DEPRESCRIBING TO REDUCE INJURIOUS FALLS AMONG OLDER ADULTS WITH DEMENTIA

Principal Investigator:
Elizabeth A. Phelan, MD, MS
Professor, Medicine/Gerontology and Geriatric Medicine, School of Medicine
Adjunct Professor, Health Systems and Population Health, School of Public Health
University of Washington

Kaiser Permanente Washington Site Investigator:
Benjamin Balderson, PhD
Senior Collaborative Scientist
Kaiser Permanente Washington Health Research Institute
Kaiser Permanente Washington

Supported by:

The National Institute on Aging

IMPACT Collaboratory (U54AG063546) Pilot Grants Program

FY22_Pilot4_Phelan

Version 2
Approved November 17, 2022

TABLE OF CONTENTS

PRÉCIS

Study Title: Deprescribing to Reduce Injurious Falls among Older Adults with Dementia

Objectives

The overarching objective of this project is to assess the feasibility and acceptability of implementing STOP-FALLS, an evidence-based, deprescribing intervention that targets central nervous system (CNS)-active medications, with older persons with dementia (OPWD) and their care partners, including those from diverse backgrounds. To accomplish this objective, we have the following aims:

Aim 1. Adapt STOP-FALLS for OPWD and their care partner(s). Stakeholder (primary care provider and care partners of OPWD) perspectives will be elicited to inform and guide adaptations. These activities are considered "not human subjects research," and have been reviewed and determined to be IRB exempt by Kaiser Permanente Washington (KPWA) IRB.

Aim 2. Conduct a one-arm pilot trial of the adapted STOP-FALLS intervention to determine 1) feasibility of reaching OPWD and their care partners, 2) acceptability of the intervention, and 3) whether the intervention was implemented as intended (implementation success).

Aim 3. Establish feasibility of using pragmatic methods to ascertain the following outcomes: 1) medically treated falls (primary outcome), 2) all-cause emergency department visits and hospitalizations (secondary outcome), and 3) nursing home placement (secondary outcome).

Design and Outcomes

The study design for Aims 2 and 3 is a one-arm, health-system embedded pragmatic pilot trial. Outcomes are described above and will be obtained from the virtual data warehouse (VDW) of the health system.

Interventions and Duration

The intervention consists of patient-facing, written brochures on six classes of CNS-active medications and provider decision support in the form of pharmaceutical aids (evidence-based pharmaceutical opinions, or EBPOs). Patient participants will receive a one-time mailing of a brochure, and PCP will receive decision support materials synchronous with the patient participant mailing. Subsequent actions around deprescribing (discussion, tapering) of the medication will be at the discretion of the patient participant and the PCP.

Sample Size and Population

The target sample size is 120 older adults with diagnosed dementia.

STUDY TEAM ROSTER

Principal Investigator:

Elizabeth A. Phelan, MD, MS
University of Washington
Harborview Medical Center
325 9th Ave Box 359755
Seattle, WA 98104
Telephone: (206) 744-9112
Fax: (206) 744-9976
Email: phelane@uw.edu

Dr. Phelan will provide overall leadership and oversee all operational issues for the project, including management of the research team, intervention refinement and implementation, data collection, analysis and interpretation, IRB and Data and Safety Monitoring Board reporting, and report and manuscript preparation and results dissemination.

Co-Investigators:

Benjamin Balderson, PhD
Kaiser Permanente Washington Health Research Institute
1730 Minor Ave
Ste 1600
Seattle, WA 98101
Telephone: (206) 326-2568
Fax: (206) 287-
Email: Benjamin.h.balderson@kp.org
Site Principal Investigator, Kaiser Permanente

Dr. Balderson will provide overall administrative and scientific oversight of the project at KPWA. Dr. Balderson will be heavily involved in data collection, preliminary analyses/ interpretation of results, and presentations. He will play a key role in the study intervention by being the liaison with primary care and will work with Kaiser Permanente leaders.

Shelly Gray, PharmD
University of Washington
Health Sciences Building, H-361D
Box 357630
Seattle, WA 98195
Telephone: (206) 616-5061
Fax: (206) 543-3835
Email: slgray@uw.edu
Co-Investigator, University of Washington

Dr. Gray will help guide all scientific decisions, participate actively in project team meetings, lead refinement of patient-facing intervention

materials, assist with finalizing the research evaluation, assist with interpretation of study data, and engage in preparation of reports, presentations, and manuscripts.

Sascha Dublin, MD, PhD
Kaiser Permanente Washington Health Research Institute
1730 Minor Ave
Ste 1600
Seattle, WA 98101
Telephone: (206) 287-2870
Fax: (206) 287-2871
Email: Sascha.Dublin@kp.org
Co-Investigator, Kaiser Permanente
Dr. Dublin will provide expertise as a practicing KPWA provider to inform intervention strategies and the integration of the study into KPWA clinics.

