Title: Can Value Champions Reduce Inappropriate Prescribing for People With Dementia?

NCT: NCT05359679

Dated: 9/13/2021

Last updated: 9/26/2023

Clinical Interventional Study Protocol Template

PREFACE

The Clinical Intervention Study Protocol Template is a suggested format for clinical trials sponsored by the National Institute on Aging (NIA). Investigators are encouraged to use this format, as appropriate, when developing protocols for their studies. Large multi-site observational studies will also benefit from this protocol template.

Note that instructions and explanatory text are indicated by italics and should be replaced in your protocol with appropriate text. Section headings and template text formatted in regular type should be included in your protocol document as provided in the template.

The goal of this template is to provide a general format applicable to all single- and multicenter clinical intervention trials (e.g., drug, surgery, behavioral, nutritional, device, etc).

As you can see the version number and date are on the bottom of each page. When making changes to an approved and "final" protocol, please provide a summary of the changes, with the date, at the front of the protocol.

CAN VALUE CHAMPIONS REDUCE INAPPROPRIATE PRESCRIBING FOR PEOPLE WITH DEMENTIA?

Study Chairman or Principal Investigator:

Lorella Palazzo, PhD

Senior Investigator

Kaiser Permanente Washington Health Research Institute

Supported by:

The National Institute on Aging

Study Intervention Provided by:

N/A

Sponsor of IND/IDE:

N/A

Version 2
October 20, 2022

TABLE OF CONTENTS

Page

PRÉCIS

Study Title

Can Value Champions Reduce Inappropriate Prescribing for People with Dementia?

Objectives

The primary objective is to assess the effectiveness of training a clinician to be a 'value champion' within their clinical setting to decrease the use of three classes of potentially inappropriate prescription medications (PIMs) among people living with dementia. (PLWD) Secondary objectives include determining if the intervention is associated with a reduction in emergency department (ED) visits or hospitalizations due to a fall, and examining five implementation outcomes: appropriateness, feasibility, fidelity, penetration, and equity.

Design and Outcomes

This study is a pragmatic cluster-randomized trial to test the effectiveness of a primary care clinician value champion for de-implementing potentially inappropriate medications among patients 65 years of age and older with a diagnosis of dementia. Medicare Part D pharmacy claims data will be analyzed at the end of the 12-month intervention for the primary outcome, the medication possession rates (MPR) for three groups of potentially inappropriate medications: antipsychotic medications, benzodiazepines, and hypoglycemic medications (sulfonylureas and insulin). In a similar fashion, a hospital admission, or an emergency department visit for a fall will be assessed at the end of the intervention using Medicare claims data. Finally, the five implementation outcomes – Appropriateness, Fidelity, Feasibility, Penetration and Equity - will be evaluated through analysis of interviews conducted with participating clinician value champions.

Interventions and Duration

Primary care clinics within each of the two participating ACOs will be randomized to either the intervention or control arms of the study. Prior to random assignment, we will stratify practices based on high versus low historic prescribing rates, with the cut-point for including a clinic in the study based on the distribution of overall rates for all 3 therapeutic classes using data for 2019-2020. A primary care clinician from each clinic selected for the trial in the intervention arm (n=30 across the two ACOs) will be recruited as a clinician value champion for their clinic. They will participate in twice monthly clinician value champion training webinars for six months and then launch a 12-month initiative within their clinic to reduce PIM prescribing among PLWD. Study outcomes will be assessed 12 months after they launch their initiative.

Sample Size and Population

Medicare beneficiaries from claims data provided by each ACO will be included in the final outcome analysis if they meet all of the following criteria prior to the start of the intervention: a) they are seen by a clinician at a participating clinic as evidenced by one or more evaluation and management claims, b) they have continuous coverage in Medicare Parts A, B and D and no months of Part C (Medicare Advantage), and c) they have two or more claims with an ICD-10 diagnosis for Alzheimer's or Alzheimer's related dementia 30 days apart or 1 inpatient stay with a principal diagnosis of Alzheimer's. We anticipate a total of approximately 5,000 patients will be included in this final analysis across both ACOs.

STUDY TEAM ROSTER

Principal Investigator: Lorella Palazzo, PhD

KPWHRI
1730 Minor Ave, Suite 1600
Telephone: 206-287-2173
Fax: 206-287-2871

lorella.g.palazzo@kp.org

Main responsibilities/Key roles*:* Dr. Palazzo will provide scientific direction and supervision for all aspects of the study. She will be responsible for the management and integrity of the design, conduct, and reporting of the study and for managing, monitoring, and ensuring the integrity of collaborative relationships between all participating organizations.
Dr. Palazzo will take an active part in manuscript preparation.

PARTICIPATING STUDY SITES

Brandeis University

Co-Investigators: Jennifer Perloff, PhD

Heller School for Social Policy and Management
415 South St. MS035
Waltham, MA 02453-2728
Telephone: 781-736-3935
Fax: N/A
perloff@brandeis.edu

Main responsibilities/Key roles: Dr. Perloff will work with Drs. Parchman and Palazzo to develop a detailed study design, help create prescription reporting templates for participating ACOs, join in data collection activities related to fidelity assessment and implementation and lead the data analysis in close collaboration with Brandeis biostatistician, Dr. Ritter.

Institute for Accountable Care

Co-Investigators: Robert E. Mechanic

601 13th Street NW, Suite 900 South
Washington, DC 20005
Telephone: 202-640-2648
Fax:
rmechanic@institute4ac.org

Main responsibilities/Key roles: Mr. Mechanic will serve a co-Investigator for this study and lead the IAC subcontract. In this capacity, he will oversee the work of the IAC statistical analysis as well as provide the team with feedback on the design and results of the study. Mr. Mechanic will also join in team meetings and contribute to written reports and manuscripts.

