B. SIGNIFICANCE: R61/R33

Cognitive decline is a significant burden for patients, family caregivers, healthcare providers, and society. Subjective cognitive decline (SCD) affects significant numbers of older adults.[1] Patients with SCD report reduced cognitive ability to function at expected levels,[29-31] disengagement from meaningful activities,[25,32] and diminished confidence in ability to manage daily challenges[25,33,34] and other chronic illness issues.[35-38] Patients with SCD also experience poor communication that contributes to decreased dyadic agreement regarding patient functional ability,[33,39,40] poor quality of life (QoL),[8,9,41-43] anxiety, depressive symptoms,[44,45] and poor patient/caregiver relationship satisfaction.[39,40,46] Family caregivers (family or friends; henceforth referred to as "caregivers") often feel unprepared and lack confidence to deal with their new caregiving duties and daily challenges.[23,46-49] With our aging population, our society faces increased numbers of people with SCD, high, complex demands on home health services,[50,51] and increased burden for millions of older persons, their families, healthcare providers, and the health care system.[51-54]

SCD provides a critical window of time to provide early interventions to slow the onset of dementia and improve negative outcomes. SCD patients and their caregivers need early, supportive interventions from home health services staff to slow functional decline and improve health outcomes. While there are no proven cures or treatments for Alzheimer's disease and related dementia (ADRD), there is strong evidence that combining four or five healthy lifestyle behaviors (i.e., heathy diet, regular exercise, cognitive stimulation, non-smoking, social activity) decreases risk of AD, compared to having none or only one of the five behaviors.[55,56] However, two of these behaviors, cognitive stimulation and exercise, are less likely to be meaningful enough be sustained by older persons' over time or foster engagement in additional activities.[55-58] Very few interventions focus on SCD patients and their caregiver in home health services settings.[55,59] The Institute of Medicine recommended research on active engagement of <u>both</u> patients and their caregivers as a fundamental feature of successful interventions,[60] but few dyadic interventions are developed, tested, or evaluated in the home health setting.[12] **Tailored positive health interventions for SCD patients living at home are sorely needed,[61] and opportunities to intervene before progression to moderate/advanced dementia are few.**

Patient-driven care and meaningful activity engagement are critical components of home health services. Sustained engagement in meaningful activities is essential for patient QoL.[15,62] Home health services *should* optimize the abilities of patients with SCD and QoL, through engagement in meaningful activity.[63] Unfortunately, healthcare teams often lack important information regarding patient goals, values, and preferences necessary to develop appropriate plans of care. Also, very few supportive care interventions focus on SCD patient-informal caregiver dyads and none promote reengagement in preferred meaningful activities to maximize QoL, preserve activity performance, prolong independence, and delay institutionalization. Current SCD interventions are rarely tailored to patient preferences, do not involve caregivers,[55,58] and are not easily integrated into the well-established, daily routines. Dyadic engagement in self-selected meaningful activities may be an efficient means to: 1) improve patient and caregiver confidence to manage patient's daily challenges,[15,64] 2) promote long-term engagement in meaningful activities;[14,18,65] 3) foster feelings of pleasure, connectedness, identity,[14,64] autonomy, and goal directedness;[14,26-28] and, 4) enhance patient activity performance over time[14,15]—all of which are important to maintain patient abilities. **Mutual engagement in daily meaningful activities can enhance the patient-caregiver relationships ,[15,66] and enhance both patient and caregiver QoL.[25]**

The Daily Engagement in Meaningful Activities (DEMA) intervention is a practical, promising solution to improve QoL for home health service patients with SCD and reduce caregiver burden. To ensure effective health promotion and quality engagement, DEMA fosters full patient engagement, with caregiver support, to identify meaningful activities, assess capacity, problem-solve barriers, and establish routines for engagement. Our previous studies found prevention of patient disengagement requires a structured, goal-setting approach to foster continued or renewed engagement in diverse meaningful activities.[26-28] DEMA's highly person-centered approach to activity engagement begins with the patient identifying valued activities and addressing the individual's unique barriers to engagement. Meaningful activity engagement promotes patient and caregiver life satisfaction by coaching the dyad on problem-solving, self-management, active listening, and communication skills, and by enhancing naturally occurring patient/caregiver interactions to accomplish self-identified and mutually agreed upon goals.[26,27,49]

Regardless of whether patients progress to ADRD, remain stable, or improve,[67] patients and caregivers can benefit from DEMA-Pro. This R61 will lead to an R33 pragmatic trial by: 1) creating the organizational structure in the R61 (pilot) phase to be used in the R33 phase; 2) recruiting participants across 4 home health service locations; 3) adapting the DEMA training protocol in collaboration with the KAH professional team to create DEMA-Pro; and, 4) using blended learning modules (i.e. electronic and in-person delivery).

IMPACT. SCD is a risk factor for developing Alzheimer disease (AD).[68] Over five million Americans had dementia in 2019, with projections of 7.1 million by 2025.[51] Innovative interventions to address the growing demands for high quality care in this population, and foster both health-related quality of life, quality of life as overall sense of well-being are needed. The interprofessional, telephone delivered DEMA-Pro program, aimed to improve quality of care and patient health outcomes, offers an efficient, cost-efficient care model.

