Care partner assisted intervention to improve oral health of individuals with mild dementia

National Clinical Trial (NCT) Identified Number: NCT04390750

Principal Investigator: Bei Wu, Brenda L. Plassman, and Ruth A. Anderson

Sponsor: New York University

Grant Title: Care Partner Assisted Intervention To Improve Oral Health for Individuals with Mild Dementia

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Statement of Compliance

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

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

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

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

INVESTIGATOR'S SIGNATURE

Principal Investigator or Clinical Site Investigator:

Signed: Date:

Name: Bei Wu

Title: Professor

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For multi-site studies, the protocol should be signed by the clinical site investigator who is responsible for the day to day study implementation at his/her specific clinical site:

Signed: Date:

Name: Brenda Plassman

Title: Professor

Affiliation: Duke University

Signed: Date:

Name: Ruth Anderson

Title: Professor Emeritus

Affiliation: Duke University

1 PROTOCOL SUMMARY

1.1 SYNOPSIS

Title: Care partner assisted intervention to improve oral health of individuals with mild dementia

Grant Number: U01DE027512

Study Description: Open label, randomized, multisite trial to study oral health intervention in individuals with mild dementia and their care partners at two sites. The recruited dyads, each consisting of an individual with mild dementia (participants) and his/her care partner will be randomly assigned to one of three groups, treatment group 1, treatment group 2, and control group. The first three months will be the active treatment phase and the final three months will be the maintenance phase. Data from each dyad will be collected over a period of six months. Oral health outcomes will be compared between the control and treatment groups.

Objectives:

Objective 1: To evaluate the efficacy of an intervention to improve oral hygiene clinical outcomes (i.e. plaque index and gingival index) by improving oral hygiene behavior (i.e., frequency and duration of toothbrushing) and oral health skills among individuals with mild dementia.

Objective 2A: To determine whether effects of the **intervention [X]** on **oral hygiene behavioral outcomes [Y]**, are mediated by the following variables from the care partners' perspective: 1) oral care self-efficacy; 2) care partner self-efficacy; 3) use of cueing methods; 4) and FOCUSED Communication.

Objective 2B: To determine whether effects of the **intervention [X]** on **oral hygiene clinical outcomes [Y]**, are mediated by the following variables from the care partner's perspective: 1) oral care self-efficacy; 2) care partner's self-efficacy; 3) use of cueing methods; 4) and FOCUSED Communication.

Objective 3a: To determine whether effects of the **intervention [X]** on **oral hygiene clinical outcomes [Y]** are mediated by **oral hygiene behavioral outcomes [M]**.

Objective 3b: To determine whether effects of the intervention **[X]** on oral hygiene clinical outcomes [**Y**] is mediated by the **care partner's**

factors [M1], which then mediates the **oral hygiene behavioral outcomes [M2]** on **oral hygiene clinical outcomes [Y]**.

Endpoints:

Primary Endpoint:

Oral Hygiene Clinical Outcomes

1. Plaque Index
2. Gingival Index

Secondary Endpoints:

Oral Hygiene Behaviors

1. Frequency of brushing
2. Duration of brushing

Oral hygiene skill

- Hygienist assessment of thoroughness and technique of participant's usual brushing and flossing

Study Population:

120 Individuals with mild dementia and their care partners. This number may be increased up to 150 if attrition rates are higher than the initial prediction.

Phase or Stage:

Phase II

Description of Sites/Facilities Enrolling Participants:

At NYU, we will recruit participants from:
1) NYU Alzheimer's Disease Center (ADRC), a part of the Department of Neurology at NYU School of Medicine. The ADRC currently has an active cohort of 363 participants, of which 20% are mildly cognitively impaired, and 9% have Alzheimer's disease or related dementia.
2) Pearl I. Barlow Center for Memory Evaluation and Treatment at NYU Langone School of Medicine. Approximately 420 patients with mild dementia visit the Center annually.

At Duke, we will recruit from:
1) Duke Memory Disorders Clinic (Duke MDC). The Duke MDC sees an estimated 600 new patients and about 1700 return patients each year; about 40% of these are in the mild dementia range.

At both sites, we will also recruit via alliances with clinical specialists at other medical facilities and at various venues including medical centers, dementia support groups, and community facilities, organizations and events.

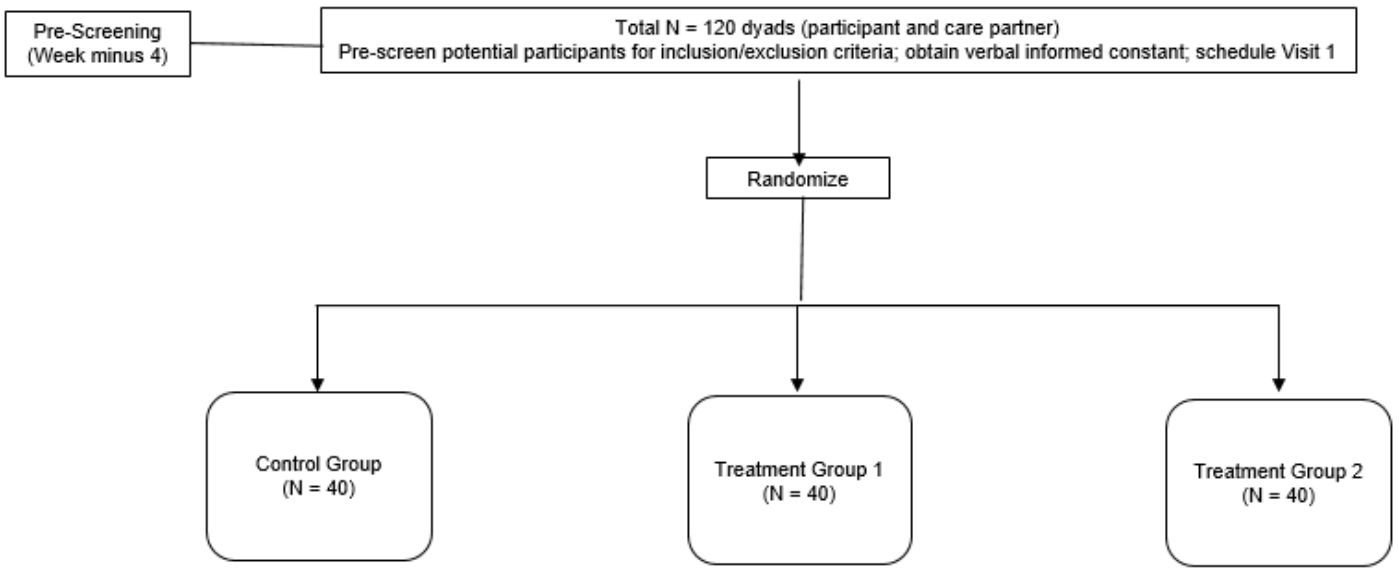
Description of Study Intervention:

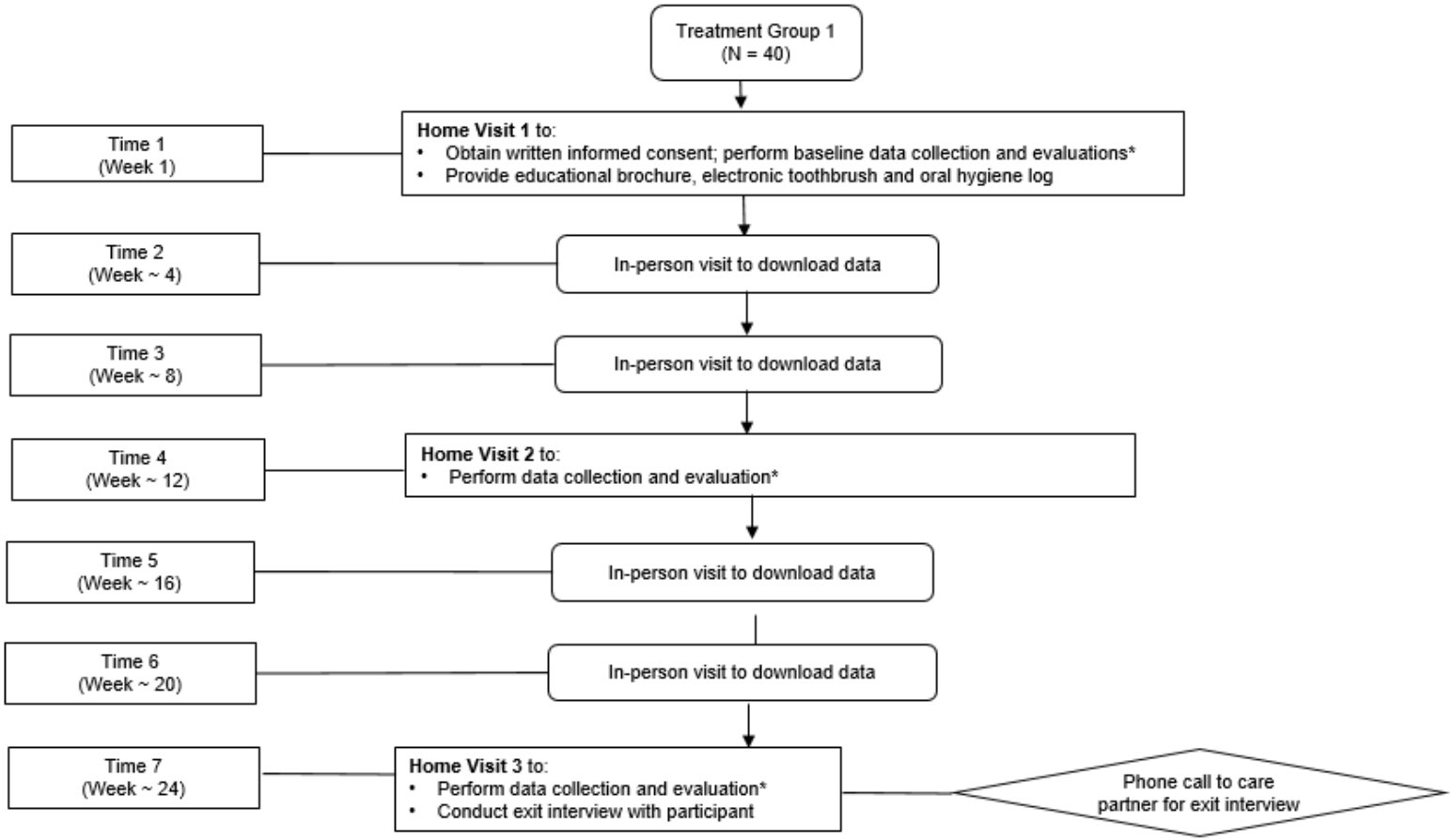
Our design includes three groups:

- Control Group will receive an educational booklet only and will continue their usual brushing techniques (manual or electric).
- Treatment Group 1 will receive educational booklet and a smart electronic toothbrush.
- Treatment Group 2 will receive the booklet, a smart electronic toothbrush, and in-home and telephone coaching.

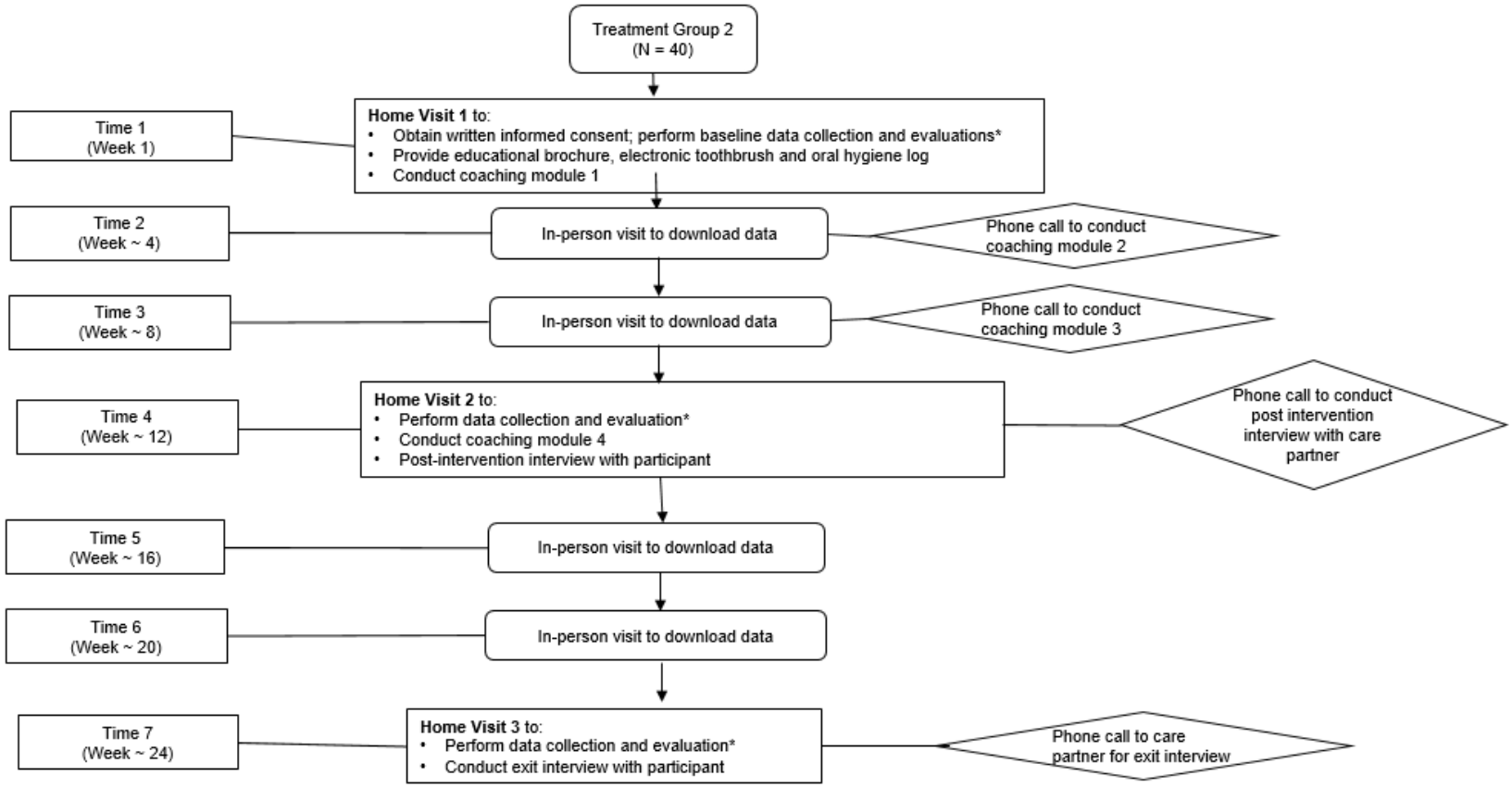
Study Duration:	36 months
Participant Duration:	6 months

