Title:
Shared Decision Making About Medication Use for People with Multiple Health Problems
NCT05156073

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eForm A – Protocol

1. Abstract

a. Provide no more than a one page research abstract briefly stating the problem, the research hypothesis, and the importance of the research.

The U.S. burden of Alzheimer's disease and related dementias is expected to grow to 13.9 million people by 2060 as a result of population aging, leading to substantial morbidity, mortality and health care costs. These effects are exacerbated in patients with dementia and multiple chronic conditions (MCC). Having multiple diseases at the same time (e.g., diabetes and hypertension and dementia) inevitably leads to the use of multiple drugs (polypharmacy) and potentially inappropriate medications, in which the risks of medications outweigh benefits, or medications do not align with the patient's treatment goals. For individuals with dementia and MCC, taking more medications is associated with greater risk of adverse drug events, drug interactions and treatment burden. Studies suggest that as many as 56% of people with dementia are taking at least one potentially inappropriate medication, including medications that can negatively affect cognitive function.

Given the growing dementia population, novel interventions are needed to improve the quality and safety of prescribing and patient-centered outcomes. Optimizing medication use through **deprescribing** (the process of reducing or stopping the use of potentially inappropriate medications or medications unlikely to be beneficial) can improve outcomes for patients with dementia and MCC. Existing deprescribing interventions have excluded patients with dementia, have been limited to inpatient or skilled nursing settings, or have focused on specific drug classes such as benzodiazepines. The most effective deprescribing interventions for older adults in general have been multidisciplinary and have involved the provision of direct-to-patient educational materials. Because primary care is typically the major point of contact for patients with dementia, there is a need to develop deprescribing interventions for this population that target multiple medications and can be integrated into the primary care setting.

Our multidisciplinary team has developed a primary care-based deprescribing intervention (OptiMize) for patients with mild cognitive impairment, dementia and MCC consisting of a patient and family component focused on education and activation about deprescribing, and a clinician component to increase awareness about processes and language for deprescribing. Patient activation refers to the willingness and ability to take independent actions to manage one's health and health care (i.e., understanding one's role in the care process and having the knowledge, skill, and confidence to manage one's health and health care). We have recently completed a multisite trial of OptiMize within Kaiser Permanente Colorado. **There are several reasons to adapt OptiMize and replicate it in diverse settings.** First, because OptiMize is a pragmatic trial, all of the outcome measures are being extracted from the EMR. **Previous deprescribing trials have, for the most part, not assessed patient-reported outcomes related to deprescribing, including measures of shared decision making and health-related quality of life.** Adapting OptiMize and replicating it in another setting would enable us to assess these important patient-centered outcomes. Second, Kaiser Permanente is often described as a model, fully integrated health delivery system, meaning that it combines a nonprofit insurance plan with its own hospitals and clinics and provides all patient services, from a primary care physician to hospitalization and pharmacy services. It has a long history of partnering with its clinical practices to conduct research and quality improvement programs, using the integrated care system as a laboratory for health services research. It has a particularly sophisticated electronic medical record (EMR) system that integrates all aspects of care across the care delivery system, including inpatient, outpatient and pharmacy settings, which enables longitudinal observation for health research. Unlike most U.S. medical practices, Kaiser's information systems and infrastructure have been

designed to address the needs of clinical research. As most patients in the U.S. receive primary care at sites that are not part of such systems, much remains to be learned about how to implement deprescribing broadly throughout diverse primary care settings. To begin filling these gaps, we propose a 3-4 month pilot trial of a patient-centered deprescribing intervention for older adults with mild cognitive impairment or dementia and/or MCC, generalizable to a range of primary care settings.

2. Objectives (include all primary and secondary objectives)

Primary objective: To establish the **feasibility and acceptability** of the intervention among patients, care partners, clinicians and medical assistants by assessing:

- Acceptability and process measures from a qualitative analysis of debriefing interviews with patients, care partners, clinicians, and medical assistants.