C. INNOVATION: R61/R33

DEMA is the first telephone-delivered intervention for patients with SCD and caregivers with demonstrated high feasibility, acceptability, and positive preliminary effects on health outcomes (physical function, mood, and QoL).[27,28] DEMA is primarily telephone delivered (1 in-person and 5 telephone session) and 5 preliminary studies demonstrated very high feasibility: 98% participant consent and 94% completion,[27] indicating *unusually high* patient and caregiver acceptance, minimal burden, and intervention value, compared to other studies of older adults with cognitive impairment (completion rates 60 to 78%).[69-72] DEMA participants reported high satisfaction with the intervener information provided over time. Group comparisons, DEMA mean scores were significantly higher for overall satisfaction subscale: usefulness (p=.025) and ease of use (p=.038).[28] Participant's post intervention interviews support the helpfulness of DEMA (e.g., Patient: *"(DEMA) let me know I'm not the only one…There are things that you can do…to resolve or make them not as big of a problem … the daily logs showed I was doing much more than I believed*." Caregiver: "*A program like this is extremely important. If nobody pays any attention…there's no improvement, there's nothing. Most helpful [was] understanding the challenges of memory impairment, learning and practicing a variety of coping skills, and realizing I need to reach out for help without guilt feeling*".[28]

The DEMA-Pro intervention will be the first to address the engagement constraints of older persons with SCD using a Positive Health approach to *foster sustainable engagement in meaningful activities* that are based on the shared values and priorities of both patients' and caregivers'. There is emerging evidence that regular, personalized, and self-identified engagement in any meaningful activities can improve quality of life, depressive symptoms, anxiety, and dyad communication.[14,15,65,73,74] The DEMA-Pro Program is: 1) tailored to patients' activity priorities and functional abilities; 2) flexible in activity selection (e.g. one long-term or several short-term activities); 3) collaborative between the patient and caregiver in developing and executing the personalized meaningful activity plan; and; 4) relevant and tailored to patient/caregiver's priority needs for written information related to the 6 priority topics identified and evaluated by focus groups.[27,28,30,31]

DEMA-Pro will be the first large-scale pragmatic RCT to evaluate a telephone intervention embedded in existing home health services teams' care for patients with SCD and their family caregivers (Aims 1-3). DEMA-Pro delivery within a pragmatic RCT increases likelihood of success and sustainability. Advantages of this pragmatic trial approach include: 1) coordinated training; 2) DEMA-Pro delivery by dedicated KAH Call Center coaches in collaboration with home health services providers in the field; and, 3) flexible incorporation of DEMA-Pro into home health services policies and procedures. For example, KAH home health service teams will train the KAH Call Center care coordinators to deliver DEMA-Pro and create DEMA-Pro care plans to be implemented by clinical staff in the field with the aim to enhance patient and caregiver engagement in self-selected meaningful activities in home settings. The field staff will be meeting regularly to support the patients in reaching their goals based on the plan created by the coach in the call center. DEMA-Pro will also be integrated into the home health services culture and existing administrative structures, which drives change in home health services settings. For example, the DEMA-Pro Coach will have accountability to their supervisors for their activities as part of their position. Internally generated benchmarking will increase willingness to devote time and resources by elevating the profile of this important staff function.

DEMA is efficiently delivered in home settings and DEMA-Pro will leverage DEMA's lessons-learned through delivery as a demonstration project in one of the largest home health services companies in

the USA (Aim 1). The DEMA-Pro Program capitalizes on our team's experiences delivering a highly person-centered approach to activity engagement based on patient-identified valued activities and addressing the individual's unique barriers to engagement. Meaningful activity engagement fosters better patient physical function and quality of life (sense of well-being) by coaching dyad problem-solving, self-management, active listening, communication skills, and by enhancing the naturally occurring patient/caregiver interactions to accomplish self-identified and mutually agreed upon goals.[26,27,49] Regardless of whether patients with SCD progress to AD, remain stable, or improve,[67] patients and caregivers can benefit from DEMA-Pro.

Our proposed study combines multiple sources of data to comprehensively evaluate quality and effectiveness of DEMA-Pro when delivered through home healthcare services (Aim 3). Use of multiple existing databases to evaluate the quality of home health services for patients with SCD is extraordinarily difficult. Our use of combined data from the Medicare OASIS electronic health record and from KAH's Electronic DEMA-Pro care plan is innovative and will enable us to meaningfully evaluate DEMA-Pro's influence on home healthcare quality of care.

D. APPROACH: R61/R33

Following the instruction and requirements provided in RFA-18-585, this section includes description of: (1) preliminary studies relevant to the R61/R33 phases; (2) a conceptual model; (3) detailed methods to assess R61 milestones prior to R33 phase; (4) R33 milestones; and, (5) Potential problems and alternative solutions.

D.1. Preliminary Studies. Our combined expertise is necessary for the success of this DEMA-Pro pragmatic pilot project. PI (Lu) has developed and led a DEMA program of research focused on positive health, strength-based and family-center interventions to improve the meaningful activities, physical function, and quality of life of older adults with cognitive impairment and their family caregivers in past 15 years. Dr. Hickman (Co-I) has significant experience with implementing and evaluating evidence-based interventions for older adults in real world clinical settings, including serving as an 8-year Co-I on a Centers for Medicare and Medicaid Services funded demonstration project in which they are implementing systematic advance care planning in 19 nursing facilities. Dr Haase (Co-I) has extensive experience developing psychosocial behavioral interventions and evaluating them in multi-site randomized clinical trial. Dr. Ellis (Co-I), Vice-President, Research and Business Development, Kindred at Home, has extensive experiences coordinating and leading efforts to guide large-scale implementation of healthcare delivery innovation via translation of evidence to real-world application in large, complex and highly-matrixed healthcare delivery organizations for over 15 years. Dr. Perkins (Co-I) is has extensive statistical experience, serving as biostatistician or Co-Investigator on 33 funded studies (including NIH). Dr. Jones (Consultant), has successful experiences with recruitment and stakeholder engagement in home healthcare setting and recently conducting improving care coordination between clinicians to optimize care transitions to home health care (AHRQ, K08HS024569).

DEMA-Pro is adapted from DEMA. DEMA was developed using NIH's Stage Model for Behavioral Intervention Development[95] across five preliminary studies (T32NR007066, P30AG10133-pilot study, K01NR010854, R21NR013755); [23-28] all five studies were consistently focused on patients' and caregivers' self-identified needs and experiences. The studies demonstrated DEMA's high feasibility and acceptability in home settings. Compared to other studies of older adults with cognitive impairment in which completion rates ranged from 60% to 78%,[69-72] we had a 98% consent rate and a 94% completion rate, indicating unusually high acceptance, minimal burden, and high intervention value.[27,28] This pilot offers the unique opportunities to adapt DEMA to the home health service setting, delivered by centralized health care professionals and with evaluation support.

