Expanding and Promoting Alternative Care and Knowledge in Decision-Making: The ExPAND Study (Improving Shared Decision-Making and Access to Non-Dialytic Treatment for People with Kidney Disease)

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NCR235148

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Sponsor
PCORI

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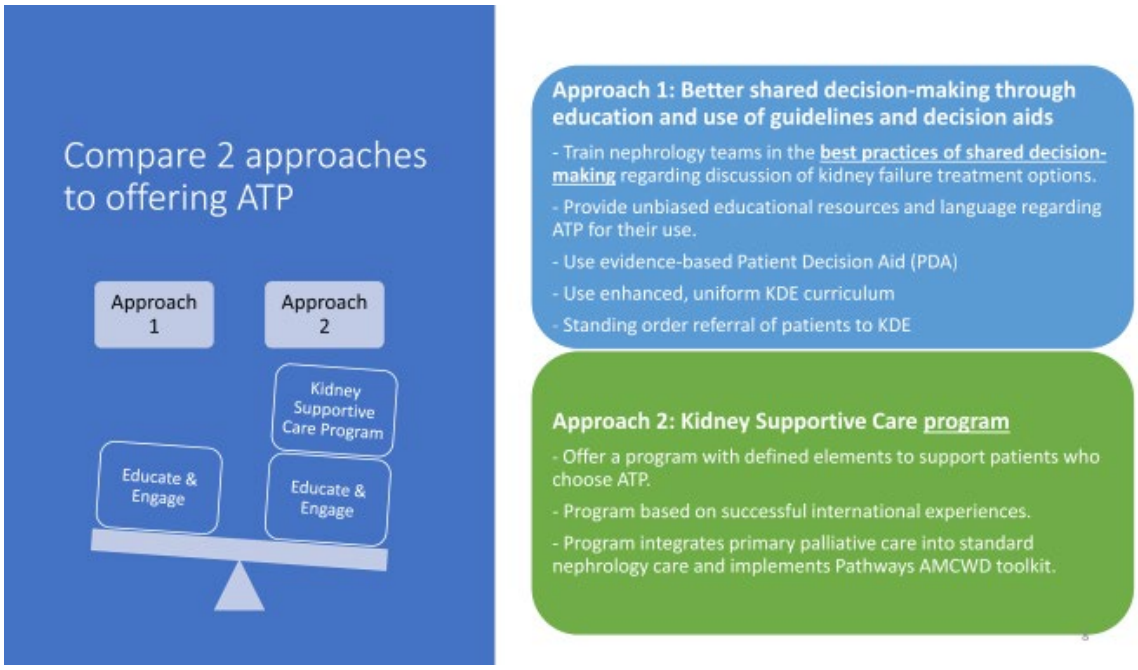
SYNOPSIS

Primary Objective

The primary objective of this study is to compare two health system-based approaches for offering kidney failure treatment options to older patients with kidney failure, to ensure they are actively involved in a shared decision making (SDM) process covering a full range of choices and have meaningful access to that full range of choices, including standard in-center or home dialysis (SIHD) and alternative treatment plans (ATPs): active medical care without dialysis (AMCWD), time-limited trial of dialysis (TLT), palliative dialysis, and deciding not to decide (DND).



Aim 1: Compare the effectiveness of two approaches: 1) improved kidney disease education (KDE) and SDM or 2) improved KDE and SDM plus the creation of a kidney supportive care program in a) increasing proportion of patients choosing ATP and b) reducing patient decisional conflict.

Secondary Objectives (if applicable)

Aim 2: Compare the patient and family experience of an ATP between Approach 1 and Approach 2, with particular emphasis on TLT and AMCWD in terms of quality of life, services used, and end-of-life (EOL) experience through medical record review and interviews with a

sample of bereaved family members. Aim 2a will focus on experience while patients are receiving an ATP (several months to several years). Aim 2b will describe the EOL experience.

Aim 3: In order to evaluate implementation of each intervention (Approaches 1 and 2), the ExPAND research team will cooperate with a separate tandem evaluation conducted by an independent evaluation team based at NORC. The implementation evaluation is a mixed-methods design based on the expanded Reach, Effectiveness, Adoption, Implementation, Maintenance (RE-AIM) framework. The implementation evaluation will consist of staff surveys, interviews, and site visits conducted by the NORC evaluation team. Regulatory oversight of AIM 3 will be handled by the NORC IRB.

General Design Description

This will be a repeated, cross-sectional stepped wedge cluster randomized trial (SW-CRT) with randomization at the nephrology clinic level. Clinics are randomly assigned to one of three sequences. Each sequence consists of four 10-month time periods during which patients are accrued and followed for study outcomes. To minimize contamination in the primary analysis, we will exclude patients recruited during the 4 months before each sequence moves to Approach 2 (see white squares in the table below). These patients will be included in a sensitivity analysis. In the 4th study period, accrual of new patients will stop at 10 months, allowing a closing 4-month follow-up period to collect primary outcomes at the end of the study. All practice sites begin by implementing Approach 1 (Educate and Engage). Practice sites then add Approach 2 (Kidney Supportive Care Program) at the assigned period based on their sequence. We have prepared for 15% drop-out of sites, leaving 21sites in the final analysis sample.

Periods of patient accrual and follow-up for 24 practices randomized to 3 sequences

Sequence	Period 1 Sep 2024-Jun 2025	Period 2 Jul 2025-Apr 2026	Period 3 May 2026-Feb 2027	Period 4 Mar-Dec 2027
S1 (8 clinics)	**	*	*	**
S2 (8 clinics)	*	**	*	**
S3 (8 clinics)	*	*	**	**

* N = 307 for each of these 10-month periods.
** N = 184 for each of these 6-month periods.
Total sample size = 307*6 + 184*6 = 2,946

Approach 1 (Educate & Engage)
Approach 2 (Supportive Care)
No recruitment

Patients will receive the intervention based on the approach (condition) in which the site is enrolled at the time of accrual. When a practice site begins implementation of Approach 2, referral to the kidney supportive care program for patients considering ATPs will become

standard care at that site. All patients still alive who chose ATPs in prior periods will be offered the option of receiving care from the newly organized supportive care program.

There are several advantages to a SW-CRT design vs. standard cluster-randomized trial. First, SW-CRT gives every practice the opportunity to implement both approaches, which is something that the physician practice leaders have told us they value. Second, SW-CRT means that from the patient perspective, they will be receiving the standard care delivered by the practice site at any given time, and there is no need for patients to opt in or out of a trial to receive this improved access to best practice care.

In addition to the primary SW-CRT comparing the two intervention approaches, we will do a pre-post comparison of primary outcomes, comparing clinic practices at baseline with each of the interventions.