Secondary objective: To assess the **preliminary efficacy of the intervention by measuring**:
a) The proportion of patients who deprescribe 1+ medicine
b) The proportion of patients who add 1+ new medicine
c) Clinical documentation of deprescribing, defined as medication discontinuation or dose-reduction
d) Clinical documentation of a discussion about medication appropriateness, safety or effectiveness (yes/possible vs. no/absent).

Our overall goal for the pilot study is to inform a future randomized controlled trial of a patient- and family/care partner-centered deprescribing intervention scalable across a range of primary care practices.

3. Background (briefly describe pre-clinical and clinical data, current experience with procedures, drug or device, and any other relevant information to justify the research)

Our research team has substantial experience in observational, qualitative, and interventional research focused on patients with cognitive impairment, MCC and polypharmacy, and is well positioned to complete the proposed project. We completed a pilot of OptiMize and a multisite randomized trial (Bayliss et al. Trials. 2020 Jun 18;21(1):542. Bayliss et al. JAMA Intern Med. 2022 May 1;182(5):534-542).

Preliminary results of qualitative interviews done as part of OptiMize have revealed that patients, care partners and clinicians are enthusiastic about deprescribing. In addition, clinicians have expressed a desire for guidance relating to deprescribing communication with patients and families, including “pearls” for specific clinical scenarios. Some of the scenarios include: How to elicit patients’ goals of treatment and connect them to deprescribing; how to talk with patients about deprescribing potentially inappropriate medications that are often taken for bothersome symptoms, such as overactive bladder and insomnia; and how to introduce the concept of deintensifying glycemic and blood pressure targets as a result of aging and multimorbidity. These communication pearls have become the cornerstone of the clinician intervention. Patients and care partners have suggested specific language for clinicians to use in initiating conversations about deprescribing. For example, they emphasized using language that develops a partnership with the patient and family and acknowledges the tradeoffs implicit in using medications for symptom management in dementia; and framing deprescribing as a routine, positive step, rather than a withdrawal of care. We further investigated patient preferences regarding clinician deprescribing communication with a national survey of approximately 800 older adults in early 2020 (Green et al. JAMA Netw Open. 2021 Apr 1;4(4):e212633. Green et al. J Am Geriatr Soc. 2022 Jun 6).

All of our educational materials in OptiMize were developed and refined with patient and care partner input. The materials in our pilot intervention in Reading, PA will build off of these existing materials and will be further refined with patient, care partner and clinician input.

Because OptiMize was a pragmatic trial designed to leverage Kaiser Permanente's robust information systems, all of our outcome measures have come from the EMR and administrative claims; we have not collected any process measures. In addition, further research is needed to determine how best to implement and adapt a patient-centered deprescribing intervention in diverse primary care settings and with members of health disparity groups. The pilot we are proposing would enable us to test Optimize in a different setting from KPCO and to explore how the intervention works in a clinic with a large proportion of low-income patients, a large Spanish-speaking/Latino population, and with trainees (residents).

4. Study Procedures

a. Study design, including the sequence and timing of study procedures (distinguish research procedures from those that are part of routine care).
b. Study duration and number of study visits required of research participants.
c. Blinding, including justification for blinding or not blinding the trial, if applicable.
d. Justification of why participants will not receive routine care or will have current therapy stopped.
e. Justification for inclusion of a placebo or non-treatment group.
f. Definition of treatment failure or participant removal criteria.
g. Description of what happens to participants receiving therapy when study ends or if a participant's participation in the study ends prematurely.

a. Study design, including the sequence and timing of study procedures: We propose to do a pilot test for a randomized controlled clinical trial of medication optimization through increased awareness of deprescribing for older adults with cognitive impairment and/or MCC. The intervention will have two components: a patient/ care partner component focused on education and activation about deprescribing, and a clinician component focused on increasing clinician awareness about options and processes for deprescribing in the cognitive impairment and/or MCC population. The intervention is designed to be simple, have broad inclusion/exclusion criteria, and be scalable across a range of primary care settings. The pilot intervention will be delivered to a single clinic – the Reading Hospital Family Health Care Center, a primary care practice in Reading, PA that is part of the JHCRN. The full randomized trial will be conducted in multiple outpatient primary care clinics in MD/DC/VA/PA. The goal of the pilot study is to assess feasibility and acceptability of the intervention.