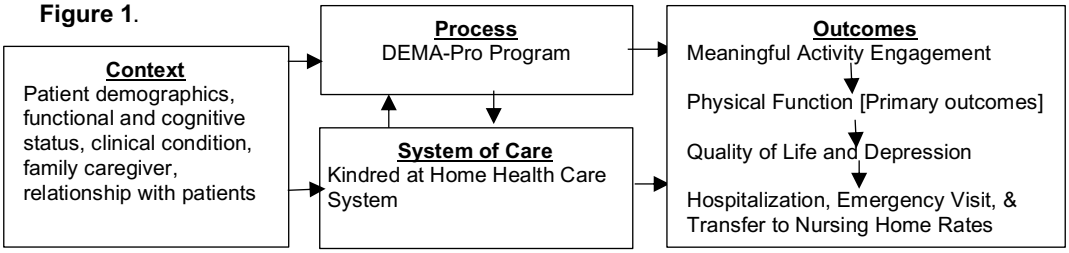
Indiana University & Kindred at Home, Gentiva Health Services academic/corporate research partnership. Kindred at Home (KAH) is one of the largest home health services in the United States (> 400 sites in 40 states).[75] Dr. Lu (PI) and KAH Vice President Dr. Ellis have collaborated since 2015 on preliminary studies of DEMA, which yielded 2 publications,[28,76] 1 manuscript in progress, and 2 poster presentations at national and international conferences.[77,78] In her role as Vice President of Research and Business Development, Dr. Ellis facilitated a formal memorandum of understanding (MOU) between IU School of Nursing and KAH to collaborate on research and share data (Data Use Agreement No.1153529). This call for pilot proposals is timely, since Drs. Lu, Ellis, and the Chief Officers of KAH had already started exploring adapting the DEMA program for use in the home health services settings—this funding mechanism provides

the ideal opportunity to both adapt and rigorously evaluate the implementation of DEMA for dissemination both within and potentially beyond KAH. (See attached of **Letter of Support**).

Team experience conducting pragmatic RCTs with Alzheimer's patient, caregivers, and healthcare providers. As an MPI on a R21/R33 APPROACHES pragmatic clinical trial to implement an advance care planning intervention for persons with ADRD in nursing facilities (R21 AG057463; R33 AG057463), Dr. Hickman established the infrastructure to conduct a pragmatic RCT, developed a training plan, collaborated with corporate partners to adapt intervention protocols, and is using existing federally collected data (Claims, MDS) along with electronic health record (EHR) data to evaluate target outcomes.

D2. Conceptual Framework (see Figure 1.) A modified Donabedian[79] approach to quality measurement guides this study. The 4 elements of the model are: 1) context, 2) process, 3) systems of care, and 4) outcomes. In this framework, DEMA-Pro is a process that is influenced by context (e.g. patients/caregiver characteristics) and systems of care (e.g. the KAH home health services sites), to improve intermediate (e.g. meaningful activity engagement) and longer-term outcomes (e.g. physical function, QoL, and reduced depression, hospitalization, emergency visit, and/or transfer to nursing home rates).

Figure 1.



D.3. APPROACH R61 Pilot Phase

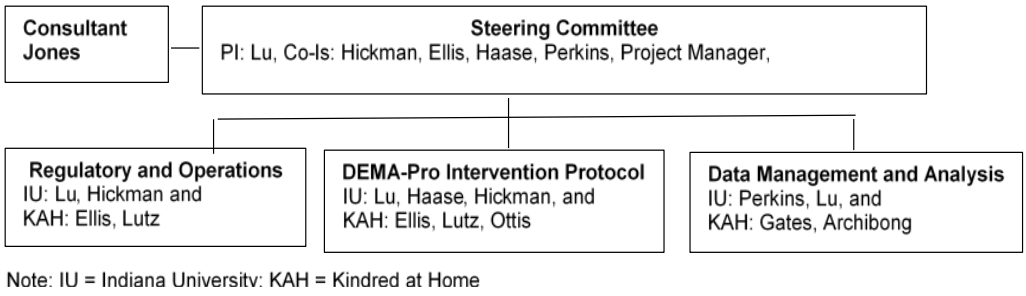
Activities to Support Aim 1: **Establish the organizational infrastructure and programmatic processes needed to conduct a pragmatic cluster-randomized control trial of the DEMA-Pro intervention versus usual care.**

D.3.1. Establish Memorandum of Agreement. PI Lu and Dr. Ellis will work with the IU Office of Research Administration and KAH. Electronic copies of the signed MOU will be securely filed in the IUPUI research office and sent to the NIA Agency. In the R61 phase, patient recruitment and assessment will be done by Assessment Associates at 4 KAH sites; DEMA-Pro will be delivered by protocol-trained personnel at KAH's Centralized Call Center and the resulting DEMA-Pro care plans will be implemented by site clinical staff.

D.3.2. Establish Organizational Structure. As PI, Dr. Lu will oversee all aspects of project development, implementation, and analysis including human resources, NIH/NIA Program Officer communication, and budgetary decisions. **Figure 2** depicts the organizational structure for both the R61 and R33 phases.

Steering Committee. Responsibilities are: 1) project oversight, including collaboration between IU and KAH partners, coordinating workgroup tasks, and achieving project milestones, including primary oversight of the pilot pragmatic phase, and transition to the R33 phase; 2) monitoring KAH electronic and Medicare OASIS data to ensure quality of all DEMA-Pro outcome data.

Figure 2 Organizational Structure



Note: IU = Indiana University; KAH = Kindred at Home

Regulatory and Operations Workgroup. Responsibilities are: 1) obtain a signed MOU from KAH, Gentiva Health Services for the DEMA-Pro trial; 2) follow the signed data use agreements from KAH to ensure access

to electronic health record OASIS data[80] and other relevant data; 3) oversee human subjects' protection, obtaining Indiana University Institutional Review Board of Record (IRB of record) approval, and requesting an informed consent waiver for patients and caregivers; 4) coordinate data safety monitoring board (DSMB), convening meetings and supporting data safety and monitoring reporting.