Primary Outcome Variables

Co-primary outcomes:

- Proportion of patients 65 years and older who choose alternative treatment plans (ATP)
- Decisional conflict score 4 months after decision initiated

Secondary and Exploratory Outcome Variables (if applicable)

- Know-CKD score: assessment of patient knowledge about chronic kidney disease (CKD) and treatments 4 months after decision initiated
- Patient experience of shared decision-making as on SDM Q-9 and COLLABORATE scales 4 months after decision initiated
- Patient reported decision regret 9 months after decision initiated
- Advance care planning documentation in chart 4 months after index visit
- End of life intensity of treatment (ATP patients)
- Unplanned start of dialysis in last 30 days of life (ATP patients)
- Advance care planning at end of life for patients who die

Additional secondary and exploratory outcomes detailed further in section 5.2.2

Number of Participants

Table 6.1.1 Number of Participants

Population	Description	N
1. Patients of the nephrology practices (Aims 1 and 2)	Patients 65+ years old with eGFR less than 30. Within this population, patients are grouped according to their treatment choice (within first 10 months).	2,948 • Choose dialysis: 2,240 • Choose ATP: 560 • Lack decision-making capacity: 147
2. Family/care partners of ATP patients (Aim 2)	Sample of family members and care partners of patients who choose an ATP	35 • Longitudinal Interviews: 15 • Bereavement interviews: 20
3. Employees of the nephrology practices (Aim 3)	Administrators/leaders (n = 50), other clinicians and staff (including doctors, advanced practice provider (APP)s, nurses, social workers, dieticians, palliative care specialists, and staff, n = 90)	140 • Administrators: 50 • Other employees: 90

Visit Schedule Table (Optional)

Synopsis Table 1. Schedule of Study Activities

Time	Activity	Population

Screening (approx. weekly)	Research coordinator (RC) reviews upcoming appointments to identify eligible patients.	All
Post-screening	RC notifies treating nephrologist/APP of plans to enroll patient at upcoming visit.	All eligible
Time 0 / Index visit	Eligible patients enrolled in study for chart monitoring.	All eligible
Time 0 / Index visit	Under a practice protocol for ExPAND including a provider standing order, patient is referred to kidney disease education (KDE). Provider introduces topic of treatment decision.	All eligible
Time 0 / Index visit	RC consents patient for surveys and administers first Decision Conflict Survey: DCS-1	Survey eligible (Has decision-making capacity and speaks English or Spanish.)
4 months after Time 0	RC administers DCS-2	Survey eligible
4 months after Time 0	Chart audit of advance care planning documentation	All eligible

4 months after Time 0	RC reviews chart, records current treatment preference and other outcomes	All eligible
9 months after Time 0	RC administers DCS-3	Survey eligible
10 months after Time 0	RC reviews chart for missing outcomes, records current treatment preference, and enters Aim 1 completion status for patient (completed all study activities; followed for 10 months but did not complete all activities; died, lost to follow-up)	All eligible
After treatment decision	RC begins monthly chart audit of ATP patient.	ATP patients
After treatment decision	RC requests permission from ATP patient and/or care partner to share contact information with external research team, (addendum to previous informed consent form).	ATP patients who participated in DCS surveys and their family/care partners
Every 4 months after treatment decision	ExPAND Research Team interviewers conduct longitudinal interviews	Sample of ATP patients and family/care partners

3 Months after ATP patient death	RC conducts end-of-life chart audit	ATP patients who died during study	
4 Months after ATP patient death	ExPAND Research Team interviewers conduct bereavement interviews	Sample of family/care partners of ATP patients who died during study	

Study Flow Chart (Optional)

See *Flowchart of Study Activities and Outcomes* (Appendix) for schematic flow of Aim 1 and Aim 2 activities and outcomes.

ABBREVIATIONS

Abbreviation	Explanation
AE	Adverse Event
AMCWD	active medical care without dialysis
APP	advanced practice provider
ATP	alternative treatment plan
DCS	Decisional Conflict Scale
DND	deciding not to decide, measured here as not making a treatment decision within the 10 ½ month follow-up period
DSMB	Data Safety Monitoring Board
ED	emergency department
EOL	end-of-life
ICC	intraclass correlation
IRB	Institutional Review Board
NKF	National Kidney Foundation
NP	nurse practitioner
PDA	patient decision aid
RC	research coordinator
RE-AIM	Reach, Effectiveness, Adoption, Implementation, Maintenance

REDCap	Research Electronic Data Capture
SAE	Serious Adverse Event
SIHD	standard in-center or home dialysis
SW	stepped wedge
SW-CRT	stepped wedge cluster randomized trial
TLT	time-limited trial of dialysis

Table of Contents

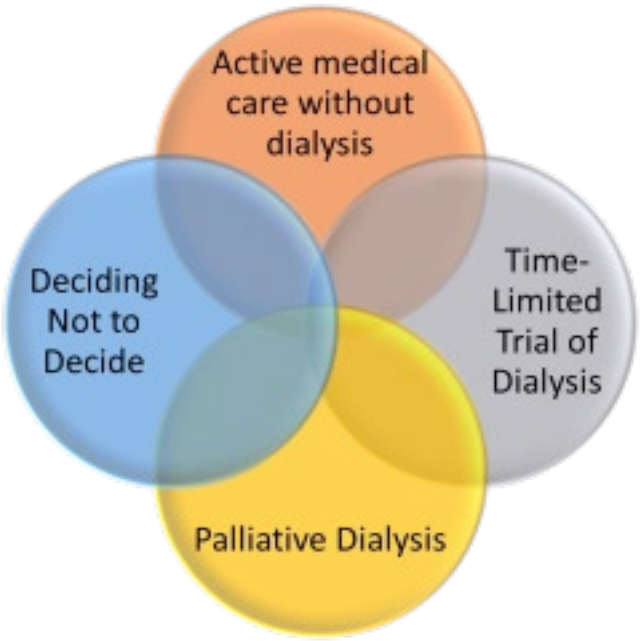
1. Statement of Compliance

This document is a protocol for a human research study. The purpose of this protocol is to ensure that this study is to be conducted according to the Common Rule at 45CFR46 (human subjects) and other applicable government regulations and Institutional research policies and procedures.

2. Background

Why this project is needed:

Over 130,000 patients with kidney failure start dialysis annually (1) . Older patients constitute the fastest growing segment (1) . Those who are frail or have other serious medical conditions may not live any longer with dialysis than without it (2) . US healthcare policy has created a powerful "dialysis default," where virtually all patients with kidney failure who do not receive a transplant are treated with a standard dialysis regimen in a dialysis center regardless of whether it will help them live any longer or better. About 20% of patients regret the decision to start dialysis, yet non-dialysis alternatives are rarely offered to them (3) . Most report they were unaware they had a choice about kidney failure treatment. Many older patients with kidney disease value independence over staying alive longer. Not aware of their patients' values, most nephrologists do not offer alternatives to standard dialysis such as active medical care without dialysis (AMCWD), a time-limited trial of dialysis (TLT), palliative dialysis, or deciding not to decide (DND) until a later date.



