

Clinical Interventional Study Protocol Template

THE AGING BRAIN CARE VIRTUAL PROGRAM (ABCV)

An embedded, pragmatic, cluster randomized, usual care-controlled trial to test the effectiveness of a virtual dementia collaborative care program in 24 IUH primary care clinics (12 intervention, 12 control) across the state of Indiana with 860 persons living with dementia (PLWD) (430 intervention, 430 control) and their care partners. The primary aim of the study is to reduce emergency department utilization and the secondary outcome is appropriate medication use. Additionally, this study will explore the implementation context, process, and outcomes of the Aging Brain Care Virtual program (ABCV).

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I. Procedures Schedule

II. Informed Consent Form Template

III. Other (add as many appendices as necessary)

PRÉCIS

Study Title

The Aging Brain Care Virtual Program (ABCV)

Objectives

The objective of this project is to conduct a statewide pragmatic trial of collaborative care delivered to persons living with dementia and their care partners virtually, by trained care coordinators. If we are successful in decreasing the outcomes of emergency department utilization and inappropriate medication use, we will provide further evidence that pragmatically embedded high-quality dementia care coordination is able to be implemented in health systems. The specific aims of the project are:

Specific Aim 1: Evaluate the impact of the ABCV Program on utilization of emergency department care in a sample of 860 persons living with dementia (PLWD).

Specific Aim 2: Evaluate the impact of the ABCV Program on appropriate medication use.

Specific Aim 3: Evaluate the implementation of the ABCV Program using the Consolidated Framework for Implementation Research (CFIR) framework in preparation for widespread implementation.

Design and Outcomes

We will conduct a 12-month cluster randomized, usual care controlled, pragmatic clinical trial of the ABCV program in 24 Indiana University Health (IUH) primary care clinics (12 intervention, 12 control) across the state of Indiana. The objective of the project is to test the effects of the ABCV Program on the primary outcome of all cause emergency department (ED) use and secondary outcomes of appropriate medication use as measured by a change in anticholinergic medication use and initiation of new prescriptions for benzodiazepines and antipsychotics.

Interventions and Duration

The ABCV intervention will be tailored to the needs of each PLWD and their care partner, but, in general, will have two phases:

1. Initial Assessment Phase includes the initial contact with the dyad to describe the ABCV intervention and the first few visits with the ABCV care coordinator. These visits may include both the patient and care partner (the dyad) or only the care partner. The goal of this phase is to build trust between the ABCV team and the dyad and to collect information about current status of the PLWD and care partners' needs to develop the care plan.

Potential participants (PLWD and their care partners) will be identified via the electronic medical record (EMR). Following an initial EMR review for all enrolled participants, the interventionist (registered nurse (RN) or social worker (SW) care coordinator) will conduct an initial virtual visit by phone or video to (a) introduce themselves; (b) introduce the ABCV program; (c) confirm the name and contact information for the PLWD and name and contact information and relationship to PLWD from the care partner; and (d) begin an initial assessment of the PLWD's home safety, medical and biopsychosocial needs, and other issues noted by the care

partner, using standardized assessment tools and semi-structured questions.

2. The Collaborative Care Phase includes monthly follow-up visits when the care plan is being implemented in which concerns will be addressed with standardized protocols. Protocols include management of behavioral/ psychological symptoms of dementia, caregiver stress, medication management, comorbidity management and advance care planning.

Following the initial visit the care coordinator will have monthly follow-up for the first three months of the intervention, and if after three months the dyad is stable, contact will be reduced to quarterly.

All interactions for the 12-month duration of the study will be documented by the care coordinator in the EMR and will be visible to the primary care team and the PLWDs' other providers. Consistent with federal law and IU Health policy, this information, like other clinical notes, can also be viewed by the patient or care partner if they have access to the patient's IU Health Patient Portal.

Case review for all enrolled dyads will occur for approximately one hour weekly with the Virtual Hub physician, with back up provided by one of the MD ABCV investigators. During these sessions, the challenges of both the PLWD and the care partner will be reviewed, and actions identified to support the dyad. The results of this initial assessment are forwarded to the patients' PCP with requested feedback and further direction as needed. Throughout the duration of the follow-up phase, the team will continue to work with the dyad and the patient's primary care team to monitor, implement, and adjust the individualized care plan, as necessary.

To study the implementation of ABCV (Aim 3), a subset of care partners and up to 30 additional stakeholders (clinicians and other health care staff) will be interviewed after the 12-month intervention period has ended. These interviews will be semi-structured and audio or video-recorded. They will be conducted within 6 months of the conclusion of the intervention.

Sample Size and Population

The intervention will enroll 860 patients. Patient participants will be 860 community-dwelling patients aged 65 or older, living with dementia (PLWD) (430 intervention, 430 control). Each intervention participant will enroll with a care partner aged 18 or older for an additional 430 participants.

STUDY TEAM ROSTER

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The Regenstrief Institute

Regenstrief Institute Data Services is the honest data broker for IU Health. RI will prepare lists of patients for the study using ICD-10 and other eligibility criteria, organized by clinic. They will also provide data for outcome analysis, including ED visits and medication usage.

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Study objectives

1.1 Primary Objective

Evaluate the impact of the ABCV Program on all cause utilization of emergency department utilization in a sample of persons living with dementia (PLWD).

1.2 Secondary Objective

Evaluate the impact of the ABCV Program on appropriate medication use, in particular anticholinergic medicines, benzodiazepines, and antipsychotics.

2 BACKGROUND AND RATIONALE

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

The majority of PLWD are cared for in primary care settings and receive considerable care and assistance from family members.^{1,2} We and others have shown that primary care patients with dementia have twice the rate of ED visits and hospitalizations compared to people without dementia and that they and their care partners have substantial unmet needs including management of cognitive and behavioral symptoms, management of comorbidities, support for care partners, and the need for better coordination of services.³⁻⁵ Family care partners are critical to the well-being and quality of life of PLWD, but often lack experience in how to manage behavioral and psychological symptoms of dementia as well as the common comorbidities that people with dementia frequently have. Symptoms of dementia can be worsened by certain medications used in primary care such as anticholinergics and inappropriate medications are sometimes used to treat dementia symptoms.^{6,7} It is also well documented that care partners experience high rates of distress and burden as well as social isolation, loneliness, and financial hardship, all of which impact the physical health of the care partner and the PLWD.⁸ There is a tremendous demand for primary care-based interventions that address these crucial needs, are pragmatic, able to be scaled across urban, rural, and suburban settings, and focused on improving care and outcomes for PLWD and their care partners.