Study procedures for the pilot:
Primary care physician cohort:

1) All eligible (N=35) Primary Care Physicians (PCPs) and medical residents (≥ 18 years) at the Reading Hospital Family Health Care Center study site will receive an IRB-approved invitation via their work e-mail from the principal investigator (addresses will be requested from the clinic medical director). We may also place hard copies of the invitations in their mailboxes at the clinic or hand them out at a team meeting. The invitation will be co-signed by the clinic medical director or a clinical "champion," who will be identified from the practice. We will ask clinicians and residents to opt out if they are not interested in participating.
2) PCPs will receive education on deprescribing through an initial 15-minute presentation, and medical residents will receive a 45-minute lecture. The presentation will be conducted by the PI (Dr. Green) at a regularly scheduled team meeting. PCPs and residents will receive 12 one-page tip sheets on managing

deprescribing in specific clinical situations during the presentation. We may also send a single tip sheet each week for 12 weeks. We will deliver the tip sheets through the clinicians' and residents' work e-mail and/or hand them out at team meetings or place them in their mailboxes.

3) At the end of the pilot, PCPs and residents will be asked to participate in a 30–45-minute debriefing interviews via Zoom, FaceTime or telephone and to complete a brief demographic questionnaire. The debriefing interviews will be audio recorded. PCPs and residents who wish to participate will provide written informed consent at the educational session prior to recruitment of patients.

Medical assistant cohort:

1) During the course of the pilot, Medical Assistants (MAs) (N=8) at the clinic will be invited to participate in a 30–45-minute interview via Zoom, FaceTime or telephone and to complete a brief demographic questionnaire. MAs will receive an invitation via their work e-mail from the principal investigator/or research staff (addresses will be requested from the clinic medical director). We may also place hard copies of the invitations in their mailboxes at the clinic or hand them out at a team meeting. The invitation will be co-signed by the clinic medical director or clinical "champion". We will ask MAs to opt out if they are not interested in participating. The research staff will obtain oral consent from MAs who express interest in participating before conducting the interview. The research assistant will read the oral consent script and inform them that their participation in the interview is voluntary, that they can withdraw from the interview at any time, and that they can decline to answer any question without providing an explanation. Participants will be given as much time as they would like to ask questions regarding the study. No interviews will be conducted until the participant has full understanding of the study and informed consent is obtained.

Patient and care partner dyad cohort:

Study procedures for the intervention

We will have two separate cohorts in this study: A Mild Cognitive Impairment (MCI)/Dementia cohort and a non-dementia cohort.

1) All established patients of PCPs and residents at the pilot clinic who meet eligibility criteria will be identified by JHCRN staff in conjunction with the research team using EMR data. We will be requesting a Waiver of HIPAA Authorization to identify eligible patients via the EMR.
    - For the purpose of this study, a care partner is defined as family or other non-related companion ≥21 years (not acting as a paid home health aide) who regularly helps the patient with managing medications.

    Additional methods for the identification of patients

    - **For the MCI/Dementia cohort**, in addition to identification through ICD-10 code diagnosis, we will also ask clinicians and residents to identify patients who:
        - meet eligibility criteria, and
        - may not have a dementia or MCI diagnosis in their problem list, but the provider is confident that the patient has dementia or MCI.

      And to provide their information to the to the local research nurse or coordinator at the pilot clinic.
    - **For the non-dementia cohort**, in addition to identification through ICD-10 code diagnosis, we will also ask clinicians and residents to identify patients who meet the eligibility criteria and to provide their information to the to the local research nurse or coordinator at the pilot clinic.
    - The research nurse or coordinator at the pilot clinic may also identify patients who are potentially eligible to participate and due for a primary care visit (i.e., have not had a visit in at least one year), create a list and share it with the clinic's staff so they can call the patient to offer an appointment.