1.2 SCHEMA

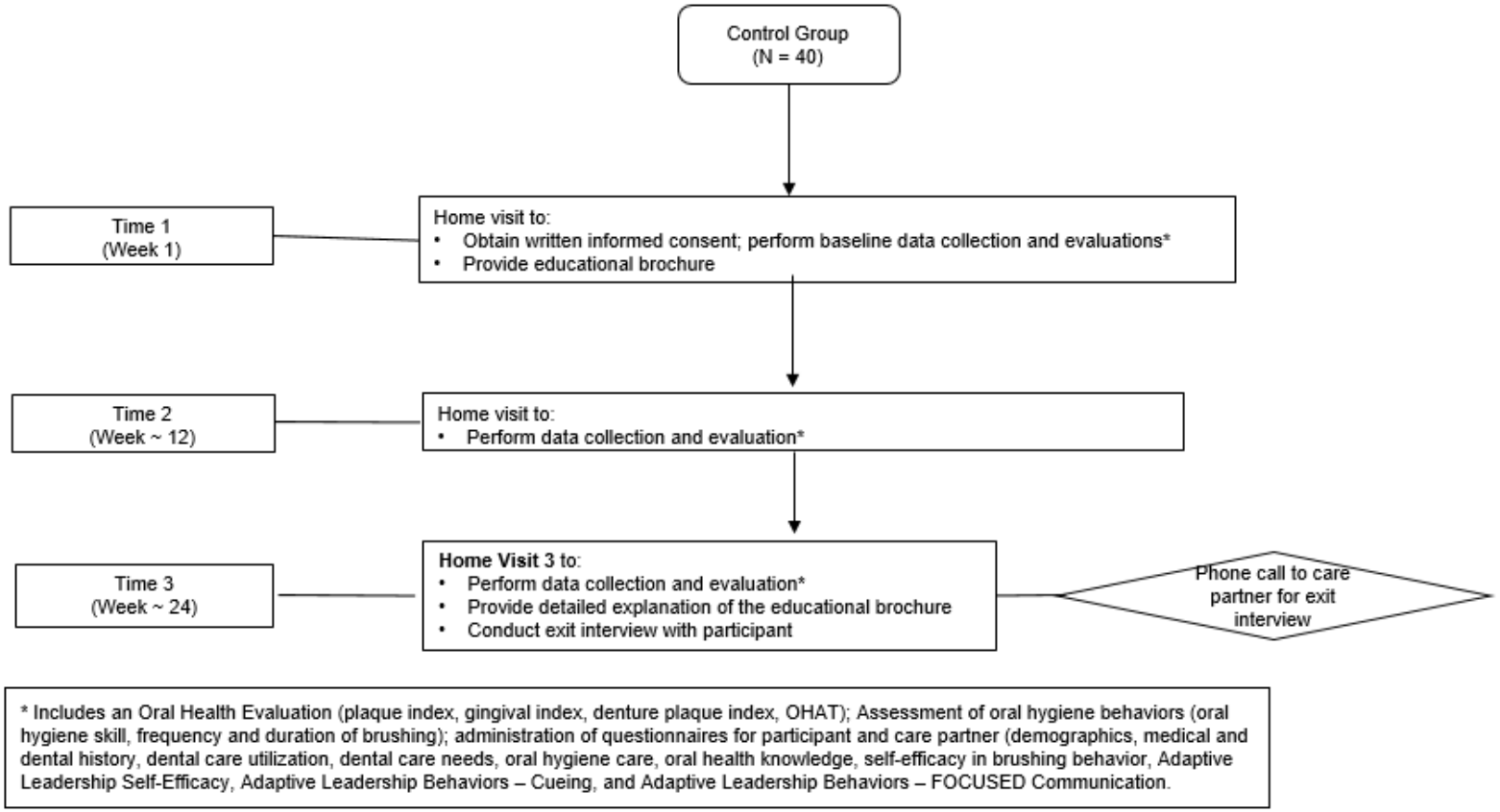

Pre-Screening
(Week minus 4)
Total N = 120 dyads (participant and care partner)
Pre-screen potential participants for inclusion/exclusion criteria; obtain verbal informed constant; schedule Visit 1
Randomize
Control Group
(N = 40)
Treatment Group 1
(N = 40)
Treatment Group 2
(N = 40)



* Includes an Oral Health Evaluation (plaque index, gingival index, denture plaque index, OHAT); Assessment of oral hygiene behaviors (oral hygiene skill, frequency and duration of brushing); administration of questionnaires for participant and care partner (demographics, medical and dental history, dental care utilization, dental care needs, oral hygiene care, oral health knowledge, self-efficacy in brushing behavior, Adaptive Leadership Self-Efficacy, Adaptive Leadership Behaviors – Cueing, and Adaptive Leadership Behaviors – FOCUSED Communication.



* Includes an Oral Health Evaluation (plaque index, gingival index, denture plaque index, OHAT); Assessment of oral hygiene behaviors (oral hygiene skill, frequency and duration of brushing); administration of questionnaires for participant and care partner including demographics, medical and dental history, dental care utilization, dental care needs, oral hygiene care, oral health knowledge, self-efficacy in brushing behavior, Adaptive Leadership Self-Efficacy, Adaptive Leadership Behaviors – Cueing, and Adaptive Leadership Behaviors – FOCUSED Communication.


Control Group
(N = 40)
Time 1
(Week 1)
Home visit to:
• Obtain written informed consent; perform baseline data collection and evaluations*
• Provide educational brochure
Time 2
(Week ~ 12)
Home visit to:
• Perform data collection and evaluation*
Time 3
(Week ~ 24)
Home Visit 3 to:
• Perform data collection and evaluation*
• Provide detailed explanation of the educational brochure
• Conduct exit interview with participant
Phone call to care partner for exit interview
* Includes an Oral Health Evaluation (plaque index, gingival index, denture plaque index, OHAT); Assessment of oral hygiene behaviors (oral hygiene skill, frequency and duration of brushing); administration of questionnaires for participant and care partner (demographics, medical and dental history, dental care utilization, dental care needs, oral hygiene care, oral health knowledge, self-efficacy in brushing behavior, Adaptive Leadership Self-Efficacy, Adaptive Leadership Behaviors – Cueing, and Adaptive Leadership Behaviors – FOCUSED Communication.

1.3 SCHEDULE OF ACTIVITIES

Treatment Group 1

Treatment Group 1	**Screening**	**Time 1 (Home Visit 1)** Week 1: (within 42 days of screening)	**Time 2** Week 4: (± 7 Days)	**Time 3** Week 8: (± 7 Days)	**Time 4 (Home Visit 2)** Week 12: (± 14 Days)	**Time 5** Week 16: (± 7 Days)	**Time 6** Week 20: (± 7 Days)	**Time 7 (Home Visit 3)** Week 24: (± 14 Days)
Screen for eligibility	X							
Obtain verbal informed consent	X							
Schedule Visit 1	X							
Obtain written informed consent		X						
Care Partner Questionnaire		X			X			X
Study Participant Questionnaire		X			X			X
Oral Health Evaluation		X			X			X
ADCS-ADL		X						
Oral Hygiene Skill Assessment Sheet		X			X			X
Coaching Module								
Tailored Oral Hygiene Instruction								

Treatment Group 1	**Screening**	**Time 1 (Home Visit 1)** Week 1: (within 42 days of screening)	**Time 2** Week 4: (± 7 Days)	**Time 3** Week 8: (± 7 Days)	**Time 4 (Home Visit 2)** Week 12: (± 14 Days)	**Time 5** Week 16: (± 7 Days)	**Time 6** Week 20: (± 7 Days)	**Time 7 (Home Visit 3)** Week 24: (± 14 Days)
Montreal Cognitive Assessment (MoCA)		X			X			X
Educational booklet provided		X						
Electronic Toothbrush Data Download			X	X	X	X	X	X
Detailed explanation of education booklet								X
Exit Interview w/participant								X
Exit Interview w/care partner								X (via phone)

Treatment Group 2

Treatment Group 2	**Screening**	**Time 1 (Home Visit 1)** Week 1: (within 42 days)	**Time 2** Week 4: (± 7 Days)	**Time 3** Week 8: (± 7 Days)	**Time 4 (Home Visit 2)** Week 12: (± 14 Days)	**Time 5** Week 16: (± 7 Days)	**Time 6** Week 20: (± 7 Days)	**Time 7 (Home Visit 3)** Week 24: (± 14 Days)
Screen for eligibility	X							
Obtain verbal informed consent	X							
Schedule Visit 1	X							
Obtain written informed consent		X						
Care Partner Questionnaire		X			X			X
Study Participant Questionnaire		X			X			X
Oral Health Evaluation		X						
ADCS-ADL		X						

Treatment Group 2	**Screening**	**Time 1 (Home Visit 1)** Week 1: (within 42 days)	**Time 2** Week 4: (± 7 Days)	**Time 3** Week 8: (± 7 Days)	**Time 4 (Home Visit 2)** Week 12: (± 14 Days)	**Time 5** Week 16: (± 7 Days)	**Time 6** Week 20: (± 7 Days)	**Time 7 (Home Visit 3)** Week 24: (± 14 Days)
Oral Hygiene Skill Assessment Sheet		X			X			X
Coaching Module		X	X (via phone)	X (via phone)	X			
Tailored Oral Hygiene Instruction		X			X			
Montreal Cognitive Assessment (MoCA)		X			X			X
Educational booklet provided and reviewed		X						
Electronic Toothbrush Data Download			X	X	X	X	X	X

Treatment Group 2	**Screening**	**Time 1 (Home Visit 1)** Week 1: (within 42 days)	**Time 2** Week 4: (± 7 Days)	**Time 3** Week 8: (± 7 Days)	**Time 4 (Home Visit 2)** Week 12: (± 14 Days)	**Time 5** Week 16: (± 7 Days)	**Time 6** Week 20: (± 7 Days)	**Time 7 (Home Visit 3)** Week 24: (± 14 Days)
Post Intervention Interview—participant					X			
Post Intervention Interview-Care partner					X (via phone)			
Exit Interview w/participant								X
Exit Interview w/care partner								X (via phone)

Control Group

Control Group	**Screening**	**Time 1 (Home Visit 1)** Week 1: (within 42 days)	**Time 2** Week 4: (± 7 Days)	**Time 3** Week 8: (± 7 Days)	**Time 4 (Home Visit 2)** Week 12: (± 14 Days)	**Time 5** Week 16: (± 7 Days)	**Time 6** Week 20: (± 7 Days)	**Time 7 (Home Visit 3)** Week 24: (± 14 Days)
Screen for eligibility	X							
Obtain verbal informed consent	X							
Schedule Visit 1	X							
Obtain written informed consent		X						
Care Partner Questionnaire		X			X			X
Study Participant Questionnaire		X			X			X
Oral Health Evaluation		X			X			X
ADCS-ADL		X						
Oral Hygiene Skill Assessment Sheet		X			X			X
Coaching Module								
Tailored Oral Hygiene Instruction								

Control Group	**Screening**	**Time 1 (Home Visit 1)** Week 1: (within 42 days)	**Time 2** Week 4: (± 7 Days)	**Time 3** Week 8: (± 7 Days)	**Time 4 (Home Visit 2)** Week 12: (± 14 Days)	**Time 5** Week 16: (± 7 Days)	**Time 6** Week 20: (± 7 Days)	**Time 7 (Home Visit 3)** Week 24: (± 14 Days)
Montreal Cognitive Assessment (MoCA)		X			X			X
Educational booklet provided		X						
Detailed explanation of education booklet								X
Electronic Toothbrush Data Download								
Post Intervention Interview—participant								
Post Intervention Interview-Care partner								
Distribution of a smart electronic toothbrush								X
Exit Interview w/participant								X
Exit Interview w/care partner								X (via phone)

2 INTRODUCTION

2.1 BACKGROUND

Oral health is a critical but often overlooked component of health and well-being in older adults. Oral health problems accumulate over the life span, but occur with increased frequency in later life. Evidence shows that oral health is associated with systemic diseases such as diabetes and cardiovascular diseases, and functional impairment, and mortality.[1-3] Oral health is an integral part of general health, quality of life, functional impairment, and mortality. Individuals with mild dementia are a subgroup of the older population that is at higher risk of poor oral health and significantly worse oral health related quality of life [4]; they have more oral plaque, more severe periodontal disease, more caries, and fewer teeth than cognitively intact older individuals. [5-7] Our study found that individuals with cognitive impairment (CI) are less likely to have regular dental visits.[8] These problems are not just an issue for those with advanced cognitive impairment. [9] One study has shown that individuals with dementia are 12 times more likely to have plaque on at least 50% of their teeth compared to individuals without dementia.[10] Another study reported that individuals with mild dementia have almost 3 times more decayed surfaces than individuals without dementia.[11] Participants in these studies ranged from mildly to severely demented, thus highlighting that oral health problems begin early in the long, insidious course of dementia. There is a critical need to address the health of this population because the number of the individuals impacted will increase exponentially due to the rapid expansion of the aging population in the U.S.[12,13]

Although there is clear evidence that persons with dementia have poor oral hygiene, there are a lack of interventions for this population. A few studies conducted in nursing homes have shown that with routine oral hygiene care, the oral health of persons with dementia improves notably in a short period of time.[14,15] However, there are many more individuals with dementia, particularly at the early stages of dementia, living in the community than in nursing homes. [16] Thus, our intervention aims to improve oral health and reduce the risk of oral health problems among individuals with mild dementia living in the community. Strong evidence suggests that inadequate oral hygiene practices are a major contributing factor for poor oral health. Our previous study found that only 36% of individuals with CI brushed their teeth twice per day, as compared to 72% of those with normal cognition. Frequency of toothbrushing was associated with better oral health outcomes among people with cognitive impairment.[8] This finding was consistent with well-established evidence that regular and proper toothbrushing helps prevent plaque build-up. Plaque control can lessen or prevent severe oral health conditions such as dental caries and periodontal disease. We propose that an intervention to improve the quality and frequency of toothbrushing for community dwelling individuals with CI would have similar positive results.

We are targeting the mild stage of dementia in this study because we believe that doing so will delay or prevent deterioration of oral health diseases and problems, maintain oral function, and minimize oral

discomfort as dementia progresses. Addressing oral health problems early in CI is a reasonable stage to intervene since the individual is still able to perform oral hygiene tasks with minimal assistance from an informal caregiver. Interventions for individuals with more advanced dementia may be more extensive. In the mild dementia or mild CI stage, the individual can be an active partner in solving the problem, increasing the likelihood of them cooperating. **To our knowledge, no oral health intervention studies have been conducted among community-dwelling individuals with mild dementia.** By intervening at this point, we aim to delay or prevent severe oral health problems, maintain oral function and minimize oral discomfort as the dementia progresses.

Informal caregivers play a pivotal role in caring for individuals with mild dementia and thus are an important resource for individuals with mild dementia. Three-fourths of the about 1.5 million individuals with mild dementia[17] in the U.S. receive assistance, reminders, or supervision for daily activities from caregivers such as spouses or adult children. [18] Yet, oral hygiene tasks are often neglected.[19] Structured assistance in the form of caregiver-assisted interventions has proven to be useful in studies of other outcomes involving individuals with mild dementia, such as improved memory performance.[20] Including the caregiver as a partner (i.e. care partner) in the intervention has distinct benefits in preventing oral health decline among individuals with mild dementia. To our knowledge, this will be the first intervention incorporating assistance of informal caregivers to improve oral health for individuals with mild dementia[21,22]. Our rationale is that individuals with mild dementia characteristically have trouble learning complex new tasks or performing multi-step tasks, such as following a recipe or performing complex household chores; yet they retain procedural memory, the ability to remember how to perform simple well-learned everyday tasks. The basic steps and motions involved in toothbrushing use procedural memory.[23] Thus, individuals with mild dementia often can continue to perform routine hygiene tasks to a large extent independently. In this intervention, care partners will learn to create routines and break oral care into discrete steps that will help lead the participant through the procedures of oral self-care.

The third significant aspect of our study is our use of an objective measure of toothbrushing behavior. Most interventions have relied on self-reported information on frequency and duration or toothbrushing. Even cognitively intact adults are susceptible to recall errors.[24] Among memory impaired individuals, this issue is even more of a problem. Thus, we will use a smart electronic toothbrush that records time and duration of use, providing a more reliable and valid assessment of behavior than self-report.