2.2 Study Rationale

Results of preliminary studies at IU Health to identify dementia in the primary care setting have tested the use of digital dementia detection and screening as a part of routine primary care delivery for adults ≥ 65 years old, which have highlighted a need for additional system-level support for patients and their care partners following a dementia diagnosis. A previous study testing the efficacy of a dementia collaborative care model in other health systems resulted in fewer behavioral and psychological symptoms of dementia and care partners showed improvement in symptoms of depression and caregiver burden.⁹ In the last ten years these studies led to the development of the Aging Brain Care (ABC) program, which assists PCPs in achieving recommended standards of care in the care and management of PLWD and their care partners, using evidence-based practice and standardized, validated assessment tools.¹⁰ ABC has been

evaluated in over 5,000 patients at Eskenazi Health and validated in multiple trials demonstrating its effectiveness in the care and management of PLWD and their care partners. ABC has been shown to reduce symptoms of depression, reduce incidence of acute care utilization, improve quality of life for both PLWD and their care partners, improve behavioral and psychological symptoms, and reduce the cost of care for PLWD. In recent years the ABC model has been combined with the Palliative Excellence in Alzheimer's Care Efforts (IN-PEACE) program, to include advance care planning (ACP), goals of care conversations, and counseling about hospice and end of life care when appropriate.

The Aging Brain Care Virtual (ABCV) program at IUH will deliver the ABC model using video or telephone so it can be expanded throughout the state of Indiana. It includes components and protocols derived from several core strategies essential for successful care management: 1) building connection and trust with dyads to increase engagement; 2) use of structured validated assessments that are comprehensive but pragmatic to limit patient and care partner burden and to increase scalability for future translation; 3) increasing 'on-demand' care partner access to program resources; 4) ensuring flexibility in relationships with primary care physicians in establishing allocation of responsibility; 5) ensuring minimum standards of expertise that cover the range of medical and biopsychosocial needs of dyads through the use of interdisciplinary care management teams.

The ABCV intervention relies on a tailored approach in which patient and care partner needs are identified during virtual visits and addressed with standardized protocols, each of which include a care partner handout and a script for the care coordinator. Other components are based on dyad need. Protocols include management of behavioral and psychological symptoms of dementia, care partner stress, medication management, management of the patient's comorbidities and the occurrence of common geriatric syndromes and medical conditions that result in acute care utilization. Palliative care interventions including advance care planning and goals of care discussions, counseling about feeding tubes, nurse home placement and hospice use, will be added from the ongoing IN-PEACE randomized controlled trial given that there is evidence that advance care planning and goals of care discussions can reduce ED use by avoiding visits that are inconsistent with patient or family goals.

3 STUDY DESIGN

The trial design is as follows:

- This is a usual care controlled, pragmatic clinical trial comparing ABCV to usual care.
- Cluster randomization will occur by primary care clinic.
- 24 IUH primary care clinics (12 intervention, 12 control) across the state of Indiana are participating.
- Patient participants will be active, primary care patients, community dwelling, and have a diagnosis of ADRD in their primary care EMR.

- Care partner participants will be self or patient-identified care partners of the enrolled patients with ADRD.
- The duration of the enrollment for each participant (patient and care partner) is 12 months from initial engagement in the ABCV intervention.
- The intervention involves a tailored approach in which patient and care partner needs are identified during visits and addressed with standardized protocols.
- A subset of patients, care partners, clinicians, and non-clinical staff at participating primary care clinics will be invited to participate in implementation surveys and qualitative interviews. Clinicians and non-clinical staff members must be employed at an IU Health Clinic randomized to the intervention group and be able to participate in an audio-recorded interview in English.

4 SELECTION AND ENROLLMENT OF PARTICIPANTS

A list of patients will be generated from the EMR based on study inclusion criteria. Patients appearing on these lists will be considered enrolled in the study. Patient lists for each clinic in the intervention group will be divided between the two care coordinators. For each patient, the assigned care coordinator will review the chart, identify a care partner, and approach them by telephone. If no care partner can be identified via the EMR the care coordinator will call the patient first, introduce themselves and the ABCV Intervention and ask for the name and the contact information for a family member *“who helps them get to the doctor, or with things around the house.”* If the patient states that they do not have a family member who meets these criteria, the care coordinators will ask *“who would your doctor call if they needed to reach someone for you?”*

4.1 Inclusion Criteria

Participants must meet all inclusion criteria to be enrolled in ABCV.

Patient inclusion criteria are:

- 65 years or older
- Community dwelling at the time of enrollment
- Ability to complete all study steps in English
- A diagnosis of ADRD based on ICD-10 codes in the EMR. Patients at all stages of dementia are eligible for the study.
- Is not enrolled in hospice
- Currently an “active” patient, as defined as having at least one primary care visit in the past 14 months as indicated in the EMR.
- Must have an eligible care partner who is able to participate with the patient.

Care partner inclusion criteria are:

- 18 years or older
- Ability to complete all study steps in English
- Ability to understand the ABCV program and to implement the program with the PLWD for the entire length of the study

4.2 Exclusion Criteria

Individuals meeting any of the exclusion criteria at screening will be excluded from engagement in the ABCV intervention but will be followed for outcomes data.

Patient exclusion criteria are:

- Under the age of 65
- Not community dwelling at the time of enrollment (e.g., long-term care or nursing facility)
- Non-English speaking
- No diagnosis of ADRD in the EMR
- Enrolled in hospice
- Not a currently “active” patient (e.g., has not had at least one primary care visit in the last 14 months)
- No eligible care partner to participate in the study with the patient

Care partner exclusion criteria are:

- Under the age of 18
- Non-English speaking

Potential participants may also be excluded from engagement in ABCV Program at any time based on the following:

- Clinical judgment on the appropriateness of the intervention, as indicated by the PCP, care coordinator, and/or the ABCV Virtual Hub Physician or other study physician.

4.3 Study Enrollment Procedures

- Eligible patients will be identified by the IUH data and analytics team and Regenstrief Data Services (RDS) to provide lists of patients at each clinic who are eligible for engagement with an ABCV care coordinator. Lists will be stored in a secure REDCap database, secure Microsoft Teams folder, or on a secure, encrypted file server at the Regenstrief Institute, where all files with identifiable information will include password protection.
- Care partners will initially be identified from the EMR (e.g., patient’s documented caregiver, medical power of attorney, or emergency contact) then verified through contact with the patient and/or the contact listed. If no care partner is identified via the EMR the care coordinator will reach out to the patient (See Section 4 above).

- Reasons for ineligibility and for non-participation of eligible candidates will be documented in a screening log. This screening log will be maintained on REDCap.
- We will obtain a waiver of informed consent for all aspects of the study involving the patients and care partners except for the qualitative interviews for Aim 3.
- We will obtain a waiver of documentation for qualitative interview participants. We will obtain verbal consent from each interviewee since these interviews will occur by phone or virtually.

5 STUDY INTERVENTIONS

5.1 Interventions, Administration, and Duration

The intervention will be delivered to the care partner or dyad based on the care partner's availability. The intervention will be conducted via video platform (e.g., Amwell Now, IUH Zoom, or similar video platform that is PHI approved and secure). Care partners who do not have access to the virtual platform will participate securely by phone.