2) All eligible patients with upcoming appointments within the study period will be mailed an introductory letter and the educational brochure informing them of the study (see attached). We will stop mailing letters once N=20 patients who receive the brochure have also completed their primary care visit. In addition, we may use several approaches that we have discussed with the local research coordinator and clinical champion and that they have recommended as being well-aligned with clinic workflows:
    - We may also send materials through the patient portal to registered patients.
    - As a reminder, we will give patients and care partners a copy of the introductory letter and brochure a second time in the waiting room or during rooming.
    - In order to expand eligibility to patients who schedule primary care visits in the last minute – in which case, there would not be enough time to mail the introductory letter and brochure in advance – a study staff member will hand the introductory letter and brochure to eligible patients and care partners in the waiting room before their clinic appointment or during rooming.
    - We may also send a list of patient's names and appointments dates to the clinic's nursing manager and a note will be added to the pre-visit planning section of Epic to notify MAs to give study materials to eligible patients and care partners during rooming.
    - The English version of the introductory letter and educational brochure will be sent/given to English-speakers. A Spanish version of the letter and brochure will be sent/given to patients who have identified Spanish as their preferred language in the EMR or where there is evidence in the chart that a translator has been used during their previous visits.
    - The introductory letter will be signed by the clinic medical director and the study PI, Dr. Green, using joint letterhead. It will be addressed to patients and care partners. The letter will say that patients and care partners are receiving the educational brochure as part of a research study focused on how doctors and patients discuss decisions to continue or discontinue medications during office visits. It will encourage patients and care partners to review the materials before their next appointment with their PCP. The letter will include a phone number that patients/care partners can call if they have further questions.
3) We will send PCPs and medical residents notification via staff message (see attached) in Epic when study materials have been given to patients with upcoming appointments.

Data collection from the EHR

Local study team members at the clinic will collect the following information from the EHR:

1) Screenshots of the patient's medication list:
    - At baseline (defined as the day they are identified as eligible),
    - On the day before their primary care visit,
    - Immediately after their primary care visit (within 1 day), and
    - 3 months $\pm$ 7 days after the primary care visit.

The medication lists will be uploaded to JH OneDrive and/or the REDCap database.

2) The PCP's clinical note from the day of the patient's primary care visit.

Study team members will also abstract the following information from eligible patients' medical records: demographics (age, gender, race/ethnicity), contact information (home address/telephone), care partner/legally authorized representative (LAR), medical diagnoses and medications, and the PCP's visit note from the primary care visit. A data dictionary will guide uniform abstraction.

Intervention consent process

We are requesting a waiver of informed consent for the intervention (mailing of educational brochure to patients/care partners) and data collection from the EHR, as in our team's previous studies ALIGN (IRB00286353) and OPTIMIZE (IRB00222685).

Options for pragmatic trial consent range from 1) full individual level recruitment and written informed consent, to 2) recruitment information sent to all eligible candidates with an 'opt out' clause, to 3) general information on the intervention provided to all eligible patients with an option for further inquiry. We request a waiver of informed consent (option 2) as an acceptable approach for the intervention and data collection from the EHR based on the following factors:

(i) The research involves no more than minimal risk to the subjects.
- Any changes in medication regimens will be made by the PCP and patient/care partner through shared decision making. This is consistent with usual care.
- Comprehensive medication management is already part of the Reading Hospital standard of care.
- There is no requirement for patients/ care partners or PCPs to engage in discussions about medication optimization upon receipt of intervention materials.
- Potential risks of deprescribing can be minimized or prevented by using a patient-centered, structured process, as this study proposes to do. Any medication believed to have increased potential for physiologic withdrawal, such as benzodiazepines, will undergo a prescribed drug taper under the clinician's supervision according to standard clinical procedure. In addition, patients and care partners may contact the clinician with concerns about drug withdrawal effects or medical condition exacerbation, as is standard clinical procedure. Further, medications can be restarted or increased at any time should concerns arise on the part of the patient, care partner or clinician. The intervention brochure includes language that instructs the dyad not to stop any medications without talking to the PCP.