1 STUDY OBJECTIVES

1.1 Primary Objective

The Primary Outcome is medication possession rates (MPR) per quarter, for any of the 3 classes of potentially inappropriate medications. Our hypothesis is that for each medication class, the intervention will produce clinically relevant decreases in mean possession rates of 10% of a standard deviation in patients seen in intervention clinics compared to those who are seen in control group clinics.

1.2 Secondary Objectives

As a secondary outcome, we will also assess the incidence of emergency department visits or hospitalizations due to a fall during the study window.

2 ADDITIONALLY, DATA COLLECTED THROUGH TWO INTERVIEWS WITH APPROXIMATELY 8 CLINICIAN VALUE CHAMPIONS WILL PROVIDE US WITH THE MEASURES WE NEED TO ASSESS FIVE IMPLEMENTATION OUTCOMES: APPROPRIATENESS, FIDELITY, FEASIBILITY, PENETRATION AND EQUITY. BACKGROUND AND RATIONALE

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

For people living with dementia (PLWD) the overuse of Potentially Inappropriate Medications (PIMs), those for which the potential for harm outweighs benefit, remains a persistent problem despite evidence-based guidelines supporting their de-adoption.[1,2] A group of geriatric experts convened by the Choosing Wisely initiative identified three classes of PIMs for PLWD: antipsychotics, benzodiazepines, and hypoglycemics (sulfonylureas and insulin) with adequate glycemic control.[1,3] In a systematic review the prevalence of PIMs when cognitive impairment was reported ranged from 20.6% to 80.5%.[1] Approximately 14.3% of Medicare Part D enrollees with dementia residing in the general community are prescribed an antipsychotic.[4] The prevalence of potentially inappropriate benzodiazepine prescriptions has been reported to be as high as 20% among elderly persons with dementia living in the community.[5] The proportion of elderly patients with an A1c < 7% who received a prescription for sulfonylurea, insulin or combined insulin and sulfonylurea therapies was 35.2%, 24.2% and 16.3% respectively and was as prevalent in those with dementia as in those without.[6] Park and colleagues compared rates of prescribing low-value medications in the elderly from 2006-2015 in both traditional Medicare and Medicare Advantage.[7] Not only was there no difference in rates between the two groups, there was also no evidence of any decline in rates of prescribing over time, including use of benzodiazepines in PLWD.

Study Rationale

The rationale for decreasing the use of PIMs is that their use in this population of patients results in a greater likelihood of harm than benefit. Documented harms in the medical literature includes falls, worsening cognitive impairment, hospital admission, functional impairment, and death.

Name and Description of the Intervention:
This embedded pragmatic trail will test the effectiveness of a Clinician Value Champion on the primary outcome by randomizing primary care practices within two accountable care organizations to the intervention or control arm of the study. One clinician value champion from each clinic in the intervention arm will complete a value champion training program led by the P.I. and then implement care redesign activities in their practice to reduce the use of low value prescribing in older adults with dementia. The 6-

month training phase (months 4-9 of the study) will consist of twice monthly webinars followed by a 12-month project phase. A formative and summative evaluation of a recently completed Robert Wood Johnson funded Value Champion Fellowship program resulted in the development of a training curriculum comprised of 10 learning modules (see Table 1) for the training phase of the intervention and a project workbook to guide the value champion during the 12-month project phase. Following the 6 months of training, value champions will participate in a monthly 1-hour shared learning webinar to share successes, challenges, and brainstorm solutions for 12 months (months 10-22 of the study). We will invite former value champion fellows and faculty from the RWJF fellowship to participate in these meetings to support this new cohort of value champions.

Table 1: Value Champion Learning Modules

Module 1: High Value Care and Health Equity Understanding the intersection between "value" and "equity" can inform conversations between value champions, leadership and stakeholders and inform project planning.
Module 2: Engaging Leadership for High Value Care Provides participants with an overview of how to engage leadership throughout the project and provides practical tips on how to create and sustain this engagement
Module 3: So Many to Consider: Choosing an Overused Service Overuse of low-value care is common, selecting a target area of overuse requires careful consideration of multiple factors that will impact subsequent success
Module 4: How to Conduct a Stakeholder Assessment and Why it Is Important Identifying, assessing and engaging stakeholders who will be impacted by reducing the use of a service is critical to project success.
Module 5: The patient voice: engaging patient participation in your project This module explains why incorporating the patient voice is important in reducing overuse and provides examples of how to do so.
Module 6: Measurement, data and trust: Supporting change with data This module discusses common challenges and a range of solutions for collecting and reporting overuse data when taking action on overuse
Module 7: Engaging health care professionals: the Taking Action on Overuse Change Package The framework and change package provides suggested key activities to select from when designing an intervention
Module 8: Strategies Employed by Value Champions This module provides examples of intervention strategies used by clinician value champions in their setting to engage providers, staff, and patients in change efforts
Module 9: **Choice Architecture and Overuse Reduction** This module helps participants understand how concepts from the field of behavioral economics can be applied to their overuse reduction initiative.
Module 10: **Planning for Sustainment** An understanding of how value champions can incorporate plans for sustainment into every aspect of their overuse reduction initiative is provided in this module

Justification for the Intervention:

Training and supporting a clinician value champion is a simple and pragmatic approach that any health system can deploy to address overuse of PIMs in their PWLD population. They are front-line clinicians who can advocate for and influence practice-driven change and may be particularly effective in de-implementing PIMs because they can: 1) be a trusted source of information about the potential harms of PIMs, 2) provide feedback and discuss prescribing behaviors with their colleagues, 3) serve as a role model for how to

provide guideline-concordant care for PLWD, and 4) identify contextual barriers and facilitators and leverage them to reduce PIMs use in their local setting. The clinician champion model is widely recognized as effective in implementing evidence-based practices in health care settings.

