DUHS IRB Application (Version 1.48)

General Information

*Please enter the full title of your protocol:		
Deprescribing for Older Dialysis Patients		
***Please enter the Short Title you would like to use to reference the study:**		
Deprescribing and Dialysis * This field allows you to enter an abbreviated version of the Study Title to quickly identify this study.		

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Research Abstract

Please type your Research Abstract here:

The Research Abstract should summarize the main points of your study in one paragraph. The following guidelines may help you:

1. Purpose and objective (1-2 sentences)
2. Study activities and population group (2-4 sentences)
3. Data analysis and risk/safety issues (1-2 sentences)

The purpose of the proposed research is to acquire evidence to inform an evidence-based strategy to reduce inappropriate prescribing in older dialysis patients. The research aims are to: 1) identify elements of a deprescribing intervention that are acceptable to nephrologists, primary care providers, pharmacists, dialysis staff, and patients, and 2) determine the feasibility of a deprescribing intervention tailored for older dialysis patients. The study activities will first involve semi-structured interviews and focus groups with key stakeholders. The qualitative analyses will inform the design, outcomes, and measures of a pilot deprescribing study. Then, we will conduct the pilot study. Although we plan to use the qualitative study to refine the pilot study design. We currently propose the pilot study will be a pharmacist-led intervention of deprescribing potentially inappropriate medications (PIMs) in dialysis patients aged greater than or equal to 65 who are prescribed PIMs. In the pilot study, we will assess for acceptability, demand, practicality, limited efficacy, and monitoring for adverse events.

Research Summary

State your primary study objectives

The primary objectives are to: 1) identify elements of a deprescribing intervention that are acceptable to nephrologists, primary care providers, and patients, and 2) determine the feasibility of a deprescribing intervention tailored for older dialysis patients.

State your secondary study objectives

Please select your research summary form:

Standard Research Summary Template

This is the regular (generic) research summary template which is required for all regular applications (unless your protocol fits under the other research summary templates in this category). Use of these instructions is helpful for ensuring that the research summary contains all necessary elements.

Standard Research Summary

Purpose of the Study

- Objectives & hypotheses to be tested

Purpose of the Study: This protocol describes a research study that is supported by the National Institute on Aging. The scientific premise is that potentially inappropriate medications (PIMs) are a modifiable contributor to adverse outcomes that commonly develop in older dialysis patients. There is insufficient epidemiologic and contextual evidence to guide development of a deprescribing intervention tailored to older dialysis patients. The overall objective of the proposed research is to develop an evidence-based strategy to reduce inappropriate prescribing in older dialysis patients.

Aim 1. Identify the elements of a deprescribing intervention that address contextual factors specific to dialysis.

Hypothesis: Understanding contextual factors in the clinical decision-making process for deprescribing in dialysis units (e.g., multiple prescribers with unclear terms of shared responsibility, organizational culture and policies, and patient attitudes) is important for development of a dialysis deprescribing intervention.

Aim 2. Determine the feasibility of a deprescribing intervention tailored for older dialysis patients.

Hypothesis:
A deprescribing clinical program that provides deprescribing recommendations and guidance to dialysis providers and patients will be acceptable and practical to dialysis providers and patients.

Background & Significance

- Should support the scientific aims of the research

PIMs are associated with the Geriatric Problems that are common in Older Dialysis Patients: Olde r patients make up 46% of adults on dialysis in the U.S. Compared to older adults without kidney failure, older dialysis patients have at least double the rates of geriatric problems including falls, cognitive impairment, hospitalizations, and polypharmacy. Potentially inappropriate medications (PIMs) are a major modifiable risk factor for these conditions, not yet explored in dialysis patients. PIMs convey greater risks than benefits for most older adults. This risk is attributable to age-related changes in pharmacokinetics and pharmacodynamics. Older dialysis patients also have uremic toxins that can alter hepatic drug metabolism (i.e., cytochrome p450 inhibition). Older dialysis patients commonly take PIMs to treat symptoms associated with end-stage renal disease (ESRD), such as anxiety, muscle cramps, or pain (e.g., benzodiazepines, muscle relaxants, opioids), or to lower blood pressure (e.g., α-blockers and central α agonists). Because older dialysis patients have increased vulnerability to PIMs, reducing PIM use may prevent geriatric problems and related hospitalizations.

A Deprescribing Intervention Designed for Dialysis Units may Improve Health Outcomes: Deprescribing interventions have been effective at reducing both PIM use and hospitalizations in community dwelling older adults. Such interventions frequently involve multidisciplinary care teams and/or patient education tools. However, no reports describe deprescribing interventions in U.S. dialysis units. To identify an effective approach, the contextual factors of dialysis need to be considered. Dialysis units often place a high priority on efficient patient turnover, are highly regulated, and have a separate electronic health record. Also, there are unclear terms of shared responsibility for medication management among multiple prescribers (primary care, nephrology, other specialists). Given this unique context, there are critical needs both for key stakeholder input on deprescribing intervention elements and mode of delivery, and for an evaluation of a novel deprescribing program's acceptability and practicality.

Design & Procedures

- Describe the study, providing details regarding the study intervention (drug, device, physical procedures, manipulation of the subject or the subject's environment, etc.). Discuss justifications for placebo control, discontinuation or delay of standard therapies, and washout periods if applicable. Identify procedures, tests and interventions performed exclusively for research purposes or more frequently than standard of care. Include alternative therapies, concurrent therapies discontinued per protocol, risk benefit ratio, and use of tissue/specimens. Discuss monitoring during washout periods if applicable. Include brief description of follow-up, if any.