2.2 STUDY RATIONALE

Close to 9% of adults age 65 and older in the U.S. have dementia [25] and individuals with dementia have significantly poorer oral health (e.g., more oral plaque, more severe periodontitis, more caries, and fewer teeth) than cognitively intact older adults.[5-9] Even individuals with cognitive impairment (CI) are at higher risk of poor oral health and evidence is strong to suggest that inadequate oral hygiene practices are a major contributing factor.[8,9] Maintaining good oral hygiene is a critical step in preventing

deterioration of oral health. Because care partners play an essential role in supervising and caring for individuals with mild dementia at home, intervention with both the individual with mild dementia and their care partners on methods for improving oral health may have long term oral health benefits for the individuals with mild dementia. Yet, few interventions have addressed oral health problems among older adults in general or among individuals with mild dementia in particular, and to our knowledge, no oral health interventions have been conducted among community-dwelling individuals with mild dementia. To address this gap in knowledge, we developed a novel intervention to help care partners learn to guide the individual with mild dementia to carry out oral hygiene care.

The overall aim of the intervention is to help care partners learn to guide the individual with mild dementia to carry out oral hygiene care. Specifically, *we help care partners to become "adaptive leaders" defined as someone who has ability to foster others to change behaviors and develop new skills[26] such as better oral care, while optimizing their independence.*[27] Oral hygiene is an activity of daily living that can be easily overlooked, as participants in our pilot study reported, particularly when the individual with cognitive impairment has challenges in execution due to cognitive changes.[28] In our intervention, care partners will learn a variety of approaches to reduce or eliminate the challenges the individual with mild dementia has with oral care. We expect that the flexibility and creativity gained by care partners as adaptive leaders will help the individual with mild dementia maintain better oral health outcomes and thus a higher quality of life. Heretofore, we will use the term participant for the individual with mild dementia.

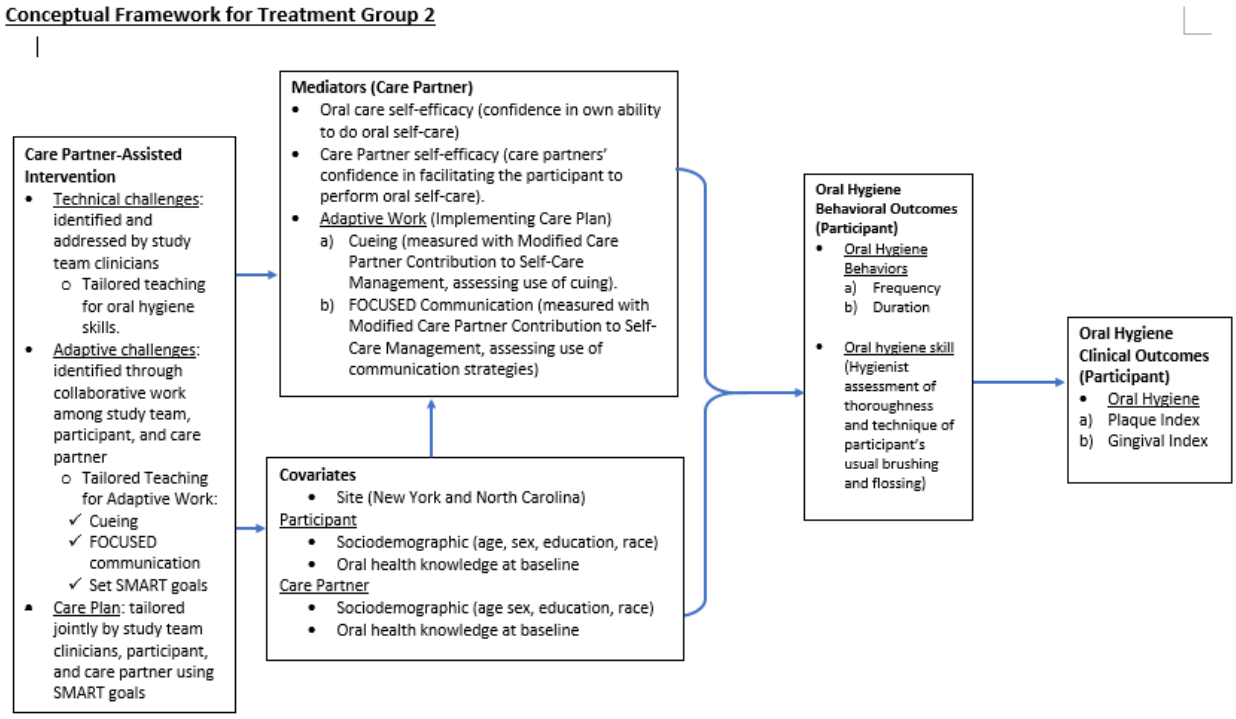
We used the Adaptive Leadership Framework for Chronic Illness[26] to guide development of the care partner-assisted intervention. The framework specifies four main concepts that we have embedded into the intervention: technical challenges, adaptive challenges, collaborative work and adaptive leadership. Because we view the care partner as the leader of change in the dyad, we propose that the intervention works through the mediators of 1) oral care self-efficacy of care partner; 2) care partner adaptive leadership self-efficacy, that is, confidence facilitating the participant to perform oral self-care; and 3) care partner adaptive work which entails the adaptive leader behaviors of cueing and focused communication (Figure 1). In turn the mediator variables will relate to better oral hygiene behavioral outcomes (i.e., frequency and duration of toothbrushing and oral hygiene skill of the participant) and finally to oral hygiene clinical outcomes (i.e., plaque and gingival indexes of the participant).

Fully combined, the intervention activities suggest these propositions:

- Tailored teaching to identify and address technical challenges combined with tailored teaching for adaptive challenges and adaptive leadership, and a jointly tailored care plan with SMART goals will lead to improved oral hygiene behavioral outcomes and better oral hygiene clinical outcomes of the participant (Objective 1).
- Care partner factors (oral care self-efficacy of care partner, adaptive leadership self-efficacy and use of adaptive leadership behaviors by the care partner) will mediate the relationship between the intervention (tailored teaching to identify and address technical challenges combined with

tailored teaching for adaptive challenges and adaptive leadership, and a jointly tailored care plan with SMART goals) and oral hygiene behavioral outcomes and better oral hygiene clinical outcomes of the participant (Objective 2a, 2b).

- Changes in oral hygiene behavior outcomes will mediate the relationship between the intervention and oral hygiene clinical outcomes of the participant. The impact of the intervention on oral hygiene clinical outcomes will be mediated by care partner's factors, and then further mediated by the oral hygiene behavioral outcomes (Objective 3a, 3b).



2.3 RISK/BENEFIT ASSESSMENT

2.3.1 KNOWN POTENTIAL RISKS

Oral health evaluation: The clinical oral evaluations involve some manipulation of the gingiva, which may cause mild discomfort and bleeding. No periodontal probing will be performed during the oral health evaluation, and thus risk to participants is minimal.

Breach of Confidentiality: There is a small risk that unauthorized persons could get access to personal or study-related participant information.

Questionnaires and Cognitive Screening: Individuals may feel self-conscious about their cognitive weaknesses when completing the cognitive screening instrument. However, they will have completed similar tests before since they currently have a diagnosis of mild dementia; thus, it is expected that this familiarity will attenuate any discomfort. In addition, our study coordinators will be trained specifically to address the individual's concerns and to provide appropriate reassurances. The other questionnaires may seem somewhat tedious, but there is no other negative risk related to completing the measures.

2.3.2 KNOWN POTENTIAL BENEFITS

If the study shows that the intervention does improve oral hygiene status and oral hygiene behaviors, then the use of such an intervention could potentially benefit future persons with mild dementia. In addition, the oral evaluations performed as part of the study might help to detect oral health needs for which the participant can be referred for care.

The intervention is also expected to help the dyad improve communication to aid in accomplishing oral hygiene. As our participants and care partners have reported in post-intervention interviews of a pilot study, they have been able to use these communication skills in several other areas of personal care or home life.[45]

2.3.3 ASSESSMENT OF POTENTIAL RISKS AND BENEFITS

Protections Against Risk

Oral health evaluation: The dental hygienists are experienced in oral evaluations for older adults with mild dementia. Additionally, the study dentists and hygienists have expertise working with this population and they will receive training in study and safety protocols. Procedures are in place to address the risk of bleeding, should it occur.

Breach of Confidentiality: Paper and pencil copies of all study materials are coded with a unique participant ID number and do not contain participant names. Complete questionnaires will be kept in the possession of the study staff, such as in a locked car trunk or locked brief case, until they are delivered to a locked file cabinet in the study office. Several portions of the home visits and telephone coaching modules will be recorded on encrypted audio recording devices. After each evaluation or coaching module, the digital, audio recording will be downloaded into the secure server within 24 hours and stored with the unique ID code. During the period prior to the file transfer from the recording device, the device will be in the secure possession of the study team such as in a locked car trunk or locked brief case. Upon verification that the recordings have been transferred securely into the secure study server, the audio recordings residing on the recording devices will be destroyed. All study data will be stored separately from signed consent forms.

Questionnaires and Cognitive Screening: To address potential for self-consciousness about their cognitive weaknesses when completing the cognitive screening instrument or answering questions about personal oral hygiene, our study staff will be trained specifically to address the individual's concerns and to provide appropriate reassurances. The participant will have completed similar cognitive tests before since they currently have a diagnosis of mild dementia; thus, it is expected that this familiarity will attenuate any discomfort. In addition, the study staff will receiving training in how to ask potentially sensitive questions regarding oral hygiene to reduce potential for discomfort by participants.

Depression Symptoms: If a participant endorses significant clinical symptoms and is not being treated for depression, the study team will encourage the dyad to discuss the problem with the primary care physician. In the unlikely event that a participant reports suicidal ideation with a plan to carry it out, then the study team would page an MD on call. At Duke, this would be co-investigator James Burke, M.D., PhD, Professor of Medicine and Psychiatry, Bryan Alzheimer's Disease Research Center. At NYU, this would be Thomas Wisniewski, MD, Neurologist at NYU Langone School of Medicine.

Potential benefits weighted against risks

The potential benefits outweigh the relatively minimal risks in this study. The risks discussed above will all be minimized by the procedures to be implemented as part of the data collection protocol and data processing procedures. Confidentiality risks are virtually eliminated by the special procedures adopted to separate identifying information from data records and by interviewer training procedures, which guard against breach of information in the field.

3 OBJECTIVES AND ENDPOINTS

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS	PUTATIVE MECHANISMS OF ACTION
Primary			
To evaluate the efficacy of an intervention to improve oral hygiene clinical outcomes (i.e. plaque index and gingival index) by improving oral hygiene behavior (i.e., frequency and duration of toothbrushing) and oral health skills among individuals with mild dementia.	Oral Hygiene Clinical Outcomes 1. Plaque Index 2. Gingival Index Oral Hygiene Behavioral Outcomes 3. Frequency of toothbrushing • Duration of toothbrushing Oral Health Skill	Both the plaque and gingival indexes are objective measures. Plaque has an etiologic role in causing gingival inflammation. Gingivitis is preventable with good oral hygiene and plaque removal.	Tailored teaching to identify and address technical challenges combined with tailored teaching for adaptive challenges and adaptive leadership, and a jointly tailored care plan with SMART goals will lead to better oral hygiene behavioral outcomes and better oral hygiene clinical outcomes of the participant**.**
Secondary			
2A. To determine whether effects of the **intervention [X]** on **oral hygiene behavioral outcomes [Y]**, are mediated by the following variables from the care partners' perspective: 1) oral care self-efficacy; 2) adaptive leadership self-efficacy; 3) use of cueing methods; 4) and FOCUSED Communication **2B.** To determine whether effects of the **intervention [X]** on **oral hygiene clinical outcomes [Y]**, are mediated by the following variables	Endpoints as above. Mediators: • Oral care self-efficacy • Adaptive leadership self-efficacy • Cueing • FOCUSED Communication	As above.	Tailored teaching to identify and address technical challenges and coaching to address adaptive challenges will increase care partner's oral care self-efficacy and adaptive leadership self-efficacy, and use of adaptive leadership behaviors by the care partner. Oral care self-efficacy of care partner, adaptive leadership self-efficacy and use of adaptive leadership behaviors by the care partner will mediate the relationship between the intervention (tailored teaching to identify and address

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS	PUTATIVE MECHANISMS OF ACTION
from the care partner's perspective: 1) oral care self-efficacy; 2) adaptive leadership self-efficacy; 3) use of cueing methods; 4) and FOCUSED Communication.			technical challenges combined with tailored teaching for adaptive challenges and adaptive leadership, and a jointly tailored care plan with SMART goals) and oral hygiene behavioral outcomes and better oral hygiene clinical outcomes of the participant.
3a. To determine whether effects of the **intervention [X]** on **oral hygiene clinical outcomes [Y]** are mediated by **oral hygiene behavioral outcomes [M]**. **3b.** To determine whether effects of the intervention [X] on oral hygiene clinical outcomes [Y] is mediated by the care partner's factors [M1], which then mediates the oral hygiene behavioral outcomes [M2] on oral hygiene clinical outcomes [Y].	Oral Hygiene Clinical Outcomes 4. Plaque Index 5. Gingival Index	As above.	As stated above, the proposed intervention will increase care partner's oral care self-efficacy and adaptive leadership self-efficacy, and use of adaptive leadership behaviors by the care partner. Prior research is clear about the relationship between oral hygiene behaviors and oral hygiene clinical outcomes. Thus, in our model, we propose that the endpoint outcomes (plaque and gingival index) follow from improving care partner's factors, and improving oral hygiene behaviors.

4 STUDY DESIGN

4.1 OVERALL DESIGN

This study is an open-label, randomized, multi-site trial to evaluate the effectiveness of an oral health intervention among individuals with mild dementia.

There will be two sites for the intervention: Duke University in Durham, North Carolina, U.S., and New York University, NY. At these sites, recruited dyads will be randomly assigned to one of three groups; Treatment group 1, Treatment group 2, and Control group. IRB approval will be obtained from these two participating sites.

The study lasts 6 months. The first three months is the active intervention phase in which coaching and educational modules are delivered to Treatment group 2. The second three months is the maintenance period in which no coaching or educational modules are presented to participants or care partners. As a team, the study coordinator, the dental hygienist, and the interventionist will conduct three visits with the participants and their care partners; baseline, 3-month (end of the active intervention phase), and 6-month (end of three-month maintenance phase).

Prior to the first study visit, Study Coordinators will pre-screen potential participants based on the inclusion and exclusion criteria. They will obtain basic medical history and verbal informed consent. If participants qualify for the study, the coordinator will schedule the first study visit with the participant and their care partner within the six weeks. Because the procedures and personnel involved in the study visits differ based on the arm of the study to which a participant is assigned, randomization must be done prior to the first visit.

The study participants will be instructed not to eat or brush their teeth for one hour before the scheduled visit and oral health evaluation. During the visit, the dental hygienist will conduct an oral health evaluation. A standard booklet of oral health educational materials will be given to all participants. Additional intervention elements apply to the treatment groups:

Participants in Treatment Group 1 and Treatment Group 2 will receive two smart electronic toothbrushes that collect the time, date and duration of brushing (each toothbrush stores approximately 15 days of the brushing data). The study coordinator will download the toothbrush data on a monthly basis to allow sufficient memory storage space for subsequent data collection. Participants in Treatment Group 2 will be asked to self-report oral hygiene behavior using a calendar log throughout the study. They will also receive individualized instruction on oral hygiene technique, cueing strategy development, oral hygiene monitoring, and coaching four times over the course of the first 3 months of the study. One module is delivered at the first visit, the next 2 are delivered telephonically at 1 month and 2-month time points, and the final module is delivered at home visit 2.