Initial Assessment Phase

- Prior to initial contact with the patient or care partner, the care coordinator will review the patient's EMR with a special emphasis on previous ED visits and hospitalizations, review of comorbidities, and a review of medications.
- Care coordinators will reach out to the care partner, once identified, and complete the following steps:
 - Review the overall structure of ABCV with the care partner and PLWD.
 - Provide the care partner with contact information for the care coordinators for non-emergent needs that arise in between scheduled calls, including symptom changes, ED or urgent care visits, hospitalizations, or with questions, concerns, and referral/resource requests.
- During the Initial Assessment Phase of ABCV, the care coordinator will:
 - Conduct a medical and biopsychosocial needs assessment using standardized assessment tools for co-morbid, chronic disease management.
 - Document all contact related to the initial assessment phase in the patient's EMR.
 - Review findings with the Virtual Hub physician or one of the other study physicians (ABCV investigators) from prior EMR data and the initial assessment.
 - Finalize an initial care plan and identify areas needing further assessment.

- Forward a summary of assessment results and the care plan to the PCP via the EMR.

The Collaborative Care Phase

- The care coordinator will conduct follow-up visits virtually or by telephone with the patient and care partner as follows:
 - Monthly check-in for at least the first three months of enrollment.
 - After three months check-in frequency will be reduced to quarterly if the patient is stable.” as indicated by scores on the Healthy Aging Brain Care (HABC)-Monitor and/or other standardized protocols to assess stability of the patient and care partner.
 - The care partner may reach out in between visits with other concerns, that may trigger other study protocols and/or more frequent contact with the care coordinator.
 - The collaborative care phase will end when the patient had been in the program for a total of 12 months.
- In general, each visit will include:
 - Open-ended questions about the patient’s most bothersome symptoms, and management of comorbidities and common geriatric syndromes, and the care partner’s experience and reactions within the care partner role.
 - Administration of the HABC-Monitor may be repeated, including items for rating a care partner’s reaction to or distress from behavioral problems. Ratings of the patient’s symptoms and the care partner’s overall stress levels will be recorded in the patient’s EMR. (There are no questions for the care partner that address clinical symptoms of depression or suicidal ideation.)
 - Responses to assessment tools indicating frequent symptoms or those causing distress in the patient or care partner will trigger the appropriate protocols for managing those symptoms.
 - Note that non-pharmacological and behavioral strategies have an early and important role in the protocols.
 - Some of the protocols may trigger follow up sooner than the next scheduled monthly contact.
 - Protocols may be tailored to address needs of the specific dyad to focus on areas, for example, the reduction of unnecessary ED visits via
 - Identification of symptoms of acute illness
 - Management of chronic disease
 - Prevention of falls and injuries
- Data from the HABC monitor will be stored in detail in a REDCap

database. REDCap is a secure, HIPAA compliant research database. The data will also be synthesized into a report that will be placed in the Cerner EMR so that the primary care provider and other clinicians are able to see it.

- The care coordinator will also set up one visit to discuss goals of care and advance care planning with the care partner.

5.2 Handling of Study Interventions

Care coordinators will be a registered nurse (RN) and a social worker (SW) with extensive experience in care of older adults with ADRD. We selected interventionists from these two disciplines because they have overlapping but complementary experiences highly relevant to geriatric patient care and can consult one another for particular areas of expertise (e.g., complex medical management is the domain of the nurse, and difficult community resource issues are the domain of the social worker).

5.3 Concomitant Interventions

5.3.1 Allowed Interventions

Not applicable

5.3.2 Required Interventions

Not applicable

5.3.3 Prohibited Interventions

Not applicable

5.4 Adherence Assessment

To monitor fidelity to the intervention we will develop two new instruments to assess the ABCV program:

- Develop a pre and post-test for the interventionist to ensure that they have the needed knowledge about dementia care and the ABCV assessments and protocol.
- Develop an interventionist adherence checklist to ensure that ABCV is delivered as intended, consistent with established methods to ensure intervention fidelity, as outlined by the NIH Treatment Fidelity Workgroup.
- Document the delivery of protocols at each patient visit.

6 STUDY PROCEDURES

6.1 Schedule of Evaluations

Study Components	Prior to Study Start	Chart Review/Screen	Initial Contact & Engagement in ABCV	ABCV Visit 1	Advance Care Planning Visit	Monthly visits (months 2-12)	Post-emergency room visit	Post Study
Study Data Collection (from IU Health Cerner data, pulled by Regenstrief Data Services)								
Data Pull data to Identify Eligible PLWD using ICD-10 codes	X							
Data pull to identify study outcomes								X
Implementation Qualitative interviews								X
Implementation surveys*								X
ABCV Intervention Components**								
Abuse (physical, emotional, financial)								
Acute concerns/symptoms of new medical issues								
Advance Care Planning					X			
Adult day services, need for and places to receive it								
Anxiety PLWD				X		X		

Study Components	Prior to Study Start	Chart Review & Screen	Initial Contact & Engagement in ABCV	ABCV Visit 1	Advance Care Planning Visit	Monthly visits (months 2-12)	Post-emergency room visit	Post Study
BPSD				X		X		
Care partner activation (knowledge, skills, and access to support)				X				
Care partner burden				X		X		
Caring and Coping								
Communication with PCP (questions re: f/u of orders, etc.								
Communication with PLWD								
Co-morbidity mgmt.; chronic disease mgmt.		X		X				
Dementia history, severity, staging		X		X				
Depression, PLWD				X				
Depression, CP								
Engagement eligibility		X	X					
Home and community-based services								

Study Components	Prior to Study Start	Chart Review/Screen	Initial Contact & Engagement in ABCV	ABCV Visit 1	Advance Care Planning Visit	Monthly visits (months 2-12)	Post-emergency room visit	Post Study
Introduction, why you are calling, what is ABCV, invitation engagement, etc.			X					
Hospice								
Medications		X		X				
Mobility								
Pain and Discomfort								
Personal Care								
Psycho Social History				X				
Root cause analysis after ED visit							X	
Respite Care, need for and places to receive it								
Safety (Home, falls, guns, driving, etc.)								
Transitional care								

*Acceptability of Intervention Measure (AIM); Feasibility of Intervention Measure (FIM), and Intervention Appropriateness Measure (IAM).

** "X's" indicate time points at which that intervention is required as part of ABCV. Other interventions are used at the care coordinator's discretion based on PLWD/CP need.

6.2 Description of Evaluations

6.2.1 Screening Evaluation

These evaluations occur to determine if the PLWD and Care Partner will be invited to engage in the ABCV intervention.

Consenting Procedure

This is a pragmatic, primary care embedded clinical trial of the ABCV dementia collaborative care intervention. We will apply for a waiver of informed consent for all study activities except the qualitative interviews that are part of the implementation evaluation. Participants may decline to engage with the care coordinators at any point in the project. Refusal to engage in ABCV or a request by the patient or care partner not be contacted again will be documented in the screening log.

We will obtain a waiver of written documentation of informed consent for individuals who participate in a qualitative interview. Verbal consent will be obtained for the sample of care partner participants and primary care providers and clinic staff who agree to participate in the implementation surveys and interviews. We will obtain a waiver of written documentation of informed consent for individuals who participate in a qualitative interview, however a record of verbal consent will be recorded by the study team.

Screening

- Lists of patients assigned to each participating primary care clinic will be finalized after IRB approval.