Aim 1 – This qualitative study is designed to understand views of providers and patients that are critical for development of an effective deprescribing intervention.

The Principal Investigator, research coordinator, or other trained member of the research team will conduct the consent process with dialysis patients meeting the study inclusion criteria and who are willing to participate. A Duke approved and encrypted tablet (iPad) will be used to electronically consent the participant. The participant will be given a paper copy of the consent to review as the electronic version of the consent is being reviewed with them. They will be given opportunity to ask questions regarding study inclusion and study procedures before being asked to electronically sign the approved informed consent document. The participant will be asked to sign the paper consent as well and will keep this copy for their records. Alternatively, an electronic version of the signed consent may be

emailed to participants who prefer this, or a physical copy of the signed consent mailed to the participants' home address. For patients who will be approached about this study, the consent process will be conducted in their home or in a private manner in the dialysis unit. If there is concern about privacy by the potential subject, the study team will accommodate the potential subject to enhance privacy (e.g., privacy curtain at the dialysis chair or private room in the dialysis unit).

We will conduct semi-structured interviews with patients to understand why patients may hold specific attitudes towards deprescribing and to identify preferences in delivery method and approaches to patient engagement in a deprescribing intervention. If patients participating in interviews have a caregiver or spouse who assists with their medications, the caregiver will be asked if they would be willing to participate in the interview with the patient to assist them in answering any of the interview questions. There will be some specific questions to engage caregivers in order to understand their values with respect to potential adverse events from medications in their loved one and their potential role in the deprescribing process. The caregiver / spouse will be asked to sign an information sheet with a brief explanation of the study, the purpose of their participation in the interview, a statement that the interview will be audio recorded, and a statement explaining that research is voluntary. By signing the information sheet, the caregivers agree to participate in the interview and allow their voice to be audio recorded. Beside the audio recording, no PHI will be obtained from spouses / caregivers. Interviews will be will be held at local dialysis units or at their home or other location on a day/time convenient for study subjects. We anticipate each interview would last up to one hour, be audio recorded, and later transcribed by an experienced research transcriptionist. We anticipate theme saturation will be achieved after 12-15 unique patient interviews with patients age 65 and older, and 12-15 interviews with patients age 55-64.

We will conduct separate focus groups (and/or interviews) with nephrologists, pharmacists, primary care providers, and dialysis staff. In these sessions, we will explore ways to increase shared decision-making between nephrologists, patients, and other providers; attributes of a deprescribing intervention that would be acceptable and feasible (including study protocol training); and concerns from providers about risk associated with deprescribing specific PIMs (i.e., adverse drug withdrawal events). Focus group sessions (or semi-structured interviews) will be held at local dialysis units or other location on a day/time convenient for study subjects. Each group will include 8-12 participants per session. Sessions would last up to one hour and will be led by study team members, audio recorded, and later transcribed by an experienced research transcriptionist. When a focus group cannot be assembled, study team will conduct 1:1 interviews. During the course of the study, we will conduct key informant interviews with the following types of providers: 1) individuals with particular experience and/or expertise in pharmacist-led interventions, deprescribing, dialysis medication therapy management, or other related topics, and 2) individuals who are unable to complete focus group but express desire to contribute perspectives to the study. Focus groups and/or interviews will continue until theme saturation is achieved (which is anticipated after 2-3 focus groups of each provider type).

Data collection: The study team will collect the following information from nephrologists, pharmacists, PCPs, and dialysis staff who consent for this study: demographics, email address, quantity of older dialysis patients in their practice, practice setting, proportion of time spent in patient care, length of time in their current role, and their role on the dialysis care team (for dialysis staff) (e.g., social worker, physician, nurse, nurse manager, and administrator).

Study team members will collect the following information from patients by medical record, in person (either at the dialysis clinic, or at the subject's home) by study team, or by REDCap survey link provided to each subject.:

- Demographics
- Contact information (phone, mailing address, email address)
- Dialysis characteristics (from medical records and/or patient self-report: length of time on dialysis, type of dialysis, dialysis access type, cause of end-stage renal disease, dialysis schedule)
- Clinical characteristics [comorbidities from medical records (per Charlson index categories) and/or self-report],
- Medications by self-report, bottle review, and/or medical records (including pharmacy records); If recruiting from a dialysis unit, we will conduct medication reconciliation by comparing participants' medication bottles to the dialysis unit's medication list. If there is significant discrepancy, we will discuss the medication reconciliation process with dialysis staff to identify the source and ways to minimize discrepancies.
- Cognitive evaluation (using Trails Making Test A and B, and Saint Louis University Mental Status (SLUMS) instrument),
- functional status (basic and instrumental activities of daily living)
- falls history
- the revised Patient Attitudes Towards Deprescribing (rPATD) questionnaire.
- Delirium assessment by 3DCAM instrument

- Symptoms index using Question#2 from the IPOS-renal 7 day recall instrument, and additional symptoms commonly managed by opioids, benzodiazepines, muscle relaxants, and anticholinergic medications (e.g., anxiety, depressed mood, muscle cramps, and headaches)

There will be no follow-up for this study aim.

Recruitment for Aim 1 has now been completed.