DEMA-Pro Intervention Protocol Workgroup. Responsibilities include adapting the DEMA protocol, training protocol and toolkits according to KAH's blended learning modules for use as DEMA-Pro to be implemented as a new KAH initiative. In collaboration with KAH Gentiva Health Servcies, relevant corporate policies will be reviewed and potentially modified or created to support the roll-out of this new initiative. The Chief Officer (O'Sullivan) of KAH Home Health Services confirmed her willingness to make modifications to policies and procedures to support DEMA-Pro. DEMA training and intervention protocols and toolkits will be revised as DEMA-Pro to assure the home health services call-center care coordinators delivering DEMA-Pro coach are able to follow the intervention protocol. DEMA-Pro will be refined based on collaboration and consensus, national standards, and existing research evidence.

Separate meetings will be conducted with each KAH site (n=4) recruiting participants and with home health services corporate leadership to discuss opportunities and potential barriers to implementing DEMA-Pro at the site. DEMA-Pro will be refined based on this feedback and further reviewed with representatives from all 4 sites. Based on feedback, DEMA-Pro materials will be refined and finalized for KAH training and delivery. A minimum of three KAH call-center care coordinators will be designated DEMA-Pro coaches will receive in-depth training (approximately 8 hours) and hard-copies of the protocol, sample template workflows, educational handouts (i.e. Self-Management Toolkits), and tips for navigating common barriers. Training will include specific information about the principles of problem-solving for patients with SCD and their family caregivers. Core expectations for DEMA-Pro include education provided to KAH staff with dedicated time to coordinate and facilitate discussions with SCD patients and their caregivers. Based on our previous DEMA study personnel training, DEMA-Pro delivery to SCD patients and caregivers requires 60 minutes for each of the six weekly calls. Dedicated time and flexible schedules are important for the DEMA-Pro coach to facilitate conversations with SDC patients and their caregivers. Consistent with the principles of a pragmatic trial, instructions for the DEMA-Pro coach will be highly flexible.[81]

Per standard operating procedures, a Clinical Assessment Associate at each KAH site will collect and enter data into the electronic health record-OASIS. This Associate will receive one-hour of training to ensure data collection fidelity at both admission and discharge data collection times. In addition, a 20 minutes online video will be provided to other home health services field-based staff to orient them to the goals and processes of DEMA-Pro and to support their use of the DEMA-Pro care plans with patients in the home setting. These KAH home health services field-based staff include registered nurses, physical therapists, occupational therapists, and social workers. The DEMA-PRO coach communicate with to the field-based staff through electronic DEMA-Pro care plan. Adaptations to the DEMA-Pro Self-Management Toolkit, workflows, and educational materials will be made following the pilot.

Data Management and Analysis Workgroup. This group is responsible for obtaining and monitoring all KAH facility and patient data. Based on power calculations, we need 40 KAH home health services locations (20 intervention and 20 control sites, 25 patients/per site; a total of 1000 patients) for the R33 clinical trial phase. This workgroup is responsible for: 1) data management required to link data sources in preparation for analysis and for the actual analysis; 2) data collection protocol and data transfer processes; and 3) the REDCap data management system for the QoL outcome. In Month 2, initial data collection protocol and process for integrating KAH electronic data sources will be tested to determine if any data revisions are necessary. To assess completeness and accuracy of , an electronic health record-OASIS dataset tool,[80] will be compared to the KAH hospitalization rate, or/and transfer to nursing home rate to determine whether the process of merging was accurate. For example, validity checks will be performed to insure all participant hospitalizations and transfers to nursing homes are captured. This also will provide an opportunity to pilot test data cleaning procedures and initial analytic capabilities of the merged data set.

<u>Activities to Support Aim 2</u>, Pilot test the DEMA-Pro training protocol in 4 KAH North Region sites and refine as indicated.

D.3.3.1 Pilot Study Setting. KAH, Gentiva Health Services is a subsidiary of Humana and annually provides home health services to >500,000 patients at > than 400 United States sites in over 40 states.[75] KAH employs teams of clinicians who provide in-home visits with the support of clinicians who provide support and monitoring by phone from the KAH-wide call-center. Call-center care coordinators will deliver DEMA-Pro intervention via telephone. The expected outcome of each session is a DEMA-Pro plan/revised plan for engagement in meaningful activity over the next week. The home health field-base staff will review the electronic weekly DEMA-Pro care plan with participants and support patient and caregiver engagement in meaningful activity according to latest plan. See **Table 1** for R61 (pilot) phase potential number of staff and admissions rates at potential sites.

Table 1. R61 KAH North Region Sites and Numbers of Site Staff and Patient Admissions in 2018

Location	Number of Staff*	2018 Patient Admissions
North Region Location No. 1	20	659
North Region Location No. 2	20	554
North Region Location No. 3	38	900
North Region Location No. 4	18	347
Total	**96 Staff**	**2460 Patient Admissions**

*Staff includes nurses, physical therapists, occupational therapists, and speech therapists.

D.3.3.2. R61 Study Population. There are two study populations.

1) KAH staff including call-center care coordinators, clinical assessment associates, field-based therapists, and clinical operational coordinator;

2) Home health service patients aged ≥ 60 years with SCD, with an OASIS- Cognition Function Subscale Score of 1 or 2 (0 = alert/oriented, able to focus and shift attention, comprehends and recalls task directions independently; 1 = Requires prompting [cuing, repetition, reminders) only under stressful or unfamiliar conditions; 2 = Requires assistance and some direction in specific situations [for example, on all tasks involving shifting of attention] or consistently requires low stimulus environment due to distractibility; 3 = Requires considerable assistance in routine situations. Is not alert and oriented or is unable to shift attention and recall directions more than half the time; 4 = Totally dependent due to disturbances such as constant disorientation, coma, persistent vegetative state, or delirium.

D.3.3.3. R61 Data Elements.

Data elements include home health services characteristics (size, rural/urban location), patient characteristics (demographics, cognitive status, and functional status), patient outcomes, and feasibility of DEMA-Pro training and delivery. Consistent with the principle of pragmatic clinical trials,[82,83] primarily existing data will be used to evaluate outcomes. See **Table 2** for Outcomes, Measures and Electronic Data Sources.