6.2.2 Enrollment, Baseline, and/or Randomization

Enrollment

All patients included on the lists generated from the EMR will be considered enrolled in the study. If a patient and/or care partner declines interactions with the care coordinator at any time throughout the intervention this will be documented in a secure screening log. Given that this study is a pragmatic trial, all data collected to measure the intervention effectiveness will be existing clinical data recorded in the patients EMR. The following variables will be collected from the EMR at the beginning of the study:

- | | |
|-----------------------------|--|
| • Clinic name | • Date of first ADRD diagnosis in EMR |
| • Clinic address | • Patient current medication list |
| • Providers at clinic | • Patient comorbidities |
| • Patient name | • Prior advance directives/advance care planning |
| • Care partner name | • Dementia evaluations and dementia specialty care |
| • Patient address | |
| • Care partner phone number | |

Randomization

Randomization occurs at the clinic level prior to patient enrollment and screening.

6.2.3 Follow-up Visits

Not applicable

6.2.4 Study Completion

There is no research follow-up visits for this study as it is a pragmatically embedded clinical trial. All outcomes will be obtained via the EMR and qualitative interviews.

7 **SAFETY ASSESSMENTS**

Participant safety will be monitored once an individual is enrolled in the study. A patient is considered “enrolled” after meeting inclusion criteria as indicated by inclusion on the patient lists received from IUH. Due to the nature of this virtual intervention we anticipate that safety risks are no greater than what a patient or care partner might experience in a similar clinical encounter. Participants may indicate discomfort with individual topics or questions posed by the care coordinator and may always refuse to respond to items that make them feel uncomfortable.

The Principal Investigators (PIs) will be responsible for overseeing participant safety throughout the course of the study. We will review cases at monthly study meetings to ensure that additional safety concerns do not arise. Any concerns for a participant’s safety that rises to the level of intervention will be discussed with the research team and communicated with the patient’s primary care team as needed.

In addition, the NIA IMPACT Collaboratory Data and Safety Monitoring Board (DSMB) and Safety Officer (SO) will oversee all data and safety monitoring activities for this study. The DSMB/SO will act in an advisory capacity to the NIA Director to monitor participant safety, to evaluate the progress of the study, and to review procedures for maintaining the confidentiality of data, the quality of data collection, management, and analyses. Advarra IRB will conduct the ethical review required for the protection of human subjects. NIA PO, in consultation with the DSMB, will make a determination regarding the level and format of data and safety monitoring this study requires, i.e., how often reporting is required.

Refer to the [IMPACT Collaboratory DSMB Charter](#) for details.

There are currently two identifiable risks to participation on the ABCV intervention. First, there is the risk of potential breach of confidentiality. Second, individuals who participate in semi-structured interviews following the ABCV intervention, may encounter questions that they would prefer not to answer. If this occurs, the participant can decline to respond. Additionally, participants may choose not to participate in an interview. There will be no penalty if a person chooses not to participate in an interview and all patients and care partners will be informed that choosing not to participate will not affect their clinical care.

7.1 **Specification of Safety Parameters**

Not applicable

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

All adverse events, unanticipated problems and potential risks will be monitored and collected on an ongoing basis, and throughout the study by the research staff. Events, which are anticipated because they are related to the worsening or advancing of the underlying disease, or symptoms related to the disease, will be monitored through patient or care partner report. Events related to any patient, care partner, and provider loss of privacy or confidentiality, or related to fatigue, frustration, or distress related to

completing the intervention will be assessed by the research staff via monitoring of the delivery of the study protocols and procedures within the EMR and by patient and care partner reports to the ABCV team.

7.3 Adverse Events and Serious Adverse Events

The study will adhere to the definitions for AEs and SAEs stipulated in the NIH Policies for Data and Safety Monitoring and NIA Guidance on Clinical Trials as outlined below.

AE Definition: AE is any untoward or unfavorable medical occurrence in a human study participant, including any abnormal sign (e.g., abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the participants' involvement in the research, whether or not considered related to participation in the research.

SAE Definition: SAEs consist of any adverse event that:

- Results in death
- Is life threatening, or places the participant at immediate risk of death from the event as it occurred
- Requires or prolongs hospitalization
- Causes persistent or significant disability or incapacity
- Results in congenital anomalies or birth defects
- Is another condition which investigators judge to represent significant hazards

Unanticipated Problem (UP) Definition: 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 IRB-approved research protocol and informed consent document; and (b) the characteristics of the study population;
- related or possibly related to participation in the research;
- 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.

For all participants, adverse events will be collected starting at enrollment and continue until after the participant has completed the study.

All **unanticipated problems (UPs)** will be reported to the IMPACT Collaboratory Regulatory and Data Team Leader (Dr. Julie Lima), Advarra IRB, NIA IMPACT Collaboratory PO (Dr. Partha Bhattacharyya), and the IMPACT Collaboratory DSMB Chair (or the project's Safety Officer) within 48 hours of the study's knowledge of the event.

Adverse events associated with this study are likely to be infrequent. The IMPACT Collaboratory adverse event form will be used by research staff to report all adverse events caused by the intervention.

AEs for this study include: Some participants may feel increased stress or anxiety while participating in the intervention. Breach of confidentiality would also constitute an

AE.

SAEs for this study include: PLWD have an increased risk of hospitalization, nursing home admission, and death and these SAEs may occur during the course of the study.

7.3.1 Reporting Procedures

- All adverse events that are serious (SAE) and unexpected (i.e., have not been previously reported for the study's intervention) will be reported to the IMPACT Collaboratory Regulatory and Data Team Leader (Dr. Julie Lima), NIA IMPACT Collaboratory PO (Dr. Partha Bhattacharyya), and the IMPACT Collaboratory DSMB Chair (or the project's Safety Officer) within 48 hours of the study's knowledge of SAE.
 - Only those adverse events that are serious (SAE), unexpected, and related to the intervention must also be reported to Advarra IRB. Unexpected and unrelated SAEs will be reported to Advarra IRB on a case-by-case basis if requested by the IMPACT Collaboratory DSMB Chair (or the project's Safety Officer) or NIA IMPACT Collaboratory PO.
- All UNEXPECTED deaths will be reported to IMPACT Collaboratory Regulatory and Data Team Leader (Dr. Julie Lima), NIA IMPACT Collaboratory PO (Dr. Partha Bhattacharyya), and the IMPACT Collaboratory DSMB Chair (or the project's Safety Officer) within 24 hours of study's knowledge of death.
 - Advarra IRB does not require the specific reporting of death outside of the SAE reporting requirement above, but they will be notified on a case-by-case basis if requested by the IMPACT Collaboratory Chair (or the project's Safety Officer) or NIA IMPACT Collaboratory PO.
- All unanticipated problems (UPs) will be reported to the IMPACT Collaboratory Regulatory and Data Team Leader (Dr. Julie Lima), Advarra IRB, NIA IMPACT Collaboratory PO (Dr. Partha Bhattacharyya), and the IMPACT Collaboratory DSMB Chair (or the project's Safety Officer) within 48 hours of the study's knowledge of the event.
- The summaries of all previously reported unexpected and related SAEs, deaths, and UPs, as well as all other SAEs and AEs will be reported to IMPACT Collaboratory Regulatory and Data Team Lead (Dr. Julie Lima), Advarra IRB, NIA IMPACT Collaboratory PO (Dr. Partha Bhattacharyya), and the IMPACT Collaboratory DSMB Chair (or the project's Safety Officer) at a minimum every 6 months, or at a frequency requested by the IMPACT Collaboratory DSMB Chair (or the project's Safety Officer) or NIA IMPACT Collaboratory PO.