3 STUDY DESIGN

Type/Design of Trial:

We will conduct a pragmatic cluster-randomized clinical trial of this simple non-pharmacologic intervention by training a cohort of Clinician Value Champions in primary care clinic settings across two large accountable care organizations (ACOs); Oschner Health, and United States Medical Management (USMM).

Primary & Secondary Outcomes by Specific Aim:

Specific Aim #1: The primary outcome for this study will be medication possession rates (MPR) per quarter, for the 3 therapeutic classes of PIMs - antipsychotics, benzodiazepines, and hypoglycemics using currently available Medicare claims data from each participating ACO. These beneficiary-level measures are calculated as quotients with denominator equal to the length of the quarter and the numerators equal to the days supply for prescriptions within the class filled during the quarter, plus excess days-supply from the previous period minus excess days-supply remaining at the end. Unlike many studies using medication possession rates to exam adherence, we are interested in reducing, not increasing, the percent of days covered.

Specific Aim #2: As a secondary outcome, we will also assess the incidence of falls during the study window. Falls are difficult to monitor using claims data, but Min and colleagues have developed a method that IAC and Brandeis staff (Co-Investigator Perloff) have helped test for ICD-10.[9] We will use the most conservative definition that looks for the presence of fall 'reason for visit' code on ED, ambulatory, or inpatient visit as indicated by a clinician bill (Part B).

Specific Aim #3: The five important implementation outcomes: appropriateness, fidelity, feasibility, and penetration will be assessed by analysis of interviews conducted with a group (approximately 8) of clinician value champions who have completed the webinar training.

Study Population:

Clinician practices within each ACO will be eligible for participation in the study if they include 3 or more primary care providers (defined as a primary care physician (specialty code of 08 or 11), nurse practitioner (specialty code = 50) or physician's assistant (specialty code = 97)) and treat 10 or more Medicare beneficiaries with Alzheimer's or Alzheimer's related dementia in the base years (2019-2020). Medicare beneficiaries within the claims data provided by the two ACOs will be included in the study if they meet all of the following criteria during the intervention year: a. they are seen by a clinician at a participating practice as evidenced by one or more evaluation and management claim, b. they have continuous coverage in Medicare Parts A, B and D and no months of Part C (Medicare Advantage), they have two or more claims with an ICD-10 diagnosis for Alzheimer's or Alzheimer's related dementia 30 days apart or 1 inpatient stay with a principal diagnosis of Alzheimer's. Specific ICD-10 diagnoses to identify beneficiaries with Alzheimer's or Alzheimer's related dementia will be derived from a forthcoming paper by Dr. Julie Bynum and colleagues from the Technical Data Core of the Impact Collaboratory (personal communication, April 4, 2021). This definition is more inclusive than the CMS Chronic Condition Data Warehouse (CCW) definition of Alzheimer's and was

specifically designed for ICD-10. Patients with a diagnosis of metastatic cancer or enrolled in hospice any time in the 6 months before the start of the intervention will be excluded.

Randomization:
The unit of randomization will be the primary care practice. We anticipate 32 out of 39 teams from USMM to meet eligibility and 26 out of 28 practices for Ochsner. Within each ACO, we will randomly select half of the practices for participation in the value champion training and the remaining practices will continue with care as usual. Prior to random assignment, we will stratify all clinics/practices based on high versus low historic prescribing rates, with the cut-point for inclusion in the study based on the distribution of overall rates for all 3 therapeutic classes using data for 2019-2020. Once randomized, a clinician value champion will be recruited from each of the clinics randomized to the intervention arm of the study in partnership with the ACO leadership.

Study Locations: Primary care clinics within each of the two participating ACOs.

Duration of Enrollment and Follow-up: Using Medicare claims data for our primary outcome, with a follow-up period of one year after completion of the 6-months of value champion training, and with mediation possession rates calculated per patient each quarter, we will have approximately 4 MPR observations per patient or 8,000 observations per group for USMM analyses and 2,000 per group for Ochsner.

4 SELECTION AND ENROLLMENT OF PARTICIPANTS

4.1 Inclusion Criteria

Clinician practices within two ACOs will be eligible for participation in the study if they meet the following criteria:

a. They include 3 or more primary care providers (defined as a primary care physician (specialty code of 08 or 11), nurse practitioner (specialty code = 50) or physician's assistant (specialty code = 97)) and
b. They have clinical encounters with 10 or more Medicare beneficiaries with Alzheimer's or Alzheimer's related dementia in the base years (2019-2020).

Medicare beneficiaries will be included in the study if they meet all of the following criteria during the intervention year:

a. They are seen by a clinician at a participating practice as evidenced by one or more evaluation and management claim,
b. They have continuous coverage in Medicare Parts A, B and D and no months of Part C (Medicare Advantage),
c. They have two or more claims with an ICD-10 diagnosis for Alzheimer's or Alzheimer's related dementia 30 days apart or 1 inpatient stay with a principal diagnosis of Alzheimer's.

4.2 Exclusion Criteria

For our analytic sample from secondary Medicare claims data we will exclude:

a. Medicare beneficiaries with a diagnosis of metastatic cancer or

b. Medicare beneficiaries enrolled in hospice any time in the 6 months before the start of the intervention

4.3 Study Enrollment Procedures

Patient Subjects

We will partner with two ACOs with primary care clinic locations. Prior to random assignment, we will stratify all clinics/practices based on high versus low historic prescribing rates, with the cut-point for inclusion in the study based on the distribution of overall rates for all 3 therapeutic classes using data for 2019-2020. These clinics will be randomized 1:1 to either the intervention or control arms of the study. We will work closely with leadership in each ACO over months 1-3 of the study to recruit an appropriate clinician from each clinic in the intervention arm of the study to participate in the study. A total of 30 clinicians across the two ACOs will participate in the intervention, with 30 clinics in the control group without a clinician value champion.