Andrea Cook, PhD
Kaiser Permanente Washington Health Research Institute
1730 Minor Ave
Ste 1600
Seattle, WA 98101
Telephone: (206) 287-4257
Fax: (206) 287- 2871
Email: Andrea.J.Cook@kp.org
Co-Investigator, Statistician, Kaiser Permanente
Dr. Cook will be involved in all issues related to study design and statistical analyses.

PARTICIPATING STUDY SITES

We anticipate submitting 1 site application, for Kaiser Permanente Washington, where the research will be conducted.

Benjamin Balderson, PhD
Kaiser Permanente Washington Health Research Institute
1730 Minor Ave
Ste 1600
Seattle, WA 98101
Telephone: (206) 326-2568
Fax: (206) 287- 2871
Email: Benjamin.h.balderson@kp.org

1. STUDY OBJECTIVES

1.1. Primary Objective

To assess the feasibility and acceptability of implementing STOP-FALLS, an evidence-based, deprescribing intervention that targets central nervous system (CNS)-active medications, with older persons with dementia (OPWD) and their care partners.

1.2. Secondary Objective

To determine the feasibility of using pragmatic methods to ascertain the primary and secondary outcome measures. These outcomes are: 1) medically treated falls (primary outcome), 2) all-cause emergency department visits and hospitalizations, and nursing home placement (secondary outcomes).

2. BACKGROUND AND RATIONALE

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

Falls among older adults are a major public health concern given their multiple adverse consequences including severe injury, functional decline, nursing home placement, and mortality.[1] Older people with dementia (OPWD) have eight to ten times more incident falls compared to age-matched peers without dementia.[2, 3] OPWD are also less likely than those without dementia to make a full functional recovery after a fall-related injury,[4] and falls increase burden on care partners.[5, 6]

Medications and particularly those that affect the central nervous system (CNS) are a key modifiable risk factor for falls.[7] Research has found that reducing CNS-active medications can reduce falls.[8] CNS-active medications are considered potentially inappropriate for older adults, especially for OPWD, and guidelines recommend avoiding their use.[9] However, use remains common and is increased among OPWD.[10, 11]

2.2. Study Rationale

STOP-FALLS-D seeks to address the guideline-practice gap described under 2.1., above. Our research team adapted a set of best practices[12, 13] for reducing use of CNS-active medications and is currently testing it with older adults *without dementia* in a pragmatic, cluster-randomized trial in primary care clinics of Kaiser Permanente Washington (KPWA). The intervention, called **STOP-FALLS**, (PI: Phelan, 1 U01CE002967) is a nudge intervention designed to activate patients and providers.[14] It delivers direct-to-patient education and provider decision support about the risks of five classes of CNS-active medications: opioids, sedative-hypnotics, skeletal muscle relaxants, tricyclic antidepressants, and first-generation antihistamines. The intervention is delivered via mail (to patients) and via the electronic medical record (to PCPs). Care partners are not an intervention target, and dementia is one of the exclusion criteria. From the health

equity perspective, given that OPWD are more susceptible to the side effects of CNS-active medications, and also given that they are more likely to be prescribed these medications, it seems reasonable and indeed imperative to attempt to reach them with the proposed intervention.

3. STUDY DESIGN

This study consists of three aims.

The study design for Aim 1 is qualitative, one-on-one interviews with stakeholders. This aim was reviewed and determined to be IRB exempt by KPWA's IRB. The purpose of this aim is to adapt STOP-FALLS intervention materials for older adults living with dementia by conducting interviews with stakeholders (KPWA primary care providers and care partners of OPWD receiving care within KPWA).

The final intervention materials, revised based on the input obtained from stakeholders who participate in Aim 1 interviews, will be submitted in a modification to Advarra to be used for Aims 2 and 3.

Aims 2 and 3 will be reviewed by Advarra. <u>The remainder of the protocol thus pertains to Aims 2 and 3 only</u>.

The study design for Aim 2 is a one-arm, pragmatic, health-system-embedded pilot trial to determine 1) feasibility of reaching OPWD and their care partners, 2) acceptability of the intervention, and 3) whether the intervention was implemented as intended (implementation success).

Aim 3 involves data collection for the pilot trial to establish the feasibility of using pragmatic methods to ascertain the following outcomes: 1) medically treated falls (primary outcome), 2) all-cause emergency department visits and hospitalizations (secondary outcome), and 3) nursing home placement (secondary outcome).

4. SELECTION AND ENROLLMENT OF PARTICIPANTS

4.1. Inclusion Criteria

Participants must meet the following inclusion criteria to participate: 1) KPWA enrollees aged 60 years or older, 2) diagnosed dementia, based on either a dementia diagnosis code or prescription for a cholinesterase inhibitor or memantine, 3) receiving primary care at a KPWA integrated group practice outpatient clinic, and 4) taking at least one

CNS-active medication on a chronic (≥3 month) basis, as determined by KPWA prescription fill records. The classes of CNS-active medications targeted by the intervention will be: antipsychotics, opioids, sedative-hypnotics, skeletal muscle relaxants, tricyclic antidepressants, and first-generation antihistamines.