Similarly, these options, which we have collectively labeled alternative treatment plan (ATP)s, are rarely included in kidney disease education (KDE) sessions for patients funded by Medicare. Other countries—notably Australia, Canada, and the United Kingdom—have found that about 15% of older patients with kidney failure prefer AMCWD (4) . They have created programs within their healthcare systems that integrate primary palliative care into care for patients who choose an ATP. These programs report excellent outcomes in terms of patient quality of life, care according to patient's wishes, and patient survival on average for over a year. They have

shown it is possible to avoid complications at the end of life such as patients who wanted AMCWD being started on dialysis because their symptoms were not well managed. These programs provide an extra layer of support and prepare patients and families for when the patient's kidney failure worsens.

Shared decision-making is recognized as the preferred approach to implementing patient-centered care and assuring that patients receive treatment that matches their goals. For over a decade, shared decision-making (SDM) has been recommended by nephrology professional societies before initiating dialysis (5). Despite the recommendation and preference for SDM (6) (7) of people with advanced chronic kidney disease (CKD), it remains poorly implemented, and observers have noted a "powerful [dialysis] default option with few perceived alternatives." (8) There is an urgent need for strategies to increase adoption and implementation of SDM in nephrology practices and elsewhere in healthcare systems where CKD patients receive care.

3. Rationale/Significance

3.1 Problem Statement

For older patients with advanced CKD and comorbidities, frailty, and/or dementia, dialysis may not provide a survival advantage for them once they have reached end-stage kidney failure. In the United States in contrast to other countries including Australia, Canada, and the United Kingdom, there are **not** well-established programs to care for these patients if they choose NOT to start dialysis. The problem to be addressed in this project is how best to implement a kidney supportive care program that will 1) fully inform patients of all their treatment options including in-center and home dialysis, kidney transplantation, a time-limited trial of dialysis, palliative dialysis, deciding not to decide about dialysis till a later date, and AMCWD; and 2) provide an infrastructure to support patients who choose an alternative to in-center or home dialysis and kidney transplantation that will manage their symptoms, conduct advance care planning with them, refer them to hospice as appropriate, and support them in a symptom crisis so that they have the options to stay at home or be treated in an inpatient hospice as an alternative to going to a hospital emergency department (ED).

3.2 Purpose of Study/Potential Impact

Using a *comparative effectiveness* approach, the purpose of this study is to determine, in real-world nephrology practices, whether 1) KDE using a shared decision-making approach and patient decision aids alone OR 2) improved KDE plus the creation of a kidney supportive care program is the most feasible and effective way to educate and provide alternative treatment plans to older patients with kidney failure, including those who do NOT want standard in-center or home dialysis. Although we hope to see a shift from in-center hemodialysis to home dialysis consistent with recently implemented federal value-based care initiatives, and although we expect that the intervention may contribute to such a shift, this study will evaluate change in the proportion of the less commonly offered alternate treatments (AMCWD, TLT, palliative dialysis, and DND). The choice of this outcome reflects the specific goals of the project as well as the need to avoid confounding by secular trends in the take-up of home dialysis.

The potential impact of this study is immense. Patients with advanced chronic kidney disease 75 years of age and older are the age group with the highest incidence and prevalence of patients on dialysis. Dialysis is a labor-intensive and expensive life-prolonging intervention. Once fully informed, approximately 15-20% of older patients with advanced chronic kidney disease in other countries choose a non-dialysis option for their kidney failure treatment. There is a paucity of data on the number of such patients who make this decision in this country, but it is thought that it is only about 1-3%. If one of the approaches in this study proves effective and acceptable to patients and the number in this country increases to a number comparable to other countries, 15,000 or more patients each year in the US could benefit from a non-dialysis treatment approach according to their wishes.

It is important to note that we are NOT trying to compare the experience or outcomes of ATP to the experience or outcomes of hemodialysis. Such descriptive comparisons already exist in the evidence base, especially for AMCWD. (9) (10) (11) (12) (13) These cited comparison studies provide evidence for the rationale for making ATP more widely available to the subset of patients who might not do well with dialysis and who might want and benefit from AMCWD, since the quality and quantity of life outcomes are non-inferior for older, frail patients. This evidence base has been criticized because few of the studies involved randomization, but such a randomized trial comparing patients who choose to prepare for dialysis to those who prepare for AMCWD is currently underway in the United Kingdom (14) . We have designed a trial whose primary aim is to test HOW best to increase SDM and access to ATP's. A second aim is to provide a comprehensive description of patient and family experience during ATP.

3.3 Potential Risks and Benefits

3.3.1 Potential Risks

Patients: Because this study is implementing recommended best practices in the care of older patients with advanced chronic kidney disease, there are no anticipated major risks associated with it. Clinicians will employ recommended communication approaches and ask for permission to provide information about the patient's kidney disease and possible treatment options before doing so. Nonetheless, some patients might experience distress once informed that they have advanced chronic kidney disease if they were not previously aware of it. This distress is comparable to that experienced by patients in routine clinical practice who receive bad news. This study may differ from standard care in that patients might become better informed and more aware of the range of treatment options they have. Also, in taking the Decisional Conflict Scale and other surveys, they might realize more clearly that they don't know 1) what are the benefits of treatment that matter most to them, 2) what risks and side effects are most troublesome to them, and 3) overall, what treatment option is best for them. Interviewers will be trained to watch for indications of emotional distress and will be trained in how to respond calmly and empathetically. If the situation persists or worsens, the interview will be terminated, and the incident will be reported within 24 hours to the patient's treating clinician, who will develop a plan for supporting the patient including referral for further mental health services, as indicated.

Care partners and clinic employees: The main risk to these participants is loss of confidentiality of research data. Specific steps to minimize these risks are described in section 8.3.

Before data collection starts, all research personnel will be required to undertake appropriate training in the conduct of human subjects research, such as Collaborative Institutional Training Initiative (CITI) or Association of Clinical Research Professionals (ACRP) coursework. All staff will complete a training program developed by the study PIs. This training will include modules covering: 1) study overview, 2) recruitment procedures, 3) study arm procedures, 4) collection and management of study data, and 5) adverse event reporting and managing emergencies. The trial will be registered on ClinicalTrials.gov and Advarra will be the Central IRB (IRB of

record). Participant recruitment will begin at each site only after that site's clinical trials office (or equivalent) has approved the study materials containing IRB-approved protocol, surveys, and data collection instruments.

3.3.2 Potential Benefits

Because this study mirrors recommended best clinical practices such as the use of shared decision-making, patient decision aids, and kidney supportive care to address unmet palliative care needs in the population of older patients with advanced chronic kidney disease, the investigators believe that there will be significant benefits for the participants. These include being aware that they have a choice about treatment to make, being fully informed of all treatment options, participating as co-equals in treatment decisions and in the development of a treatment plan, being offered the opportunity to participate in advance care planning, being routinely assessed for symptoms and being treated for them, and being referred to palliative care and/or hospice in a timely manner as appropriate.