We will request a waiver of informed consent and waiver of HIPAA authorization for including patient data in this study. The intervention will be embedded within the health care system at the clinic level as a training program for clinicians. No patients will be recruited into this study. Although data from human subjects are involved, no contact will ever be made with patients as this project involves the use of secondary data only. Attempting to obtain authorization or consent would not be feasible as this study will involve a study population of an estimated 5,000 patients. Consent and authorization of patients for enrollment in this study would create bias, generate prohibitive study costs rendering the study unfeasible, and produce results that would not be generalizable to other health care organizations. Furthermore, contacting 5,000 subjects for written consent would increase the only risk for patients - breach of confidentiality. We will ensure subjects' protection against risk by following the measures outlined in the section below.

Clinician Subjects:
Clinical leaders at the two ACOs with an understanding of the scope of the project will identify and approach clinicians at each intervention clinic to take part in the Value Champions training sessions. Clinical leadership will support VCs participation in the project in re: time needed for training and de-implementation efforts.

The clinician VCs are the de-implementation intervention. The control group (clinics) have no clinician VC embedded at the clinic. We will conduct 2 interviews with approximately 8 VCs that have completed the webinar training to measure implementation outcomes. Each VC who agrees to be interviewed will be interviewed approximately 5-7 months after webinar training is complete, and a second time approximately 10-12 months after training is complete. The implementation measures are not used to assess the VCs themselves (no personal information, or health information about the VCs will be collected). These interviews will be analyzed to provide insight into the de-implementation process at each ACO; how the de-implementation intervention was tailored and taken up in the clinical setting, for example. We will report each implementation outcome, both within each ACO and across the two ACO.

An email with an information sheet attached will be sent to the Value Champions after they are identified by clinical leaders, and before the first Webinar training. Included in this email is contact information to ask questions. At the first Webinar training session, we will start

the meeting by reminding Value Champions about the information sheet, ask if there are questions, and provide contact information to use in order to ask questions privately.

We are requesting a waiver of documentation of consent to enrolled clinician Value Champions in the study.

We will mention the interviews to the clinician champions during the monthly shared learning phone calls, and in emails reminding the group of the upcoming phone calls. We will then send an email inviting the clinician Value Champions to participate, with an information sheet explaining the interviews. The email and information sheet will note that they may opt out of the interviews. The email and information sheet will also give contact information if the clinicians have questions about the interviews.

If we have not reached recruitment goals (at least 4 clinicians at each ACO – 8 clinicians total) in one week, we will ask clinical leaders at the ACOs to remind clinicians to respond to the emails by opting in or out. If we still have not reached recruitment levels two weeks after the invitation email is sent, we will ask the clinic manager to forward the recruitment email to ask for a response.

We are seeking a Waiver of Documentation of Consent in order to conduct these interviews.

5 STUDY INTERVENTIONS

5.1 Interventions, Administration, and Duration

No drugs or devices will be studied. The intervention is a quality improvement strategy consisting of a clinician value champion who will engage other clinicians within their clinic in an effort to decrease the use of PIMs in PLWD. Typical methods of engagement include educational meetings, facilitating conversations about evidence of harm, providing current provider-specific data on rates of prescribing, etc.

5.2 Handling of Study Interventions

No drugs, devices or dietary or nutritional supplements will be used in this study. No patient level interventions will be used either.

5.3 Concomitant Interventions

N/A.

5.3.1 Allowed Interventions

N/A

5.3.2 Required Interventions

N/A

5.3.3 Prohibited Interventions

N/A

5.4 Adherence Assessment

There is no adherence assessment for enrolled patients, as this study uses secondary data only. Although Clinician Value Champions are not study subjects, they are key to the intervention and will take part in study activities as part of their clinical care. The study team will work closely in partnership with ACO leadership to facilitate study participation and retention of the clinician value champion from each clinic in the intervention arm of the study. In addition, each champion will be assigned a mentor from the former value champion fellows to increase the likelihood of engagement.

6 STUDY PROCEDURES

There are no study visits, no patient-level evaluation or schedule of such evaluations planned. We will use existing Medicare claims data from each ACO to inform selection of clinics for randomization. The primary outcome (Specific Aim #1) and one of the secondary outcomes (Specific Aim #2) will be evaluated using secondary Medicare claims data 12 months after completion of the clinician value champion training program. The secondary outcome for Aim #3 will be evaluated by analyzing interviews with approximately 8 value champions conducted following the completion of the training program.

6.1 Schedule of Evaluations

Assessment	*Months 1-3: Selection of Clinics for Randomization*	*Months 18-24: Evaluation of Primary & Secondary Outcomes*
Medicare Claims for each ACO	***X***	
Rates of Prescribing of PIMs (Specific Aim #1) from Medicare Claims		***X***
ED Visits or Hospitalization for a fall (Specific Aim #2) from Medicare Claims		***X***
Implementation Outcomes From Clinician Interviews (Specific to Aim #3)		***X***

6.2 Description of Evaluations

6.2.1 Screening Evaluation

Screening for eligibility will be done by review of existing Medicare claims data from each ACO as described in Section 4.1 above.

Consenting Procedure

Patient Subjects

We are seeking a Waiver of Informed Consent in order to identify and include patients in the study. Although data from human subjects are involved, no contact will ever be made with patients as this project involves the use of secondary data only. Attempting to obtain authorization or consent would not be feasible as this study will involve a study population of an estimated 5,000 patients. Consent and authorization of patients for enrollment in this study would create bias, generate prohibitive study costs rendering the study unfeasible, and produce results that would not be generalizable to other health care organizations. Furthermore, contacting 5,000 subjects for written consent would increase the only risk for patients - breach of confidentiality.