Specific Modifications During COVID-19 Pandemic

- Recruitment letters will be mailed out to patients.
- Utilizing a HIPAA compliant phone script, a follow up call will be made to the patient and the details of the study and participation will be reviewed. Patients will be given at least one day to consider participation if needed. Verbal consent will be obtained by phone, as allowed by a waiver of documentation.
- A copy of the unsigned consent will be mailed or emailed to the patient if they desire.
- Patient interviews will be done remotely by phone and audio recorded. If a spouse / caregiver would like to participate, they will be informed that the interview will be audio recorded, and verbal permission to record their voice will be obtained on the phone.
- Medication reconciliation will be done over the phone by comparing the patient's medications listed in the DaVita Falcon EMR to what the patient verbally says they are taking.
- Since the TRAILS and SLUMS tests require patients to complete a written portion, these tests will not be administered during the COVID-19 restrictions.
- An alternative cognitive assessment, a modified MOCA test, will be administered over the telephone during COVID-19 restrictions.
- We will not administer the chair stand test during COVID-19 restrictions.
- After the physical distancing orders are lifted, we will attempt to complete any incomplete study procedures in-person: memory testing with modified MOCA (or the TRAILS and SLUMS tests), as well as the chair stand test required for assessment of frailty in subjects age 55-64.

Aim 2 -

We used the qualitative data from Aim 1 to design a deprescribing quality improvement program (QIP) for dialysis patients. We are seeking IRB approval for evaluation of this deprescribing QIP.

Brief Description of Deprescribing QIP: The dialysis deprescribing team (pharmacist, nurse, physician) will conduct the process of deprescribing in patients aged 55 and older who have been undergoing dialysis for at least 3 months and have regular use of a PIM based on their Duke electronic medical record (EMR). PIMs for deprescribing will include antihypertensive PIMs (alpha blockers and central alpha agonists) and psychoactive
medications, such as gabapentinoids, muscle relaxants, and Z-drugs (e.g., zolpidem). The team will also conduct chart review to discern if the patient is a candidate for deprescribing the specific PIM. After identification of eligible patients, the deprescribing team will provide a deprescribing recommendation (including instructions for deprescribing the PIM) to the nephrologist (or other dialysis provider). If a patient agrees to attempt deprescribing a PIM, the team will supervise implementation and monitoring of the deprescribing.

Deprescribing PIMs is considered a best practice for providing care to older adults with multiple comorbidities. It can improve quality of life, reduce medication related problems and lower financial burden to patients.[1] It is consistent with the American Geriatrics Society's guiding principles to make clinical decisions that optimize benefit and minimize harm.[2] Deprescribing, as part of routine geriatrics care, carries minimal risk. It is not routine for dialysis clinics; however, a Canadian dialysis deprescribing QIP demonstrated favorable preliminary outcomes on reducing polypharmacy.[3]

1. Woodford HJ, Fisher J. New horizons in deprescribing for older people. *Age and Ageing.* 2019;48 (6):768-775.
2. Boyd C, Smith CD, Masoudi FA, et al. Decision Making for Older Adults With Multiple Chronic Conditions: Executive Summary for the American Geriatrics Society Guiding Principles on the Care of Older Adults With Multimorbidity. *J Am Geriatr Soc.* 2019;67(4):665-673.
3. McIntyre C, McQuillan R, Bell C, Battistella M. Targeted Deprescribing in an Outpatient Hemodialysis Unit: A Quality Improvement Study to Decrease Polypharmacy. *American Journal of Kidney Diseases.* 2017;70(5):611-618.

Aim 2 Research Activities. Because personnel designated to conduct deprescribing decision-making has not been clearly defined in dialysis units, we want to evaluate the program with and without team assistance with shared decision-making. We plan to evaluate the QIP when delivered in two formats:

1. QIP- Provider Communication Only: Deprescribing team communicates only with the dialysis providers. Dialysis providers leads decision-making with patient.
2. QIP- Provider/Patient Communication: Deprescribing team includes either a pharmacist or a nurse who communicates with providers and patients. After dialysis provider buy-in, the deprescribing team leads decision-making with patient.

Whether a patient falls into the Provider Communication Only or Provider/Patient communication is based on availability of the nurse or pharmacist. For example, if the team nurse or pharmacist is available only on Tuesdays and Thursdays, then the patients and providers that they can communicate with on those two days will be part of Provider/Patient Communication QIP.

The table below delineates deprescribing steps for each format (QIP – Provider Communication Only and QIP – Provider / Patient Communication) in parallel to demonstrate similarities and differences (italics):