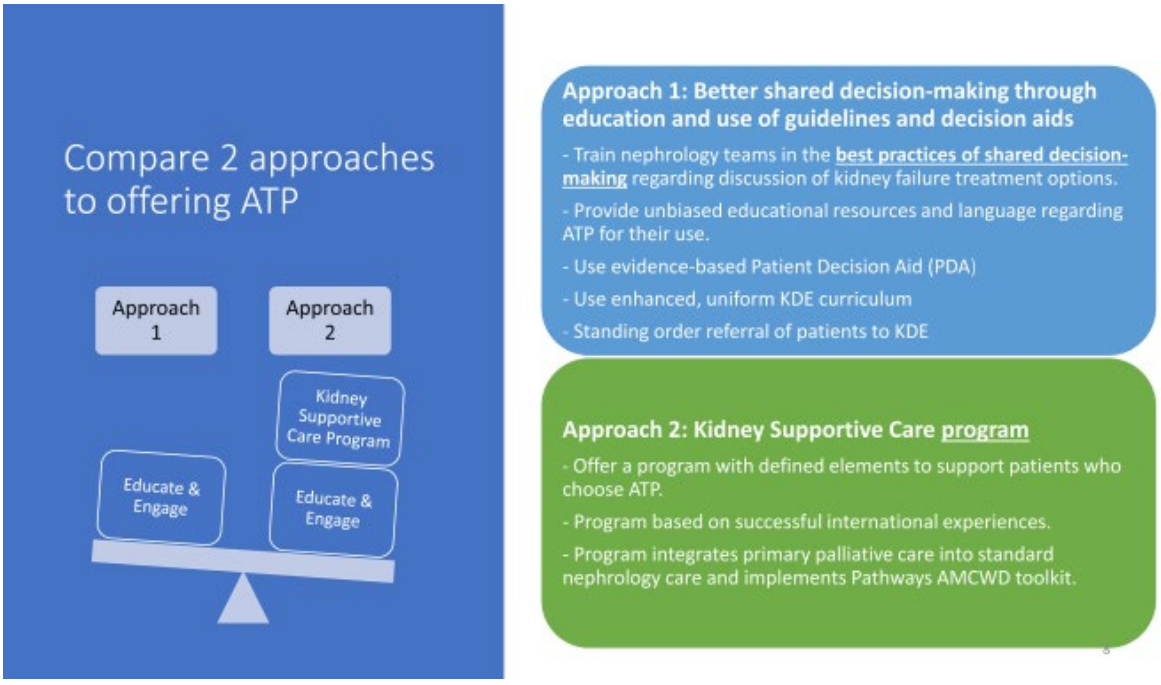
4. Study Objectives

4.1 Hypothesis

Primary hypothesis: Approach 1 (Educate and Engage) will be less effective than Approach 2 (Provide Primary Palliative Care) in a) increasing proportion of patients choosing ATP and b) reducing patient decisional conflict. **Subgroup hypothesis**: The difference in primary outcomes (selection of ATP and decisional conflict) will be more pronounced for older/frailer patients and for patients with heart disease.

4.2 Primary Objective

The primary objective of this study is to compare two health system-based approaches for offering kidney failure treatment options to older patients with kidney failure, to ensure they are actively involved in a shared decision making (SDM) process covering a full range of choices and have meaningful access to that full range of choices, including standard in-center or home dialysis (SIHD) and alternative treatment plans (ATPs): active medical care without dialysis (AMCWD), time-limited trial of dialysis (TLT), palliative dialysis, and deciding not to decide (DND).



Aim 1: Compare the effectiveness of two approaches: 1) improved kidney disease education (KDE) and SDM or 2) improved KDE and SDM plus the creation of a kidney supportive care program in a) increasing proportion of patients choosing ATP and b) reducing patient decisional conflict.

4.3 Secondary Objectives (if applicable)

Aim 2: Compare the patient and family experience of an ATP between Approach 1 and Approach 2, with particular emphasis on TLT and AMCWD in terms of quality of life, services used, and end-of-life (EOL) experience through medical record review and interviews with a sample of bereaved family members. Aim 2a will focus on experience while patients are receiving an ATP (several months to several years). Aim 2b will describe the EOL experience.

Aim 3: In order to evaluate implementation of each intervention (Approaches 1 and 2), the ExPAND research team will cooperate with a separate tandem evaluation conducted by an independent evaluation team based at NORC. The implementation evaluation is a mixed-methods design based on the expanded Reach, Effectiveness, Adoption, Implementation, Maintenance (RE-AIM) framework. The implementation evaluation will consist of staff surveys, interviews, and site visits conducted by the NORC evaluation team. Regulatory oversight of AIM 3 will be handled by the NORC IRB.

5. Study Design

5.1 General Design Description

This will be a repeated, cross-sectional stepped wedge cluster randomized trial (SW-CRT) with randomization at the nephrology clinic level. Clinics are randomly assigned to one of three sequences. Each sequence consists of four 10-month time periods during which patients are accrued and followed for study outcomes. To minimize contamination in the primary analysis, we will exclude patients recruited during the 4 months before each sequence moves to Approach 2 (see white squares in the table below). These patients will be included in a sensitivity analysis. In the 4th study period, accrual of new patients will stop during a 4-month follow-up period (to collect primary outcomes) at the end of the study. All practice sites begin by implementing Approach 1 (Educate and Engage). Practice sites then add Approach 2 (Kidney Supportive Care Program) at the assigned period based on their sequence. We have prepared for 15% drop-out of sites, leaving 24 sites in the final analysis sample.

Periods of patient accrual and follow-up for 24 practices randomized to 3 sequences

Sequence	Period 1 Sep 2024-Jun 2025	Period 2 Jul 2025-Apr 2026	Period 3 May 2026-Feb 2027	Period 4 Mar-Dec 2027
S1 (8 clinics)	**	*	*	**
S2 (8 clinics)	*	**	*	**
S3 (8 clinics)	*	*	**	**

* N = 307 for each of these 10-month periods.
** N = 184 for each of these 6-month periods.
Total sample size = 307*6 + 184*6 = 2,946

Approach 1 (Educate & Engage)
Approach 2 (Supportive Care)
No recruitment

Patients will receive the intervention based on the approach (condition) in which the site is enrolled at the time of accrual. When a practice site begins implementation of Approach 2, referral to the kidney supportive care program for patients considering ATPs will become standard care at that site. All patients still alive who chose ATPs in prior periods will be offered the option of receiving care from the newly organized supportive care program.

There are several advantages to a SW-CRT design vs. standard cluster-randomized trial. First, SW-CRT gives every practice the opportunity to implement both approaches, which is something that the physician practice leaders have told us they value. Second, SW-CRT means that from the patient perspective, they will be receiving the standard care delivered by the practice site at any given time, and there is no need for patients to opt in or out of a trial to receive this improved access to best practice care.

In addition to the primary SW-CRT comparing the two intervention approaches, we will do a pre-post comparison of primary outcomes, comparing clinic practices at baseline with each of the interventions.