Care partners will be identified as individuals aged 18 years or older who self-identify as a care partner for the person with dementia and return a completed research questionnaire.

4.2. Exclusion Criteria

Participants meeting any of the following criteria will be excluded from study participation: a) residing in a skilled nursing facility; b) cancer diagnosis in the prior 12 months; c) receiving hospice or palliative care; d) legally blind (unable to see print materials.

4.3. Study Enrollment Procedures

1. This project will request a waiver of consent to send out the educational brochure and collect data from the electronic medical record (EMR), because mailed educational material could reasonably be sent to patients from their healthcare home as part of routine care, and because decisions about any changes to medications will rest with the patient, their care partner, and their PCP. Therefore, there will not be a process for the participant to opt-out of the study. See section 11.2 for details. The project will request a waiver of documentation of consent for the questionnaire; completing and returning the questionnaire indicates permission to use responses for research.

2. Before commencing data pulls, the study team will email the Medical Chief at each intervention clinic to alert them that this pilot intervention is going to commence. Because the intervention and implementation are very comparable to that of STOP-FALLS, which these clinicians are already familiar with due to having been based in intervention clinics for the STOP-FALLS trial, a more in-depth clinic presentation to providers is not deemed necessary.

3. Using KPWA automated data under a waiver of HIPAA authorization, the study programmer will identify all potential participants who meet inclusion criteria. The programmer will oversample participants who are of Hispanic ethnicity and whose race is not white. Of this potential participant pool we will identify a total study sample of 120 participants to whom we will mail the study materials.

5. STUDY INTERVENTIONS

5.1. Interventions, Administration and Duration

Aim 2

The study design is a one-arm, pragmatic pilot trial. The intervention will be implemented with up to four clinics and up to 120 OPWD and their care partners. The intervention consists of an educational brochure about a CNS-active medication that the OPWD has been prescribed along with decision support for that individual's PCP. To assess the acceptability of the intervention, a brief questionnaire will be mailed to the OPWD shortly after mailing of the intervention materials. Follow-up for outcomes ascertainment will start at the time of mailing of intervention materials to eligible participants.

1. After the sample has been identified, the study team will send a packet to all eligible participants containing:

a. A cover letter addressed to the participant and any care partner they may have. The letter will also contain a study phone number with voicemail to call if either participant or care partner has questions. This voicemail line will be monitored by study staff;
b. Educational brochure for the medication class that the participant has been prescribed on a chronic (3 months or longer) basis;
c. For most drug classes, a corresponding non-pharmacological self-care sheet, previously approved for STOP FALLS that has been modified based on dementia care partner input (Aim 1 interviews).

2. At the same time, the study team will use the Epic (electronic medical record) "staff message" functionality to send a message letting the PCP know that their patient is included in the study and a link to the EBPO of the relevant medication class. The purpose of this message is to enable the PCP to be prepared to have conversations with participants about their medication use and for these conversations to be guided by the evidence and talking points in the EBPO. The timing of these messages is not aligned with an upcoming clinic visit; it is anticipated that a participant/care partner may initiate the conversation with the provider on their own time schedule.

3. When the participant/care partner receives the mailed packet, they can choose to read the materials or not. Reading all the materials in the packet should take approximately 10 minutes. If they choose, they can discuss the information in the brochure with their PCP.

4. Approximately 1-3 weeks after brochure mailing, the study team will send a brief questionnaire to OPWD and their care partners to ascertain intervention acceptability including the perceived usefulness of the educational materials and the likelihood of starting conversations about their medications with their providers. Care partner sociodemographics will also be obtained via this questionnaire for descriptive purposes. If the participant/care partner choose to complete and return the questionnaire, that activity should take approximately 5 minutes. (see **Supplements/Appendices**: **Participant questionnaire**)

5. Returned questionnaires will be data-entered, and a survey response dataset will be created.

Aim 3

The automated data pulls and chart review associated with Aim 3 involve data collection for the pilot trial to establish the feasibility of using pragmatic methods to ascertain the following outcomes: 1) medically treated falls (primary outcome), 2) all-cause emergency department visits and hospitalizations (secondary outcome), and 3) nursing home placement (secondary outcome).

Automated data pull

1. The study programmer will modify existing code from STOP-FALLS to pull data from KPWA automated data sources for the following three outcomes:
   1) medically treated falls (primary clinical outcome), 2) all-cause emergency department visits and hospitalizations (secondary outcome), and 3) nursing home placement (secondary outcome).
2. An analytic dataset will be created and outcomes data summarized. We anticipate this will take 3-6 months.