Deprescribing steps	**QIP - Provider communication only**	**QIP - Provider/Patient communication**
Identify eligible patients (medication review)	Deprescribing team reviews medical records to identify potential patients Deprescribing team gives recommendation to nephrologist (or other dialysis provider).	Deprescribing team reviews medical records to identify potential patients Deprescribing team gives recommendation to nephrologist. *Deprescribing team waits for nephrologist approval.*
Decision-making	*The nephrologist decides whether to proceed with the recommendation and talk with the patient on their own.* *Research activity: Questions to nephrologist about acceptability of the recommendation (see text)*	*If approval from nephrologist, study team talks to patient about recommendation and that nephrologist supports the recommendation. education to patient about medication risk and process for deprescribing. Team asks if patient is willing to proceed with deprescribing*
Deprescribing	If patient agrees, *Nephrologist* will provide instructions for deprescribing. *Research activity: Questions to nephrologist about acceptability of the recommendation (see text) and deprescribing attempts* Research activity: After a patient decides (either for or against deprescribing), they will be approached for consent for an interview and/or survey. This approach will be by recruitment letter mailed and/or provided in person at the dialysis clinic. We will document deprescribing in medical record and to pharmacy.	If patient agrees, the *deprescribing team* will provide instructions for deprescribing. Research activity: After a patient decides (either for or against deprescribing), they will be approached for consent for an interview. This approach will be by recruitment letter mailed and/or provided in person at the dialysis clinic. We will document deprescribing in medical record and to pharmacy.
Monitoring	Deprescribing team will assist patient with any issues during deprescribing step AND contact patient after a month to check on progress and ask about symptoms.	Deprescribing team will assist patient with any issues during deprescribing step AND contact patient after a month to check on progress and ask about symptoms.

Aim 2 Data collection: We are collecting data for program evaluation. we will assess demand, deprescribing attempts, change in PIM burden (number of PIMs) and feasibility (acceptability and practicality),

Demand: We will assess demand from chart review and define demand as the proportion of patients with a specific PIM divided by all patients with PIMs.

Deprescribing Attempts: We will assess number (and %) of deprescribing attempts in each format of the QIP. The denominator would be total number of patients who were approached for deprescribing decision-making. The approach for each format:

- QIP – Provider Communication Only: We will ask dialysis providers if the patient agreed to deprescribe after a month.
- QIP – Provider / Patient Communication: We will collect information from the deprescribing team on whether the patient agreed to deprescribe.

participants who agreed to deprescribed were called after 3 months to see if they remained off PIM or at a lower dose of the PIM

Change in PIM burden: We will assess change in PIM burden as measured by Sustainability at 3 months; of those who can be reached, proportion of patients who remain off PIM at at a lower dose at 3 months. Participants who agree to deprescribe will be called after 3 months to see if they remain off PIM or at a lower dose of the PIM.
Time frame: 3 months.

Provider Acceptability: For the QIP-Provider Communication only format, we want to assess provider acceptability of the QIP recommendation. Specifically, When the nephrologist (or other dialysis provider) receives the recommendation from the deprescribing team, they will receive a short survey with two primary questions: 1) Will you implement this deprescribing plan? 2) If not, would you support implementation of this deprescribing plan if you had assistance from the deprescribing team? At the end of the month, we will ask the nephrologist some questions about the deprescribing plan: What worked about the deprescribing program recommendation? What did not work?

Patient acceptability: In both formats, we will assess patient acceptability. After a patient decides (either for or against deprescribing), they will receive a recruitment letter (either mailed to them, or given to them by a member of their care team) or may be called or approached in-person at the dialysis clinic to invite them to participate in an interview and a set of surveys. Patients will be able to choose to participate in data collection alone (baseline surveys and again at 3 months), or complete both an interview and the surveys. The consent process and interview will either be by phone or in person at the dialysis clinic. A description of the logistics for interviews is as described for Aim 1. The interviews will be audio recorded and later transcribed by an experienced transcriptionist. We expect to conduct interviews in 12-15 subjects. The focus of the interviews will be on acceptability of the clinical program (e.g., experience, perceived burden, negative consequences or side effects).

Practicality: We can assess practicality in the QIP – across both Provider Only and Provider/Patient communication formats in the following measures:

- Time (in days) spent awaiting provider response to recommendation
- Time (in days) to initial patient communication
- Number of attempts to reach patient, number of conversations, and length of conversations

Additional data collected for Aim 2 is listed below. This data will be obtained from the medical record and through patient communication for the clinical program. We will also assess for clinical events by self-report and/or medical records.:

- Age / DOB (if age >89, will record as age 90)
- Gender
- Race
- Ethnicity
- PIM prescription
- Length of time on dialysis
- Comorbidities
- Medication counts
- Presence of adverse drug withdrawal event (ADWE), type of ADWE, and if associated with unscheduled clinic visit and/or serious adverse event.

Geriatric Assessment: Recent studies suggest that decisions around medications are related to other geriatric problems, such as mobility, cognitive dysfunction, and patient preferences. Therefore, we plan to ask patients to complete a geriatric assessment. The geriatric assessment will be administered via REDCap survey. Either study staff will assist patients with completion of the assessment remotely (via telephone call or zoom), or patients may complete the assessments on their own via an emailed REDCap link. Surveys include: geriatric assessment of mood, medication adherence, nutritional status, social support, what matters most, and mobility via the following survey instruments: Patient Health Questionnaire-9, Morisky Medication Adherence Survey, Health Outcomes Priorities, CDC Falls risk checklist, Modified Medical Outcomes Study Social Support Scale, Received Social Support & Satisfaction Measure, Simplified

Nutritional Appetite Questionnaire, Modified Gait Efficacy Scale, Functional Assessment, Patient and Caregiver Participant Survey, Cognitive Change Index, and Questions on Your Experience Completing the GOLD.

At a 3 month follow up, patients will be asked to repeat 4 of these surveys (Patient Health Questionnaire-9, CDC Falls Risk Checklist, Cognitive Change Index, and Functional Assessment), as well as an additional question: "Have you fallen in the last 3 months?" The 3-month surveys and additional question will be completed within 2 weeks of the exact 3 months date of baseline data collection.