The primary study outcome is physical function, assessed using existing OASIS Activity Daily Living and Instrumental Activity Daily Living (ADL/IADLs) subscales.[80] Secondary outcomes are QoL, depression, the rates of hospitalization, emergency room admission, and transfers to a nursing home. We will use OASIS to assess rates of hospitalization, emergency room visits, and transfer to nursing home.[80] QoL (Sense of Well-being) will be measured with the NIH Toolbox-Psychological Well-being Short-From.[84,85] Depression will be assessed using the OASIS-PHQ-2 subscale. DEMA-Pro training acceptability, delivery confidence, and ability to meet goals will be assessed using of the existing KAH online learning management system and tools and will be analyzed by the Data Management Workgroup.

Table 2. R61 Data Elements: Patient, Staff, and Outcomes

***Patient* Data**	**Measure(s)**	**OASIS-D[a]**	**Other Sources**
Demographics	Patient Characteristics	*M0010, M0014, M0020, M0030, M0050, M0066, M0069, M0140, M0100, M1000, M1021; M1023, M1028, M1033, M1100, M1200*	
Cognitive status	Cognitive Function	M1700	

DEMA-Pro care plan	DEMA-Pro Care Plan and Daily Meaningful Activity Log		KAH - DEMA-Pro care plan [b]
***Staff* Data**			
Staff Experiences of DEMA-Pro training and delivery	Feasibility and Acceptability of DEMA-Pro training and delivery survey		KAH LMS[c]
***Outcomes* Data**			
Physical Function, (Primary Outcome)	Activities of Daily Living/Instructive Activities of Daily Living	M1800, M1819, M1820, MM1830, M1840, M1845, M1850, M1870,	
QoL (Sense of Well-Being)	NIH ToolBox: Psychosocial Well-being-Short-Form		REDCap
Depression	PHQ-2	M1730	
Hospitalization Rate	Frequency of rehospitalization rate	M2410	
Number, Types of ER visits	Frequency unplanned urgent care or hospital ER care	M2301, M2041	
Nursing Home Transfers	Frequency of transfers to nursing home care	M2410	

[a]OASIS-D = Outcome and Assessment Information Set Data; [b]KAH electronic DEMA-Pro Care Plan; [c]KAH LMS = Kindred at Home Learning Management Systems.

D.3.3.4. R61 Data Collection Protocol. Patient data will be obtained by a KAH Clinical Assessment Associate at start of care date, date of any re-admission, and discharge date, using existing KAH electronic data sources including electronic health record-OASIS, Electronic DEMA-Pro Care Plan, learning management system (LMS) and REDCap.

Staff data related to orientation, training, DEMA-Pro delivery and data collection will be obtained from DEMA-Pro coaches, Clinical Assessment Associates, and home health field-based staff. The KAH call-center Care Coordinator will complete the Weekly Activity Engagement Form through the electronic KAH E DEMA-Pro care plan data are used by KAH to identify quality improvement opportunities, evaluate the quality of service provided and guide operational decisions. Items specific to DEMA-Pro outcome s (i.e., QoL) will be added to the KAH home health services REDCap system. KAH staff perception of feasibility of and satisfaction with DEMA-Pro training and delivery survey questions will be added to and entered into KAH LMS.

To establish acceptability of the blended learning modules to train home health providers to deliver DEMA-Pro, the Intervention Protocol Workgroup will: 1) review corporate policies relevant to DEMA-Pro implementation at KAH; 2) adapt the DEMA intervention protocol, training protocol, and Self-Management Toolkit, into blended learning modules and training materials; 3) develop the 15-minute orientation video for KAH home health services field-based staff in Month 4, at the KAH Education/Training Center in Atlanta, and 4) work with KAH clinical operational coordinators to ensure the training protocols are aligned with KAH policies.
The Data Management and Analysis Workgroup will: 1) integrate the feasibility and satisfaction survey questions of DEMA-Pro training and delivery into the KAH online system; 2) ensure the KAH trained staff (i.e. call-center care coordinators, clinical assessment associates, home health service field-based staff) complete the feasibility DEMA-Pro training survey after training sessions and the satisfaction survey (within 48 hours of completing training session) in the KAH online system as following the KAH policies; 3) complete the survey data analysis; and 4) provide the results to the steering committee and the funding agency quarterly. PI Lu and the project manager will work with the DEMA-Pro intervention protocol work group to train KAH staff using the modified training protocol, developed blended teaching modules, and training materials.

To assess feasibility of the DEMA protocol as delivered by trained call-center care coordinators, PI Lu will work with the Project Manager and the DEMA-Pro Intervention Protocol Workgroup to ensure trained KAH call-center care coordinators can follow the DEMA-Pro protocol and deliver the sessions through telephone.
To assess acceptability and quality of study data using the electronic health record- OASIS data collection tool, KAH Electronic DEMA-Pro care plan, and other measures (e.g., QoL), Dr Lu, the (TBD) Project Manager, and the Data Management and Analysis Workgroup will: 1) extract necessary home health services OASIS administrative data, and generate preliminary statistics; 2) access the acceptability and quality of study specific data such as electronic health record from the OASIS data set, the KAH electronic DEMA-Pro care plan, the REDCap Data (e.g. QoL), and KAH online learning management system (e.g. feasibility of DEMA-Pro training and delivery survey data).

D.3.3.5. R61 Intervention Monitoring data will be obtained and monitored within the DEMA-Pro REDCap and KAH electronic DEMA-Pro care plan data bases, as modified by the Steering Committee. These modifications are necessary both to monitor the use of the intervention and to support best clinical practice. A goal will be to minimize the burden on staff and maximize the integration of monitoring into existing clinical systems, consistent with the goals of a pragmatic clinical trial. Specifically, the KAH electronic DEMA-Pro care plan will capture: 1) When a DEMA-Pro is held; 2) what is discussed (check box), 3) who are involved; 4) length of discussion, and 5) outcomes (e.g. code status documentation "Weekly Activity Engagement"). The DEMA-Pro coach will be given an assignment list of 5 home health patients with SCD with a total of 20 telephone session monthly approach; the project staff will work with the DEMA-Pro coach and the KAH Clinical Operations Coordinator to determine procedures for generating this monthly assignment list. If a patient or family caregiver is approached by phone, but declines or does not engage (e.g., passive refusal) after three phone call attempts, the DEMA-Pro coach will document this outcome in the electronic DEMA-Pro care plan.