5.2 Outcome Variables

5.2.1 Primary Outcome Variables

Table 5.2.1 Primary Outcomes

Primary Outcomes				
Name of outcome	**Specific measure**	**Timepoints**	**Power** **(effect size)**	**N**
Aim 1: Effectiveness - compare 2 approaches to offering ATP				
Proportion of patients choosing ATP*	$\frac{ATP}{ATP + SIHD}$	Month 4 (return nephrology visit)	.96 (medium)	2,800
Decisional conflict score at return nephrology visit	Decisional Conflict Scale (Month 4 score, adjusted for baseline score)	Month 0 (covariate) **Month 4 (return nephrology visit; outcome)** Month 9 (exploratory)	.89 (medium)	780

* ATP: alternative treatment plan, including active medical care without dialysis (AMCWD), time-limited trial of dialysis (TLT), palliative dialysis, and deciding not to decide (DND). DND is defined as not making a treatment decision within the 10 ½ month follow-up period.

5.2.2 Secondary and Exploratory Outcome Variables (if applicable)

Table 5.2.2.A Secondary Outcomes for Aim 1

Secondary Outcomes				
Name of outcome	**Specific measure to be used**	**Timepoints**	**Power (effect size)**	**N**
Aim 1: Effectiveness - compare 2 approaches to offering ATP				
Knowledge about CKD and treatments at return nephrology visit	Know-CKD (Month 4 score, adjusted for baseline score)	Month 0 (covariate) **Month 4 (return nephrology visit; outcome)** Month 9 (exploratory)	.89 (medium)	780
Patient-reported experience of SDM	SDM-Q-9	Month 4	.83 (medium)	780
Patient-reported experience of SDM	CollaboRATE	Month 4	.83 (medium)	780

Patient reported decision regret	Modification of dialysis decision regret: Do you regret your decision to start (treatment selected)	Month 9	.84 (large)	780
Advance care planning (ACP) documentation	Complete ACP measure (Three elements present in chart: a surrogate, a goals of care discussion, and either an accessible advance directive or medical order such as POLST or DNR.)	Month 4	.99 (medium)	2,800

Table 5.2.2.B Secondary Outcomes for Aims 2 and 3

Aim 2a: Descriptive - experience during ATP				
Proportion of AMCWD patients who change to dialysis at any time	Proportion of patients who initially choose AMCWD who subsequently switch to dialysis (standard in-	At study end or patient death	.79 (large)	280

(*Primary for Aim 2*)	center hemodialysis, home dialysis, TLT, or palliative).			
Proportion of ATP patients who "crash" into dialysis	Proportion of patients who initially chose an ATP who have unplanned dialysis start: defined as starting dialysis urgently in the hospital during an unscheduled admission. (See examples below.)	At study end or patient death		560
Planned Admission for Dialysis Start. Example: Patient with congestive heart failure (or other condition such as hypotension that could increase the risk of dialysis) and ESKD who is admitted as a precaution to monitor cardiac status during the first or several sessions of hemodialysis. Because dialysis is planned, the patient has a "permanent" access, an arteriovenous fistula, an arteriovenous graft, or a tunneled cuffed catheter. _____ *Unplanned Admission for Dialysis Start*. Example: Patient with advanced CKD who does routine lab work for next nephrology appointment and labs reveal one or more of the following: life-threateningly high potassium, very low CO2, and/or BUN is very high (>75 mg/dL), OR patient has symptomatic uremia or volume overload with dyspnea/hypoxia. Patient is requested to go to the Emergency Department or is a direct admit to the hospital. Patient will need a temporary (non-tunneled) dialysis catheter for urgent start hemodialysis.				

Aim 2b: EOL experience during ATP				
EOL intensity scale	Measure based on hospitalization, ICU admission, intensive procedures during last 30 days of life and death in hospital.	Chart review 3 months after death		173
AMCWD & DND patients who initiate dialysis in the last month of life	Proportion of AMCWD & DND patients who die who used dialysis in last 30 days of life. Sensitivity analysis - also examine change to dialysis 60 days and 90 days before death.	Chart review 3 months after death		173
Advance care planning (ACP) documentation	Complete ACP (same measure as in Aim 1, but performed over different time period.)	Chart review 3 months after death		173

Table 5.2.2.C Exploratory Outcomes			
Name of Outcome	**Specific measure to be used**	**Timepoints**	**N**
Aim 1: Effectiveness - compare 2 approaches to offering ATP			
Decisional conflict scale subscale scores	Decisional Conflict Scale (Month 4 score, adjusted for baseline score)	Month 0 (covariate) **Month 4 (return nephrology visit; outcome)** Month 9 (exploratory)	780
Aim 2a: Descriptive - experience during ATP			
Patient reports of their experience of an ATP	Open-ended qualitative questions about their experience One item (Part A) from the McGill Quality of Life Questionnaire	Reported by sample of patients in longitudinal cohort every 4 months	40
Care partner reports of their experience	Open-ended qualitative questions	Reported by sample of care partners in	15

caring for patients who have selected an ATP	about their experience = One item (Part A) from the McGill Quality of Life Questionnaire	longitudinal cohort every 4 months	
Aim 2b: EOL experience			
Hospice Use	Proportion of deaths with hospice care, length of use of hospice	Chart review after death	173
Care partner reports of their experience of end-of-life care	Open-ended qualitative questions about their experience	Family members/care partners approached 4 months after patient death	20

6. Study Population

6.1 Study Population

Study Population 1: Patients at participating clinics

Patients at participating CKD clinics who are 65+ years old and have eGFRs < 30. These patients are at the point in their disease course when they should make a decision about treatment for kidney failure.

Study Population 2: Family and care partners of patients who choose ATPs

To learn about family/care partner perceptions of the healthcare received by patients who choose an ATP, we will survey/interview a sample of family members and care partners a) throughout care and b) after patient's death.

Study Population 3: Employees of participating clinics

Employees who participate in the training to deliver the interventions will be asked to complete surveys measuring the impact of the training.

6.1.1 Number of Participants

Table 6.1.1 Number of Participants

Population	Description	N
1. Patients of the nephrology practices (Aims 1 and 2)	Patients 65+ years old with eGFR less than 30. Within this population, patients are grouped according to their treatment choice (within first 10 months).	2,948 • Choose dialysis: 2,240 • Choose ATP: 560 • Lack decision-making capacity: 147
2. Family/care partners of ATP patients (Aim 2)	Sample of family members and care partners of patients who choose an ATP	35 • Longitudinal Interviews: 15 • Bereavement interviews: 20

3. Employees of the nephrology practices (Aim 3)	Administrators/leaders (n = 50), other clinicians and staff (including doctors, advanced practice provider (APP)s, nurses, social workers, dieticians, palliative care specialists, and staff, n = 90)	140 • Administrators: 50 • Other employees: 90

6.1.2 Eligibility Criteria/Vulnerable Populations

Study Population 1: Person with CKD, cared for at participating clinic

Inclusion Criteria (screened by research coordinator):

- Age 65 years or older
- Most recent eGFR <30 at time of screening AND meets practice site criteria for KDE referral
- Treatment naïve (no dialysis or kidney transplant prior to enrollment)

Exclusion Criteria (assessed by treating nephrologist, APP, or other clinician):

- The patient is a transplant candidate.
- The current decrease in eGFR is thought to be due to an acute event.
- Education and initiation of shared decision-making process are not yet indicated for the patient, (per practice protocol and/or provider's judgment).
    - The patient will continue to be screened to see if their kidney function falls to the point where education and shared-decision making are indicated.
    - Note that patients who lack decision-making capacity should be enrolled when they would otherwise be eligible.