We will also enroll a subset of participants to complete only the geriatric assessment surveys. We are seeking input on the questionnaires from patients as preliminary data for a geriatric program for dialysis patients. Such a program would not be limited to those who are eligible for deprescribing.

Selection of Subjects

- List inclusion/exclusion criteria and how subjects will be identified.

Selection of Nephrologists and Nephrology staff participants for Aim 1:

- Nephrologists: Identify subjects from the list of National Kidney Foundation annual meeting registrants. Aim for variation in practice setting (rural vs. urban; academic vs. private)
- Renal Pharmacists: Identify subjects from the list of National Kidney Foundation meeting registrants or other professional pharmacist organizations.
- Primary Care Providers: Identify through the Duke Primary Care Research Consortium. For inclusion, the provider would have at least 3 dialysis patients in their clinical practice that are routinely followed every 3-6 months.
- Dialysis unit staff: Nurses and advanced practice providers (e.g., nurse practitioner or physician assistant) will be identified using list of National Kidney foundation meeting registrants. We will also identify staff through direct communication with individual dialysis units or communication through the American Nephrology Nurses Association and National Association of Nephrology Technicians.

The only exclusion criterion is inability to speak and understand English and individuals younger than 18 years.

Aim 1 Patient selection:

Potential subjects will be identified by the primary provider (dialysis physician, nurse, or social worker) who will provide names of potential study subjects to the research team, OR they may be identified by the research team utilizing medical records of dialysis patients, and confirming eligibility requirements with dialysis clinic social workers if needed. Alternatively, potential subjects may be identified from a list of previously enrolled subjects from past dialysis studies where the research coordinator is known to the patient. If we conduct chart review, we will be screening for subjects who meet the inclusion criteria. Then, we will work to recruit potentially eligible subjects (see Recruitment section). Inclusion and exclusion criteria are below:

- Aim 1 Inclusion Criteria: Patients aged ≥ 55 years receiving dialysis.

- Aim 1 Exclusion Criteria: Advanced dementia, those receiving hospice, and non-English speaking.

For Aim 1, our purposive sampling plan is to obtain a sample of older dialysis patients age ≥55 that includes at least two individuals in each of the following categories: 1) PIM (taking one vs. not), 2) dialysis vintage (≥6 months or < 6 months), and 3) level of independence in activities of daily living (independent or some dependence) this will often be indicated by whether they require assistance daily with medication administration. We will aim to include at least 50% under-represented minority patients.

Aim 2 Selection of Nephrologists and Nephrology staff participants:

For QIP Provider Communication Only, we will enroll Nephrologists and Advanced Practice Providers. Inclusion criteria for provider participation is that they must be employed by Duke and see patients at a

Duke affiliated DaVita hemodialysis (HD) clinic where Duke nephrologists serve as medical directors and rounding physicians.

Aim 2 Patient selection:

While this is a clinical program, the research evaluation part of Aim 2 will involve interviews and surveys with patients who participate in the program. Potential subjects will be identified by the research team utilizing Duke and DaVita dialysis medical records of dialysis patients, and confirming eligibility requirements with the nephrologist.
Consent will be required for patients to participate in this portion of Aim 2.

Aim 2 **Inclusion** Criteria: Patients must be aged ≥ 55, have received dialysis for at least 3 months and have at least one active target PIM prescription. Subjects must be receiving dialysis at a Duke affiliated DaVita hemodialysis (HD) clinic where Duke nephrologists serve as medical directors and rounding physicians. Study participants must have a Duke primary care physician or prescriber of their PIM, and must use a pharmacy that utilizes electronic prescribing (i.e., Surescripts) so that we can examine medication usage by verifying 2 refills of a PIM (gabapentin, muscle relaxant, or anticholinergic) within prior 6 months.

Aim 2 **Exclusion** Criteria: Patients may not participate if they have been diagnosed with advanced dementia, are receiving hospice, do not speak English, or reside in a long-term care facility.

Subject Recruitment and Compensation

- Describe recruitment procedures, including who will introduce the study to potential subjects. Describe how you will ensure that subject selection is equitable and all relevant demographic groups have access to study participation (per 45 CFR 46.111(a) (3)). Include information about approximately how many DUHS subjects will be recruited. If subjects are to be compensated, provide specific prorated amounts to be provided for expenses such as travel and/or lost wages, and/or for inducement to participate.

Aim 1 – We will use different recruitment approaches for each provider type:
We plan to have 8-12 particpants form each provider focus group. We may have 2-3 focus groups for each of the 4 provider type. This could be up to 144 providers. At most 50% of these providers will be from Duke (n=72). Of note, if we are unable to conduct focus groups, we will conduct 1:1 semi-structured interviews with representatives of each provider group. Sample email recruitment letters are provided.

- Nephrologists/Pharmacists: Email invitations will be sent to individuals who designate themselves as nephrologists or pharmacists in their registration for the 2019 National Kidney Foundation Spring meeting. The study team will work with the National Kidney Foundation meeting planning committee who will provide an updated list of registrants in months prior to the meeting.
- Primary Care Physicians: We will send email invitations to local physicians affiliated with Duke Primary Care Research Consortium.
- Dialysis staff: For nurses and advanced practice providers, email invitations will be sent to those who designate themselves in these professions when they register for the 2019 National Kidney Foundation Spring meeting. (see description above for nephrologists/pharmacists). We will send emails or display fliers at local dialysis unit to solicit for study subjects and/or solicitations through the American Nephrology Nurses Association and National Association of Nephrology Technicians (for semi-structured interviews).