D.3.3.6. R61 Phase Data Analysis. **Analytic Plan.** Aim 1 will not require quantitative analysis. The data collected for Aim 2 will be analyzed with descriptive methods. Item responses will be tabulated and scale scores for acceptability and feasibility summarized by means and standard deviations (or medians and 25th and 75th percentiles if the data is skewed). Acceptability, feasibility, and satisfaction data will be summarized separately for DEMA-Pro coaches, clinical assessment associates, and home health field-based staff. With respect to patient outcomes, our primary goals are to examine the data collected from the EHR for quality and ensure it can be captured and merged efficiently and appropriately. We will also generate descriptive statistics for all patient outcomes collected through the EHR to help us to identify any data issues, such as missing data patterns, that could influence the implementation of the pragmatic RCT. Cronbach's alpha will be calculated for multi-items scales.

D.3.3.7. R61Go/No-Go Criteria, Milestones and Timeline. The Go/No-Go Criteria are established per the RFA guidance to identify the milestones that must be achieved during the R61 phase to qualify for the transition from the R61 to the R33 phase**.** The R61 Go/No-Go criteria are: 1) Establish partnerships with the KAH home health services as demonstrated by executed memoranda of understanding and data use agreements; 2) Obtain access to necessary administrative data including OASIS, KAH electronic DEMA-Pro care plan, REDCap and KAH LMS; 3) Produce the DEMA-Pro protocol; and 4) Pilot test the DEMA-Pro Program and generate preliminary feasibility data. Milestones and the study timeline are in **Table 3.**

Table 3. R61 (Pilot) Milestones and Timeline.

Milestones Months:	1	2	3	4	5	6	7	8	9	10	11	12
Start-UP: hire staff, obtain IRB approvals; establish goal timelines the Steering Committee and the three Workgroups												
Obtain MOU with the KAH, and establish DMSB												
Submit data access requests to: HHS for OASIS database and to KAH for access to DEMA-Pro care plan and LMS data bases												
Identify pilot sites and DEMA Program interveners, Review/adapt HHS EHR policies and procedures.												
Refine DEMA in-person training delivery to blended learning models for DEMA-Pro												
Pilot test DEMA-Pro training and revise as needed												
Access and analyze process and outcome data from OASIS and KAH DEMA-Pro care plan and LMS databases												
Extract, link and verify accuracy of data												
Assess value of and ease of obtain outcomes measures for use in R33												

Note: IRB = Institutional Review Board; MOU = Memoranda of Understanding; HHS = Home Health Services; EHR= Electronic Health Record; DSMB = Data Safety and Monitoring Board; OASIS = Outcome and Assessment Information Set; LMS = Learning Management System; DEMA-Pro = Daily Engagement Meaningful Activity Professional

D.4. APPROACH: R33 Phase.

D.4.1. R33 Phase Overview. The overarching goal of the 4 year R33 phase is to conduct a pragmatic cluster RCT of DEMA-Pro in 40 home health services locations in multiple states. The intervention will be the DEMA-

Pro program and control condition will be usual care. The telephone delivered DEMA-Pro intervention will be implemented for 30 months. The target population will be home health services patients with SCD. Outcomes will be ascertained using existing data resources (OASIS, REDCap- patient QoL). The primary trial outcome is level of physical function. Secondary outcomes are: 1) hospital transfer (admissions within 30 days and emergency department visits per 1000/ person-days alive); 2) nursing home transfer; and 3) patient QoL; and 4) depression). The detailed methods for the R33 phase are described below. Information about the organizational structure of the project, data collection measures and other relevant information are contained above in the R61 and are not repeated here.

D.4.2. R33 Home Health Service and Patient Characteristics. KAH, Gentiva Health Services, is a subsidiary of Humana and annually provides home health services to more than half a million patients at over 400 United States locations in over 40 states.[75] **Table 4** indicates that in 2018, the KAH Home Health Services had a total of 321,297 new patients (excluding home hospice patients); 92% were aged ≥ 60 year old (n = 295,092) and 89% of were ≥ aged 65 years old; an average 615 new patients/per locations annually and the average lengths of home health services were 58 days. KAH employs teams of clinicians (or field-based staff) who provide in-home visits with the support of care coordinators who provide support and monitoring by phone through a centralized call-center.

Table 4. KAH Patients Meeting Eligibility Criteria in 2018[a]

	N (%)
Age: % ≥ 60 years old	295,092 (92%)
Mean (Median)	77.7 (78.5)
Gender: Female	63%
Race: White	82%
Black	13%
Latino	2%
Number/Percent of Patients with SCD[a]:	112,135 (38%)
Mean Time on Home Health Service: (days)	58
Risk for Hospitalization:	45%
Fall Risk	98%

[a]Subject cognitive decline (SCD) is verified based on OASIS Cognitive Function a score of 1 or 2 (0 is normal).

D. 4.3. R33 Home Health Service Site Eligibility. Criteria for home health services sites are: 1) a minimum 300 or more new patients/per site annually; 2) at least 50% w/ length of service ≥ 60 days; 3) staff-to-patient ratio complies with Home Health Agency requirements; 4) no severe state issues. Prior to randomization, sites meeting these criteria will be determined in consultation with the KAH, Clinical Operations Coordinator.