Medication taper ascertainment from medical records

1. The study programmer will modify existing code from STOP-FALLS to create flags indicating which participants' medical records have deprescribing text in the "sig field" (i.e., prescribing instructions) for each CNS-active medication.
2. The KPWA study team members (Dr. Balderson and Ms. Fujii) will review up to a 20% random sample of records to adjudicate whether or not the flags correctly identified evidence of a medication taper, completing the following shell table for each record:

Field	***Description***	**Notes:**

Study ID	*Pre-populated study ID*	
ConsumerNo	*Pre-populated Consumer Number*	PHI
Medication class	*Pre-populated med class (e.g. opioid, TCA, benzo)*	
Date	*Pre-populated date*	PHI
Taper flag	*Pre-populated (yes/no)*	Did the program identify a potential deprescribing plan for the sig field?
KPWA_sig	*Pre-populated text*	Actual text from sig field
Taper flag correct?	*Yes/No/Not sure*	Does the adjudicator find information in the medical record to support the "Taper flag"?
Notes:	*Text box*	Any additional information to support decision making of "taper flag correct" score.

5.2. Handling of Study Interventions

Due to the nature of the intervention, participants cannot be masked.

There is no "training fidelity" plan given the nature of this intervention.

There is no "intervention fidelity" plan given the nature of this intervention.

5.3. Concomitant Interventions

We do not have any concomitant interventions.

5.4. Adherence Assessment

There is no "adherence assessment" plan given the nature of this intervention.

6. STUDY PROCEDURES

6.1. Schedule of Evaluations

Measure	Baseline	1-3 month follow-up	3-6 month follow-up
Aim 2			
Feasibility (Participants meeting eligibility criteria are identified and mailed intervention materials)	X		
Acceptability (Participants find the intervention acceptable)		X	
Implementation Success (Taper plans for CNS-active medications are documented in the participants' medical records)		X	X
Aim 3			
Feasibility of obtaining outcomes data from the medical records (e.g., falls, nursing home placement, etc.)			X

6.2. Description of Evaluations

The pilot study evaluation (Aim 2) will assess 1) feasibility of reaching the target population, 2) acceptability of the intervention, and 3) success of intervention implementation.

Intervention feasibility will be measured by the ability to pull baseline data such as participant contact information, eligibility/ineligibility criteria, and demographics. If no more than 30% of intervention materials are "returned to sender," we will deem it feasible to reach the target population.

Intervention acceptability will be measured by responses on returned questionnaires. If at least 65% of returned questionnaires indicate the intervention is acceptable and [if applicable] open-ended comments are positive >50% of the time, we will deem the intervention to be acceptable to the target population.

Intervention implementation success will be measured by documentation of a plan to taper in the "sig" field in the participant's medical record; if at least 35% of participants have a documented taper plan, we will consider the intervention to have been successfully implemented.

Feasibility of obtaining outcomes data from the medical record will be assessed in Aim 3. Outcomes (clinical and utilization) data will be summarized and presented as percent of the study sample with the event (e.g., percent with a medically treated fall; percent with any ED visit or hospitalization, percent with a skilled nursing facility stay). Time to first medically treated fall will also be recorded.

7. SAFETY ASSESSMENTS

7.1. Specifications of Safety Parameters

Comprehensive medication management is part of the KPWA standard of care, and any medication changes will be made by the participant and their PCP. This is consistent with usual care. There is no requirement for participants, care partners or PCPs to engage in discussion about medication safety or deprescribing. The intervention is education and designed to offer participants and their care partners information to understand the risks of CNS-active medications for older adults with dementia. The intervention does not alter a participant's medication prescriptions.

There is still the possibility for adverse effects from the intervention. These are described under 7.3., below.

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

This research involves testing an educational intervention, and therefore the main risk is breach of confidentiality. For more detail on the steps we will take to ensure patient confidentiality, see section 11.3.

To allow for the possibility that adverse events may result from the intervention, we define adverse events and reporting procedures in the following section.

Throughout the study period, any clinic champion or PCP will be able to report safety concerns via the study's project manager's voicemail.

7.3. Adverse Events (AE) and Serious Adverse Events (SAE)

AEs for this study include:

- Medication withdrawal symptoms (e.g., for opioids – nausea, vomiting, diarrhea)

- Worsening of underlying condition for which medication was prescribed (e.g., for antipsychotics – behavioral and psychological symptoms of dementia (BPSD) (e.g., agitation, aggression, psychosis)

The severity of AE is likely to be moderate and would be *expected* as a result of reduction in medications especially if the medication were withdrawn rapidly or abruptly.

SAEs for this study include:

- Emergency department visit or hospitalization for management of medication withdrawal symptoms
- Emergency department visit or hospitalization for management of BPSD or re-emergence of other symptoms for which the medication was prescribed
- Hospitalization due to any cause
- Death due to any cause

The above events would be *expected* given the nature of the intervention and the population under study (i.e., older adults with dementia).

7.3.1. Reporting Procedures

Contact information (telephone / voicemail) for the study's project manager will be provided to intervention clinics, and clinic champions and PCPs will be invited to report any possible adverse events resulting from the trial. For each report, the site PI and study PI will review the potential concern. Review of the electronic medical record for adverse events will be restricted to SAE.

Adverse events that are serious and unexpected will be reported to the IMPACT Collaboratory Regulatory and Data Team Leader, the NIA IMPACT Collaboratory Program Officer, and the project's Safety Officer and, if related to the intervention, to the Advarra IRB, within 48 hours of the study team's knowledge of the event.