Severity of Event

All AEs will be assessed by a qualified medical professional using a protocol defined grading system. For adverse events (AEs) not included in the protocol defined grading system, the following guidelines will be used to describe severity.

- **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”.

These terms should match those collected on the Adverse Event Form.

Expectedness

- **Unexpected** -- nature or severity of the event is not consistent with information about the condition under study or intervention in the protocol, consent form, product brochure, or investigator brochure.
- **Expected** -- event is known to be associated with the intervention or condition under study.

Unexpected events will be subject to expedited reporting requirements as described in the [NIA Guidance on Clinical Trials](#) and in Section 1.2.4, below.

Relationship To Study Intervention

All adverse events (AEs) must have their relationship to study intervention assessed by a qualified medical professional who examines and evaluates the participant based on temporal relationship and his/her clinical judgment. The degree of certainty about causality will be graded using the categories below. In a clinical trial, the study product must always be suspect.

- **Definitely Related:** The adverse event is clearly related to the investigational agent/procedure – i.e., an event that follows a reasonable temporal sequence from administration of the study intervention, follows a known or expected response pattern to the suspected intervention, that is confirmed by improvement on stopping and reappearance of the event on repeated exposure and that could not be reasonably explained by the known characteristics of the subject’s clinical state.
- **Possibly Related:** An adverse event that follows a reasonable temporal sequence from administration of the study intervention follows a known or expected response pattern to the suspected intervention, but that could readily have been produced by a number of other factors.
- **Not Related:** The adverse event is clearly not related to the investigational agent/procedure - i.e., another cause of the event is most plausible; and/or a clinically plausible temporal sequence is inconsistent with the onset of the event and the study intervention and/or a causal relationship is considered biologically implausible. Follow-up for Adverse Events

The occurrence of an adverse event (AE) or serious adverse event (SAE) may come to the attention of study personnel during intervention visits or research interviews, or upon review by a study monitor.

All AEs including local and systemic reactions not meeting the criteria for SAEs will be captured on the appropriate case report form (CRF). Information to be collected includes event description, time of onset, qualified medical professional's assessment of severity, relationship to study product (assessed only by those with the training and authority to make a diagnosis), and time of resolution/stabilization of the event. All AEs occurring while on study must be documented appropriately regardless of relationship. All AEs will be followed to adequate resolution.

Any medical condition that is present at the time that the participant is screened will be considered as baseline and not reported as an AE. However, if the study participant's condition deteriorates at any time during the study, it will be recorded as an AE.

Changes in the severity of an AE will be documented to allow an assessment of the duration of the event at each level of severity to be performed. AEs characterized as intermittent require documentation of onset and duration of each episode.

The care coordinator will record all reportable events with start dates occurring any time after study enrollment until 7 (for non-serious AEs) or 30 days (for SAEs) after the last day of study participation. At each intervention visit, the care coordinator will inquire about the occurrence of AE/SAEs since the last visit. Events will be followed for outcome information until resolution or stabilization.

After the completion of the 12 month participation window, outcomes data will be obtained from the EMR, via regular data transfers to the Regenstrief Institute Data services. Additional AE's will be identified during this period. The research manager will record all reportable events obtained from this data. This data will be pulled within 6 months after the completion of the intervention by the last dyad.

7.4 Safety Monitoring

The NIA Guidelines on Data and Safety Monitoring generally require that a NIA-appointed Data and Safety Monitoring Board or Safety Officer monitor clinical trials. Please see the [Data and Safety Monitoring Guidelines](#).

The study PI will present their safety reports at the intervals described below. Safety reports will be provided to the SO and NIA PO.

Data will be presented in a blinded manner in SO reports. SO reports, data and discussion are confidential. Participant identities will not be known to the SO.

For the study, the frequency of DSM will proceed as follows:

1. Prior to the start of participant enrollment and data collection, the study PI must submit a DSMP for approval by the SO, DSMB and/or the NIA PO;
2. Six months after the initiation of participant enrollment and/or data collection, the study PI must provide a DSM report to the SO, through submission to the IMPACT IRB and Regulatory Team. This interim report will be reviewed by the SO to determine whether there are any human subjects or data safety concerns; and
3. At the end of the study, the PI must submit a final DSM report to the SO, through submission to the IMPACT IRB and Regulatory team.

The SO will sign a Conflict of Interest Statement which includes current affiliations, if any, with pharmaceutical and biotechnology companies (e.g., stockholder, consultant), and any other relationship that could be perceived as a conflict of interest related to the study and / or associated with commercial interests pertinent to study objectives.

SO Responsibilities

The role of the SO is described in the [IMPACT Collaboratory DSMB Charter](#).

A detailed list of SO responsibilities includes:

- Review the research protocol, informed consent documents and plans for data safety and monitoring;
- Recommend subject recruitment be initiated after receipt of a satisfactory protocol;
- Evaluate the progress of the trial, including periodic assessments of data quality and timeliness, recruitment, accrual and retention, participant risk versus benefit, performance of the trial sites, and other factors that can affect study outcome;
- Consider factors external to the study when relevant information becomes available, such as scientific or therapeutic developments that may have an impact on the safety of the participants or the ethics of the trial;
- Review study performance, make recommendations and assist in the resolution of problems reported by the PI;
- Protect the safety of the study participants;
- Report to NIA on the safety and progress of the trial;
- Make recommendations to the NIA and the PI concerning continuation, termination or other modifications of the trial based on the observed beneficial or adverse effects of the treatment under study;
- If appropriate, review interim analyses in accordance with stopping rules, which are clearly defined in advance of data analysis and have the approval of the DSMB;
- Ensure the confidentiality of the study data and the results of monitoring; and,
- Assist the NIA by commenting on any problems with study conduct, enrollment, sample size, and/or data collection.

8 INTERVENTION DISCONTINUATION

If there were unanticipated serious adverse events that were possibly or probably related to the study, we would review with the institutional review board and the DSMB to consider discontinuation.

Note that subjects may withdraw voluntarily from participation in the study at any time and for any reason. Participants will continue to be followed via the EHR, even if the study intervention is discontinued.