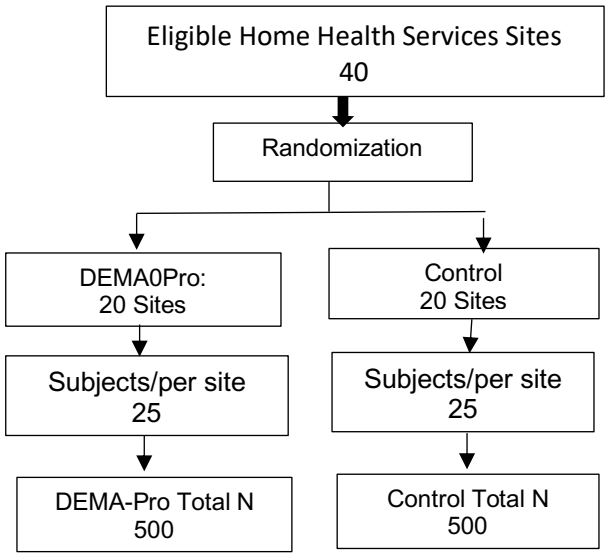
D. 4.4. R33 Home Health Services Location Recruitment. The DEMA-Pro Program will be rolled out as a corporate initiative and the KAH Home Health Services Clinical Operations Coordinator will be supported in participating in the initiative by the KAH corporate leadership**.** The KAH Clinical Operations Coordinator has agreed to participate in the study. The KAH Clinical Operations Coordinator will use the home health service eligibility check list to identify the KAH home health service locations meeting eligibility criteria and provide the list to the PI and Co-I Susan Perkins, who will randomize sites.

D. 4.5 R33 Sample Size and Power. Kindred at Home (KAH) has generously agreed to support 40 home health services sites (20 sites for intervention; 20 sites for control) with 25 subjects per site to recruit 1000 patients at 40 sites in R33 (implement) phase over a 4 years intervention period. Sample sizes of 500 subjects in the Intervention group and 500 subjects in the Control group will be obtained by sampling 25 patients at each of the 20 Intervention group sites and 25 at each of the 20 Control group sites, to achieve 90% power to detect an effect size of 0.5 standard deviations assuming an intracluster correlation coefficient of 0.1. A two-sided t-test with a significance level of 0.05 was used for this calculation. KAH pilot data indicates the intra-cluster correlation for physical function (primary outcome) is 0.07, so our power calculation is conservative. The power calculation was done using NCSS PASS 2019, v19.0.1.[86] Because each home health service setting delivers care across a large catchment area (i.e. city, surrounding suburbs and rural areas), we anticipate diversity in the sample of patients and caregivers across all sites.

D. 4.6. R33 Random Assignment. Figure 3 describes randomization levels. More than forty eligible home health services locations who agree to participate in the trial will be randomized to either the intervention or control group at a 1-to-1 ratio. Specifically, randomization will occur at the facility level, all patients with SCD in

the intervention home health services sites are eligible for inclusion in the trial and, depending on site randomization status, will receive either the DEMA-Pro or Control intervention.

Figure 3.



D. 4.7. R33 Programmatic RCT Procedures. Following site randomization, the intervention will first be implemented in one home health service site selected in consultation with the KAH Clinical Operations Coordinator. This initial "selection" is to identify any implementation problems as the intervention is disseminated beyond the R61 (pilot) phase and without the hands-on involvement of the study team. The Regulatory and Operations Workgroup and DEMA-Pro Protocol Workgroup will work closely with the home health system partners to troubleshoot and identify any necessary refinements. After a 2 month period, the DEMA-Pro program will be rolled out to the rest of selected intervention home health service sites. All communications with the clinical care coordinators and clinical operations coordinator will be drafted by the Regulatory and Operations Workgroup and tailored to fit the KAH corporate branding. The Clinical Operations Coordinator and an IT Specialist will be designated for the KAH home health services by Dr. Jennifer Ellis (Co-I, the Vice President of Research and Operational Development, KAH) and supported by the grant. All communications about the DEMA-Pro program with individual home health service sites will be delivered through the DEMA-Pro coach during regularly planned monthly Zoom meetings with the DEMA-Pro Project Intervention Team where in any issues and unmet needs are address. Following the 18 month pragmatic cluster RCT, we will merge data from the 40 sites and analyze primary and secondary outcomes.

D. 4.8. <u>R33 DEMA-Pro Intervention</u>. Trained DEMA-Pro coaches will follow the adapted DEMA intervention protocol to deliver six weekly, 1-hour sessions. The first session is an orientation to the DEMA-Pro intervention, including DEMA- Pro goals, processes, review of educational materials, timelines, and development of the initial Weekly Activity Plan based on the patient's self-identified meaningful activity. Over the next five weekly sessions, the coach uses problem-solving strategies to facilitate dyad collaboration to mutually identify meaningful activities and make a realist plan to achieve the patient-identified meaning activity goals. In subsequent weekly sessions, the KAH-trained coaches review patient-caregiver dyad progress towards their previously set goals and engages the dyad in additional problem-solving strategies for achieving their current goal, refining their plan as needed, and/or identifying additional meaningful activities and establishing plans to achieve them with caregiver support. In each session, the patient and caregiver also select, review, and discuss one of six topics in the Self-Management Toolkit (e.g., planning meaningful activities; learning strategies for living with SCD; finding resources, planning for the future).

As dyads gain skills to enact the patient's meaningful activity, they work with KAH trained call-center care coordinator to establish a pattern of problem solving for engagement in additional meaningful activities. At the end of a session, the Coach enters the Weekly Activity Plan into the electronic health record (HER) system so field-based staff can integrate the plan into their care.

Between weekly sessions, the patient and caregiver will work with their home health services field-based staff in support of intermediate goals (e.g. adjusting pain medication or physical therapy treatment plan to gain lower body strength with minimum pain) necessary to achieve longer-term goals (e.g, painting a portrait of grandson; engaging in social or physical activities such as playing bridge or golfing.) The patient and caregiver work together to incrementally achieve the patient's planned meaningful activity goals and document their daily progress in their activity log (activity type, frequency, and time spent engaged in each specific activity, and any problems/concerns).