Initial provider recruitment letters will be sent through the RedCap data entry system. The recruitment email will contain a link to the self-directed electronic consent and demographics survey. Due to the limitations of RedCap, any other email communications with participants, or potential participants, will be done through Outlook. Types of email communications will include: responding to questions and coordinating study activities (e.g., event reminders, scheduling events, arranging subject compensation).

We plan to recruit up to 90 total patients between Aim 1 and 2.

Patient Recruitment for Aims 1:

We aim to recruit a total of 24-30 patients for Aim 1. Duke does not have an outpatient dialysis unit, but we expect at least 50% of Aim 1 patients also receive care from Duke (n=27).) We will identify dialysis patients from 9 local DaVita hemodialysis units:

1. DaVita Durham Dialysis (Hood Street)
2. DaVita Southpoint Dialysis
3. DaVita Durham West Dialysis
4. DaVita Research Triangle Park
5. DaVita Bull City Dialysis
6. DaVita Durham Regional
7. DaVita Roxboro
8. DaVita Kerr Lake
9. DaVita Vance County

We have received approval from DaVita Clinical Research to conduct research in DaVita dialysis units. We have two unique approaches to recruitment and data collection described below:1) independent of DaVita units, and 2) engagement of DaVita units.

Independent of DaVita units: We may recruit patients who were previously enrolled in past dialysis studies and are known to the Research Coordinator. Recruitment letters may be mailed and / or a phone call may be made by the coordinator to inquire about interest in participation. Alternatively, eligible patients may be identified by Duke attending physicians in the Division of Nephrology who care for these patients. Recruitment letters may be provided to these patients on behalf of the nephrologist. The consent process will occur outside of the dialysis unit setting. If consent is subsequently obtained, all study activities will be conducted outside of the dialysis unit.

Engagement of DaVita units: We will identify eligible patients with the help of each unit's dialysis care providers (e.g., social worker, dietician, physician, nurse, or mid-level clinical provider (physician assistant, nurse practitioner) by utilizing a list of subjects previously enrolled in past dialysis studies, or via screening of medical records. To introduce the study to potential subjects at the dialysis clinics, a primary dialysis care provider or social worker who knows the patient will talk to the patient and hand out the recruitment letter in person. The letter will include a description of the study and a telephone number for the potential subject to call and inform the research team if they are, or are not, interested in additional research contact. When the care provider offers a copy of the letter and the patient is not interested, the study team will not approach the patient. If the patient is interested, the care provider will inform the study team, and the study team will proceed with recruitment. Only interested patients will be contacted by the research team about participating in the study. This contact will be by phone or in person at the dialysis clinic. In this initial contact, the research team will screen the subjects for eligibility, describe the study to eligible patients, and conduct the consenting process. If this initial contact occurs at the dialysis clinic, the research team will first communicate with a member of the dialysis care team (e.g., nurses, technicians, social work, or physician) to confirm if timing of contact is appropriate and does not interfere with standard dialysis care protocols. If consent is subsequently obtained, study activities may occur at the dialysis unit or another location preferred by patient.

In order to identify frailty in patients aged 55-64 we will use the SOF Frailty Index. Frailty defined by the SOF index is identified by the presence of 2 or more of the following 3 components: 1.) Weight loss (irrespective of intent to lose weight) of 5% or more within the last year 2.) The subject's inability to rise from a chair 5 times without using their arms 3.) Reduced energy level, as identified by an answer of "no" to the question, "Do you feel full of energy?" on the Geriatric Depression Scale. At least 2 of the 3 components must be present for the patient to be considered frail.

Specific Modifications for Recruiting and Consenting During COVID-19 Pandemic:

- After screening for eligibility from a DaVita census list at each unit, recruitment letters will be mailed out to patients. Patient addresses will be obtained from their medical record, as per the waiver for screening and recruitment.
- Patients will be given at least one week to opt out before a phone call will be made to determine their interest.
- Utilizing a HIPAA compliant phone script, a follow up call will be made to the patient and the details of the study and participation will be reviewed. The patient will be given the opportunity to ask questions.
- Patients will be given at least one day to consider participation if needed. Verbal consent will be obtained by phone, as allowed by a waiver of documentation.
- A copy of the unsigned consent will be mailed or emailed to the patient if they desire.

These modifications apply to both Aim 1 and Aim 2

Provider Recruitment for Aim 2:
The Deprescribing QIP team will have an introductory meeting with nephrologists (and other dialysis providers) to describe the QIP. During this meeting, we will explain that we will collect data on acceptability and would like to get verbal consent from them (waiver of documentation of consent).

Patient Recruitment for Aim 2:
We plan to recruit up to a total of 30 patients from both formats of the dialysis deprescribing QIP. After the patient has decided about deprescribing their medication, the study team will reach out to the patient with a recruitment letter (either mailed to them or given to them by a member of their care team), or may call them or approach them in-person at the dialysis clinic. The recruitment letter provides a phone number and an email address if the patient would like to opt out of being contacted regarding study participation.