4.2 SCIENTIFIC RATIONALE FOR STUDY DESIGN

Our design includes three groups:

- Control Group participants will receive an educational booklet only and will continue their usual brushing techniques (manual or electric). They will receive a smart electronic toothbrush at the end of the study (at home visit 3)
- Treatment Group 1 participants will receive an educational booklet and 2 smart electronic toothbrushes.
- Treatment Group 2 participants will receive an educational booklet, 2 smart electronic toothbrushes, and in-home and telephone coaching.

In our pilot study, both the treatment (treatment group 2) and the comparison group (treatment group 1) improved in their oral hygiene outcomes. Thus, in the present study, we have added a usual care control group to address the possibility that the smart electronic toothbrush itself may serve as an intervention ingredient.

4.3 JUSTIFICATION FOR INTERVENTION

Mode of intervention delivery: The intervention uses a combination of in-home face-to-face and telephone delivery. Recent meta-analyses demonstrate that both face-to-face and telephone (or other technology) intervention delivery are effective when the caregiver is the focus of the intervention[29,30] but a combination of approaches was found to be most effective.[31] A systematic review found face-to-face delivered interventions with caregivers were most effective for skill-building intervention such as ours.[30] Because of this evidence and because our intervention includes both the individual with mild dementia and the care partner, we chose to use a combination of face-to-face and telephone contact.

Minimum-acceptable participation in, or exposure to, the intervention in order to have evaluable data.

Three months is the Minimum acceptable length of participation in order to have evaluable data. See section 6.1.2 for dosing determination.

4.4 END-OF-STUDY DEFINITION

A participant is considered to have completed the study if he or she has completed the baseline assessment, all 4 coaching modules (if applicable), the 3-month study visit, and the final 6-month study visit.

The end of the study is defined as completion of the 6-month follow up visit shown in the Schedule of Activities, Section 1.3.

5 STUDY POPULATION

5.1 INCLUSION CRITERIA

Participant eligibility is determined according to the following criteria:

- The participant is 60 years or older.
- The participant has been given a diagnosis of mild dementia within the past year. The following guidelines will be used to differentiate between a diagnosis of mild dementia vs moderate/severe dementia: a) a diagnosis of dementia by a physician with dementia expertise, b) from medical records, a recent Montreal Cognitive Assessment (MoCA) score > 14 or a Mini-Mental Status Examination (MMSE)score > 16, and c) can follow 2 to 3-step commands.
- The participant has at least 4 natural teeth.
- The participant is community dwelling.
- The participant lives with an informal, unpaid, care partner who is 18 years or older and who is willing to participate in the study.
- The participant is physically able to brush their own teeth.
- Able to speak and understand English.

5.2 EXCLUSION CRITERIA

Any participant who meets any of the following criteria will not qualify for entry into the study:

- The participant is unable to have an oral health evaluation.
- The participant is prescribed anti-biotics prior to a regular dental visit.
- In the opinion of the investigator, the participant has sensory or physical problems that prevent participation in the intervention.
- In the opinion of the investigator, the participant has a terminal illness or behavioral or psychiatric disorder that would interfere with participation in the intervention.
- The participant has a medical condition that places him/her at greater risk of infection from the manipulation of the gums to measure the gingival index. These conditions are serious congenital heart conditions, previous infective endocarditis, prosthetic cardiac valves, and cardiac transplantation with cardiac valvulopathy.
- The participant has a medical condition that suppresses the immune system.
- The participant has had a total joint replacement and has had an infection in the replaced joint.
- The participant is at increased risk of bleeding due to a bleeding disorder such as having hemophilia or the use of antiplatelet or anticoagulant medications.

5.3 LIFESTYLE CONSIDERATIONS

There are no lifestyle considerations once a person is enrolled in the study. However, individuals who recently have had a periodontal treatment including a regular cleaning will have their study visit postponed until three weeks after the dental visit. We will document all dental visits during the active treatment phase.

5.4 SCREEN FAILURES

Screen failures are defined as individuals who agree to participate in this study but are not subsequently assigned to the study intervention or entered in the study.

Individuals who do not meet the criteria for participation in this trial (screen failure) because of meeting one or more exclusion criteria that are likely to change over time may be rescreened. Examples include the discontinuation of a prohibited medication or the recent availability of a care partner. Rescreened individuals will be assigned the same participant number as for the initial screening.

5.5 STRATEGIES FOR RECRUITMENT AND RETENTION

We anticipate screening by telephone about 680 individuals to enroll 120; this number increases to about 850 if our targeted enrollment is increased to 150 for this study. Our experience has shown that we generally need to screen a proportionally higher number of males and racial/ethnic minority groups to enroll the targeted number in those groups.

At both sites, we will recruit from local clinical sites with large numbers of individuals diagnosed with mild dementia. At NYU, we will recruit participants from NYU Alzheimer's Disease Research Center (ADRC), a part of the Department of Neurology at NYU Grossman School of Medicine. Dr. Thomas Wisniewski (Co-Investigator) is Director of the NYU ADRC. The NYU site will also recruit from the Pearl I. Barlow Center for Memory Evaluation and Treatment at NYU Langone. The Center sees about 420 patients with mild dementia annually, of which about 79% are White, and the others come from diverse racial/ethnic groups.

At Duke University, we will recruit from the Duke Memory Disorders Clinic (Duke MDC). James Burke, MD, PhD, a Co-Investigator on this project was the director of the Duke MDC for several years. The Duke MDC sees an estimated 600 new patients and about 1700 return patients each year; about 40% of these are in the mild dementia range.

At the medical clinics and centers at both NYU and Duke, potential participants will be identified by the provider or medical records. These individuals will be sent a letter from the provider or contacted by recruitment staff introducing the study and stating that a study coordinator will call them to explain more about the study and to inquire of interest and assess eligibility for participation in the study.

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At NYU, DataCore or EPIC information will be one method used for recruitment, including the use of SlicerDicer. Recruitment staff will submit a request form to DataCore. The results of any EPIC search will be accessed by the study coordinator, recruitment coordinator, and the principal investigator. Initial queries will be based on age and gender, as well as the studies inclusion/exclusion criteria. Unless eligibility criteria changes, Epic DataCore will be used up to every six months to sufficiently identify patients who have been seen in the six-month time period. Staff will only be contacting patients who have previously agreed to be contacted for future studies as filtered by DataCore. Potential subjects will be contacted via telephone or email. Once contact is made, approved recruitment language will be used to communicate the reason they are being contacted and potential subjects will be asked if they are interested in participating in this specific study. Since participants will be recruited primarily from the Barlow Center where the recruitment coordinator is located, the treating physician agrees to permit study team to directly contact potential subjects on behalf of the treating physician. Should the potential subjects agree; the study team will provide the subjects with information regarding the next steps for participation. Potential subjects obtained through DataCore who express interest in participating will be administered an IRB approved phone screening by a study team member, mainly by the study coordinator (refer to Section 8.1). Any recruitment information sent by email will utilize Send Safe email.

In addition to utilizing Epic and DataCore to procure a list of potentially eligible participants, the NYU team will be also utilizing Epic/DataCore for MyChart recruitment. Epic MyChart has the ability to send IRB approved research recruitment messages to patients with an active MyChart account. Epic MyChart recruiting has the ability to identify highly qualified patients and electronically communicate with them directly using the MyChart patient Inbasket system. Similar to obtaining a DataCore list, a study team member will submit a request utilizing Epic SlicerDicer to identify a cohort of individuals that may be eligible for study participation. Only those individuals who select that they would like to learn more will be moved to a research recruitment Epic folder for further contact.

At both sites, we will also recruit participants via alliances with clinical specialists at other medical facilities and via contacts with dementia support groups, community facilities, organizations, and at outreach events. Study related presentations and flyers will be used at the above noted venues.

Screening forms for potential subjects who are deemed ineligible or who refuse to participate will be discarded. Study team will have a database of the ineligible subjects to ensure that the study does not unnecessarily contact an individual multiple times. This database will only include the name and phone number of the potential subject and no additional PHI.

We have extensive experience in recruiting and retaining older adults, including historically under-represented populations, in longitudinal studies. In regard to under-represented groups, particularly minorities, for several years, the Duke Bryan Alzheimer's Disease Research Center (Duke ADRC) has focused efforts on developing relationships with minorities in the community through targeted outreach events. These efforts have resulted in our meeting goals of between 15 – 50% enrollment of African Americans for various studies. We will leverage these already established relationships to recruit for the present study.

We expect these recruitment sources will meet our enrollment goals because of large volume of patients at these sites. In addition, often those patients who seek treatment at academic sites have an interest in participating in clinical trials. More importantly, we have successfully recruited a diverse group of participants from the two Duke sources for our pilot studies described above and numerous prior other studies.

Our plans to retain participants in this six-month intervention include 1) ensuring that the individuals understand the purpose and benefit of the study, 2) being responsive to their inquiries, and 3) sending visit confirmation letters and visit reminder phone calls. Our incentive fee schedule is structured to pay a larger amount at the last visit, which may have some influence on retention. We think the factor that most impacts participants' decision to complete a study is a sense that the research team respects them as individuals and is committed to improving the lives of those with mild dementia.

We will pay the participant and the care partner each the following amounts: $20 at Visit 1, $20 at Visit 2 and $40 at Visit 3. This amount provides some compensation for their time, but is not sufficient to be coercive.

6 STUDY INTERVENTION(S) OR EXPERIMENTAL MANIPULATION(S)

6.1 STUDY INTERVENTION(S) OR EXPERIMENTAL MANIPULATION(S) ADMINISTRATION

6.1.1 STUDY INTERVENTION OR EXPERIMENTAL MANIPULATION DESCRIPTION

Control Group

The Control group intervention includes a standard educational booklet and clinical oral health evaluation with no instruction on oral hygiene technique. The educational booklet is the same one delivered to the intervention groups. The oral health evaluation is detailed in procedures below. The dental hygienist will observe the participant's normal toothbrushing technique, interdental cleaning procedures, and the cleaning of partial dentures. No instruction is provided.

Treatment Group 1

The Treatment group 1 intervention includes the standard educational booklet, clinical oral health evaluation and a smart electronic toothbrush with no instruction on oral hygiene technique. The educational booklet is the same standard one that is delivered to all groups. The oral health evaluation is detailed in procedures below. The dental hygienist will observe the participant's normal toothbrushing technique, interdental cleaning procedures, and the cleaning of partial dentures. No instruction is provided. The hygienist will provide basic instruction on proper use of the smart electronic toothbrush.

Treatment Group 2

The Care Partner-Assisted Intervention includes the standard educational booklet, clinical oral health evaluation with tailored instruction on oral hygiene technique, and care partner coaching. These components are summarized in Table 2 (below). The two intervention components (i.e., tailored instruction and coaching) are interrelated and thus the hygienist and interventionist work together as described below.

Table 2: Care Partner (CP) Assisted Intervention Components

Component	Who/Where	When
1. In-home oral exam • Oral health educational booklet, given on first visit • Oral health evaluation • Assessment of technical challenges and tailored instruction on oral hygiene technique • **Create Oral Hygiene Treatment Plan using Dental Hygienist's Guidance), given on baseline visit and 3-month visit** • List tailored recommendations for oral care for dyad (to be integrated in care partner assisted coaching modules), given on baseline visit and 3-month visit • Monitoring of oral hygiene by dyad	Participant, CP, hygienist, and interventionist Home visit	· Baseline · 3 months. · 6 months.
2. **Care Partner- Assisted Coaching Modules** 1. **Module 1**: Assessment of adaptive challenges; and teach cueing strategies for CP to support collaborative work with participant; review hygienist's oral hygiene treatment plan and integrate into goal setting; evaluate motivation and self-efficacy.	CP, participant, interventionist Home visit, (participant joins for final 10 minutes.)	Baseline
2. **Module 2:** Review module 1 content; CP learns and practices advanced communication strategies (e.g., FOCUSED) and reviews cueing strategies. Assess adaptive challenges and problem solve applying learned communication and cueing strategies; update goals, and re-establish SMART goals and support motivation and self-efficacy.	CP, participant and interventionist Phone	4 weeks
3. **Module 3:** Reassess adaptive challenges and progress on goals; review and apply communication and cueing approaches, problem solving to support collaborative work between the CP and participant to establish oral hygiene behaviors.	CP, participant and interventionist Phone	8 weeks
4. **Module 4:** Review hygienist's plan of care; engage dyad in assessing successes and challenges in meeting oral care goals; Review communication and cueing strategies as needed; address self-efficacy and motivation for sustaining oral care behaviors.	CP, participant, interventionist Home visit, (participant joins for final 10 minutes.)	3 months

Intervention Components, At-Home Visits:

Each dyad will receive 3 at-home visits: baseline, 3-month (end of the active treatment phase) and 6-month (end of the maintenance phase).

Educational booklet. (All groups) We created an educational booklet that includes information on: 1) connections between oral health and systemic diseases and ways to improve awareness of dental problems; 2) importance of oral hygiene and recommended daily practices; 3) potential risk to oral health of unhealthy lifestyle behaviors and medication side effects; 4) common signs of oral diseases and conditions; and 5) preventive oral care strategies. The material is written at a 6th grade level.[21] The booklet is given to dyads at the first visit. The booklet is reviewed at different visits for the various groups. Because the booklet is given to both intervention and control groups, it does not address adaptive challenges. However, it addresses some common technical challenges and solutions, such as proper brushing technique.

Clinical Oral Health Evaluation. (All groups) The hygienist performs an oral health evaluation (see detailed procedures in Section 8.1 Endpoint and other Non-Safety Assessments). The evaluation is used by the hygienist to guide tailored recommendations for the treatment plan for participants assigned to Treatment Group 2.

Assessment of technical and adaptive challenges and instruction. (Treatment Group 2) This assessment is completed in the location where the dyad normally does oral care, usually a bathroom with a large mirror over the sink. Because the interventionist and the care partner must integrate the tailored instruction, they both will observe. Standing in front of a mirror, the dental hygienist will ask the participant to brush using his/her normal toothbrush to assess the participant's toothbrushing technique and begin to identify technical challenges and areas for specific feedback on technique, including areas of the dentition missed in brushing. S/he will then demonstrate the proper technique on a mouth model using a smart electronic toothbrush. Standing in front of a mirror, participant will then be asked to brush her/his teeth again, using the smart electronic toothbrush and the technique demonstrated. This approach is based on the approach developed by others[32] for the clinical setting and adapted for the in-home setting. We will recommend use of interdental cleaning aids. Using the same approach as above, the hygienist will assess interdental cleaning by participants and assess cleaning partial dentures, if applicable. The hygienist will demonstrate the correct cleaning techniques and ask the participant to return-demonstrate. The participant and care partner will then be shown how to use a disclosing tablet to identify areas of dentition missed in brushing. The care partner is given an electronic toothbrush to support the collaborative effort of the dyad in regular and appropriate oral hygiene behavior. The care partner is also asked to demonstrate use of the electronic toothbrush to ensure that s/he understands. The oral hygiene technique assessment will be conducted at each visit. Examples of technical challenges that might be identified include limited hand dexterity which will guide selection of the right tool for interdental cleaning, or gum conditions that might guide recommendations

for reducing pressure during brushing and eliminating "sawing" motions. Associated adaptive challenges might include knowledge deficits regarding effective frequency for toothbrushing, lack of motivation for oral hygiene, or a dislike of flossing. These challenges become part of the treatment plan and coaching modules as described below.