All deaths will be reported to the IMPACT Collaboratory Regulatory and Data Team Leader, the NIA IMPACT Collaboratory Program Officer, and the project's Safety Officer within 24 hours of the study team's knowledge of death.

All unanticipated problems (UPs) will be reported to the IMPACT Collaboratory Regulatory and Data Team Leader, Advarra IRB, NIA IMPACT Collaboratory Program Officer, and the project's Safety Officer within 48 hours of the study's knowledge of the problem.

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, Advarra IRB, NIA IMPACT Collaboratory PO, and the project's Safety Officer at a minimum every 6 months, or at a frequency requested by the IMPACT Collaboratory.

7.3.2. Follow-up for Adverse Events

Adverse events will be reviewed by the Safety Officer for the study as described above, who will determine the need for any follow-up actions and define the exact nature of those actions.

7.4. Safety Monitoring

An independent Safety Officer has been appointed by the NIA IMPACT Collaboratory to serve as the data safety monitor.

8. INTERVENTION DISCONTINUATION

For this pilot study of a one-time, pragmatic, educational intervention, we do not have intervention discontinuation criteria.

9. STATISTICAL CONSIDERATIONS

9.1. General Design Issues

This is a one-arm pilot study to inform a future full-scale, stage 4 embedded pragmatic clinical trial (ePCT). The one-arm design is justified because the primary objective is to establish feasibility and acceptability of the intervention. We hypothesize that the intervention will be feasible to implement, acceptable to patients and clinicians, and that outcomes will be feasible to assess via pragmatic methods.

9.2. Sample Size and Randomization

For Aims 2 and 3, our sample size calculations are based on the framework of "green", "yellow" and "red" lighting for pilot feasibility trials.[39] Based on our primary endpoint, which is implementation success,[17] assuming the upper boundary of the "red" zone is 20% and the lower boundary of the "green" zone is 35%, the sample size required for analysis given 90% power and one-sided 5% alpha is n=78 (intervention arm only). Specifically, if the true rate is in the "green" zone with a sample size of 78, we have 90% power for the study to not be defined as "red" lighted. We will increase the sample size to 120 to be able to have 90% power across all secondary endpoints as well.

9.2.1. Treatment Assignment Procedures

This is a one-arm pilot trial, and as such all participants will receive the intervention.

9.3. Interim analyses and Stopping Rules

No interim analyses are planned. There are no stopping rules.

9.4. Outcomes

9.4.1. Primary outcome

The primary outcome is medically treated falls, defined as falls for which medical care is received. Our measure of the primary outcome will be time to first medically treated fall. The time window of observation for the primary outcome will be 6 months subsequent to the patient-facing materials being distributed to study participants. We will ascertain this outcome from health plan utilization files using International Classification of Disease-10 injury diagnosis and fall-related (V-code or W-code) external cause of injury codes.[20-22] We will describe fall events according to sex and race/ethnicity.

9.4.2. Secondary outcomes

Secondary outcomes are 1) all-cause emergency department visits and hospitalizations, and 2) nursing home placement. Secondary outcomes will be ascertained from utilization files of the health plan.

9.5. Data Analyses

We will summarize measures of feasibility and acceptability using binary outcomes and calculating proportions and 95% confidence intervals using simple descriptive analysis. For our primary endpoint of implementation success, following the framework proposed for pragmatic pilot trials,[39] if 35% have a documented taper plan, the trial will be "green" lighted to move forward to a confirmatory study; if 20%-<35% have a documented taper plan, it will be "yellow" lighted, meaning that the intervention needs be modified if to move forward; and if <20% have a documented taper plan, it will be "red" lighted, meaning that the intervention is a "no go". The same framework will be applied across secondary endpoints. We will examine differences by relevant sociodemographic characteristics (e.g., race, ethnicity, sex) for each outcome using the same criteria.

10. DATA COLLECTION AND QUALITY ASSURANCE

10.1. Data Collection Sources

There will be two sources of data collection for this research project: 1) KPWA automated data sources and 2) a mailed questionnaire.

1) **KPWA automated data sources and electronic medical records:** KPWA automated data sources will be used to complete both Aims 2 and 3. Automated data sources such as demographics, prescription medication fills, and diagnoses will be used to identify and mail to eligible participants for Aim 2. In order to ascertain the occurrence of deprescribing, we will look at the electronic medical records of participants to determine whether a plan to taper the target medication was documented. For Aim 3, we will use automated data sources to collect and summarize the following outcomes of interest: 1) medically treated falls (primary clinical outcome), 2) all-cause emergency department visits and hospitalizations, and 3) nursing home placement.