9 STATISTICAL CONSIDERATIONS

9.1 General Design Issues

A 0.05 significance level will be used for all statistical tests. The analyses in Aims 1 and 2 will include 860 PLWD (approximately 430 in the control clinics and 430 in the intervention clinics) identified by the baseline EMR search who are determined to have dementia based on our ICD-10 selection algorithm. We will include patients in the

intervention group for analysis whether or not they engage in the intervention, in order to prevent bias in sample selection between the intervention and control groups. For the primary outcome, the number of ED visits during the one-year observation period will be determined for each patient. We will use a mixed-effects Poisson regression model, with a random effect for clusters, to compare control versus intervention on this outcome. We will use the offset option in Poisson modeling to account for the person-time followed on study while alive; specifically, we will model the ED event rate per person-years. The planned follow-up is 1 year for each person, but if a person dies, then they will contribute less than 1 year of time to the person-year rate. We specify the Poisson error distribution in the primary analysis plan; however, we may explore other error distributions such as zero-inflated Poisson, negative binomial, or zero-inflated negative binomial. All models will account for clustering and variables we a priori think may affect the outcome, including race, ethnicity, sex, SES and rurality. Additionally, although the study is not powered to assess racial differences, we will examine an interaction term of race by intervention group to test for differences in the effect of the intervention between Black/African American and White patients. Such an outcome would require revision of the intervention to ensure that it did not widen disparities. The exploratory outcome for Aim 1 is total preventable ED visits. The sample and analysis for this secondary outcome will be the same as described above for the primary outcome. This outcome will include potentially preventable ED visits, based on the definition by Anderson et al. that relies on ICD-10 codes.

Guided by recent studies and guidelines for prescribing studies, we will first create a dichotomous variable for receipt of a new prescriptions for antipsychotic medications (excluding patients with a diagnosis of a psychotic disorder such as schizophrenia) and a similar variable for benzodiazepines. The outcome will be an overall dichotomous variable of any new antipsychotic or benzodiazepine medication. In secondary analyses, we will develop separate models for the outcomes: (1) A new antipsychotic medication and (2) A new benzodiazepine. A mixed-effects logistic regression model (with a random effect for clusters) will be used to compare control vs. intervention on each of these dichotomous outcomes. Second, we will use the Anticholinergic Cognitive Burden Scale total score,¹ measured at baseline and at 12 months. A mixed-effects linear regression model (with a random effect for clusters) will be used to compare control vs intervention on this scale score. All models will account for clustering and variables we a priori think may affect the outcome, including race, ethnicity, sex, SES and rurality.

We will use the CFIR to evaluate the ABCV Program. We chose CFIR because it contains a comprehensive array of addressable context and process factors known to drive implementation outcomes positively as facilitators or negatively as barriers. Each CFIR construct is well defined, has established measures, and can be depicted in both rich qualitative detail and with a structured quantitative rating scale on a +3 (facilitator) to -3 (barrier) scale. Importantly, CFIR posits relationships between context, process, and outcome. CFIR is well validated and highly practical because it is often used to both explore and subsequently optimize future implementation context and process. Thus, if our primary aim reveals that the ABCV Program is effective, the CFIR-guided implementation analysis will produce guidance on how to optimally implement it across

PC practices in a dissemination-and-implementation study. Data collection and analysis of the implementation constructs is accomplished using a mixed-method quantitative and qualitative approach.

Measuring Implementation Context and Processes. Interview data guided by CFIR will be collected from a purposeful sample of dyads in the intervention and from clinic stakeholders (clinical and non-clinical staff) following the intervention. We will conduct semi-structured interviews and administer three quantitative, standardized measures of the outcomes of the ABCV Program: acceptance, feasibility, and appropriateness. These measures will be the short form versions of Weiner et al.'s Acceptability of Intervention Measure (AIM); Feasibility of Intervention Measure (FIM), and Intervention Appropriateness Measure (IAM). Qualitative interview data will be thematically analyzed to identify presence and nature of implementation barriers or facilitators for the ABCV Program. Qualitative content analysis will be performed primarily using a deductive framework (CFIR)-based analysis, while secondarily allowing for the inductive development of new themes, categories, and relationships as they arise from the data.

9.2 Sample Size and Randomization

Sample Size Calculations

We determined our power calculations based on our clinic capacity and the capacity of the dementia care coordinators, within the constraints of the funding mechanism. Based on our experience with the ABC model, we anticipate that each care coordinator could manage about 108 dyads over the study, for a total of 215. We anticipate that when dyads are approached, about 50% either cannot be reached or will refuse care coordination for various reasons including lack of time, other obligations, or lack of interest. We will therefore double our sample size to 430 per group. We will select 24 primary care sites that will be equally randomized to intervention and control, stratified into low and high numbers of PLWD in each clinic and location in an underserved area. For Aim 1 and Aim 2, power was calculated for the primary outcome of number of ED visits using PASS software (NCSS, LLC, Kaysville, Utah, USA) based on a cluster-randomized design. For aim 1, we assumed a mean number of ED visits per 1 year period equal to 0.50 for the control group, based on the review by Hunt et al.⁶⁰ We desired at least 80% power to detect a control-intervention event rate ratio of 1.50. Because Hunt et al. reported a range across studies for the mean number of annual ED visits for controls, we also present power for two other values (1.0 and 2.0) for the control 1-year ED event rate. A sample of 430 patients per arm will yield 408 person-years per arm which will provide 80% power for a two-sided test to detect a difference in 1-year ED event rates of 0.50 for control vs 0.33 for intervention (i.e., event rate ratio of 0.6667 for intervention vs control, or equivalently 1.50 for control vs intervention), assuming a between-cluster coefficient of variation of 0.20 in both the control and intervention groups. This power calculation assumes that 430 persons per arm will contribute 408 person-years per arm, based on assuming 90% of persons will contribute 1 year of data, and the 10% of persons who are projected to die sometime during the 12 months of observation will contribute ½ year of data. The anticipated 0.17 absolute difference between arms in the event rates (0.50 vs 33%) assumes zero intervention-control effect (0.50 vs 0.50) among the projected 50% of persons who do not answer the

phone calls or refuse to participate, and a 0.34 absolute intervention-control difference (0.50 vs 0.16) among the projected 50% who will participate.

9.2.1 Treatment Assignment Procedures

Cluster randomization will occur at the level of the primary care practices. We chose cluster randomization to avoid contamination as patients may see more than one provider within practices. Additionally, providers within a practice are more likely to collaborate in the care of patients. We chose this approach over a stepped-wedge design at the recommendation of the IMPACT Design and Statistics team to concerns about the effects of temporal trends that may affect not only analysis, but also enrollment and successful study implementation, as well as other logistic concerns. Prior to randomization, clinics will be selected to ensure that we can enroll at least 20% Black participants and 5% Latino participants. Sites will be stratified by number of PLWD in the practice (low versus high) to ensure adequate numbers of dementia patients in each group, and by clinic location in an underserved area (yes vs no) in order to balance socioeconomic status between groups (4 strata). Clinics in the control groups will provide usual care to PLWD and their care partners. Control clinics will not be given additional information about the intervention.

9.3 Interim analyses and Stopping Rules

We will not conduct any interim analyses for this trial. Reports will be provided to the DSMB every 6 months or more often as requested. A close-out DSM report will be provided at the conclusion of the study.