***Create Oral Hygiene Treatment Plan*.** (Treatment Group 2) The dental hygienist reviews findings from the participant oral health evaluation with the participant and care partner, with the interventionist present, and provides detailed feedback on treatment and prevention of oral health conditions and symptoms. S/he also develops the written Oral Hygiene Treatment Plan. The tailored plan is provided at baseline and Visit 2.

Tailored Recommendations. (Treatment Group 2) The hygienist will present a list of tailored recommendations which outline the options for technical work for the participant to accomplish during the next 3 months. These recommendations are delivered at the end of the care partner session (see below) at which time the hygienist, interventionist and the participant and care partner together develop an individualized program which integrates any additional adaptive challenges identified in the care partner session.

Monitor Oral Hygiene. (Treatment Groups 2) Oral hygiene will be monitored using 3 approaches. A data recording toothbrush will be used to measure frequency and duration of participant's toothbrushing. Plaque disclosing tablets will be used by the dyad to assess the quality of the brushing behavior and the dyad will record oral care activities on a paper calendar log. First, participants will be given a smart electronic toothbrush that has been adapted to record the date, time, and duration of use, providing an objective measure of oral hygiene behavior. To monitor the quality of oral hygiene behavior, care partners will be asked to assist the participant with using plaque disclosing tablets to check the quality of toothbrushing once per week, taking about 10 minutes. Disclosing tablets temporarily stain plaque red to help individuals see the areas of accumulation of plaque that need more attention when brushing. The care partner and participant will be instructed to document on a log the frequency and duration of toothbrushing. In Treatment Group 2, this information will be discussed during the monthly phone calls and the completed log will be collected at home visit 2 and home visit 3.

Intervention Components, Coaching Modules: (Treatment Group 2)

Interventionists will conduct 4 coaching modules, 2 in home, face to face (baseline and 3 months) and 2 by phone, evenly spaced between baseline and 3 months. The 4 coaching modules build from basic to more advanced and provide opportunities for role-playing by the care partner to practice cueing and communication techniques that s/he can use to motivate and encourage the participant to carry out oral self-care. The participant joins in the final portion of the coaching modules for assessment of motivation and goals setting. To maximize fidelity of delivery, the modules are scripted with directions to the interventionist for how to deliver it conversationally with probes where appropriate. The module details are described in Table 2. An overview of the main therapeutic strategies are described below.

Three primary sets of tools are learned by caregivers, 1) cueing, 2) dementia specific communication, and 3) goal setting. Cueing and goal setting are introduced in module 1 and communication strategies are introduced in module 2. All strategies are reviewed in succeeding modules following their introduction.

Cueing Strategies: Cueing strategies are considered adaptive because they encourage the participant's independence and use his/her existing capacity for self-care. The interventionist will help the participant and their care partner design visual cues, such as placing the toothbrush in plain sight, putting a week's supply of flossing tools in a cup so they can visually monitor use as the number declines over the week, or taping a reminder to the mirror. The interventionist also will help the care partner learn to use verbal and tactile cueing strategies. The care partner will learn to use verbal cues that are simple and direct, such as "pick up the toothbrush," and tactile cues such as touching the participant's hand to guide a new way of angling the toothbrush head and moving it across the tooth surface. The interventionist and care partner will discuss how to use the cues when the participants travel away from home. Because cueing, if not done properly, might be interpreted by the participant as nagging, the coaching modules address this potential; care partners learn and practice cueing in ways that are focused on doing things together, rather than "telling" the participant what to do. Furthermore, interpersonal relationships between the participant and the caregiver will vary, thus the modules address how to establish the most effective plan for improving oral hygiene activities that preserves and/or improves the relationship.

Communication Strategies: FOCUSED stands for encourage face-to-face communication; orienting participant to topic; continuity—avoid shifting from topic to topic; helping the participant unstick when s/he is word searching; use structure by posing clear yes/no choices; speaking in ways that encourage conversation; and using direct, short, simple sentences. When introduced, and in subsequent coaching sessions, the interventionist engages the care partner in role playing to practice each strategy. Particular attention is paid to the dyad relationship and how to use the strategies in ways that support the relationship and the participant. The strategies also aim to maintain as much independence by the participant as possible.

Goal Setting: For goal setting we use the SMART recommendations,[33] defined as specific, measurable, attainable (agreed), realistic, and timed, which have been used successfully in a variety of fields, including occupational therapy,[34] rehabilitation,[33] and nursing.[35,36] At the end of the coaching modules delivered in-home (i.e., 1 and 4), the participant and hygienist join the care partner and interventionist to review hygienist recommendations and then the care partner and interventionist engage the participant in setting 1 to 3 SMART goals. They will discuss how to advance a goal each week if successful performance is achieved. Progress on goals is assessed during each coaching session and new goals are set if appropriate. If goals are not met, the interventionist and care partner explore barriers, discuss strategies to overcome using the cueing and communication tools and then work with the participant to revise the goal. Typical goals in our pilot have included reducing pressure while brushing, using the correct angle and downward sweep of the brush head, and increasing frequency of flossing.

6.1.2 ADMINISTRATION AND/OR DOSING

Dose of the of this behavioral intervention is captured by length, number and frequency of intervention contacts.

Length: The intervention has an active period (3 months) and a maintenance period (3 months) for a total of 6 months from baseline to final endpoint measure. The active period of 3 months was chosen to allow time for participants to learn the oral care techniques and then have time to engage in the new oral hygiene behaviors to impact plaque and gingival indexes. We determined the appropriate length in preliminary work done during in the R34 with internal pilot funded. The length of the study visit was refined during the pilot to take about 2 hours and occur in 15-minute increments to accommodate the various activities and roles of study staff, while minimizing burden on the participant and care partner. During the visit, both the participant and care partner alternate between joint intervention activities (done with both the participant and care partner) and individual activities. For example, while the hygienist is doing the oral hygiene evaluation on the participant, the care partner is engaged in the coaching session with the interventionist.

Number and Frequency: The intervention includes 3 home visits and 2 telephone contacts (for care partner coaching). The rationale for 3 home visits is to minimize burden on the participant and care partner while meeting study objectives of obtaining baseline measures, measures following the active period (3 months) and measures following the end of the maintenance period (6 months from baseline). The baseline and month 3 home visit serve also to provide for face-to-face intervention delivery during which the focus is on skill building.[30] The two phone contacts are equally spaced between baseline and 3 months to continue the intervention coaching with the care partner and participant. This timing allows use of the combination of face-to-face and telephone delivery which are found to be effective in prior research[31] and provide for efficient use of participant and care partner's time.

6.2 FIDELITY

6.2.1 INTERVENTIONIST TRAINING AND TRACKING

We use the NIH Behavior Change Consortium's treatment fidelity model [16] to ensure design fidelity, we developed the care partner intervention components to closely align with the study's guiding framework [16] and we standardized the protocols to a specified dose in terms of number, frequency, and length of contact.

Hygienist Training

The hygienists will be trained on the key points that differentiate intervention activities for the three study groups, in particular, we will emphasize that the tailored care plan occurs only for Treatment Group 2. To ensure the fidelity of the hygienist delivered intervention components, a PI or designee will

be present at the home visits of the two dyads within the first five enrolled to evaluate fidelity to the protocol. Also, all encounters will be audio recorded digitally and will be checked on a random schedule by a PI or designee to assess adherence. The team members and PIs will discuss adherence results and problem-solve barriers to adherence with repeat of concepts and role-play as needed.

Interventionist Training

To ensure design fidelity, we developed the care partner intervention components to closely align with the study's guiding framework and we standardized the protocols to a specified dose in terms of number, frequency, and length of contact.

The interventionists are trained on the coaching modules separately from the other staff and do not interact with the Control group or Treatment Group 1, reducing potential for contamination. To ensure that interventions are delivered as intended, a PI or designee will be present at the home visits for two dyads within the first five enrolled to evaluate fidelity to the protocol, completing standardized checklists for adherence to protocol. Also, all encounters will be audio recorded digitally and will be evaluated on a random schedule by a PI or designee to assess adherence using the standardized checklist. The team members and PIs will discuss adherence results and problem-solve barriers to adherence with repeat of concepts and role-play as needed.

Study Coordinator Training

To further reduce potential for contamination, training for the study coordinator also will clearly differentiate intervention activities for the three groups; we will emphasize that the tailored care plan and Adaptive Leadership Behavior training occurs only for Treatment Group 2. To ensure the fidelity of coordinator to consenting and data collection procedures, a PI or designee will be present at the home visits for two dyads within the first five enrolled to evaluate fidelity, completing standardized checklists for adherence to protocol. Also, portions of all encounters will be audio recorded digitally and will be checked on a random schedule by a PI or designee to assess adherence using the standardized checklist. The team members and PIs will discuss adherence results and problem-solve barriers to adherence with repeat of concepts and role-play as needed.

Intervention Tracking:

Debriefing with study coordinators and the PIs will occur in weekly meetings. The PIs and coordinators from both sites will meet quarterly with theinterventionist, and hygienist at each site. Our debriefing process involves a discussion of issues encountered, problem-solving among the team members, and assessment of threats to fidelity and consistency across settings and across time. To ensure that any actions taken during the study balance research integrity with practical issues, we use the TECH Tool (Simpson et al., 2013), an algorithm for evaluating challenges and solutions that preserve fidelity. One of the PIs will facilitate the discussion of areas for improvement and lessons learned, using a developmental intent and incorporating multiple sources of information such as other team members,

protocols or literature. Lessons learned will be documented in meeting minutes where they can be accessed for use in planning future interventions.

6.3 MEASURES TO MINIMIZE BIAS: RANDOMIZATION AND BLINDING

The study team plans to take numerous steps to ensure a rigorous, unbiased study. Prior to the first visit, the statistician will be blinded when randomizing participant and care partner to study groups.

The procedures for the study visits differ based on which arm of the study a participant is assigned; thus, the research staff is not blind to the participant's assigned group. The randomization group determines which research staff members attend the home visits. The Research staff who conduct the study visits with participants and care partners will be trained to adhere to study procedures and interventions appropriately based on group assignment. The interventionist does not attend the visits for the Control Group and Treatment Group 1, reducing risk of contamination through delivery of in-person coaching. The participants will be recruited from local clinics and the intervention will be conducted at each participant's home, so the chances of contamination between the Treatment groups and the Control group is small.

Blinded randomization assignments will be determined by the statistician at the beginning of the study using a block (by sex) random allocation algorithm generated a *priori* by the statistician assuring there will be equal allocation to arms by site. Because the interventionist does not attend study visits for participants in the Control Group and Treatment Group 1, randomization must be done prior to the first visit.

This is a three-group randomized trial [Treatment Group 1, Treatment Group 2 and the Control Group] using randomization blocks by site to ensure balance within this potential confounder. Each randomization block will be composed of two units male and female in each treatment arm by site and randomization error will be minimized by ensuring that an equal number of all of units are randomized to each group. As minorities are recruited, they will sequentially be assigned to each group. To assess for randomization balance, we will use chi-square tests to examine if there are any statistically significant differences between race, and site by the three groups.

6.4 STUDY INTERVENTION/EXPERIMENTAL MANIPULATION ADHERENCE

Receipt of Treatment. During home visits, participants return-demonstrate oral hygiene skills. For intervention group participants, we discuss the skills with them and provide tailored feedback for improvement if necessary. Similarly, for care partners, each module includes discussion of the individual's impressions of progress, barriers and challenges and new strategies are developed as needed.

Enactment of Skills. Researchers will systematically assess enactment using data from the smart electronic toothbrush that record the date, time, and duration of use, providing an objective measure of oral hygiene behavior.

To further ensure enactment of skills by the care partner, we will assess the fidelity of the explicitly named behavior change techniques such as goal setting and goal implementation which are part of the scripted intervention using recorded or transcribed care partner coaching sessions and on a random schedule.

6.5 CONCOMITANT THERAPY

6.5.1 RESCUE THERAPY

N/A

7 STUDY INTERVENTION/EXPERIMENTAL MANIPULATION DISCONTINUATION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

7.1 DISCONTINUATION OF STUDY INTERVENTION/EXPERIMENTAL MANIPULATION

When a participant discontinues from the study intervention, he/she will be withdrawn from the study. Section 7.2 describes the data to be collected if a participant withdraws from the study.

7.2 PARTICIPANT DISCONTINUATION/WITHDRAWAL FROM THE STUDY

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

1. Any event or medical condition or situation occurs such that continued collection of follow-up study data would not be in the best interest of the participant or care partner or might require an additional treatment that would confound the interpretation of the study
2. The participant no longer meets the inclusion criteria or meets an exclusion criterion (either newly developed or not previously recognized) that precludes further study participation
3. Death of participant or moving away from study site area
4. Lost to follow-up; unable to contact participant

The reason for participant discontinuation or withdrawal from the study will be recorded on the Discontinuation/Withdrawal Case Report Form (CRF). Participants who sign the informed consent form and are randomized but do not receive the study intervention may be replaced. Participants who sign the informed consent form, and are randomized and receive the study intervention, and subsequently withdraw, or are discontinued from the study, will be replaced if the enrollment window is still open.

7.3 LOST TO FOLLOW-UP

A participant will be considered lost to follow-up if study staff are unable to contact the participant or care partner after many attempts by phone, email and/or mail. This is unlikely to occur given the relatively short time period of the intervention and the regular contact that most participants and care partners will receive as part of the intervention. If study visits are cancelled multiple times, the study coordinator will counsel the participant and study partner on the importance of maintaining the assigned visit scheduled and ascertain if the participant wishes to and/or should continue in the study. Before a participant is deemed lost to follow-up, the investigator or designee will make every effort to regain contact with the participant and care partner; this will include multiple telephone calls, emails, and/or mailed letter to the participant and care partner. These contact attempts will be documented in the study tracking program with a copy saved in the participant's study file. If the participant continues to be unreachable, he or she will be considered to have withdrawn from the study with a primary reason of lost to follow-up.

8 STUDY ASSESSMENTS AND PROCEDURES

8.1 ENDPOINT AND OTHER NON-SAFETY ASSESSMENTS

Screening

Telephone screening will be conducted to determine eligibility. The study coordinator will first confirm that both the participant and the care partner are interested in participating in the study. After obtaining permission from the participant to ask the care partner questions about the participant's health and every day activities, the care partner will then be asked questions about the functional abilities and health conditions of the potential participant to determine eligibility (See Oral Health Study Phone Screening Report Form). Preliminary eligibility will be determined by the study coordinator at the end of the call. The PI or designee at each site will then review the responses to the health conditions and determine final eligibility. The screening interview should occur within 42 days of enrollment.

Home Visits

The care partner and participant will complete the questionnaires in separate rooms from one another.