We will recruit approximately 40 community-dwelling hemodialysis patients (aged 55 and older) to be consented for ONLY completion of the GOLD surveys to assess feasibility of the GOLD instrument (time spent, amount of help needed).
Patients will be recruited from Duke affiliated DaVita Dialysis clinics utilizing DaVita patient census lists to identify those who are age 55 and older. We will ask a member of the DaVita clinical team to give the patient a recruitment letter that we will later follow up with, either in person or over the phone. Alternatively, we may mail recruitment letters and/or call patients who have participated in prior studies with this research team, or approach hospitalized dialysis patients at Duke.

Compensation:

Aim 1: Compensation for patients who consent to participate in the interview will be a gift valued at approximately $30, or a check in the amount of $30. Providers will be compensated with a $75 gift card, and light refreshments will be provided at the focus group sessions.

Aim 2: Compensation for patients who complete the GOLD surveys **only** will be either a gift valued at approximately $30, or a check in the amount of $30. Patients who enroll to participate in an interview will be compensated with either a gift valued at approximately $30, or a check in the amount of $30. Patients who complete both the GOLD surveys and the interview will be compensated with either a $60 check, or gifts with a total value of $60, or a combination of a $30 check and a gift valued at $30 for completion of both portions of their study participation.

Patients will receive a gift valued at $20 or a check for $20 for completing the 3-month follow-up surveys.

Subject's Capacity to Give Legally Effective Consent

- If subjects who do not have the capacity to give legally effective consent are included, describe how diminished capacity will be assessed. Will a periodic reassessment occur? If so, when? Will the subject be consented if the decisional capacity improves?

Aim 1-
Providers and dialysis staff will be considered to be capable of consent by virtue of employment status (staff). Periodic reassessment will not occur.

Patients:
We plan to exclude patients with advanced dementia; therefore, potential subjects for this study are not expected to have diminished decision making capacity. If a potential subject does not appear to comprehend the study and its minimal risk during the informed consent process, we will assess for diminished capacity. This capacity determination will involve asking potential subjects to describe in their own words what the purpose, procedures, and/or risk of the study. If a potential subject is not able to restate the primary study procedures and risks, we will exclude the patient.

Study Interventions

- If not already presented in #4 above, describe study-related treatment or use of an investigational drug or biologic (with dosages), or device, or use of another form of intervention (i.e., either physical procedures or manipulation of the subject or the subject's environment) for research purposes.

This is a descriptive study with no study intervention

PI Attestation Statement Regarding DaVita's Engagement in Research

According to the protocol, DaVita staff (e.g., social worker, nurse, dietician, physician, advanced practice practitioner or technician) will only perform the following activities:

1. **Identify potentially eligible subjects and provide the study team the following list of information to facilitate eligibility screening:**

a. Patient's name and age
b. Location of patient's hemodialysis clinic
c. Patient's HD treatment schedule
d. Date of first HD treatment

2. **Present recruitment letter to eligible patients that describes the study and provides patients with information about study participation.**
    a. Patients may indicate to DaVita staff if they would like to be contacted by study staff or not. This information will be shared with study staff, who will only contact those patients who have agreed.
    b. Patients may also contact study staff themselves using the contact information provided in the recruitment letter.
    c. Patients will be instructed by DaVita to contact the study staff if they have any questions about study participation.
    d. Patients may choose to meet with study staff at DaVita sites to discuss enrollment but DaVita staff will not participate in the consent process in any way.

3. **Print patient information from electronic medical record for patients who meet with study staff and agree to participate by signing the informed consent form.**
    a. Medication history
    b. Medical history

"The activities listed above are considered part of DaVita's usual scope of practice, and therefore, as the PI for this study, I conclude that DaVita is not engaged in research activity and, therefore, does not require IRB oversight/approval."

Risk/Benefit Assessment

- Include a thorough description of how risks and discomforts will be minimized (per 45 CFR 46.111(a) (1 and 2)). Consider physical, psychological, legal, economic and social risks as applicable. If vulnerable populations are to be included (such as children, pregnant individuals, imprisoned persons or cognitively impaired adults), what special precautions will be used to minimize risks to these subjects? Also identify what available alternatives the person has if he/she chooses not to participate in the study. Describe the possible benefits to the subject. What is the importance of the knowledge expected to result from the research?

Potential Risks:

Aim 1: This aim involves subject interviews, and there is minimal psychological risk as the topic is not likely to be deemed sensitive by the subjects. **There is a low risk of loss of confidentiality. Every effort will be made to minimize this risk by de-identifying data obtained from subjects and by assigning a study ID number as a subject identifier.**

Aim 2: Subjects who have medications deprescribed (reduced dose or discontinued) as part of this deprescribing clinical program have potential risk of harm consistent with routine clinical care, including a low risk of adverse drug withdrawal events (ADWE). ADWE involve clinical signs and symptoms after medication removal or reduced dose, such as rebound hypertension or anxiety, and will be monitored for as per routine clinical practice. The research activities described herein (surveys and interviews) have similar minimal risk as described above for Aim 1.

For both aims: there is a minimal risk of loss of confidentiality from primary data collection (including interview transcripts) in the dialysis unit. Data from each subject will be imported directly to a secure folder behind the Duke network's firewall. Only key study personnel will have access to the data.

We will minimize risks and discomforts through the following activities:

1. data storage in a secure server in a confidential folder that is accessible only by study personnel
2. voluntary informed consent process
3. research procedures that will not interfere with or delay patient care in the dialysis unit

If potential subjects refuse to participate in the study, he/she will continue standard of care provided by dialysis providers. Because there is not an intervention for the study, the alternative therapy is to continue usual care provided by the patient's providers. The study will not include vulnerable populations.