Clinician Subjects:

We are seeking a Waiver of Documentation of Consent in order to enroll clinician Value Champions in the study. The study PI (the initial PI at the time the study commenced), Michael Parchman, will send an email prior to training webinars with an attached study information sheet. During the first webinar, VC clinicians will be reminded of the information sheet by Dr. Parchman. He will provide contact information both in the email and during webinar in case VCs have questions.

We are seeking a Waiver of Documentation of Consent in order to conduct a series of 2 interviews with clinician who have completed the Value Champions webinar training series. We will mention the interviews to the group during the shared learning phone calls, and in emails reminding the group of the upcoming phone calls. We will then send an email inviting the Value Champions to participate, with an information sheet explaining the interviews. The email and information sheet will note that they may opt out of the interviews. The email and information sheet will also give contact information if the clinicians have questions about the interviews.

If we have not reached recruitment goals (at least 4 clinicians at each ACO – 8 clinicians total) in one week, we will ask clinical leaders at the ACOs to remind clinicians to respond to the emails by opting in or out. If we still have not reached recruitment levels two weeks after the invitation email is sent, we will ask the clinic manager to forward the recruitment email to ask for a response.

Screening

Patient Subjects:

Screening of eligible participants will be done by the programmer/analyst at IAC by applying study inclusion / exclusion criteria as described above in Section 4.1. This screening and selection will take place months 1-3 of the study prior to the value champion intervention. All Medicare beneficiaries at eligible ACOs will be included if they

meet eligibility criteria during the intervention year.

Clinician Subjects

Clinician Value Champions in the intervention clinics will be identified by ACO leadership, prior to the first webinar. The ACO leadership, in consultation with Dr. Parchman, will determine the suitability of specific clinical staff for study participation.

We will enroll at least four Clinical Value Champions from the two ACOs to be interviewed twice after they have completed the webinar training. Clinicians will be enrolled on a first come basis. All clinicians that have completed the webinar series will be eligible.

6.2.2 Enrollment, Baseline, and/or Randomization

Enrollment

Patient Subjects

We are using secondary data to identify Medicare beneficiaries at eligible ACO clinics, and thus seek a waiver of informed consent. Medicare beneficiaries will be enrolled in the study when they are identified, after we receive the waiver of informed consent.

Clinician Subjects

We are seeking a waiver of documentation of consent to enroll clinician Value Champions at the intervention clinics. Clinician Value Champions will be considered enrolled when their questions about the study have been answered, and they take part in the webinar trainings.

We are seeking a waiver of documentation of consent to enroll clinician Value Champions for 2 interviews from among clinicians who participated in the Value Champions training. Clinician Value Champions will be considered enrolled in the interviews when they indicate their willingness to participate, their questions about the 2 interviews have been answered, and they take part in the interviews.

Baseline Assessments

N/A

Randomization

We will start our sample identification by identifying clinics at each ACO that meet eligibility criteria. Half of the eligible clinics will be randomized to an intervention group, and half to usual care group.

6.2.3 Follow-up Visits

N/A-there are no follow-up visits since we are using secondary Medicare claims data to measure our primary outcome.

6.2.4 Completion/Final Evaluation

Patient Subjects:

We will not assess Medicare beneficiaries at a clinic visit. Rather, the primary outcome (Specific Aim #1) and one of the secondary outcomes (Specific Aim #2) will be evaluated using secondary Medicare claims data 12 months after completion of the clinician value champion training program.

Clinician Subjects:
A clinician value champion will have completed the study once the training and shared learning sessions are over. If they have chosen to participate in the interviews, they will have completed the study once the second interview is complete.

7 SAFETY ASSESSMENTS

7.1 Specification of Safety Parameters

There are no known risks to discontinuing these potentially inappropriate medications. Instead, the purpose of discontinuing these medications is to lower the risk of an adverse event due to the medication such as a fall, changes in cognitive status, or acceleration of the course of dementia. In addition, the data used to measure the primary outcome, pharmacy claims data, is de-identified and contains no PHI, lowering the risk due to loss of confidentiality.

These three classes of medication pose significant risks to older patients with dementia including falls, changes in cognitive status, and potentially accelerating the course of their dementia. The risk of these adverse events is significantly lowered by discontinuing these medications. Each of the risks described above also has the potential to create a cascade of adverse experiences such as fractures or head trauma from falls, resulting in hospitalization and the need for skilled nursing care instead of returning home.

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

As data used to measure the primary outcome is de-identified, contains no PHI, and is collected after the intervention is completed. However, to ensure that we capture any unexpected AEs, we will ask each clinician champion to monitor for any unexpected adverse events and complete an adverse event form if they see one. Once each month, clinician value champions will be asked to send all adverse event forms to the study coordinator. No SAEs are expected as described above. All deaths within the study cohort will also be reported along with a cause of death

7.3 Adverse Events and Serious Adverse Events

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.

AEs for this study include: There are no known expected or unexpected adverse events. Rather, discontinuing these medications lowers the risk of an adverse event from these medications.