Note: patients who lack decision-making capacity should be enrolled, when otherwise eligible, but they will be excluded from the primary analysis. Outcomes for this group will be described separately.

All patients who meet the criteria above should be enrolled in the study. Additional exclusions apply for patients recruited for surveys and interviews:

- Insufficient decision-making capacity
- Non-English and non-Spanish speaking

- Treating nephrologist/APP opts patient out (for example, if contraindicated for patient's health)

Study Population 2: Family member or care partner of patient in Study Population 1

Inclusion Criteria:

- Family member or care partner of Population 1 patient who has a) chosen an alternative treatment plan and b) consented to the decision conflict surveys.
- 18+ years old
- English or Spanish speaking
- Cognitively able to participate in surveys/interviews

Study Population 3: Administrator, clinical provider, or staff at participating chronic kidney disease clinic

Inclusion Criteria:

- Currently practicing or employed at participating clinic

Employees are a vulnerable population. The intervention is at the clinic level, and supervisors at each site will decide which employees will be asked to participate in training and implementation. Participation in the *evaluation* of the training and interventions is voluntary, as described below.

In order to evaluate effectiveness of the training to implement the interventions and for quality improvement purposes, we will survey staff before and after the training. Participation in surveys will be voluntary, and employees will not be subject to firing or any other punitive action if they do not participate. We will not disclose which employees participate. In reporting aggregate results to the clinic sites, we will exclude results that would make it easy to identify participants (e.g., results for dieticians at Clinic A (n=1)); however, it may be possible in some cases for other staff members to infer participation.

7. Methods

7.1 Intervention

7.1.1 Description of Intervention

Intervention Approach 1 — Educate & Engage: This is a bundle of three components to improve SDM. Other than these activities aimed at decision-making, patients receive standard CKD care, which rarely offers what is provided under Approach 2 (care coordination, case management, active symptom management, and advance care planning). The components of Approach 1 are:

1. Practice sites encourage patients to engage with a formal KDE program using the National Kidney Foundation (NKF) Council of Advanced Practice Providers curriculum enriched by the investigators to include an expanded and balanced presentation of TLT, palliative dialysis, and AMCWD. The project will train the educators providing the KDE in best practices for engaging patients and families and for culturally sensitive and inclusive delivery of KDE. Under a practice protocol for ExPAND including a provider standing order, all eligible patients will be referred to KDE unless opted out by provider.
2. Practice sites use evidence-based decision aids that include unbiased presentations of ATP options. These will be vetted by the project with input from advisory group to assure cultural inclusivity.
3. Current CKD teams (nephrologists, APPs, nurses, social workers, and kidney educators) receive training in communication skills using the Ask-Tell-Ask approach and the 9 elements of SDM. SDM best practices include using unbiased language to describe all options and using decision aids.

Intervention Approach 2 — Provide primary palliative care to patients choosing ATP: In this comparator, practice sites implement a new systematic kidney supportive care program to manage and coordinate additional services for patients choosing ATP. In addition to the Approach 1 bundle of education and engagement activities, practice sites set up and offer a systematic program integrating primary palliative care to support patients and their families who choose any ATP regimen. This program closely follows patients on ATP treatment regimens and implements care coordination, symptom management, advance care planning, and psychosocial support. The project team will assist the CKD practice site in building a program based on the Pathways Project AMMWD toolkit (https://go.gwu.edu/ammwd), which integrates palliative care into routine CKD patient care. The original toolkit will be expanded to include support for other ATPs. Practice sites will designate a lead clinician (usually a nurse practitioner) and will be encouraged to expand the staff of the primary palliative care program to include social worker and dietician. Practices will forge a relationship with at least one community palliative care and hospice organization so that these services can help to support patients and families in their ATP care. Services provided via the primary palliative care

program include regular care coordination, frequent patient contact not normally deployed in CKD practices (such as biweekly to monthly symptom check calls), systematic advance care planning, care management, symptom assessment and management, attention to psychosocial and family concerns, early involvement of specialty palliative care/hospice, and anticipatory guidance with a plan in advance of a symptom crisis. Patients considering ATP are referred to this team for initial consultation. If they choose an ATP, they are followed by the team in addition to usual services provided by their nephrologist.

7.1.2 Method of Assignment/Randomization

Randomization will be performed at the clinic (practice site) level. The study coordinator will randomly assign (using a random number generator) each clinic to one of the three sequences. The assigned sequence determines when the clinic moves from Approach 1 to Approach 2.

Patients will receive the intervention based on the approach (condition) in which the site is enrolled at the time of accrual. When a practice site begins implementation of Approach 2, referral of patients who choose ATP to the supportive care clinic will become standard care at that site. All patients still alive who chose ATP during prior periods will be offered the option of receiving care from the newly organized supportive care program. Ethics require offering existing ATP patients the new care option once it is implemented.

7.1.3 Selection of Instruments/Outcome Measures

Table 7.1.3 Instruments and Surveys

Instrument	Measures	Items	Completed by*
Decisional Conflict Scale (DCS) — Statement Format: 16 item 5 response (15)	Decisional conflict	16	All
Know-CKD (16)	Knowledge about kidney failure	12	All
	Readiness	1	All

Stage of Decision Making: 1 item (17)			
The 9-item Shared Decision Making Questionnaire (SDM-Q-9) (18)	SDM	9	All
CollaboRATE (19)	SDM	3	All
Dialysis decision regret (modified): “Do you regret your treatment decision?” (5 point Likert scale from 1 to 5, with 1 being “no regret at all” and 5 being “a lot of regret”) (3)	Decision regret	1	All
McGill Quality of Life Questionnaire – Part A (20)	Quality of life	16	Patients and care partners in longitudinal qualitative interviews
Staff Training Evaluation Surveys (One per training session)	Self-Reported Confidence in Learning Objectives	Varies 10-15	Employees

*Population definitions: All = all survey-eligible patients who consent; Longitudinal = ATP patients, family members, or care partners who participate in the longitudinal surveys; Bereaved

= bereaved family members or care partners of ATP patients who die during the study; Employees = nephrology practice employees.

ExPAND End of Life Intensity Score for People with CKD (Adapted from Wong, O'Hare, 2012 (22)):

Intensity of Care During the Final Month (30 days) of Life		
Measure	**Points**	**Notes**
Any hospital admission	1	
Total days hospitalized > 14 days	1	Cut-off from Earle, 2004 (23)
Any intensive care unit admission	1	
Total days in ICU >= 4	1	Wong mean was 3.5 for dialysis patients
Any intensive procedure	1	Mechanical ventilation, CPR, or feeding tube
Death in hospital	1	

Total	**6**	

Complete advance care planning measure: This multi-component measure was successfully used in the Pathways Project (24) . Trained auditors use a checklist to ascertain the presence and quality of documentation for each of the following elements: designated surrogate decision-maker, narrative discussion of goals of care, an accessible advance directive, and a medical order such as a do-not- resuscitate (DNR) or orders for life- sustaining treatment (e.g. POLST or MOLST). Complete ACP documentation requires three elements: a surrogate, a goals of care discussion, and either an accessible advance directive or medical order.