Table 1: Data from KPWA to identify potential study participants

Source (specify) (i.e., from KPWA, or an existing or previous study, etc.)	List of electronic data that will be used to identify potential participants
KPWA electronic data sources	Healthcare Utilization: all outpatient visits, dates, provider id
KPWA electronic data sources	Pharmacy Dispensing Data: drug name, NDC, strength, quantity, days supply, prescriber id, and date dispensed for all medications of interest (antipsychotics, opioids, benzodiazepines, tricyclic antidepressants, Z-drugs, other sedative hypnotics, muscle relaxants, antihistamines) and medications to treat Alzheimers/dementia
KPWA electronic data sources	Diagnosis Codes: all fall and fracture related diagnoses and dates of diagnoses, all opioid use diagnoses codes and dates (exclusion criteria)
KPWA electronic data sources	Demographics: age, sex, race, and ethnicity
KPWA electronic data sources	Tumor Registry: dates of all cancer diagnosis (exclusion criteria)
KPWA electronic data sources	Procedures: all fall and fracture related procedure codes and dates of procedure
KPWA electronic data sources	Enrollment: enrollment in KPWA (start and stop dates)
KPWA electronic data sources	Provider table: provider id, specialty, provider type
KPWA electronic data sources	Referral for nursing homes and/or hospice (Exclusion Criteria)

KPWA electronic data sources	Hospice admissions database (Exclusion Criteria to confirm that these patients are not receiving hospice care)
KPWA electronic data sources	Provider ID, Specialty, Provider Type, primary practice clinic. Data collected so that we can determine who the patients' PCP is for Epic Staff Messaging the EBPO to the correct provider).

Table 2: Data from KPWA to ascertain study outcomes

Source (i.e., from KPWA, or an existing or previous study, etc.)	Key Information/Description of Variables
KPWA electronic data sources	Diagnosis codes: For outcomes including: • Injury diagnostic codes • Fall-related diagnostic codes For chronic conditions associated with falls, e.g.: arthritis, back pain, knee pain, alcohol use disorder, chronic lung disease, congestive heart failure, diabetes, heart disease, hip fracture, hypertension, obesity, peripheral neuropathy, osteoporosis, Parkinson's disease, stroke, urinary incontinence, impaired vision, impaired hearing, memory problems, non-melanoma cancers, frailty For other diagnoses related to medication prescription for the following conditions: anxiety, depression, insomnia, chronic pain
KPWA electronic data sources	All healthcare utilization for the primary outcome (falls) such as primary care visits, specialty visits, emergency department visits, inpatient stays, nursing home admissions
KPWA electronic data sources	All emergency department visits, inpatient stays, and nursing home admissions
KPWA electronic data sources	Pharmacy dispensing data (drug name, date of dispensing, strength, quantity, days supply, provider id, NDC) for the following intervention target prescription medication classes: antipsychotics, benzodiazepines, z-drugs, opioids, muscle relaxants, antihistamines, tricyclic antidepressants. In addition, the following medication classes are needed to examine whether target medications were substituted with equally unsafe medications as a result of the intervention: Gabapentinoids, other sedative hypnotics, other antidepressants, NSAIDs.

KPWA electronic data sources	KP's Center for Effectiveness and Safety Research (CESR) Med Order Table information (e.g. instruction for usage, prescription date, medication type)
KPWA electronic data sources	Demographics (e.g., age, sex, race, marital status)

2) **Questionnaire:** We will assess acceptability of the intervention (Aim 2) via a brief, mailed questionnaire. The questionnaire will be anonymous; it will not contain any identifiable information such as PHI or a study ID. Thus, this information cannot be linked to any other study data.

10.2. Data Management

KPWA automated data sources and electronic medical records: All automated data will be extracted from KPWA automated data sources. Data will be stored on KPWA password protected computers. Medication deprescribing information will be ascertained by looking at the "sig" field under the "Medication tab" of the KPWA electronic medical record. The results of that chart review, whether or not deprescribing information is indicated and the wording used, will be data-entered into a MS Excel spreadsheet stored on a KPWA password protected computer.

Questionnaires: The responses of the returned questionnaires will be data-entered into a MS Excel spreadsheet stored on a KPWA password protected computer.

10.3. Quality Assurance

For Aim 2, to ensure accuracy of the data, we will double input data from the mailed questionnaires. For sig field data, up to 20% of charts will be reviewed to determine if the sig data pulls are accurate.

For Aim 3, the data pulled will be verified as being within the follow-up time window and pertinent to the given study participant by hand-review of the data returned.

11. PARTICIPANT RIGHTS AND CONFIDENTIALITY

11.1. Institutional Review Board (IRB) Review

This protocol and patient/care partner-facing materials will be reviewed and approved by the IRB responsible for oversight of the study.