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

SAEs for this study include: None

As there are no expected AEs or SAEs, we will not capture solicited AEs or SAEs. Unsolicited AEs and SAEs will be noted during clinical care. Once each month, clinician value champions will be asked to send all adverse event forms to the study coordinator. No SAEs are expected as described above. All deaths within the study cohort will also be reported along with a cause of death

7.3.1 Reporting Procedures

All data and safety monitoring reporting will classify SAEs and AEs as to their severity, as per the definitions below:

- **Mild:** Awareness of signs or symptoms, but easily tolerated and are of minor irritant type causing no loss of time from normal activities. Symptoms do not require therapy or a medical evaluation; signs and symptoms are transient.
- **Moderate**: Events introduce a low level of inconvenience or concern to the participant and may interfere with daily activities, but are usually improved by simple therapeutic measures; moderate experiences may cause some interference with functioning
- **Severe**: Events interrupt the participant's normal daily activities and generally require systemic drug therapy or other treatment; they are usually incapacitating.

All data and safety monitoring reporting will classify SAEs and AEs as to potential relatedness to the study intervention as per the definitions below:

- **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.

7.3.2 Follow-up for Adverse Events

Adverse event reporting schedule: Once each month, clinician value champions will be asked to send all unexpected adverse event forms to the study coordinator. No SAEs are expected as described above. All deaths within the study cohort will also be reported along with a cause of death.

- All **adverse events that are both 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 (Julie Lima PhD), Advarra IRB, NIA IMPACT Collaboratory PO (Dr. Partha Bhattacharya), and the IMPACT Collaboratory DSMB Chair within 48 hours of the study's knowledge of SAE.

- The summary of all other SAEs will be reported to IMPACT Collaboratory Regulatory and Data Team Leader (Julie Lima PhD), Advarra IRB, NIA IMPACT Collaboratory PO (Dr. Partha Bhattacharya), and the IMPACT Collaboratory DSMB Chair quarterly, unless otherwise requested by the DSMB Chair.

- All deaths will be reported to IMPACT Collaboratory Regulatory and Data Team Leader (Julie Lima PhD), Advarra IRB, NIA IMPACT Collaboratory PO (Dr. Partha Bhattacharya), and the IMPACT Collaboratory DSMB Chair and to the DSMB Chair within 24 hours of study's knowledge of death.

- AEs will be reported per IRB policies and also to IMPACT Collaboratory Regulatory and Data Team Leader (Julie Lima PhD), Advarra IRB, NIA IMPACT Collaboratory PO (Dr. Partha Bhattacharya), and the IMPACT Collaboratory DSMB Chair and to the DSMB Chair at minimum every 6 months, or at a frequency requested by NIA and/or by the DSMB.

7.4 Safety Monitoring

The Principal Investigator (PI) will be responsible for ensuring participants' safety on a daily basis. In addition, the NIA IMPACT Collaboratory DSMB will oversee all data and safety monitoring activities for this study. The number of DSMB members will be determined by NIA, and one will be designated the Chairperson. DSMB members will be appointed by the NIA Director. This DSMB 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 DSMB chair, will make a determination regarding the level and format of data and safety monitoring this study requires.

8 INTERVENTION DISCONTINUATION

Patient Subjects:

N/A – The goal of the value champion intervention, deprescribing of potentially inappropriate medications, is considered acceptable and standard clinical care at

intervention clinics. We will analyze secondary data of all eligible Medicare beneficiaries whether or not they reduce use of the targeted medications in response to the value champion interventions, and thus it is not possible for subjects to discontinue early. Reduction in use is likely to improve overall health, and we do not expect needed follow up for those who reduce their use of these medications.

Clinician Subjects:

Value Champions may end participation in the study for any reason. In that case, an alternative clinician Value Champion may be identified to replace the VC at that clinic if feasible considering the timing of withdrawal during the study period.

9 STATISTICAL CONSIDERATIONS

9.1 General Design Issues

Our hypothesis is that for each medication class, the intervention will produce clinically relevant decreases in mean possession rates of 10% of a standard deviation in patients seen in intervention clinics compared to those who are seen in control group clinics.

The study design was chosen to meet the requirements of the funder for a non-pharmacologic/non-device intervention for people living with dementia, conducted in a health system setting. The 24-months of funding is for a demonstration project, intended to demonstrate the feasibility and acceptability of the intervention, but with the stipulation by the funder that the trial must be a randomized controlled trial, one with a control group. In response, we proposed a cluster-randomized trial where the intervention will be randomized at the primary care clinic level, not the patient level, and existing health systems claims data will be used to address our primary outcome (Specific Aim #1) and one of our secondary outcomes: Specific Aim #2: emergency department visits and hospitalizations for a fall.

The primary outcome measure for this study will be medication possession rates (MPR) per quarter, for the 3 therapeutic classes of medications - antipsychotics, benzodiazepines, and hypoglycemics - that are considered low-value for beneficiaries with dementia. Unlike many studies using medication possession rates to exam adherence, we are interested in reducing, not increasing, the percent of days covered. Following an intent-to-treat design, claims data from all Medicare beneficiaries meeting our dementia eligibility criteria prior to the start of the value champion intervention will be included in the analysis. To determine the impact of the intervention, we will construct hierarchical models with time period observations nested within patient. These models will be random effects or generalized estimating equations (GEE) with robust standard errors, and will be either linear, if original MPRs are used as outcome, or generalized linear, if transformation necessary. The key variable of interest in these models will be the treatment indicator (assigned based on practice randomization to intervention or control group).

9.2 Sample Size and Randomization

Our sampling plan anticipates enrolling at least 30 of the 39 practices in USMM and 26 of the 28 practices in Ochsner. Based on Medicare enrollments of 39,000 members in USMM with a 20 percent dementia rate in 2019, and 10,000 members in Ochsner with approximately 10 percent of members diagnosed with dementia om 2019, we should have

at least 2,000 patients per treatment group for USMM and 500 patients per treatment group for Ochsner. For our primary outcome, with a follow-up period of one year and with mediation possession rates calculated per patient each quarter, we will have approximately 4 MPR observations per patient or 8,000 observations per group for USMM analyses and 2,000 per group for Ochsner. Even after assuming significant correlation across time within patient and modest correlation between patients within a practice, which will reduce effective sample sizes by 20%, we should have the equivalent of 6,400 observations per treatment group for our USMM analyses and 1,600 observations per treatment group for Ochsner.