Potential benefits of research to subjects and others: This research will reveal the most acceptable approach to deprescribing PIMs in older dialysis patients.

Importance of knowledge to be gained: Knowledge gained through this study is valuable for design of a clinical trial that targets deprescribing PIMs in older dialysis patients. PIMs are potentially modifiable risk factors for geriatric syndromes, hospitalizations, quality of life in older dialysis patients. The benefits of establishing evidence that improves health in these patients outweigh the potential risk.

Costs to the Subject

- Describe and justify any costs that the subject will incur as a result of participation; ordinarily, subjects should not be expected to pay for research without receiving direct benefit.

Study participants may incur travel costs for participation in a focus group or interview.

Data Analysis & Statistical Considerations

- Describe endpoints and power calculations. Provide a detailed description of how study data will be analyzed, including statistical methods used, and how ineligible subjects will be handled and which subjects will be included for analysis. Include planned sample size justification. Provide estimated time to target accrual and accrual rate. Describe interim analysis including plans to stop accrual during monitoring. Phase I studies, include dose escalation schema and criteria for dose escalation with definition of MTD and DLT.

Qualitative analyses will start with Rapid assessment. Rapid assessment involves team-based inquiry for triangulation, iterative data analysis, and data collection. This process allows data analysis before completion of data collection to facilitate rapid identification of key issues that inform intervention development. Subsequently, we will perform traditional qualitative analyses using ATLAS.ti software to summarize themes using framework analysis. Framework analysis will proceed in five steps by a team consisting of at least two study team members. This thematic framework will be refined through interim analyses of interview data until there is theme saturation. I anticipate theme saturation for each stakeholder group will practically be achieved after 2-3 focus groups of each provider type and 10-12 patient interviews.

Descriptive statistics will be performed to describe the patient participants' demographics and clinical characteristics and provider characteristics (role, experience, and for PCP participants, quantity of dialysis patients in clinical practice).

Aim 2 - We will perform descriptive statistics on the feasibility measures described under (Design and Procedures/Data collection for Aim 2), subject characteristics, survey responses, and types of PIMs prescribed. We will calculate intracluster correlations and standard errors to inform sample size for a clinical trial. We will also conduct a qualitative analysis from semi-structured interviews as described above.

Data & Safety Monitoring

- Summarize safety concerns, and describe the methods to monitor research subjects and their data to ensure their safety, including who will monitor the data, and the frequency of such monitoring. If a data monitoring committee will be used, describe its operation, including stopping rules and frequency of review, and if it is independent of the sponsor (per 45 CFR 46.111(a) (6)).

1. **Data & Safety Monitoring:**

Adverse drug withdrawal events (ADWEs) are the primary safety concern in the deprescribing Quality Improvement program we are evaluating in Aim 2. ADWEs include a physiological withdrawal reaction or intolerance of deprescribing (worsened symptoms). However, this risk is consistent with risk involved with routine clinical care. Still, we recognize the need to have a plan for safety monitoring that is outlined below:

- The deprescribing recommendation will provide providers and patients specific information on potential symptoms that may develop and contact information to the deprescribing clinical program if intolerance develops.

- If a patient experiences intolerance (worsened symptoms), they will have instructions based on an evidence-based protocol (e.g., adjust or stop the taper or seek immediate medical attention) and to contact the deprescribing team. Such a protocol will be specific to each target PIM for the pilot study. These protocols will be developed prior to study initiation and approved by a team of physicians and pharmacists. Medications can be restarted or increased at any time should patient not tolerate deprescribing.

- We will monitor for ADWEs after a month of deprescribing onset by reviewing electronic medical records for documentation of clinical event (e.g., unscheduled visit for a symptom or sign related to deprescribing of the target PIM). We will also communicate with each patient at this point. This communication will assess 1) if patient is tolerating the deprescribing plan and 2) if patient has experienced an adverse drug withdrawal events (ADWEs). Prior to that, patients who have concerns during deprescribing can reach deprescribing team. In that communication, the team will ask specific questions to inquire about ADWEs.

- As part of the clinical program, ADWEs will be immediately reviewed by team geriatric nephrologist (Dr. Hall) for immediate management recommendations; serious ADWEs will be communicated to the dialysis provider and/or PCP within 2 business days. We will encourage documentation in the patient's medical record.

- The PI (or designee) will report ADWEs that constitute SAEs to the Duke University IRB within 24 hours of learning about the event. Within 5 business days following the initial report, a Notification of a Problem or Event Requiring Prompt Reporting Form to the Duke IRB. The PI will also report SAEs to the NIA Safety Officer according to their reporting policies (if indicated).

- [redacted], a geriatrician who is not associated with the program, will serve as Safety Monitor. ADWEs will be reviewed with him quarterly. We will adjust the protocol if needed.

Additional concerns are Loss of Protected Health Information: The study team has outlined procedures for data management to protect against loss of data (detailed below). Breaches in data security will be reported within 24 hours of detection, and a plan for management of the breach and modification of data security procedures will be developed within 3 business days, if applicable.

Additional Oversight and Reporting: The PI, Dr. Hall, will be responsible for the operation of this research study according to the study's protocol and IRB policies. In addition to adverse events described above, The PI (or designee) will submit complaints, withdrawals, and protocol violations to the Duke University IRB.