D.4.9 R33 Intervention Fidelity/adherence and Monitoring Plan. To translate and implement and evidence-based intervention in the home health services settings, we will follow the guidance of the PRECIS-2 tool[87] and PART Model[83] to implement a fidelity/adherence monitoring plan. The goal is to ensure treatment integrity, maximize flexibility in delivery and adherence, minimize experimental drift, and minimize contamination of the

control group.[88] Strategies include: 1) standardized DEMA-Pro training protocol, session delivery manual, and timing (telephone session) vs. usual care; 2) standardized procedures for documenting DEMA-Pro quality assurance and deviations; 3) documenting DEMA-Pro content and duration in the home health services electronic notes; 4) guidelines for managing adverse events of the intervention; 5) weekly documented DEMA-Pro meaningful activity engagement form that includes type of activity, engagement schedule, frequency; and 6) bi-weekly zoom meeting with the call-center care coordinators to address their concerns.

See **D.3.3.5** for a description of the intervention monitoring plan. We anticipate the intervention will be refined based on the R61 outcomes. Patients receiving home health service and randomized to the control group will receive usual care during the course of the study, meaning patients will be exposed to whatever DEMA-Pro practices are in use within the home health service sites or are adopted during the course of the trial. PI, Co-Is will closely work with our DEMA-Pro Intervention team to ensure DEMA-Pro coaches, clinical assessments associates, and home-field based staff follow the modified DEMA-Pro and data collection protocol. We will also obtain and use data to minimize staff burden and maximize integration of monitoring into existing clinical systems, consistent with the goals of a pragmatic clinical trial. Specifically, the KAH electronic call-center care coordination communication notes will capture: 1) when a DEMA-Pro session is held; 2) what was discussed (check box), 3) who were involved; 4) length of discussion, and 5) outcomes (e.g. code status documentation "Weekly activity Engagement").

D4.10. R33 Data Elements and Sources. Based on outcomes of the R61 Pilot we will make decisions about using the same measures used in the R61, including considering or dropping or adding measures. See **D3.3.7Table 2 and Human Subjects and 4.3 Outcomes and Measures**.

D 4.11. R33 Data Analysis.
Analysis will be carried out in an intention-to-treat framework (IIT), which gives a pragmatic estimate of the intervention estimate.[89] The IIT analysis will use data from all eligible patients, regardless of sites' adherence to the study protocol and patient attrition. It is well-known that clinical effectiveness can be severely underestimated if IIT analyses are not preformed.[90] Cronbach's alpha will be calculated for multi-items scales. Hypotheses will be tested in the generalized linear mixed models (GLLM) framework that include a fixed effect for intervention and random effect for site. In the context of the clustered RCT, patients from the same site share a common site-specific intercept; this random intercept helps to accommodate the within-site correlations among responses from patients in the same site. The general form of the GLLM model is $g(\mathrm{E}(Y_{ij})) = \beta_0 + U_i + \alpha \cdot DEMA\text{-}Pro_i + X^t_{ij}\beta$ where g is the link function, Yij is the response of the jth patient in the ith site, $DEMA\text{-}Pro_i$ is a binary intervention indicator, α is the regression coefficient representing the treatment effect, β_0 is the intercept, $U_i \sim N(0,\sigma^2)$ is the random site effect, and $\boldsymbol{X}^t_{ij}$ is a vector of patient characteristics (age, gender, comorbidities, etc.) and site characteristics (patients per site, staff-to-patient ratio, etc). Even though we expect the covariates to be balanced due to the randomization, here we include the covariates in the main analytical model just in case some of the factors are not sufficiently balanced by the randomization scheme. The identity or gamma link (depending on data distribution) will be used for physical function, quality of life (sense of well-being), and depression. Because hospitalizations and emergency department visits are discrete events, we use counts of hospital admissions and emergency department visits/1000 person-days alive observed during the follow-up period as the main analytical outcome. Event counts are usually analyzed with count data regression models, so we will employ mixed-effects Poisson regression. The model can be written as above but using a log link: $log((\mathrm{E}(Y_{ij})) = \beta_0 + U_i + \alpha \cdot DEMA\text{-}Pro_i + X^t_{ij}\beta$. From the fitted model, we can ascertain the incident rate ratio associated with the intervention, exp (α). Importantly, an offset parameter can be added to account for the unequal lengths of observation periods among study participants. As a result, death and early dropout can be appropriately accommodated. Other scenarios that may complicate the study include extra-Poisson variability, zero-inflation, informative missingness of data, and possible existence of nonlinear effects. Negative binomial models will be used if there is significant overdispersion and zero-inflated models will be used as needed.[91] Depending on the amount and type of missing data, we will conduct multiple imputation (for missing at random patterns) or pattern mixture models (for not missing at random patterns) analyses. The significance level will be set at 0.05.

R33 Milestones and Timelines. The R33 will be conducted over 3 years (36 months). Proposed Milestones and Timelines are outlined in **Table 5.** Per the request for applications, annual milestones will be negotiated with the program officer in the event the R33 is awarded.

Table 5. R33 (Implement) Phase Milestones and Timeline

R33 (Implement) Phase Milestone	Year 2				Year 3				Year 4				Year 5			
Month	1-3	4-6	7-9	10-12	13-15	16-18	19-21	22-24	25-27	28-30	31-33	34-36	37-39	40-42	43-45	45-48
Refine and standardize DEMA-Pro Program based on the R61 findings.																
Analysis of Pilot Data																
Site Selection and Power Calculations																
Pragmatic Trial of DEMA-Pro Program																
Data Management: Merging, Cleaning																
Data Analysis																
Dissemination: Presentations, Manuscripts																

Note: DEMA-Pro = Daily Meaningful Activity Engagement-Professional.

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Potential problems and alternative solutions Our team is aware of four potential barriers and prepared for navigating barriers to successful implementation in home health services settings: 1) Home health services leaders may not support DEMA-Pro coach, thus hindering full adoption of the program; 2) Home healthcare service leaders' may have competing priorities, leading to additional duties for DEMA-Pro coach or re-assign them to meet competing priorities; 3) Staff turnover may result in inadequate numbers of DEMA-Pro trained staff, which could result in lack of coverage for DEMA-PRO activities; and 4) There may be limited ability for monitoring the quality of the DEMA-Pro coach's work. We will identify and regularly communicate with the KAH home health service site clinical operations coordinator for early identification of issues. We will provide a clear role description and orientation to ensure the DEMA-Pro coach accountable role responsibility.