The expectation of our intervention is that for each medication class, it will produce clinically relevant decreases in mean possession rates of 10% of a standard deviation. If the effect size is this large for a medication class and using a 5% level of significance, our Ochsner sample (with effective size of at least 1,600 per group) will have 80% power to discern a significant difference, while our larger USMM sample (with effective size of at least 6,400 per group) will have almost 100% power. Indeed, our USMM sample will have 80% power to find a significant difference, even if the effect size is only 5% of a standard deviation

9.2.1 Treatment Assignment Procedures

The unit of randomization will be the primary care practice or team. We anticipate 32 out of 39 teams from USMM to meet eligibility and 26 out of 28 practices for Ochsner. Within each ACO, we will randomly select half of the practices for participation in the value champion training and the remaining practices will continue with care as usual. Prior to random assignment, we will stratify practices based on high versus low historic prescribing rates. We will select practices for randomization and inclusion using a cut-point based on the distribution of overall rates for all 3 therapeutic classes using data for 2019-2020. Once randomized, a clinician value champion will be recruited from each of the clinics randomized to the intervention arm of the study in partnership with the ACO leadership.

9.3 Interim analyses and Stopping Rules

N/A – No interim analyses are planned. The proposed activities involve the collection and analysis of secondary automated system patient data for Specific Aims 1 & 2, and interviews with clinician value champions for Specific Aim #3.

9.4 Outcomes

9.4.1 Primary outcome

The primary outcome for this study (Specific Aim #1) will be medication possession rates (MPR) per quarter, for the 3 therapeutic classes of medications - antipsychotics, benzodiazepines, and hypoglycemics - that are considered low-value for beneficiaries with dementia. These beneficiary-level measures are calculated as quotients with denominator equal to the length of the quarter and the numerators equal to the days supply for prescriptions within the class filled during the quarter, plus excess days-supply from the previous period minus excess days-supply remaining at the end. Unlike many studies using medication possession rates to exam adherence, we are interested in reducing, not increasing, the percent of days covered. As a first choice, we will try to use originally-valued MPR variables in regression modeling, but if they don't reflect adequate

fit, we will transform them or possibly convert them to ordinal variables instead. For example, Benner and colleagues in their study of statin adherence defined non-adherence as MPRs within 0-20 percent, low-adherent as between 21-79 percent and high adherence as 80 percent or higher.[8] In addition to MPRs, we will also calculate and analyze the number of 30-day prescriptions per time-period for each beneficiary in the study.

9.4.2 Secondary outcomes

As a secondary outcome, for Specific Aim #2, we will also assess the incidence of falls during the study window. Falls are difficult to monitor using claims data, but Min and colleagues have developed a method that IAC and Brandeis staff (Co-Investigator Perloff) have helped test for ICD-10.[9] We will use the most conservative definition that looks for the presence of fall 'reason for visit' code on ED, ambulatory, or inpatient visit as indicated by a clinician bill (Part B). Key covariates in all of our regression models will include age and sex, both derived from the Medicare beneficiary summary files, house at IAC.

For Specific Aim #3, the five important implementation outcomes: appropriateness, fidelity, feasibility, and penetration will be assessed by analyzing interviews with clinician value champions. The Clinician interviews will provide us with data we need to assess the implementation outcomes.

9.5 Data Analyses

Following an intent-to-treat design, all Medicare beneficiaries meeting our dementia eligibility criteria will be included in the study, regardless of level of engagement with practice clinicians. Data analysis will begin with descriptive statistics, comparing the mix of patients at each practice including demographics, chronic conditions, and incident versus prevalent dementia. This will allow us to check for balance between treatment and control practices and inform subsequent modeling. To determine the impact of the intervention, we will construct hierarchical models with time period observations nested within patient. These models will be random effects or generalized estimating equations (GEE) with robust standard errors, and will be either linear, if original MPRs are used as outcome, or generalized linear, if transformation necessary. The key variable of interest in these models will be the treatment indicator (assigned based on practice). Since there could well be a time effect of treatment, we will explore several model specifications, such as discrete indicators for the time periods or a single continuous variable. Interactions of treatment with time period will also be explored. By examining various different specifications involving time, we should be able to determine whether the intervention leads to a one-time change, a gradual trend over time, or a combination of both (an immediate jump with a further change, as time passes). Finally, we will explore the impact of this intervention on health inequities by stratifying our primary analysis by race/ethnicity.

Specific to Aim #3: Current approaches to evaluating implementation outcomes are still nascent, with few measures that have validated psychometric properties. Conceptually, these measures are inter-dependent, and are connected with service outcomes, such as patient safety. We will use data collected from interviews with the Value Champions to conduct a thematic analysis of the five implementation outcomes using a deductive approach.

10 DATA COLLECTION AND QUALITY ASSURANCE

10.1 Data Collection Forms

We have two primary data sources: the 100% Medicare claims files from each ACO, and interviews with clinicians conducted by staff at KPWHRI and Brandeis. . Secondary data from Medicare Part D pharmacy claims data will provide us with our primary outcome data: cumulative exposure to any of the PIMs among an inception cohort of PLWD. In addition, Medicare claims data will be used for the third exploratory aim: rates of ED visits or admissions for a fall. This data will be identified and collected by the study programmer / analyst at AIC.

The Clinician interviews will provide us with the data we need for our implementation outcomes. A interview protocol is submitted for review. Data Management

Clinical Site Responsibilities: The two participating ACO organizations have Data Use Agreements with the Institute for Accountable Care, to access their 100% Medicare Claims data for purposes of the secondary data analyses for Specific Aims #1 & 2.