Participant Questionnaire:

- Sociodemographics (Baseline) for the study participant including date of birth, gender, years of educated completed, race/ethnicity, marital status
- Oral Health Knowledge Scale: Our team has developed a 12-item oral health knowledge scale to assess the knowledge of oral self-care such as frequency and technique of brushing and flossing, duration of brushing, and tongue cleaning that are consistent with general recommendation by dental professionals. [37]Oral hygiene behavior (investigator developed) asks about participants' frequency of toothbrushing, flossing, and mouth rinse. The response categories will be coded as 1= Twice a day or more, 2=once a day, 3= Several times a week, 4= Once or less than once a week, 5=Hardly ever, and 6= Never. Geriatric Oral Health Assessment Index[38] asks 13 questions about self-perceived oral health. The response categories of each item range from 1=always, 2=sometimes, and 3=never. Xerostomia Inventory[39] asks 11 questions about the signs and severity of xerostomia[8]. The responses of each question range from 1=never, to 5=very often. PHQ-8[40] is an 8-item screen for depression that is administered to the participant.

Care Partner Questionnaire:

- Sociodemographics (Baseline) for the care partner including date of birth, gender, years of education completed, race/ethnicity, marital status, and medical and dental insurance for care partner and for the participant
- Oral Health Knowledge Scale: Our team has developed a 12-item oral health knowledge scale to assess the knowledge of oral self-care such as frequency and technique of brushing and flossing, duration of brushing, and tongue cleaning that are consistent with general recommendation by dental professionals. [37]
  Oral Care Self-Efficacy:[41] Oral care self-efficacy is measured using a slightly modified version of the Geriatric Self-Efficacy Scale for Oral Health measure containing 6 items that assess oral hygiene behaviors.

- Adaptive Leadership Self-Efficacy: The investigators adapted the Caregiver *Confidence* in Contributing to Self-Care to measure [42,43]the care partners' confidence in facilitating the participant to perform oral self-care. The measure was originally developed for caregiving in heart failure and has been shown to be reliable and valid in samples of heart failure caregivers. We adapted this 5-item scale (4-point scale) for this study to address care partner confidence in their ability to foster oral self-care in individuals with mild dementia.
- Adaptive Leadership Behaviors-Cueing: The investigators adapted the Caregiver Contribution to Self-Care Management scale to measure use of adaptive leadership cueing strategies by the care partner to facilitate the participant in performing oral self-care. Originally the scale was developed for caregiving in heart failure and has been shown to be reliable and valid in samples of heart failure caregivers.[43] We revised the original scale to include 5 items that measure use of verbal, visual, or touch cueing strategies Each is measured using a 4-point Likert scale (never or rarely, sometimes, frequently, always or daily).
- Adaptive Leadership Behaviors-FOCUSED communication: The investigators adapted the Caregiver Contribution to Self-Care Management scale to measure use of adaptive leadership tailored communication strategies by the care partner to facilitate the participant in performing oral self-care. Originally the scale was developed for caregiving in heart failure and has been shown to be reliable and valid in samples of heart failure caregivers.[43] We revised the original scale to 9 items that measure use of FOCUS communication strategies.
- Participant oral hygiene behavior (investigator developed) asks about the participants' frequency of toothbrushing and flossing. The response categories will be coded as 1= Twice a day or more, 2=once a day, 3= Several times a week, 4= Once or less than once a week, 5=Hardly ever, and 6= Never. This measure also includes the frequency of reminders that the care partner provides. The response categories include 1=Very often, 2=Sometimes, 3=Occasionally, and 4= Not at all
- Own oral hygiene behavior (investigator developed) asks about care partners' frequency of toothbrushing, flossing, and mouth rinse. The response categories will be coded as 1= Twice a day or more, 2=once a day, 3= Several times a week, 4= Once or less than once a week, 5=Hardly ever, and 6= Never.

Study coordinator collects data from log and a smart toothbrush

- Oral hygiene behavior data collected from log for Treatment Group 2: Duration of toothbrushing and frequency of toothbrush. Duration of brushing will be measured as a continuous variable; frequency will be coded as an ordinal variable, 1-3.

- Oral hygiene behavior data from a smart toothbrush for Treatment Group 1 and 2: Duration of toothbrushing and frequency of toothbrushing. Duration of brushing will be measured as a continuous variable; frequency will be measured as a continuous variable..

After both sets of questionnaires are completed, the dental hygienist will perform a complete oral health evaluation on the participant:

- Determination of missing teeth (Number of missing teeth coded as a continuous variable.)
- Plaque Index[44] using UNC Modified Green and Vermillion Oral Hygiene Index (1960) Plaque will be measured as 0= No plaque, 1=Plaque covers < 1/3 tooth, 2=Plaque covers >=1/3 but < 2/3 tooth, and 3=Plaque covers >=2/3 tooth.

- Gingival Index[45] using UNC Modified Loe and Silness Gingival Index. Gingival inflammation is classified as 0 = Normal gingiva, 1 = Mild inflammation, no bleeding on probing, 2 = Moderate inflammation, bleeding on probing, 3 = Severe inflammation, tendency to spontaneous bleeding.
- Score of overall oral health using the OHAT[46] assessment sheet. A modification of the Brief Oral Health Status Examination that was developed specifically for older adults with cognitive impairment. OHAT measures eight categories: lips, tongue, gums and tissues, saliva, natural teeth, dentures, oral cleanliness and dental pain. Each category is coded as 0 (unhealthy), 1 (changes), and 2 (healthy). The data collected during the oral evaluation will be manually transcribed by a dental recorder and will be audio recorded. At this point, the dental hygienist will complete the General Examination Recommendation Sheet which will inform the participant if there are any urgent dental problems present. If urgent problems are present, the participant and care partner will be informed and referred to a dentist for treatment.
- Oral hygiene skills: The hygienist measures the appropriateness, quality, and duration of toothbrushing. It is coded as continuous variable, ranging from 3-9.

- Alzheimer's Disease Cooperative Studies Activities of Daily Living Instrument (ADCS ADL). The ADCS ADL is administered to the care partner to assess the participant's functional ability during the previous 4 weeks to complete 27 daily activities. If the activity was attempted, then the care partner was asked if the participant completed the activity 'independently', 'with supervision', or 'with physical help'. Each activity will be coded as 0=need some assistance, 1=independent without any help. A summary score ranges from 0-27. This instrument will be administered at baseline to better characterize the level of cognitive and functional impairment of the participants.
- Current medications - All medications taken during the previous two weeks will be reviewed and recorded by the dental hygienist, collected by medicine chest inventory by study staff. This screening is to confirm eligibility of study participant.
- Montreal Cognitive Assessment (MoCA)[47] is a brief cognitive assessment measure with a maximum of 30 points. It has been widely used and validated in many populations, the score ranges from 0-30. We will use the actual score to measure participant's cognitive function.

In a post-intervention interview at the last visit, all participants and care partners will be asked about their experience in the study using the guide developed in the pilot study.

8.2 SAFETY ASSESSMENTS

ASSESSMENT OF SAFETY

During the oral evaluation conducted at each study visit, the hygienist will assess whether the participant's mouth has signs of inappropriate oral hygiene behaviors that are damaging the teeth or gums.

CLINICAL SITE MONITORING

Internal Monitoring: The research team will monitor safety issues on an ongoing basis. Adverse event data reports will be available to the research team on a monthly basis. All deaths and any serious

adverse events will be reported according to procedures stated in this protocol regardless of relation to the study.

Safety monitoring plan
We will document, track and report safety issues as noted elsewhere in the protocol.

8.3 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

8.3.1 DEFINITION OF ADVERSE EVENTS

An adverse event (AE) is any untoward medical occurrence which does not necessarily have a causal relationship with this study intervention. There are no safety implications from participation in the study. AEs may also include the following: Intervention complications that occurs as a result of a protocol-mandated procedure (e.g., brushing teeth with electrical toothbrush) during or after screening.

8.3.2 DEFINITION OF SERIOUS ADVERSE EVENTS

A serious adverse event (SAE) is one that meets one or more of the following criteria:

- Results in death
- Is life-threatening (places the participant at immediate risk of death from the event as it occurred)
- Results in inpatient hospitalization or prolongation of existing hospitalization
- Results in a persistent or significant disability or incapacity
    - An important medical event that may not result in death, be life threatening, or require hospitalization may be considered an SAE when, based upon appropriate medical judgment, the event may jeopardize the participant and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

8.3.3 CLASSIFICATION OF AN ADVERSE EVENT

8.3.3.1 SEVERITY OF EVENT

The following guidelines will be used to describe severity of adverse events.

- **Mild**: Events require minimal or no treatment and do not interfere with the participant's daily activities.
- **Moderate**: Events result in a low level of inconvenience or concern with the therapeutic measures. Moderate events may cause some interference with functioning.

- **Severe**: Events interrupt a participant's usual daily activity and may require systemic drug therapy or other treatment. Severe events are usually potentially life-threatening or incapacitating. Of note, the term "severe" does not necessarily equate to "serious".

8.3.3.2 RELATIONSHIP TO STUDY INTERVENTION/EXPERIMENTAL MANIPULATION

All reported adverse events (AEs) will relate to the study procedures or the intervention as assessed by an appropriately-trained investigator. The degree of certainty about causality will be graded using the categories below.

- **Related**: The AE is known to occur with the study procedures or the intervention, there is a reasonable possibility that the study procedures or the intervention caused the AE, or there is a temporal relationship between the study procedures and the event. Reasonable possibility means that there is evidence to suggest a causal relationship between the study procedures and the AE.

- **Not Related**: There is not a reasonable possibility that the study procedures caused the event, there is no temporal relationship between the study procedures and event onset, or an alternate etiology has been established.

8.3.3.3 EXPECTEDNESS

The principal investigators will be responsible for determining whether an adverse event (AE) is expected or unexpected. An AE will be considered unexpected if the nature, severity, or frequency of the event is not consistent with the risk information previously described for the study procedures. This study is considered to be at minimum risk.

8.3.4 TIME PERIOD AND FREQUENCY FOR EVENT ASSESSMENT AND FOLLOW-UP

All adverse events (AEs) and serious adverse events (SAEs) that are spontaneously reported to study personnel or elicited by them during subject interviews or contacts will be systematically assessed. The coordinator will maintain a tracking log of all AEs and SAEs. For all reportable AEs and all SAEs, details of the event will be collected and recorded in RedCap. Information to be collected includes event description, time of onset, assessment of severity, relationship to study procedures (assessed only by those with the training and authority to make a diagnosis), and time of resolution/stabilization of the event. All reportable AEs and all SAEs will be followed to adequate resolution.

Any medical or psychiatric condition that is present at the time that the participant is screened will be considered as baseline and not reported as an AE. Some participants' health conditions may decline during the study period. If the study participant's condition deteriorates significantly during the study, it will be recoded as an AE.

The principal investigators or research staff will record events with start dates occurring any time after informed consent is obtained until 7 (for non-serious AEs) or 30 days (for SAEs) after the last day of study participation.

8.3.5 ADVERSE EVENT REPORTING

In consultation with the PIs, a trained member of the study team will submit annual reports to the IRB that will contain: 1) The number of adverse events and an explanation of how each event was handled, 2) The number of complaints (reflecting participant disposition) and how each complaint was handled; 3) The number of participant withdrawals and an explanation of why the participant withdrew or was withdrawn; and 4) The number of protocol deviations/violations and how each was handled.

In addition, the study team will submit annual reports to the DSMB summarizing the AEs.

8.3.6 SERIOUS ADVERSE EVENT REPORTING

Any study related death will be reported to the IRB and NIDCR within 24 hours of the study team's knowledge of it. Any other study related SAE will be reported to the IRB and NIDCR within 5 business days of the study team being made aware of it. The written report will be prepared in consultation with the PI. In the event that a participant either withdraws from the study or the investigator decides to discontinue a participant due to study-related SAE, the participant will be monitored by the investigator via on going status assessment until 1) a resolution is reached i.e., the problem requiring hospitalization has resolved or stabilized with no further changes expected 2) the SAE is determined to be clearly unrelated to the study intervention, or 3) the SAE results in death. Outcome of SAEs will be periodically reported to NIDCR. A summary of the SAEs that occurred during the previous year will be included in the annual progress report to NIDCR.

8.3.7 REPORTING EVENTS TO PARTICIPANTS

N/A

8.3.8 EVENTS OF SPECIAL INTEREST

N/A

8.3.9 REPORTING OF PREGNANCY

N/A

8.4 UNANTICIPATED PROBLEMS

8.4.1 DEFINITION OF UNANTICIPATED PROBLEMS

This protocol uses the definition of Unanticipated Problems as defined by the Office for Human Research Protections (OHRP). OHRP considers unanticipated problems involving risks to participants or others to include, in general, any incident, experience, or outcome that meets all of the following criteria:

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

8.4.2 UNANTICIPATED PROBLEMS REPORTING

The investigator will report unanticipated problems (UPs) to the reviewing Institutional Review Board (IRB), the DSMB and NIDCR. The UP report will include the following information:

- Protocol identifying information: protocol title and number, PI's name, and the IRB project number
- A detailed description of the event, incident, experience, or outcome
- An explanation of the basis for determining that the event, incident, experience, or outcome represents an UP
- A description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the UP

To satisfy the requirement for prompt reporting, UPs will be reported using the following timeline:

- UPs that are serious adverse events (SAEs) will be reported to the IRB and NIDCR within 48 hours of the investigator becoming aware of the event
- Any other UPs will be reported to the IRB and NIDCR within 7 days of the investigator becoming aware of the problem
- UPS will be annually reported to the DSMB.

8.4.3 REPORTING UNANTICIPATED PROBLEMS TO PARTICIPANTS

Since UPs by definition suggest that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized, all participants who are still active in the protocol (i.e. have not completed in-person 6 month study visit) will be notified in writing of UPs and will be reconsented at the time of their next study visit.

9 STATISTICAL CONSIDERATIONS

9.1 STATISTICAL HYPOTHESES

Primary Efficacy Endpoint(s):

- H1 (Objective 1): There will be an improvement in the oral hygiene clinical outcomes (lower plaque index and lower gingival index) from baseline to Month 3 and Month 6, and from Month 3 to Month 6. Treatment Group 1 will have a higher rate of improvement than the control group while Treatment Group 2 will have the highest rate of improvement.
- H2b (Objective 2b): The effects of the intervention on oral hygiene clinical outcomes (i.e., plaque index and gingival index) will be mediated by a set of mediating variables controlling for selected key covariates.
- H3a (Objective 3a): The effects of the intervention on oral hygiene clinical outcomes (i.e., plaque index and gingival index) will be mediated by oral hygiene behavioral outcomes controlling for selected key covariates.
- H3b (Objective 3b): The effects of the intervention on oral hygiene clinical outcomes (i.e., plaque index and gingival index) will be mediated by care partner's factors, and then mediated by oral hygiene behavioral outcomes controlling for selected key covariates.

Secondary Efficacy Endpoint(s):

- H1 (Objective 1): There will be an improvement in the oral hygiene behaviors (better oral hygiene skills and higher frequency of toothbrushing) from baseline to Month 3 and Month 6, and from Month 3 to Month 6. Treatment Group 1 will have a higher rate of improvement than the control group while Treatment Group 2 will have the highest rate of improvement.
- H1 (Objective 1): There will be an improvement in the oral hygiene behaviors (longer duration of toothbrushing) from the first week of the intervention (average in Week 1)) to Month 3 (average in Month 3) and Month 6 (average in Month 6), and from Month 3 to Month 6. Treatment Group 2 will have longer duration of toothbrushing than the Treatment Group 1.
- H2a (Objective 2a): The effects of the intervention on oral hygiene behavioral outcomes (i.e., the duration and frequency of toothbrushing and oral hygiene skills) will be mediated by a set of mediating variables controlling for selected key covariates.