11.2. Informed Consent

Waiver of informed consent. We request a waiver of informed consent for the research to be conducted in Aims 2 (pilot trial) and 3 (outcomes ascertainment). This research meets the five criteria for a waiver of informed consent, as follows:

1) the research is minimal risk by virtue of its educational nature; participants are not required to engage in discussions about deprescribing; study materials provide guidance about how to safely taper and stop medications;
2) the research could not practicably be carried out without a waiver, because obtaining written informed consent would be highly burdensome to the target population (OPWD) and outweigh the minimal risks of the intervention; obtaining surrogate consent would be likely to render otherwise eligible participants ineligible if a surrogate were not available or identifiable and thus compromise recruitment and threaten achievement of sufficient sample size;
3) the research could not practicably be carried out without the use of identifiable data; these data are needed to identify the eligible sample of OPWD and send study materials to them and to their PCP, and to extract research measures including outcomes data from the KPWA virtual data warehouse (VDW). With regard to outcomes data extraction specifically, in prior research that we have conducted that focused on the same target medication classes, in which we initially provided participants an opportunity to opt out of use of automated data for outcomes assessments, we experienced a higher proportion of opt-outs among those who were on opioids. This imbalance represents a threat to internal validity that can be avoided through a waiver of consent;
4) the waiver will not adversely affect the rights or welfare of participants; the cover letter accompanying the educational brochure will encourage the participant to discuss their use of the medication with their PCP and share the brochure with family members and/or friends who help them with their health care but explain that they are under no obligation to do so;
5) whenever appropriate, participants or legally authorized representatives will be provided with additional pertinent information after participation; a summary of key findings from the research can be written up for publication in a patient-facing KPWA newsletter that goes out to KPWA enrollees on a periodic basis.

Alteration and waiver of documentation of consent. An alteration and waiver of documentation of informed consent is requested for the Aim 2 questionnaire. This brief questionnaire will be the source of information on intervention acceptability and care partner sociodemographic characteristics. The questionnaire will contain a statement explaining that by completing and sending the questionnaire back to the study staff, the

participant is giving us permission to use their anonymous responses for research. A cover letter containing most, but not all of the components of informed consent will be included with the questionnaire.

Waiver of HIPAA Authorization. A full waiver of HIPAA authorization is requested for study sample identification and collecting study outcomes. The use of protected health information (PHI) for this purpose involves no more than minimal risk to the privacy of individuals, because the PHI will be protected from improper use and disclosure by virtue of its being accessed only by the KPWA-based study staff. No PHI will be transmitted beyond the KPWA-based programmer, Research Specialist, and Project Manager, and any linking files created for participant tracking, extraction of data from electronic health records, and data analysis will be destroyed as soon as the research has been completed and the study findings published. The research could not practicably be conducted without the waiver and without access to and use of the PHI, as obtaining consent directly from participants for this purpose would be unnecessarily burdensome.

11.3. Participant Confidentiality

All data will be stored on the KPWA secure network folders accessible only to research study team members. Only the KPWA study programmer will have access to the linking file. The KPWA study programmer, KPWA Research Specialist, and KPWA Project Manager will have access to identifiers so that they can recruit participants, mail out study materials, and let providers know that their patient is participating in the study. Computer files will be password protected with access restricted to staff using this information to perform study-related activities. All analytic data files will be password protected. Data tables with any identifiers needed for mailing the patient brochures (i.e., name, address)) will be kept separate from all other study data tables. All employees at KPWA routinely sign a confidentiality form that covers access to all data encountered.

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

All research conducted at KPWA complies with the Department of Health and Human Services requirements for safeguarding the rights and welfare of human subjects, regardless of the source of funding. KPWA and UW each have approved Federal-wide Assurance Compliance filed with the Office for Human Research Protections (OHRP). Both institutions have agreed to cede to Advarra for IRB oversight and study approval. Advarra will also serve as the Research Privacy

Board, and ensures that the privacy and confidentiality or protected health information is maintained, as required by the Health Insurance Portability and Accountability Act (HIPAA).

13. COMMITTEES

NIA Program Officer

Partha Bhattacharyya
Program Director
National Institute on Aging
bhattacharyyap@nia.nih.gov
(301) 496-3131

14. PUBICATION OF RESEARCH FINDINGS

Publication of the evaluation of the pilot study will be determined by the study team. Our primary purpose is to inform the development of a full-scale, stage IV effectiveness embedded pragmatic clinical trial. Publication of the results of this pilot study will be governed by the policies and procedures developed by the IMPACT Collaboratory.

15. REFERENCES

1. Centers for Disease C, Prevention. Fatalities and injuries from falls among older adults--United States, 1993-2003 and 2001-2005. *MMWR Morb Mortal Wkly Rep*. Nov 17 2006;55(45):1221-4.

2. Allan LM, Ballard CG, Rowan EN, Kenny RA. Incidence and prediction of falls in dementia: a prospective study in older people. *PLoS One*. 2009;4(5):e5521. doi:10.1371/journal.pone.0005521

3. Casey CM, Caulley J, Phelan EA. The Intersection of Falls and Dementia in Primary Care: Evaluation and Management Considerations. *Med Clin North Am*. Sep 2020;104(5):791-806. doi:10.1016/j.mcna.2020.06.003

4. Shaw FE. Falls in cognitive impairment and dementia. *Clin Geriatr Med*. May 2002;18(2):159-73. doi:10.1016/s0749-0690(02)00003-4

5. Kamiya M, Sakurai T, Ogama N, Maki Y, Toba K. Factors associated with increased caregivers' burden in several cognitive stages of Alzheimer's disease. *Geriatr Gerontol Int*. Apr 2014;14 Suppl 2:45-55. doi:10.1111/ggi.12260