(ii) The research could not practicably be carried out without the requested waiver or alteration.
Requiring full individual level recruitment and written/oral informed consent would be highly burdensome to the target population, older adults with dementia, and would outweigh the minimal risks of the intervention itself. The standard procedures for assessing capacity, identifying a legally authorized representative and obtaining surrogate consent would likely cause many patients to opt out or become ineligible. Requiring that two physicians determine capacity and document it in the EMR would also be highly burdensome to the study population and would outweigh the minimal risks of the intervention itself. This requirement would likely cause many patients to opt-out or become ineligible, which would compromise the scientific validity of any evaluation of the intervention. Even if we consented care partners, the research cannot be carried out without enrolling patients.

(iii) If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format:
The intervention is pragmatic and designed to test a scalable process that can be implemented across multiple clinics to improve care for people with mild cognitive impairment or dementia and MCC. For this reason, our initial eligibility criteria and our primary outcome are derived from the EHR data under a waiver of HIPAA Authorization. The data need to be identifiable in order to send educational materials to individual patients and care partners and to link subject data over time.

(iv) The waiver or alteration will not adversely affect the rights and welfare of the subjects:

Intervention materials will include an informational cover letter that will indicate that patients may wish to discuss medication discontinuation with the PCP but are under no obligation to do so. This is consistent with usual care.

(v) Whenever appropriate, the subjects or legally authorized representatives will be provided with additional pertinent information after participation.
It is not anticipated that significant new findings that affect individual patients are likely to occur during their participation in the study, so we do not have plans to provide information to subjects or their LARs after participation.

Procedures for debriefing interviews of patients and care partners

Recruitment:
A smaller subset (N=10-15) of patients who have received study materials and completed their primary care visit will be mailed a letter informing them about the interview. The letter will be signed by the principal investigator and the clinic's medical "champion". A research assistant will contact participants by phone approximately 7-10 days after mailing the letter. The letter will include a phone number where participants may call if they would like to "opt out". Patients and care partners who do not "opt out" will be called by phone by research staff to explain the study in detail, to assess interest in participating in a 45–60-minute interview, and to schedule an interview. We will attempt no more than six calls to participants. During the course of the study, we may interview patients/care partners who have received the study materials but don't have an appointment schedule with their PCP. Interviews will be conducted via telephone or a teleconferencing platform (FaceTime or Zoom) at a time convenient to participants.

- **Recruitment of patients:**
    - For patients whose EHR records do not reflect that they are incapacitated, we will assess their interest in participating in the interview.
        - If the individual can provide informed consent based on their responses to the capacity questions, then we will obtain informed consent from them and proceed to conduct the interview.
        - If an individual is not able to answer the capacity questions correctly, then they will not be eligible to participate in the interview.
    - Patients who have incapacity documentation in the EHR will not be recruited. Care partners/LARs of these patients can still participate in the interview.

Informed consent process:
After completing the recruitment process described above, oral informed consent will be obtained by research staff trained in human subject research prior to conducting the interview. The research assistant will read the oral consent script to the patient/care partner and inform them that their participation in the interview is voluntary, that they can withdraw from the interview at any time, and that they can decline to answer any question without providing an explanation. Participants will be given as much time as they would like to ask questions regarding the study. No interviews will be conducted until informed consent is obtained.