9.4 Outcomes

All pragmatic outcomes will be obtained from patient's EMR data. First the IUH data warehouse will be searched to identify all outcomes from Aims 1 and 2. For Aim 1, CPT codes will be used to identify emergency room visits obtained during the one-year study period. To identify is the ED visit as an injury or related to an acute or chronic ACSCs, ICD-10 codes associated with these conditions will be obtained from all acute care visits. Medication data will be obtained from the patient's EMR list of active medications. Anticholinergic Burden Scale scores will be calculated at the time of enrollment and 12 months later at program completion. We will also conduct surveys and interviews with key clinical stakeholders as part of Aim 3. At the end of the 12-month intervention period for the intervention clinic, trained research staff will contact care partners who engaged in the ABCV intervention to administer the implementation measures. Data will be entered into REDCap, a secure, HIPAA compliant research data program.

9.4.1 Primary outcome

1. Evaluate the impact of the ABCV Program on all cause utilization of emergency department utilization in a sample of persons living with dementia (PLWD) during the 12-month ABCV intervention period.

9.4.2 Secondary outcomes

1. All new prescriptions for antipsychotic medications or benzodiazepines during the 12-month study period and anticholinergic burden scale score change during the 12-month study period.
2. Evaluation of implementation endpoints (acceptability, appropriateness, feasibility, fidelity, and potential for future adoption of the intervention) assessed

through chart review and semi-structured participant interviews with a subset of patient-care partner dyads, clinicians, and other non-clinical staff at clinics randomized to the intervention (see Table 1).

9.5 Data Analyses

The analyses in Aims 1 and 2 will include 860 PLWD (approximately 430 in the control clinics and 430 in the intervention clinics) identified by the baseline EMR search who are determined to have dementia based on our ICD-10 selection algorithm. We will include patients in the intervention group whether or not they engage in the ABCV intervention, in order to prevent bias in sample selection between the intervention and control groups. For the primary outcome, the number of ED visits during the one-year observation period will be determined for each patient. We will use a mixed-effects Poisson regression model, with a random effect for clusters, to compare control versus intervention on this outcome. We will use the offset option in Poisson modeling to account for the person-time followed on study while alive; specifically, we will model the ED event rate per person-years. The planned follow-up is 1 year for each person, but if a person dies, then they will contribute less than 1 year of time to the person-year rate. We specify the Poisson error distribution in the primary analysis plan; however, we may explore other error distributions such as zero-inflated Poisson, negative binomial, or zero-inflated negative binomial. All models will account for clustering and variables we *a priori* think may affect the outcome, including race, ethnicity, sex, socioeconomic status, and rurality. Additionally, although the study is not powered to assess racial differences, we will examine an interaction term of race by intervention group to test for differences in the effect of the intervention between Black/African American and White patients. Such an outcome would require revision of the intervention to ensure that it did not widen disparities. The exploratory outcome for Aim 1 is total *preventable* ED visits. The sample and analysis for this secondary outcome will be the same as described above for the primary outcome. This outcome will include potentially preventable ED visits, based on the definition by Anderson et al. that relies on ICD-10 codes.

10 DATA COLLECTION AND QUALITY ASSURANCE

10.1 Data Collection Forms

Data for qualitative interviews will be collected by the research staff at each clinical site from the EMR.

Data collection forms will be designed and securely stored within REDCap or on a password protected, encrypted server at the Regenstrief Institute Indiana University (IU) Center for Aging Research EMR data will be collected using site specific automated data repositories (e.g., Regenstrief Data Core in Indiana).

10.2 Data Management

The clinical sites will have no responsibility for data collection or management.

Data will be managed by the research team at the IU Center for Aging Research. Physical documents related to the study will be stored in a locked file cabinet, while electronic documentation will be stored on an encrypted, password-protected server at the Regenstrief Institute. Data collection instruments will be created in REDCap.

10.3 Quality Assurance

10.3.1 Training

The interventionists will undergo three workdays (about 24 hours) of training in ABCV dementia collaborative care with a study Co-I. They will receive operational training to learn how to provide the Aging Brain Care program within the existing IU Health Virtual Hub, including delivery of the intervention using virtual technology and incorporation of ABCV notes into the existing workflow.

10.3.2 Quality Control Committee

There will be no quality control committee, however, fidelity will be monitored throughout the study. See Section 5.3.

10.3.3 Metrics

Go to section 9.4 for more information on quality assurance metrics.

10.3.4 Protocol Deviations

Quality assurance procedures include observing research activities for adherence to protocol. The research team has developed internal methods for quality assurance for any data that is recorded within our study documents and REDCap database. Any deviations to the protocol will be documented and reviewed by the study team at weekly meetings. Should a reportable deviation occur, we will adhere to reporting requirements as outlined by the IRB and as noted in section 7 above.

10.3.5 Monitoring

Monitoring will include review and observation of data from clinical sites for the purpose of ensuring protocol compliance and data quality. The research team will be responsible for addressing any concerns identified through the monitoring process. Monitoring will also ensure the completion of documentation of informed consent for qualitative interview participants.

11 PARTICIPANT RIGHTS AND CONFIDENTIALITY

11.1 Institutional Review Board (IRB) Review

This protocol and the informed consent document for qualitative interviews and any subsequent modifications will be reviewed and approved by the Advarra IRB.

11.2 Informed Consent Forms

Our study consists of two separate components – the embedded intervention and a set of semi-structured participant interviews.

Embedded ABCV program

The **intervention** consists of the ABCV program, which will be embedded within clinical practice. We request a waiver of informed consent for recruitment, participation, and outcome assessment of participants, to include the use of EMR data for these purposes.

We offer the following justifications for the waiver of informed consent:

- the research involves no more than minimal risk to the subjects:
 - a. Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. The embedded design of this study aligns with this definition. Furthermore, prior research supports the minimal risk designation of ABCV. The Aging Brain Care Model is currently used as the standard of care at Eskenazi Health (where it was originally developed) and other outpatient care clinics.
- The research could not practicably be carried out without the requested waiver:
 - a. Obtaining consent prior to implementation of the study would impact the scientific integrity of the trial, in that it is contradictory to the pragmatic design of the trial. This intervention is being integrated into routine clinical practice and obtaining consent would significantly interrupt the regular flow of patient care in the clinic. The consent process would be impracticable in a busy outpatient practice and impractical given the embedded approach.
 - b. Additionally, since patients and patient/ care partner dyads are identified using ICD-10 codes for dementia, the informed consent process would involve disclosure of the methods used to identify patients, and with that the risk of sharing protected health information (such as diagnosis) with an unauthorized party.
- The research involves using identifiable private information, and could not practicably be carried out without using such information in an identifiable format:
 - a. It is necessary in this study to utilize identifiable information for the purpose of screening patients, engaging in the intervention, and assessing outcomes in the EMR. These tasks would be impossible to complete without using identifiable information from the health systems' EMR.
- The waiver or alteration will not adversely affect the rights and welfare of the subjects:
 - a. We believe that a waiver will not adversely impact participants. Because ABC is a well-established model of care, we believe the waiver is justifiable and appropriate for this study. We believe that patients and care partners will find value in the intervention. Because this is an intervention designed to improve clinician-patient communication, it is highly unlikely that study

participants would object if they knew of the waiver. However, potential participants are free to decline to participate in the intervention with the care coordinator, without penalty. Declining to participate will in no way impact their clinical care now or in the future.