7.1.4 Intervention Administration

The intervention will be administered by clinicians (nephrologists, APPs, nurses, social workers, and kidney disease educators) at the participating nephrology centers according to the schedule specified by the stepped wedge design. At each clinic, all eligible patients will receive the intervention being used by the clinic at the time of treatment.

Training and support

Approach 1: Clinicians administering the intervention receive training in communication skills using the Ask-Tell-Ask approach and the 9 elements of SDM. SDM best practices include using unbiased language to describe all options and using decision aids. Training will use learning methodologies including small group case discussion, recorded role plays with standardized patients, and video observation of SDM and critique. Our goal is to train at least 50% of existing CKD practice staff (including nephrologists).

Approach 2: The project team will assist the CKD practice sites in building a kidney supportive care program based on the Pathways Project AMMWD toolkit (https://go.gwu.edu/ammwd), which integrates palliative care into routine CKD patient care. Practice sites will designate a lead clinician (usually a nurse practitioner (NP)) and will be encouraged to expand the staff of the primary palliative care program to include social worker and dietician. Practices will forge a relationship with at least one community palliative care and hospice organization so that these services can help to support patients and families in their ATP care.

There can be considerable turnover of staff in nephrology practices for reasons beyond the influence of the research project. If there is staff turnover at clinical sites, especially the champion nephrologist, nurse practitioner or research coordinator, we will orient and train their successor. If staff such as research coordinator changes, we will re-train the replacement staff in study processes. If key clinical staff, such as champion nephrologist or NP leaves, we will attempt to orient a new champion at the site. We will provide the new champion with one-to-one orientation and training in the intervention and the study processes. The most critical problem

will be if the lead staff person running the ATP program leaves, it may take time for the site to recruit a replacement ATP clinician. If this were to happen, we might have to pause accrual at that site until the ATP clinic and approach 2 could be restarted with sufficient staffing resources at the clinic.

Core Functions/Form

To accommodate local adaptations, we will be using an implementation science framework called Core Functions and Forms. This format allows flexibility in the "forms" (specific methods) sites may use in order to fulfill the core "functions" of the intervention. The central research team (including patient advisors), together with key collaborators at the clinic sites, will finalize and develop a document describing the core (required) functions of the intervention, including functions for 1) provider discussions with patients that incorporate shared decision making and an ask-tell-ask approach, 2) patient kidney disease education (KDE), 3) patient decision aid (PDA)s, and 4) the palliative care program of Approach 2.

7.1.5 Reaction Management

Patient reactions

Because of the nature of this minimal risk study, no physical harms are expected. It is possible that patients might suffer psychological distress. Some patients may become emotionally upset when thinking about their disease progression or the decisions they are making about their treatment. In standard CKD patient care, patients also need to make decisions about what treatment they want. This study may differ from standard care in that patients might become better informed and more aware of the range of treatment options they have. Also, in taking the Decisional Conflict Scale (DCS) and other surveys, they might realize more clearly that they don't know 1) what are the benefits of treatment that matter most to them, 2) what risks and side effects are most troublesome to them, and 3) overall, what treatment option is best for them.

Interviewers will be trained to watch for indications of emotional distress and will be trained in how to respond calmly and empathetically. If the situation persists or worsens, the interview will be terminated, and the incident will be reported within 24 hours to the patient's treating clinician, who will develop a plan for supporting the patient including referral for further mental health services, as indicated.

Nephrology practice-level reactions:

As the intervention occurs at an organizational level, it is possible, although highly unlikely, that the intervention could create undesirable impacts for the staff. The most plausible would be higher than usual staff turnover due to changes in work processes due to the intervention. If an organization experiences staff turnover that the organizational leadership judges is related to the study intervention, the organizational leadership will report this to the Co-PI's. This will be discussed with the Clinical Site Council and the Data Safety Monitoring Board (DSMB) for potential adjustments to the intervention implementation.

7.2 Assessments

7.2.1 Efficacy

The efficacy of the two intervention approaches will be compared using the measures below. See 7.1.3 for more information about survey instruments.

Aim 1 - All Patients

Primary

- Chart review: Proportion of patients who choose an ATP, as reported in the medical record.
- Survey: Decisional Conflict Scale

Secondary

- Survey: Know-CKD
- Survey: SDM-Q-9
- Survey: CollaboRATE
- Question: Dialysis decision regret (modified): Do you regret your treatment decision? (5 point Likert scale from 1 to 5, with 1 being “no regret at all” and 5 being “a lot of regret”)
- Chart review: Proportion of patients with advance care planning documented in the medical record.

7.2.2 Safety/Pregnancy-related Procedure

NA

7.2.3 Adverse Events Definition and Reporting

No serious adverse events related to this minimal risk study are anticipated. However, to be comprehensive in our monitoring of adverse events, we have developed detailed policies and processes for monitoring and reporting adverse events. The key feature is distinguishing between adverse events that may be related to the study interventions from adverse events that are likely to happen in the study population but are unrelated to the study interventions. Local site PI's will assess all serious events and all unexpected events to determine whether or not they are related to study participation. Specific reporting timetables for reporting events are detailed in the appendix.

Definitions

Adverse Event (AE): Any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign, symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in

the research (modified from the definition of adverse events in the 1996 International Conference on Harmonization E-6 Guidelines for Good Clinical Practice). AEs encompass both physical and psychological harms. AEs are assessed in terms of seriousness, expectedness, and relatedness.

Serious adverse event (SAE): An AE that meets any of the following conditions:

- results in death
- is life-threatening (actually, not hypothetically)
- requires inpatient hospitalization or prolongation of existing hospitalization
- results in persistent or significant disability/incapacity
- Other 'important medical events' may also be considered serious if they jeopardize the participant or require an intervention to prevent one of the above consequences.

Unexpected Adverse Event: An AE is "unexpected" when its nature, severity or frequency is inconsistent with risk information previously reviewed and approved by the IRB in the context of the study population.

Related Adverse Event: An AE is "possibly related" to the research procedures if, in the opinion of the investigator, the research procedures may have caused the harm.