The Institute for Accountable Care will be responsible for data management of the secondary Medicare claims data. Their programmers will create a de-identified analytic file for Drs. Perloff and Ritter to use to test hypotheses for Aims #1 & 2.

The clinician interviews will be conducted and recorded by staff at KPWHRI and Brandeis University. The recorded interviews will be transcribed, and the transcriptions will be analyzed by staff at both Brandeis and KPWHRI.

10.2 Quality Assurance

10.3.1 Training

Dr. Lorella Palazzo's Current Human Subjects Training:

04/26/2021 CITI: Responsible Conduct of Research

04/30/2021 CITI: Level 1- Investigator-Initiated Behavioral Intervention

10.3.2 Quality Control Committee

N/A .

10.3.3 Metrics

N/A.

10.3.4 Protocol Deviations

We will document number of training sessions completed by each clinician value champion. Each value champion will have an assigned mentor who will conduct a monthly check-in visit to overcome challenges if they deviate from the training program and their project to tackle overuse of inappropriate medications. Mentors will keep notes of these meetings and share them with the PI and study team monthly.

10.3.5 Monitoring

See above regarding Protocol Deviation for our monitoring plan regarding compliance with the protocol.

11 PARTICIPANT RIGHTS AND CONFIDENTIALITY

\.

11.1 Institutional Review Board (IRB) Review

This protocol and any subsequent modifications will be reviewed and approved by the IRB or ethics committee responsible for oversight of the study.

11.2 Informed Consent Forms

N/A – We seek a waiver of informed consent to include secondary claims data from Medicare beneficiaries (patient subjects) in the study. We will seek a waiver of documentation of consent for enrolled clinician subjects before the start of study activities . We will provide clinician subjects an opportunity to ask questions about the study in private, and contact information if they have questions.

We will seek a waiver of documentation of consent for enrolled clinician subject before conducting interviews. (NOTE: As the interview data collection was added after consent process was completed for the enrolled clinicians, we will conduct separate consent procedures for the interviews.)

11.3 Participant Confidentiality

Multiple steps will be taken to protect participant confidentiality. Access to electronic files will be restricted to study staff on a need-to-know basis, and subject to the same security protections as other confidential health plan data. All data containing identifying information will be kept on password-protected computers using password-protected files. Identifiable information will be kept in a separate file from data used in analysis. Data used for analysis will be identified by unique study identifiers. Study data will be transferred between sites using secure methods, and appropriate Data Use agreements will be established between sites as needed. The clinician interviews will not contain any PHI or information about care specific to individual patients. No publications or reports will include any information identifying study participants.

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

We will adhere to the NIH Clinical Center researchers seven main principles of the conduct of ethical research:

- Social and clinical value
- Scientific validity
- Fair subject selection
- Favorable risk-benefit ratio
- Independent review
- Informed consent (in this case, obtaining a waiver of informed consent)
- Respect for potential and enrolled subjects

13 COMMITTEES

N/A

14 PUBLICATION OF RESEARCH FINDINGS

Any presentation, abstract, or manuscript will be made available for review by the sponsor and the NIA prior to submission.

15 REFERENCES

1. Redston MR, Hilmer SN, McLachlan AJ, Clough AJ, Gnjidic D. Prevalence of potentially inappropriate medication use in older inpatients with and without cognitive impairment: A systematic review. J Alzheimers Dis. 2018;61:1639-52. Epub 2017/12/28.

2. Delgado J, Bowman K, Clare L. Potentially inappropriate prescribing in dementia: a state-of-the-art review since 2007. BMJ open. 2020;10:e029172. Epub 2020/01/05. PMCID: PMC6955517.
3. American Geriatrics Society. Ten things clinicians and patients should question. Philadelphia, PA: Choosing Wisely, ABIM Foundation; 2013 [updated April 23, 2015; cited 2021 April 20]; Available from: https://www.choosingwisely.org/societies/american-geriatrics-society/.
4. U.S. Government Accountability Office. Antipsychotic drug use: HHS has initiatives to reduce use among older adults in nursing homes, but should expand efforts to other settings. Washington, DC; 2015 [cited 2021 March 17]; Available from: https://www.gao.gov/assets/gao-15-211.pdf.
5. Dionne PA, Vasiliadis HM, Latimer E, Berbiche D, Preville M. Economic impact of inappropriate benzodiazepine prescribing and related drug interactions among elderly persons. Psychiatr Serv. 2013;64:331-8. Epub 2012/12/18.
6. Hambling CE, Seidu SI, Davies MJ, Khunti K. Older people with Type 2 diabetes, including those with chronic kidney disease or dementia, are commonly overtreated with sulfonylurea or insulin therapies. Diabet Med. 2017;34:1219-27. Epub 2017/05/13.
7. Park S, Jung J, Burke RE, Larson EB. Trends in use of low-value care in traditional fee-for-service medicare and medicare advantage. JAMA Netw Open. 2021;4:e211762. Epub 2021/03/18. PMCID: PMC7970337.

8. Benner JS, Glynn RJ, Mogun H, Neumann PJ, Weinstein MC, Avorn J. Long-term persistence in use of statin therapy in elderly patients. JAMA. 2002;288:455-61. Epub 2002/07/23.
9. Min L, Tinetti M, Langa KM, Ha J, Alexander N, Hoffman GJ. Measurement of fall injury with health care system data and assessment of inclusiveness and validity of measurement models. JAMA Netw Open. 2019;2:e199679. Epub 2019/08/23. PMCID: PMC6707014.

SUPPLEMENTS/APPENDICES

Study information sheet provided to clinician subjects
Advance email sent to clinician subjects