Upon review of the oral informed consent, we will evaluate whether the patient/care partner may provide informed consent by asking them about the study protocol. We will ask: "What is the main purpose of the study?", "What are the benefits of the study?", "What are the risks of the study?", "Are you able to withdraw from the study at any time?" If the patient/care partner provides an inaccurate answer, the study staff member will review that section and then re-ask the question. The study staff member will then pose

the question to the patient/care partner again. If the patient/care partner answers incorrectly a second time, then will be unable to provide informed consent and will be determined ineligible to participate in the interview. Where capacity to consent is questionable participants will be excluded. Study staff will document whether the person may provide informed consent. Finally, participants who are able to provide informed consent will be asked they want to participate in the interview and their responses will be recorded. All participants will be directed to the phone number of the respective Principal Investigator and research coordinator if further questions arise. The contact information for the IRB will be provided to them for further questions concerning their rights as study subjects.

Interviews:
Patients/care partner interviews will begin with a brief demographic questionnaire. The interviews will be semi-structured, meaning that there will be a predefined interview guide based on the questions of interest and existing literature, but the interviews will also be dynamic and allow for new topics to emerge. Consistent with established qualitative research methods, we will iteratively refine the interview guide. Interviews with Spanish-speaking patients will be conducted by a research coordinator who is a native Spanish speaker. This research coordinator will do all of the recruitment phone calls with patients who have identified as Spanish-speaking in the medical record or where there is evidence in the chart that a translator has been used during their previous visits. The interviews will be audio-recorded, transcribed verbatim, translated (only for the interviews conducted in Spanish) and reviewed for accuracy by a transcription service. We plan to use a HIPAA-compliant transcription service, Production Transcripts for the English interviews, and Landmark Associates for the Spanish interviews, both approved vendors by Johns Hopkins University. If names or other personal identifiers are used in the audio recordings, the transcription service will remove them from the transcripts. All files exchanged between the transcription service and the study team will happen via a password-protected secured extranet. The transcripts will be analyzed in an iterative manner using established qualitative methods. All data will be stored on a secure Hopkins server (JH OneDrive and/or REDCap). The audio recordings will be destroyed after transcripts have been checked for accuracy, and transcripts will be destroyed at the earliest opportunity in accordance with Hopkins's policies and procedures.

b. Study duration and number of study visits required of research participants: The study will last from February 2023 – May 2024. At the end of the pilot, participants (patients and care partners) may be invited to participate in a 45-60 minute debriefing interview and will be asked to complete a demographic questionnaire. Aside from these interview, patients will only attend their routine primary care visits. Primary care clinicians and residents will each be asked to participate in a single educational session and a single, 30-45 minute, one-on-one debriefing interview at the conclusion of the pilot study, and to complete a brief demographic questionnaire. We will work with the clinic medical director to hold the clinician education session during a regularly-scheduled team meeting. Medical assistants will be asked to participate in 30-45 minute, one-on-one debriefing interview during the course of the pilot.

c. Blinding, including justification for blinding or not blinding the trial, if applicable: The pilot trial will be single-group. Due to the nature of the intervention, it will not be possible to blind the trial to patients, care partners and clinicians.

d. Justification of why participants will not receive routine care or will have current therapy stopped: N/A. Patients enrolled in the study will receive routine care. All medication decisions for the intervention and control groups, prescribing or deprescribing, will be at the discretion of the clinicians.

e. Justification for inclusion of a placebo or non-treatment group: The pilot will be single-group. As there are currently no established gold-standard deprescribing methods, we will have a usual care comparator in the full trial.

f. Definition of treatment failure or participant removal criteria: For the pilot study, we do not have treatment failure or participant removal criteria. The clinic director and physicians will be able to directly report any safety concerns. Patients, care partners and clinicians are not required to act on the educational materials or to participate in deprescribing discussions at any point. Outcomes data will be collected on all participants, regardless of whether they choose to discuss medication management or deprescribing with their primary care providers. Participants in the debriefing interviews may opt out at any point. The IRB may request study cessation.

g. Description of what happens to participants receiving therapy when study ends or if a participant's participation in the study ends prematurely: Participants will continue receiving routine care.

5. Inclusion/Exclusion Criteria

Patient and care partner dyad:

Inclusion criteria:

This study is for patients aged 65 or greater. We will expand eligibility criteria and create an MCI/dementia cohort and a non-dementia cohort, as described below.

