of stroke
4. other severe concurrent medical conditions that may prevent the participants from completing the 3-month study.

Using an estimated effect size (Cohen's d) of 0.99 based on follow-up data from a previous study of a home-based exercise program for individuals with Alzheimer's disease (N=40), 14 participants in each group will provide an 80% chance of detecting a significant difference between groups at the 0.05 significance level (one-tailed t-test). To account for 10% dropout, we will recruit 15 participants in each group. To ensure an equal number of participants in each group, we used block randomization.

Intervention

Participants will be randomly assigned to either the FitMi AD therapy group or the control group (booklet of exercises). Participants in the control group will be given a custom-designed wrist-mounted actigrapher to monitor adherence by dawning the actigrapher when they exercised. Participants will receive a thirty-minute training session on how to safely perform their assigned exercises. For both groups, the supervising therapists at Rancho or Havana Research will select the appropriate exercises for each patient based on their abilities and functional goals. All exercises for participants in both groups will be selected from the same library of exercises. Participants in the FitMi AD group will also receive an additional thirty-minute training session on how to use the FitMi AD software. After completing their training, participants will be instructed to take the FitMi AD system (with the software installed on a supplied 10" touchscreen tablet) or the booklet of exercises home to exercise, depending on their group designation. Participants in both groups will be instructed to perform self-guided therapy for at least 30 minutes per day for 3 months. Participants will receive weekly phone calls from a supervising therapist to ensure they are not having any difficulties with the exercises and to monitor them for any increases in pain or adverse events. During the weekly phone calls, the supervising therapist will also review the patient exercise data on the remote monitoring dashboard and adjusted patient recommendations accordingly. After 6-weeks,

participants will return for a mid-way assessment. Participants will return again after the 3-month exercise period for their follow-up assessment. At this assessment, participants will return the FitMi AD system and the booklet of exercises

Outcomes

The primary outcome measure will be the change in physical function from baseline to post-therapy, using the Functional Reach test (FRT), the Timed Up and Go test (TUG), and the 30 second chair stand test (30CST). Secondary outcome measure will include the duration of exercise performed throughout the study. These measures are widely used to assess balance, mobility, and lower-extremity strength. All clinical assessments will be performed by a blinded, trained evaluator.

Statistical Methods

Change in primary measures FRT, TUG, and 30CST from baseline to follow up will be compared between groups using an unpaired two-tailed t-test.