6. Leggett AN, Polenick CA, Maust DT, Kales HC. Falls and Hospitalizations Among Persons With Dementia and Associated Caregiver Emotional Difficulties. *Gerontologist*. Mar 19 2018;58(2):e78-e86. doi:10.1093/geront/gnx202

7. Seppala LJ, Wermelink A, de Vries M, et al. Fall-Risk-Increasing Drugs: A Systematic Review and Meta-Analysis: II. Psychotropics. *J Am Med Dir Assoc*. Apr 2018;19(4):371 e11-371 e17. doi:10.1016/j.jamda.2017.12.098

8. Campbell AJ, Robertson MC, Gardner MM, Norton RN, Buchner DM. Psychotropic medication withdrawal and a home-based exercise program to prevent falls: a randomized, controlled trial. *J Am Geriatr Soc*. 1999;47(7):850-3.

9. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. *J Am Geriatr Soc*. Apr 2019;67(4):674-694. doi:10.1111/jgs.15767

10. Maust DT, Strominger J, Bynum JPW, et al. Prevalence of Psychotropic and Opioid Prescription Fills Among Community-Dwelling Older Adults With Dementia in the US. *JAMA*. Aug 18 2020;324(7):706-708. doi:10.1001/jama.2020.8519

11. Growdon ME, Gan S, Yaffe K, Steinman MA. Polypharmacy among older adults with dementia compared with those without dementia in the United States. *J Am Geriatr Soc*. Sep 2021;69(9):2464-2475. doi:10.1111/jgs.17291

12. Martin P, Tamblyn R, Benedetti A, Ahmed S, Tannenbaum C. Effect of a Pharmacist-Led Educational Intervention on Inappropriate Medication Prescriptions in Older Adults: The D-PRESCRIBE Randomized Clinical Trial. *JAMA*. Nov 13 2018;320(18):1889-1898. doi:10.1001/jama.2018.16131

13. Tannenbaum C, Martin P, Tamblyn R, Benedetti A, Ahmed S. Reduction of inappropriate benzodiazepine prescriptions among older adults through direct patient education: the EMPOWER cluster randomized trial. *JAMA Intern Med*. Jun 2014;174(6):890-8. doi:10.1001/jamainternmed.2014.949

17. Proctor E, Silmere H, Raghavan R, et al. Outcomes for implementation research: conceptual distinctions, measurement challenges, and research agenda. *Adm Policy Ment Health*. Mar 2011;38(2):65-76. doi:10.1007/s10488-010-0319-7

20. Moreland BL, Burns ER, Haddad YK. National rates of non-fatal emergency department visits and hospitalisations due to fall-related injuries in older adults 2010-2014 and 2016: transitioning from ICD-9-CM to ICD-10-CM. *Inj Prev*. Mar 2021;27(S1):i75-i78. doi:10.1136/injuryprev-2019-043516

21. Hedegaard H, Johnson RL. An Updated International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) Surveillance Case Definition for Injury Hospitalizations. *Natl Health Stat Report*. Jul 2019;(125):1-8.

22. Slavova S, Costich JF, Luu H, et al. Interrupted time series design to evaluate the effect of the ICD-9-CM to ICD-10-CM coding transition on injury hospitalization trends. *Inj Epidemiol*. Oct 1 2018;5(1):36. doi:10.1186/s40621-018-0165-8

39. Lewis M, Bromley K, Sutton CJ, McCray G, Myers HL, Lancaster GA. Determining sample size for progression criteria for pragmatic pilot RCTs: the hypothesis test strikes back! *Pilot Feasibility Stud*. Feb 3 2021;7(1):40. doi:10.1186/s40814-021-00770-x

16. SUPPLEMENTS/APPENDICES

Participant questionnaire

The first question lets us know who is filling out this questionnaire. Is the person filling out this questionnaire:

- Someone who assists a Kaiser Permanente enrollee who may have memory difficulties with their medical care
- A Kaiser Permanente enrollee who may have memory difficulties
- Other; _____

The next question is about the medication information packet that you received in the mail recently. Please choose the response that best describes your impression of the medication information packet.

The medication information packet...

	Completely disagree	Disagree	Neither agree nor disagree	Agree	Completely agree
Meets my approval					
Is appealing to me					
Is likeable					
Is welcome to me					

Please tell us about yourself

1. Which of the following describes your race? Please select all that apply

- ❑ American Indian/Alaskan Native
- ❑ Asian
- ❑ Black or African American
- ❑ Native Hawaiian/Other Pacific Islander
- ❑ White
- ❑ You describe yourself as;_____

2. Do you consider yourself to be:

- ❑ Hispanic or Latino
- ❑ Not Hispanic or Latino

3. What is your age?

- ❑ Less than 65
- ❑ 65-74
- ❑ 75-84
- ❑ 85-94
- ❑ 95 and older

4. Sex

- ❑ Female
- ❑ Male
- ❑ You describe yourself as;_____