The following criteria will be used to identify potentially eligible patients:

- MCI/dementia cohort:
    - Age 65 or older.
    - Diagnosis of MCI **OR** dementia from ICD-9 and ICD-10 codes on the problem list **OR** the presence of dementia medications on their medication list **OR** identified as having MCI or dementia by their primary care provider.
    - At least one other chronic condition documented on the problem list. Chronic conditions will be defined as conditions that last 1 year or more and require ongoing medical attention, such as hypertension.
    - 5 or more medications (to include all prescription and over-the-counter medications, both scheduled and as needed) documented in the EMR medication list.
    - Have a primary care physician or resident at the pilot clinic; this will be defined as having had at least 1 previous visit with a physician at the clinic in the past year.
    - Have a scheduled visit with a primary care physician during the pilot study period.
    - Patient must be able to hear well enough to participate in interviews on the telephone.

- Non-dementia cohort:
    - Age 75 or older.
    - No MCI or dementia diagnosis
    - At least two chronic conditions documented on the problem list
    - 5 or more medications (to include all prescription and over-the-counter medications, both scheduled and as needed) documented in the EMR medication list.

  - Have a primary care physician or resident at the pilot clinic; this will be defined as having had at least 1 previous visit with a physician at the clinic in the past year.
  - Have a scheduled visit with a primary care physician during the pilot study period.
  - Patient must be able to hear well enough to participate in interviews on the telephone.

- Care partners:
  - Age 21 or older.
  - Must be able to hear well enough to participate in the interviews on the telephone.

Exclusion criteria:

- As the pilot will be based in primary care, individuals residing in long term care facilities or enrolled in hospice care at baseline will be excluded.
- Patients taking 4 or fewer different medications for all their health needs will be excluded.

Primary care physician and medical assistant cohorts:
All primary care physicians and medical assistants at the pilot site will be included. Physicians who only provide urgent care will be excluded.

6. Drugs/ Substances/ Devices

a. The rationale for choosing the drug and dose or for choosing the device to be used.
b. Justification and safety information if FDA approved drugs will be administered for non-FDA approved indications or if doses or routes of administration or participant populations are changed.
c. Justification and safety information if non-FDA approved drugs without an IND will be administered.

N/A

7. Study Statistics

a. Primary outcome variable.
b. Secondary outcome variables.
c. Statistical plan including sample size justification and interim data analysis.
d. Early stopping rules.

a. The primary outcome for the pilot study will be the feasibility and acceptability of the intervention among patients, care partner and clinicians. These data will be obtained through the qualitative analysis of the debriefing interviews with patients and care partners who have received the intervention materials, clinicians and medical assistants.

b. The secondary outcomes for the pilot study will focus on the preliminary efficacy of the intervention in diverse primary care settings. Measures will include: the proportion of patients who deprescribe 1+ medicine, the proportion of patients who add 1+ new medicine, clinical documentation of deprescribing, defined as medication discontinuation or dose-reduction, and clinical documentation of a discussion about medication appropriateness, safety or effectiveness (yes/possible vs. no/absent). These measures will be extracted from the electronic medical record.

c. Statistical plan and interim data analysis: The pilot aims to assess feasibility and acceptability of the intervention. For the pilot study, we do not have statistical hypotheses, sample size calculations or randomization.

d. Early stopping rules: There are no statistical criteria that would temporarily suspend the intervention. The clinic director and physicians will be able to directly report any safety concerns, and the IRB may request study cessation.