9.2 SAMPLE SIZE DETERMINATION

Since we will collect data from the predictors [X], mediators [M] and outcomes [Y] at all three time points (baseline, 3 months, 6 months), we will use generalized linear mixed models to account for longitudinal repeated measurements over time to produce sample based inferential effects, which is a group-specific averaged effect size slope over all three time points to estimate each pathway strength.

For the power analyses, we proposed a small to medium effect size of 0.3 for our main outcome analyses without mediators. This was based on a combination of the effect size that is needed to detect what is reasonably thought to be a meaningful change and guidance from our pilot study. Thus, for the main effect we need a minimum of 107 subjects to reach 80% power at a significance level of 0.05. For the sequential mediation models, a sample of 120 provided at least 85% power at a significance level of 0.05. Thus, our target is to have a sample size of 120 to complete the intervention. However, if our attrition rate is higher than originally predicted, the sample size will be increased up to 150.

9.3 POPULATIONS FOR ANALYSES

Per-Protocol analysis dataset will be described in the SAP.

9.4 STATISTICAL ANALYSES

9.4.1 GENERAL APPROACH

A statistical analysis plan (SAP) will be prepared and finalized prior to database lock and unblinding of participant's treatment assignment. This document will provide further details regarding the definition of analysis variables and analysis methodology to address all study objectives. A blinded data review will be conducted prior to unblinding of the participants' treatment assignments. This review will assess the accuracy and completeness of the study database, participant evaluability, and appropriateness of the planned statistical methods. The SAP will not be posted publicly or registered before the study begins.

We will conduct data analysis in the following steps:

- Descriptive analysis on the sample characteristics, potential mediators, and oral hygiene behavioral and clinical outcomes. For the categorical variables, we will present percentages. For continuous variables, we will present means (with range and standard deviations).
- We will conduct ANOVA and Chi-Square analysis to compare group differences for the variables listed above. This will be based on two-tailed hypothesis testing. We will use p-value and 95% confidence interval for statistical significance test. P value of 0.05 will be considered the level of significance.
- We will use linear mixed models for continuous outcomes (e.g., plaque index, gingival index, oral hygiene skills, and duration of toothbrushing from smart toothbrush) accounting for within-participant correlation over time.
- We will use generalized linear mixed models for ordinal variables (e.g., self-reported duration of toothbrushing) accounting for within-participant correlation over time.
- Key covariates will be specified in the SAP.
- The tests for the underlying assumptions for the models will be specified in the SAP.

9.4.2 ANALYSIS OF THE PRIMARY ENDPOINT(S)

Details of the analysis of the primary endpoints will be provided in the SAP. A summary of the planned steps are provided here.

The first step will test whether the intervention is associated with differences across groups in the primary oral hygiene clinical outcomes. We will use linear mixed models for continuous outcomes (e.g., plaque index and gingival index) accounting for within-participant correlation over time. In addition to group, all models will be adjusted for site and time point and the interaction between group and time point – to assess whether group difference varied over time – as fixed effects; we will include a random effect for participants to handle within-participant clustering. Significant interaction between group and time point ($p < 0.05$) will provide statistical evidence for the efficacy of the intervention in improving oral health outcomes in Treatment Group 2 as compared to Treatment Group1 and the Control Group.

The subsequent steps will test the strength of the indirect effect of the intervention on oral hygiene clinical outcomes through mediators such as care partner factors and oral hygiene behavior outcomes. The following step will test the indirect effects are stronger than the direct intervention effects in Treatment Group 2 compared with Treatment Group 1 and the Control Group. The final step will test whether the impact of the intervention on oral hygiene clinical outcomes is sequentially mediated first by care partner's factors and then by oral hygiene behavioral outcomes.

9.4.3 ANALYSIS OF THE SECONDARY ENDPOINT(S)

The secondary endpoints are oral hygiene behavioral outcomes.

We will test whether the intervention is associated with differences across groups in the oral hygiene behavioral outcomes. We will use linear mixed models for continuous and ordinal outcomes accounting for within-participant correlation over time. In addition to group, all models will be adjusted for site and time point and the interaction between group and time point – to assess whether group difference varied over time – as fixed effects – and include a random effect for participants to handle within-participant clustering. Significant interaction between group and time point ($p < 0.05$) will provide statistical evidence for the efficacy of the intervention in improving oral health outcomes in Treatment Group 2 as compared to Treatment Group1 and the Control Group. Similar to the approach taken with the primary endpoints, we will then test the strength of the indirect effects of intervention on oral hygiene behavioral outcomes through mediators.

9.4.4 SAFETY ANALYSES

N/A

9.4.5 BASELINE DESCRIPTIVE STATISTICS

We will compare baseline characteristics across the Control Group, Treatment Group 1, and Treatment Group 2. The following characteristics will be included: demographics, education and income, health status, dental service utilization, MoCA, and ADCS ADL. ANOVA for continuous variables and chi-square test for categorical variables will be used for the comparison across three groups.

9.4.6 PLANNED INTERIM ANALYSES

N/A

9.4.7 SUB-GROUP ANALYSES

Any sub-group analyses will be described in the SAP.

9.4.8 TABULATION OF INDIVIDUAL PARTICIPANT DATA

9.4.9 EXPLORATORY ANALYSES

For qualitative data analysis, all sites will analyze de-identified data using Dedoose Software. These programs are approved for use by the NYU Langone IRB MCIT and Duke IRB IT. DUAs are in place to allow sharing of data between sites. Due to enrollment being less than anticipated, we plan to do mixed method analysis of the following aims:

- Exploratory Aim 1: Explore a detailed explanation of the impact of behavioral change techniques (BCTs) on oral hygiene behaviors and oral health outcomes (mixed method).
- Exploratory Aim 2: Examine relationship between the measures of adaptive leadership behaviors and the interventionist use of BCTS (mixed method).
- Exploratory Aim 3: Describe care partners' assessment of the intervention content and delivery (qualitative).

10 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1 REGULATORY, ETHICAL, AND STUDY OVERSIGHT CONSIDERATIONS

10.1.1 INFORMED CONSENT PROCESS

10.1.1.1 CONSENT/ASSENT AND OTHER INFORMATIONAL DOCUMENTS PROVIDED TO PARTICIPANTS

Verbal assent to conduct the phone screen and schedule a home visit (if eligible) will be obtained prior to beginning the phone screen. Consent forms describing in detail the study intervention, study procedures, and risks will be given to the participant and care partner to read. Written documentation of informed consent is required prior to starting intervention/administering study intervention.

10.1.1.2 CONSENT PROCEDURES AND DOCUMENTATION

At the time the study coordinator screens the participant for eligibility through a telephone script, s/he will obtain verbal willingness to participate from the participant and his/her care partner for permission for the study team to conduct the visit. Written informed consent will then be obtained from both participants at the time of the first home-visit. The interventionist or study coordinator will review the consent form face-to-face with the individuals. The individuals will be invited to ask questions prior to signing the consent form. The team member obtaining consent will determine the ability of the individual with dementia to provide informed consent based on the individual's responses to the following 3 questions: 1) What is the purpose of the study? 2) What are the risks of the study? 3) Who should I contact if I have a question about this study? If the individual is able to answer 2/3 questions correctly, s/he will be deemed capable of providing informed consent. If the participant is not able to answer 2/3 questions correctly, but is willing to participate in the study, the legal representative for the individual will be asked to sign the consent form.

10.1.2 STUDY DISCONTINUATION AND CLOSURE

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to participants, care partners, investigators, funding agency, and regulatory authorities. If the study is prematurely terminated or suspended, the Principal Investigator (PI) will promptly inform participants, care partners, the IRB, and the funding agency, and will provide the reason(s) for the termination or suspension.
Circumstances that may warrant termination or suspension include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to participants
- Demonstration of efficacy that would warrant stopping

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

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

10.1.3 CONFIDENTIALITY AND PRIVACY

10.1.2 Study Discontinuation and Closure

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to participants, care partners, investigators, funding agency, and regulatory authorities. If the study is prematurely terminated or suspended, the Principal Investigator (PI) will promptly inform study participants, care partners, the IRB, and the funding agency, and will provide the reason(s) for the termination or suspension.

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

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

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

10.1.3 Confidentiality and privacy

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

All research activities will be conducted in as private a setting as possible.

The study monitor, other authorized representatives of the sponsor, and representatives of the Institutional Review Board (IRB) may inspect all documents and records required to be maintained by the investigator, including but not limited to, data collected from participants and care partners as part of the study. The clinical study site will permit access to such records.

The participant's contact information will be securely stored at each clinical site for internal use during the study. At the end of the study, all records will continue to be kept in a secure location indefinitely or at least as long a period as dictated by the reviewing IRB, Institutional policies, or funding agency requirements.

Participant and care partner's research data, which is for purposes of statistical analysis and scientific reporting, will be transmitted to and stored at the NYU Data Coordinating Center for this study. This will not include the participant's contact or identifying information. Rather, participants and care partners, and their research data will be identified by a unique study identification number. The study data entry and study management systems used by clinical sites and by the NYU Data Coordinating Center research staff will be secured and password protected. At the end of the study, all study databases will be de-identified and prepared for archiving by the NYU Data Coordinating Center.

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

10.1.4 FUTURE USE OF STORED SPECIMENS AND DATA

Data collected for this study will be analyzed and stored at the NYU Data Coordinating Center on NYU Box. After the study is completed, the de-identified, archived data will be stored in an approved data repository such as the Inter-University Consortium for Political and Social Research (ICSPR) and will be available to eligible researchers. Permission to transmit the data to the U01 de-identified data study repository will be included in the informed consent.

10.1.5 KEY ROLES AND STUDY GOVERNANCE

Principal Investigator	**Medical Monitor or Independent Safety Monitor**
Bei Wu, PhD, Dean's Professor in Global Health New York University 433 First Ave, 5th Floor	

New York, NY 10010 212-992-5951	
Ruth Anderson, PhD Professor Emeritus 2400 Pratt Street Durham, NC 27705 919-966-8785	
Brenda L Plassman, PhD Professor Duke University 2400 Pratt Street, 6th Floor, Rm 6012 Durham, NC 27705 919-668-1586	

10.1.6 SAFETY OVERSIGHT

Safety oversight will be under the direction of a Data and Safety Monitoring Board (DSMB) composed of individuals with the appropriate expertise, including dentistry and behavioral interventions. Members of the DSMB should be independent from the study conduct and free of conflict of interest, or measures should be in place to minimize perceived conflict of interest. The DSMB will meet at least semiannually to assess safety and efficacy data on each arm of the study. The DMSB will operate under the rules of an approved charter that will be written and reviewed at the organizational meeting of the DSMB. At this time, each data element that the DSMB needs to assess will be clearly defined. The DSMB will provide its input to National Institutes of Health, National Institute of Dental and Craniofacial Research.

10.1.7 CLINICAL MONITORING

External monitoring for this study will be performed by the NIDCR Clinical Research Operations and Management Support (CROMS) contractor. The monitor will evaluate study processes and documentation based on the International Council for Harmonisation (ICH), E6: Good Clinical Practice guidelines (GCP). The plan for external clinical site monitoring will be detailed in a Clinical Monitoring Plan (CMP) developed by the NIDCR.

10.1.8 QUALITY ASSURANCE AND QUALITY CONTROL

Each clinical site will perform internal quality management of study conduct, data and biological specimen collection, documentation and completion. All sites will follow a common quality management plan.

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

Oral evaluation outcomes - The dental hygienists at two sites will undergo training by the master hygienist and will complete calibration sessions. The dental hygienists will be required to achieve preset benchmarks prior to being certified to conduct the evaluations. Calibration will be done annually to assure there is no drift in procedures.

Informed consent - Study staff will review both the documentation of the consenting process as well as a percentage of the completed consent documents. This review will evaluate compliance with GCP, accuracy, and completeness. Feedback will be provided to the study team to ensure proper consenting procedures are followed.
Source documents and the electronic data - Data will be initially captured on source documents or electronically (see **Section 10.1.9, Data Handling and Record Keeping**). If captured on source documents, it will then be entered into the study database. To ensure accuracy, the data will be double entered and compared electronically for discrepancies. Any discrepancies between first and second entry will then be reconciled with the source data and corrected in the database.
Intervention Fidelity Consistent delivery of the study interventions will be monitored throughout the intervention phase of the study. Procedures for ensuring fidelity of intervention delivery are described in **Section 6.2.1, Interventionist Training and Tracking**.
Protocol Deviations The study team will review protocol deviations on an ongoing basis and will implement corrective actions when the quantity or nature of deviations are deemed to be at a level of concern.

The PIs will provide direct access to all trial related sites, source data/documents, and reports for the purpose of monitoring and auditing by the NIDCR Clinical Research Operations and Management Support (CROMS) contractor and inspection by regulatory authorities.

10.1.9 DATA HANDLING AND RECORD KEEPING

10.1.9.1 DATA COLLECTION AND MANAGEMENT RESPONSIBILITIES

Data collection will be the responsibility of the clinical trial staff at the site under the supervision of the site investigator. The investigator will be responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported.
All source documents will be completed in a neat, legible manner to ensure accurate interpretation of data.
Hardcopies of the study visit worksheets will be provided for use as source document worksheets for recording data for each participant consented/enrolled in the study. Data recorded in the electronic case report form (eCRF) derived from source documents will be consistent with the data recorded on the source documents.
Clinical data (including AEs and expected adverse reactions data) will be entered into RedCap database, a 21 CFR Part 11-compliant data capture system provided by the NYU Data Coordinating Center. The data system includes password protection and internal quality checks, such as automatic range checks, to identify data that appear inconsistent, incomplete, or inaccurate. Clinical data will be entered directly from the source documents.

10.1.9.2 STUDY RECORDS RETENTION

Study documents will be retained for a minimum of 3 years after submission of the final Federal Financial Report. No records will be destroyed without the written consent of the sponsor/funding agency, if applicable. It is the responsibility of the sponsor/funding agency to inform the investigator when these documents no longer need to be retained.

10.1.10 PROTOCOL DEVIATIONS

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

These practices are consistent with ICH GCP:

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

It will be the responsibility of the site investigator to use continuous vigilance to identify and report deviations within 10 working days of identification of the protocol deviation, or within 10 working days of the scheduled protocol-required activity. All deviations must be addressed in study source documents and reported to the Data Coordinating Center. Protocol deviations must be sent to the reviewing IRB per their policies. The site investigator is responsible for knowing and adhering to the reviewing IRB requirements. Further details about the handling of protocol deviations will be included in the MOP.

10.1.11 PUBLICATION AND DATA SHARING POLICY

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

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

This study will comply with the NIH Data Sharing Policy and Policy on the Dissemination of NIH-Funded Clinical Trial Information and the Clinical Trials Registration and Results Information Submission rule. As such, this trial will be registered at ClinicalTrials.gov, and results information from this trial will be submitted to ClinicalTrials.gov. In addition, every attempt will be made to publish results in peer-reviewed journals. The de-identified individual participant data collected during the trial will be shared between 9 months and 36 months following article publication or as required by a condition of awards and agreements supporting the research, for researchers who provide a methodologically sound proposal. Data will be made available at https://www.icpsr.umich.edu/web/pages (Note: a specific link will be provided after the study is published/when the DOI is obtained.) The protocol, statistical analysis

plan, and analytic code will be made available on Clinicaltrials.gov only as required by federal regulation or as a condition of awards and agreements supporting the research. Considerations for ensuring confidentiality of these shared data are described in Section 10.1.3.