- Whenever appropriate, the subjects will be provided with additional pertinent information after participation.
 - a. Results will be shared via published manuscripts and any other applicable formats within the healthcare systems where the study is performed.

Semi-structured Participant Interviews

We will conduct **semi-structured interviews** with a select group of clinicians, non-clinical staff, and care partners who participated in ABCV. Informed consent will be obtained for this activity. We will request an alteration and waiver of documentation of informed consent for these semi-structured interviews.

Consent forms will be Institutional Review Board (IRB)-approved that will include most but not all components of informed consent. This component of the research also involves no more than minimal risk to the participants. These are brief questionnaires that will occur over the phone or via virtual platform (such as Amwell Now or Zoom) to collect information about the stakeholders (i.e., clinicians, non-clinical staff and care partners) experience with the intervention. Research staff will review the consent document with individuals who are eligible to participate in these semi-structured interviews. Research staff will explain the research study to the interviewee and answer any questions that may arise. A verbal explanation will be provided in terms suited to the participant's comprehension of the purposes, procedures, and potential risks of participation in the interview and of their rights as research participants. Participants will be informed that participation is voluntary and that they may withdraw at any time, without prejudice, and that the quality of their medical care will not be adversely affected if they decline to participate. Participants will have the opportunity to ask questions prior to providing their verbal consent. The informed consent process will be conducted by trained research staff.

Semi-structured Interviews with Care Partners

We will approach care partners for participation by phone or mail. Care partners who cannot consent for the interview will not be eligible to participate. We will determine capacity to consent for the interview using a consent verification process, which is outlined below.

In order to comply with the requirements of the IRB, the PI or an equally qualified sub-investigator, will assess the capacity of the potential subject to provide informed consent. As a part of this assessment, the potential subject must demonstrate, at a minimum, an understanding of the following topics in order to participate in the research study:

- 1) That the potential subject is being asked to participate in a research study.
- 2) The study-related procedures involved in the research.
- 3) The anticipated risks associated with the research.
- 4) The potential benefits that might be expected from participation.
- 5) That the potential subject does not have to participate in this research study.
- 6) That the potential subject may stop participation at any time.

We will utilize a teach back consent verification process with interview participants after reviewing the informed consent information. This process will involve questions about the topic under study, what the participant would be asked to do if enrolled, and the voluntary nature of the study. This information will be repeated up to three times. If the participant is unable to correctly answer each question after three attempts, the participant will be determined to be ineligible to participate in the interview.

These interviews will be conducted by phone or virtual meeting. Care partners will receive a \$20 incentive for participating in the semi-structured qualitative interview.

Semi-structured Interviews with Clinicians and Non-clinical Staff

We will approach clinicians and non-clinical staff who have participated in the ABCV intervention by phone or email to invite them to complete a semi-structured interview with research staff. There will be no penalties for declining to participate in the interview. For those who are interested, we will conduct informed consent as outlined above. Clinicians and non-clinical staff will receive a \$50 incentive for participating in the semi-structured qualitative interview.

Documentation of Consent

All research activities including documentation of consent procedures will be recorded by research staff assigned at each site, before the participant undergoes any study-specific procedures.

11.3 Participant Confidentiality

We also request a full HIPAA waiver of authorization for the use of EHR data for this study. We offer the following justifications for the HIPAA waiver:

- Use or disclosure involves no more than minimal risk to the privacy of

individuals because of the presence of the following elements:

- An adequate plan to protect health information identifiers from improper use or disclosure,
 - An adequate plan to destroy identifiers at the earliest opportunity absent a health or research justification or legal requirement to retain them, and
 - Adequate written assurances that the PHI will not be used or disclosed to a third party except as required by law, for authorized oversight of the research study, or for other research uses and disclosures permitted by the Privacy Rule.
- Research could not practicably be conducted without the waiver or alteration; and research could not practicably be conducted without access to and use of PHI as outlined in the prior section 11.2 and as follows:
 - Obtaining consent prior to implementation of the study would impact the scientific integrity of the trial, in that it is contradictory to the pragmatic design of the trial.
 - Additionally, since patients and patient-care partner dyads are identified using ICD-10 codes for dementia, the informed consent process would involve disclosure of the methods used to identify patients, and with that the risk of sharing protected health information (such as diagnosis) with an unauthorized party and/or disclosing information from the medical record that the patient and/or care partner has not been disclosed previously.
 - To minimize the risk of breach of confidentiality, all study materials will be regarded as strictly confidential. Paper study documents will be stored in a locked file cabinet in a secure office at the IU Center for Aging Research. Computerized data entry and data storage systems are on secure Indiana University servers and password protected and will be accessible only to study personnel. The participants will be informed that representatives of the IRB or other regulatory bodies may inspect their study records to verify the information collected and that all information will be handled in strictest confidence. All analyses from the study will be performed and reported in aggregate and will exclude any personally identifiable information. A data agreement is in place between Indiana University Health and the Regenstrief Institute to facilitate access to identifiable protected health information as needed for the project. Access will be as specified per all applicable university policies and procedures, including but not limited to, secure transfer protocols, virtual private networks, and remote desktops.

Any data, specimens, forms, reports, both video and audio recordings, and other records that leave the site will be identified only by a participant identification number (Participant ID, PID) to maintain confidentiality. All records will be kept in a locked file cabinet. All computer entry and networking programs will be done using PIDs only. Information will not be released without written permission of the participant, except as necessary for monitoring by the sponsor or persons working on behalf of the sponsor (i.e., IMPACT research study staff, and/or Safety Officer (SO)), the IRB, the FDA, the NIA, and the OHRP.

11.4 Study Discontinuation

The study may be discontinued at any time by the IRB, the NIA, the OHRP, the FDA, or

other government agencies as part of their duties to ensure that research participants are protected.

12 ETHICAL CONSIDERATIONS

The research team will adhere to the following policies, guidelines, and ethical principles as described:

- Propose, conduct, and report research with integrity and honesty;
- Protect people and humanely treat animals involved in research or teaching;
- Learn, follow, and demonstrate accountability for meeting and ensuring compliance with the requirements of sponsors, regulatory bodies, and other applicable entities;
- Faithfully describe and transmit research data and findings;
- Protect rights to individual and University intellectual property;
- Ensure originality of work, provide credit for the ideas of others upon which their work is built, and be responsible for the accuracy and fairness of information published; and
- Fairly assign authorship credit on the basis of an appropriate array of significant intellectual contributions, including conception, design, and performance; analysis and interpretation; and manuscript preparation and critical editing for intellectual content.

13 COMMITTEES

IMPACT Collaboratory- Study oversight, sponsorship, and funding.

14 PUBLICATION OF RESEARCH FINDINGS

Publication of the results of this trial will be governed by the policies and procedures developed by the sponsor(s) of this study. Any presentation, abstract, or manuscript will be made available for review by the sponsor prior to submission. We will adhere to the IMPACT Collaboratory Publication and Acknowledgment Policy and Resource and Data Sharing Plan available on the IMPACT Investigator's Portal.

15 REFERENCES

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16 SUPPLEMENTS/APPENDICES

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