8. Risks

a. Medical risks, listing all procedures, their major and minor risks and expected frequency.
b. Steps taken to minimize the risks.
c. Plan for reporting unanticipated problems or study deviations.
d. Legal risks such as the risks that would be associated with breach of confidentiality.
e. Financial risks to the participants.

a. This protocol presents minimal risks to the subjects. The main risk is breach of confidentiality. Potential risks associated with deprescribing include adverse drug withdrawal events, return of symptoms, and anxiety about deprescribing. Potential risks can be minimized or prevented by using a patient-centered, physician-led deprescribing process. Additionally, potential risks of deprescribing need to be weighed against potential risks of continuing an inappropriate medication. Deprescribing studies, where the intervention involves withdrawal of medications which have been determined through shared decision making to be inappropriate for the individual (which is what our intervention will involve) have been generally shown to be safe. Our intervention involves providing patients and care partners with an educational brochure and opportunities (through increased patient/care partner engagement) for patients, care partners and clinicians to identify medications which may be suitable for withdrawal and to discuss deprescribing as a component of optimal medication management. The decision to deprescribe a medication will be made by the primary care physician together with the patient and care partner. Interviews with patients and care partners conducted as part of OptiMize reveal strong support for this approach.

b. Strategies to minimize these risks in our study include:
- Emphasis on shared-decision making between patients, care partners and their primary care physician;
- Patient and care partner directed education; and
- Use of language and approaches for discussing deprescribing that were recommended by patients and care partners in our preliminary research in preparation for this pilot.

c. Plan for reporting unanticipated problems or study deviations:
The introductory letter for patients and care partners will advise them to contact the study coordinator if they have any questions about the study or materials. The educational brochure will also advise patients and care partners to not to stop any medications without consulting with their PCP. We will provide all PCPs who are participating in the pilot study with contact information for the Principal Investigator (Dr. Green) and advise them to report any perceived adverse events resulting from the trial to her (e.g., symptom recurrence after stopping a medicine). PCPs will be advised to report such events immediately to Dr. Green, who will contact the primary care provider to review the potential concern. She will then write a report within 5 calendar days and submit it to the IRB. She will also appraise study personnel via e-mail. The clinic medical director may request that the study be stopped at any point. All potential concerns will be noted and discussed with the study team as part of reviewing pilot study results and will be reported to the IRB and discussed with the project's Safety Officer (SO).

d. Legal risks such as the risks that would be associated with breach of confidentiality: There is a small risk of breach of confidentiality. Eligible patient/care partner participants will be identified by the local research nurse or coordinator at the pilot clinic using EHR data under a waiver of HIPAA Authorization. All study staff have successfully completed HIPAA and human subjects research trainings as required by the IRB. Names and other identifiers will be kept in separate locked files. Analyses will be performed on de-identified data; participants will never be individually named. All computerized data will be kept in REDCap and on secure servers. These data will be accessible only to study team members. We will comply with the IRB's policies regarding data protection and data file destruction at the earliest date.

e. Financial risks to the participants: There are no foreseeable financial risks.

9. Benefits

a. Description of the probable benefits for the participant and for society.

Patient-centered, clinician-guided deprescribing has been shown to be safe and effective, and to improve outcomes for older patients. Participants in the pilot study may benefit from learning about deprescribing and may benefit from shared decision making with their PCPs regarding medication management.

Information obtained through this research has the potential to improve outcomes for patients with cognitive impairment and MCC. For older individuals with cognitive impairment, taking more medications is associated with greater risk of adverse drug events, drug interactions, treatment burden, and cognitive changes from medication side effects. Educating patients and clinicians on optimal medication management, and increasing patient/care partner engagement in deprescribing, can improve health outcomes. If the pilot intervention is successful, we will have an opportunity to test the intervention across multiple clinics and ultimately, in other healthcare systems and settings.

10. Payment and Remuneration

a. Detail compensation for participants including possible total compensation, proposed bonus, and any proposed reductions or penalties for not completing the protocol.

- We will offer patients and care partners a $25 gift cards for participating in the 45-60 minute debriefing interview (one per participant).
- We will offer clinicians, residents and medical assistants $25 gift cards for participating in the 30-45-minute debriefing interviews.

11. Costs

a. Detail costs of study procedure(s) or drug (s) or substance(s) to participants and identify who will pay for them.

There is no cost to participants.