10.1.12 CONFLICT OF INTEREST POLICY

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

10.2 ADDITIONAL CONSIDERATIONS

10.3 ABBREVIATIONS AND SPECIAL TERMS

AE	Adverse Event
CFR	Code of Federal Regulations
CMP	Clinical Monitoring Plan
CRF	Case Report Form
DSMB	Data Safety Monitoring Board
EC	Ethics Committee
eCRF	Electronic Case Report Forms
FDA	Food and Drug Administration
GCP	Good Clinical Practice
IB	Investigator's Brochure
ICH	International Council on Harmonisation
IDE	Investigational Device Exemption
IND	Investigational New Drug Application
IRB	Institutional Review Board
MOP	Manual of Procedures
NCT	National Clinical Trial
NIH	National Institutes of Health
OHRP	Office for Human Research Protections
PI	Principal Investigator
QC	Quality Control

SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
UP	Unanticipated Problem
US	United States

10.4 PROTOCOL AMENDMENT HISTORY

Version	Date	Description of Change	Brief Rationale

11 REFERENCES

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Sample Size as of 05/08/24

	Consented*	Completed
Treatment Group 1	**20**	**18**
Treatment Group 2	**20**	**17**
Control Group	**20**	**19**
Total	**60**	**54**

** Does not include ineligible*
**Target accrual: 120 dyads*

Study Design

This is a three parallel arm randomized controlled trial (RCT) to evaluate the effectiveness of a care partner-assisted intervention to improve oral hygiene in individuals (≥ 60 years) with mild dementia. Participant-care-partner dyads were randomized into 1 of 3 groups: Treatment Group 1 (**TG1**), Treatment Group 2 (**TG2**), and the Control Group (**CG**) stratified by site. **TG1** and **TG2** were given smart electronic toothbrushes. Only **TG2** will received in-home and telephone coaching throughout the duration of the study and were instructed to record daily brushing habits. The coaching sessions included individualized instruction on oral hygiene technique, cueing strategy development, or oral hygiene monitoring and coaching. **TG1** and **CG** did not receive coaching sessions. While randomization occurred at the dyad level (participant-care partner), primary study outcomes will be assessed at the participant level. The study duration was 6 months, including a 3 month intervention phase, in which coaching and educational modules were delivered, followed by a 3 month maintenance phase in which no coaching or educational modules were presented to participants. Data was collected by the study team at three visits: baseline, 3-months (end of active intervention phase), and 6-months (end of three-month maintenance phase). The primary endpoint is oral hygiene (plaque index, gingival index) at 3 months, with a secondary endpoint of 6 months to explore maintenance of intervention effects.

Study Aims

Aim 1: Evaluate the effectiveness of a care partner-assisted intervention to improve oral hygiene and oral hygiene behaviors in individuals with mild dementia.
Hypothesis 1a: Compared to CG, both T1 and T2 will result in improved oral hygiene as measured by reduced plaque index, and reduced gingival index, at 3 months.
Hypothesis 1b: T2 will have higher improvement than T1, relative to CG, in oral hygiene as measured by a greater reduction in plaque index, and gingival index, at 3 months.

Aim 2: Assess changes in mediating factors/process outcomes, including communication between the dyads, oral health knowledge, and self-efficacy for both participants and care partners to understand mechanisms of the intervention.
Hypothesis 2: The effects of the intervention on oral hygiene outcomes (i.e., plaque index and gingival index) will be mediated by oral care self-efficacy, leadership self-efficacy, use of behaviors cueing, leadership focused communication.

Measures

Primary outcomes:
1) Plaque index: UNC Modified Green and Vermillion Oral Hygiene Index. Plaque was measured as 0 = No plaque, 1 = Plaque covers <1/3 tooth, 2 = Plaque covers >=1/3 but <2/3 tooth and 3 = Plaque covers >=2/3 tooth. *The proportion of sites with plaque deposits on at least less than 1/3 of crown will be calculated for each participant for use in analyses.*
2) Gingival Index: UNC Modified Loe and Silness Gingival Index. Gingival inflammation is classified as 0 = Normal gingiva, 1 = Mild inflammation, no bleeding on probing, 2 = Moderate inflammation, bleeding on probing, 3 = Severe inflammation, tendency to spontaneous bleeding. *The proportion of sites with at least some mild inflammation will be calculated for each participant for use in analyses.*

Secondary outcomes:

Participant oral hygiene behavioral outcomes, note for outcomes with both participant and care-partner report, care-partner report will be used for all statistical analyses. Participant data will be presented descriptively by arm and time.

1) Participants' frequency toothbrushing *(reported by participants and care-partners).*
   Numeric scale ranging from 1-6. Data will be dichotomized into the following categories: less than twice a day or twice a day or more. Care-partner response will be used for analysis.
2) Participants' duration of toothbrushing *(reported by dental hygienist).*
   Ordinal measure, consisting of 3 response types (< 1min; ≥ 1 min & < 2min; ≥ 2 min). Data will be treated as ordinal. For sensitivity analysis we will dichotomize responses into the following categories: < 2 min vs. 2 min or more.
3) Participants' frequency of interdental cleaning *(reported by participants and care-partners).*
   Ordinal scale ranging from 1-6. Data will be treated as ordinal. For sensitivity analysis we will dichotomize responses into the following categories: < once per day or once per day or more. Care-partner response will be used for analysis.
4) Participants' interproximal cleaning technique *(reported by dental hygienist).*
   Categorical measure, consisting of 4 response types. Responses will be dichotomized into the following categories: less than optimal or interproximal surfaces cleaned using 'c' shape.
5) Participant oral hygiene skills *(reported by dental hygienist).*
   Numeric score derived by averaging across responses to Q3, Q4, Q5 of the oral hygiene assessment.
6) Modified oral health knowledge score (*reported by participants and care-partners*)
   Numeric score reflecting the proportion of correct responses for knowledge questions (C4 - C11).

Potential mediators (exploratory):

For mediators with both participant and care-partner report, care-partner report will be used for all statistical analyses. Participant data will be presented descriptively by arm and time.

1) Oral care self-efficacy *(reported by participants and care-partners).*
   Modified geriatric self-efficacy scale for oral health. Numeric care-partner self-efficacy score will be derived by averaging across items (D1 - D6). Numeric participant self-efficacy score will be derived by calculating the proportion of items responded to as "confident."
2) Leadership self-efficacy *(reported by care-partners).*
   Numeric score will be derived by averaging across item responses (I1-I4)
3) Use of behaviors-cueing methods *(reported by care-partners).*
   Numeric score derived by averaging across item responses (J1-J3). J4 will be reported separately as appropriate.
4) Leadership behaviors-FOCUSED Communication *(reported by care-partners).*
   Numeric score derived by averaging across item responses (K1-K8).

Additional variables:

Baseline participant characteristics: site (New York and North Carolina) age, sex, education, race, oral health knowledge; physical function at baseline [ADCS ADL], MOCA.
Baseline caregiver characteristics: site (New York and North Carolina), age, sex, education, race, oral health knowledge.

Statistical Analysis Plan

General Approach: The overall goal of this study is to demonstrate the effectiveness of the two intervention strategies (**TG1, TG2**) against that of **CG**. The primary outcomes are plaque index, which is quantified as the proportion of sites with plaque deposits on at least less than 1/3 of crown, and gingival index, which is quantified as the proportion of sites with at least some mild inflammation. While the unit of randomization is at the dyad level, the primary outcomes will be evaluated at the individual level. As participants and care-partners contribute repeated measures (at baseline, 3 months and 6 months), we will use a linear mixed modeling approach for the analysis of the primary hypotheses, to account for correlation among repeated measures from the same individual. Analyses for all study outcomes will be conducted according to the intention-to-treat (ITT) principle, where all participants are analyzed according to the group in which they were randomized, irrespective of their receipt of allocated treatment. For our primary analysis we will conduct a

complete case analysis, thus excluding participants who are lost to follow up. As a sensitivity analysis, we will use the strategy of last-observation-carried-forward (LOCF) (thus assuming no change), to impute missing values for participants lost to follow up, if a monotone pattern is demonstrated in complete data. A strategy of LOCF is conservative in that it may bias results towards a null effect, but eliminates bias related to differential dropout, especially in the case where participants with no improvement are less likely to complete follow-up assessments. Statistical analyses will be performed in R version 4.4.0. All statistical tests will be two-sided, and a p-value of < 0.05 will be considered statistically significant.

Statistical Analyses (Aim 1): To examine between-group differences in baseline characteristics and outcome variables, we will use Chi-square tests or Fisher's exact tests to analyze categorical variables and a one-way analysis of variance (ANOVA) for continuous variables. The effectiveness hypotheses will be analyzed using a linear mixed modeling framework with random effects. Specifically, longitudinal outcomes (e.g. plaque index) will be regressed on a treatment indicator, timepoint indicator, interaction of the two, and additional participant-specific covariates as needed. That is for the i^{th} person and t timepoint, $Plaque_{it} = \alpha_i + \beta_0 + \beta_1 \cdot Site_i + \beta_2 \cdot X_i + \beta_g \cdot Group_i + \beta_t \cdot Time_t + \beta_{gt} \cdot Group_i \times Time_t + \varepsilon_{it}$, where the terms represent the following: α_i person-specific random effects, β_0 overall mean plaque, β_1 site effects, X_i additional participant-specific covariates, β_g group effects, β_t time effects, and β_{gt} the interaction effect between group and time. Covariates determined a priori (including: baseline index scores, baseline functional status) will be included via the flexible X_i term. If data suggest a between-group difference (e.g. significant interaction between time and group) on the primary outcomes of interest, we will conduct the following pairwise comparisons using estimated means (**TG1** vs. **CG**; **TG2** vs. **CG**), at 3 months and 6 months. To control for multiple comparisons, pairwise comparisons will incorporate a False Discovery Rate-controlling procedure (e.g. Benjamini-Hochberg) which yields the desired type-I error rate of 5%. Lastly, depending on the distribution of the proportions for the primary outcomes (plaque, gingival indices) we may explore alternative distributions (e.g. beta regression) if it improves model fit. To address secondary outcomes including: 1) participants' frequency of toothbrushing, 2) participant's duration of toothbrushing, 3) participants frequency of interdental cleaning, 4) participant's interproximal cleaning technique, and 5) participants' oral hygiene skills score, and 6) participants' oral health knowledge score, we will use the same analytic approach outlined above consisting of linear mixed modeling with random effects. Given the overall sample size and number of secondary outcomes, all secondary outcome analyses will incorporate an appropriate False Discovery Rate-controlling procedure (e.g. Benjamini-Hochberg).

Exploratory Analyses (Aim 2): If findings from the analyses outlined above, for the primary outcomes of plaque and gingival indices, indicate an overall intervention effect, we will consider exploratory mediation analysis. Specifically, if a significant effect of the two treatment packages is observed (relative to control), we will explore the extent to which the proposed mediators (oral care self-efficacy, leadership self-efficacy, use of behaviors-cueing, or leadership communication) mediate the effect of the two treatment packages compared to control on the primary outcomes (plaque and gingival indices). Given the available sample size, we will consider the mediators independently and estimate preliminary single mediation effects using causal mediation analysis. Model-based causal mediation involves a two-step process. First, we specify a mediator model to obtain the conditional distribution of the mediator given the exposure, and an outcome model to obtain the conditional distribution of the outcome given the exposure and mediator. Each model is fit separately and then their fitted objects are inputted into a mediation function, which estimates the effects of interest. The mediator model will be specified as a linear regression of the mediator at 3 months post-randomization on the exposure (treatment allocation) and baseline values of the mediator. The outcome model will be specified as a linear regression of the outcome at 6 months post-randomization on the mediator at baseline, and 3 months after randomization, and the exposure (randomization assignment). Using the mediator and outcome regression models we will estimate the corresponding preliminary indirect and direct effects for each mediator. Of particular interest to the present study are the preliminary indirect effect estimates, which measure the effect of the exposure (randomization assignment) on the outcome (plaque or gingival index) via the mediator of interest (e.g. oral care self-efficacy). We will estimate corresponding standard errors and 95% confidence intervals for these effects using bootstrapping.

Should model diagnostics from our exploratory mediation analysis (e.g. RMSEA) indicate poor model fit or we observe indications of instability in effect estimates (e.g. wide confidence intervals), we will opt for a paired down assessment of potential mediators. In this paired down approach, we will explore changes in potential mediators following intervention (e.g. oral care self-efficacy) by summarizing mean change (6 months - baseline), (3 months - baseline) in potential mediators stratified by intervention group (**TG1, TG2, CG**). To inform future studies, we will calculate corresponding effect sizes (Cohen's d for independent samples) for key between-group differences (**TG1** vs. **CG**; **TG2** vs. **CG**) in mean change for potential mediators (e.g. oral care self-efficacy). These descriptive summaries will provide inputs to aid in powering a future mediation analysis to examine the underlying mechanisms of intervention effects.

Supplementary Strategies

Assessment of Modified Measures. For modified scales, which include the secondary outcome of oral care self-efficacy, and the exploratory mediators of adaptive leadership and focused communication, we will confirm unidimensionality via exploratory factor analysis, and subsequently compute Cronbach's alpha to examine reliability for each modified scale.

Electronic Toothbrush Data. The secondary outcomes of participants' frequency and duration of toothbrushing was also measured via electronic toothbrush for participants randomized to **TG1** or **TG2**, at baseline, 3 months and 6 months post-randomization. We anticipate a substantial proportion of participants may have missing data for frequency and duration of toothbrushing due to toothbrush device issues (e.g. battery, glitches etc.). Following the identification and removal of test cases in the dataset, we will examine outliers and missing data patterns via visualization to inform subsequent strategies. Our primary goal is to identify a subset of participants with complete data for frequency and duration of toothbrushing in the electronic toothbrush dataset. These data will be used as a validation set to examine agreement between participant self-report, care-partner report, and electronic toothbrush-assessed frequency and duration of toothbrushing. To align with the care-partner and participant reported toothbrushing data, we will calculate an average measure for frequency and duration based on 6 days of consecutive or non-consecutive data, surrounding the baseline, 3 month, and 6 month assessment date, which will serve as the index date for each visit. Lastly, we will compute relevant interclass correlation coefficients to explore agreement between participant self-report, care-partner report, and electronic toothbrush assessed frequency and duration of toothbrushing.

Descriptive Tables

Table 1. Participant demographics by arm at baseline.
- Variables for inclusion: age, sex, education, race, oral health knowledge score, ADL score, MOCA score

Table 2. Care-partner demographics by arm at baseline.
- Variables for inclusion: age, sex, education, race, oral health knowledge score

Table 3. Primary and secondary outcomes by arm at baseline, 3 months, and 6 months.
- Variables for inclusion: frequency toothbrushing, duration of toothbrushing, frequency of interdental cleaning, interproximal cleaning technique, oral hygiene skills score, oral health knowledge score.
- *Participant oral health knowledge score (separately – not a secondary outcome).*

Table 4. Exploratory mediators by arm, at baseline, 3 months, and 6 months.
- Variables for inclusion: oral care self-efficacy, leadership self-efficacy, behaviors cueing methods, leadership focused communication.

Table 5. Subjective responses from oral health knowledge survey (C1-C3) by arm at baseline, 3 months, 6 months.
- Variables for inclusion: responses to C1, C2, and C3 (for participants and caregivers).

Table 6. Participant oral health knowledge score, and individual cueing items by arm at baseline, 3 months, 6 months.
- Items J1-J3 (verbal, visual, touch) of cueing methods (binary categories, Yes/No cueing method used).
- Count of cueing methods used (sum of binary categories for J1-J3).
- Item J4 of cueing methods (original categories).