ExPAND study expected AEs

Unrelated AEs: Due to the nature of advanced CKD and its treatment, especially in multi-morbid frail older people, SAEs would be expected to occur frequently throughout the course of the disease. These expected SAEs include:

- Abnormal electrolyte and hematological laboratory results that can be explained directly or indirectly by their advanced CKD or comorbidities
- Hospital admissions — elective and emergency — that can be explained directly or indirectly by their advanced CKD or comorbidities
- Hospice admissions — planned and emergency — that can be explained directly or indirectly by their advanced CKD or comorbidities
- Infections and cardiovascular events, including fluid overload and swelling, that can be explained directly or indirectly by their advanced CKD or comorbidities
- Commencement of dialysis
- Death that can be explained directly or indirectly by their advanced CKD or comorbidities

Study-related AEs: Because of the nature of this minimal risk study, no physical harms are expected. It is possible that patients might suffer psychological distress. Some patients may

become emotionally upset when thinking about their disease progression or the decisions they are making about their treatment. In standard CKD patient care, patients also need to make decisions about what treatment they want. This study may differ from standard care in that patients might become better informed and more aware of the range of treatment options they have. Also, in taking the DCS and other surveys, they might realize more clearly that they don't know 1) what are the benefits of treatment that matter most to them, 2) what risks and side effects are most troublesome to them, and 3) overall, what treatment option is best for them. Interviewers will be trained to watch for indications of emotional distress and will be trained in how to respond, (see 7.1.5).

More details can be found in the document *ExPAND Adverse Event Reporting Guidelines* (Appendix).

AE Reporting

The Site Principal Investigator will assess the severity, expectedness, and relatedness of the AE, which will be reported accordingly.

Prompt reporting: The Site Principal Investigator will report the following events to the study Principal Investigator within 24 hours of becoming aware of the event. The study Principal Investigator will report the AE to the Institutional Review Board (IRB) within 48 hours of becoming aware of the event.

- SAEs, that are **study-related** (related to the research procedures)
- AEs (whether serious or not) that are both **unexpected and study-related**

Other reporting: All **study-related** adverse events will be recorded in Research Electronic Data Capture (REDCap)by the research coordinator (RC)(date, description, severity, expectedness, relatedness, and management/remediation of AE). The central data management team will assemble a list and summary of AEs, which will be reported to the IRB, DSMB, study sponsor, and site principal investigators as part of periodic reporting.

7.2.4 Pharmacokinetics (if applicable)

NA

7.2.5 Biomarkers (if applicable)

NA

7.3 Study Procedures

7.3.1 Study Schedule

Baseline chart audit:

Prior to the beginning of the intervention (Approach 1), or as soon as possible thereafter, local RC will conduct a retrospective chart audit to assess key outcomes at baseline. Section 8.5 describes the methodology and data to be collected.

Intervention (Approaches 1 and 2) - All eligible patients:

1. Local RC screens patients with upcoming appointments for eligibility and identifies candidates.

2. RC notifies treating nephrologist/APP, who determines final eligibility. They plan for research activities at patient visit, potentially including discussion about treatment options, referral to KDE and/or recruitment for decision conflict surveys (DCS).

3. **Enrollment Visit = Time 0.**

- When an eligible patient attends initial visit, the patient is enrolled. With HIPAA waiver of authorization and a waiver of consent, RC will monitor chart outcomes for all enrolled patients.
- Clinician assesses patient frailty and decision-making capacity.
- Clinician initiates discussion about treatment decision and/or refers patient to KDE.
- RC approaches survey-eligible patients (English/Spanish speaking with decision-making capacity). For patients who provide written informed consent, administer first survey (DCS-1). (May be administered up to 2 months later but not after post-enrollment KDE, if attended. May be administered in person or remotely.)

4. Four months after Time 0, RC administers DCS-2 in person or remotely. (May be up to 2 months early or 2 months late, preferably after 2nd visit with provider).

5. Four months after Time 0, RC reviews chart, records current treatment preference and other outcomes. (May be up to 2 months early or 2 months late, preferably after 2nd visit with provider).

6. Four months after Time 0, RC completes chart audit of advance care planning. (May be up to 2 months early or 2 months late, preferably after 2nd visit with provider).

9. Nine months after Time 0, RC administers DCS-3 in person or remotely. (May be up to 2 months early or 2 months late.)

7. Ten months after Time 0, RC reviews chart for missing outcomes (e.g. treatment decision) and enters Aim 1 completion status for patient (completed all study activities; followed for 10 months but did not complete all activities; died, lost to follow-up).

Patients who choose ATP:

1. After patient chooses an ATP, RC submits monthly report for each patient via REDCap. This report includes clinic visits, change in treatment plans, dialysis, hospitalizations, and death.

2. RC approaches patients who consented to DCS and, where available, care partners. Requests permission to share contact information with ExPAND research team interviewers for longitudinal and bereavement interviews. For patients and care partners who assent, RC adds addendum to ICF, and enters contact information into REDCap.

3. Purposeful sample of ATP patients and care partners selected to participate in longitudinal series of interviews. ExPAND research team interviewers contact selected subjects, provide information about the interviews, and invite them to participate. For participants who agree, they schedule and administer the interviews, starting with verbal consent. The interviewer will send thank-you cards upon completion of each longitudinal interview. Follow-up interviews are conducted every 4 months until study end or patient death.

4. If ATP patient dies, RC reports data on end-of-life service intensity and ACP documentation at end of life.

Bereaved family members or care partners:

If ATP patient dies, and family/care partner has previously assented to be contacted, ExPAND research team interviewer sends a bereavement card to family/care partner. Four month after patient death, interviewer follows up with family/care partner and invites them to participate in bereavement interview.

Clinic staff:

1. Clinic staff who participate in training activities complete pre-and post-test survey at beginning and end of training.

See *Flowchart of Study Activities and Outcomes (Appendix)* for schematic flow of Aim 1 and Aim 2 activities.

7.3.2 Informed Consent

Multiple consent processes will be employed, depending on subject population and study activity. In general,

- for chart reviews, we will ask the IRB to approve a HIPAA waiver of authorization and waiver of consent
- for surveys conducted by the local RC, we will obtain written informed consent or eConsent

- for surveys/interviews conducted remotely by the central research team (external to the site), we will obtain verbal consent and ask the IRB to approve a HIPAA waiver of documentation of consent

Patients:

Chart audits: We will ask the IRB to approve a HIPAA waiver of consent in order to conduct chart audits to gather data on treatment choice, health service utilization, and advance care planning for all patients meeting inclusion/exclusion criteria.

Decisional conflict surveys (administered by site RC): the site RC will approach eligible patients, explain the study, and obtain written informed consent to participate in the three DCS surveys. Ideally, the initial approach and consent will be in person but if needed, the RC may conduct these activities by phone, email, or US mail. The consent may be remote (e.g., US mail) or electronic. We have implemented an eConsent process in REDCap. Alternatively, patients may sign a paper copy of the consent form, scan it, and email it to the RC. Sites may also use their own Advarra-approved eConsent mechanisms. See *Informed Consent Form for Patient DCS Survey, Recruitment Letter/Email to Patients for DCS Survey, eConsent REDCap Script* (Appendix).

ATP Patients, family members, and care partners:

Longitudinal and bereavement interviews (conducted by ExPAND Research Team interviewers; waiver of documentation of consent): After patients choose an alternative treatment plan (ATP), the RC will approach those patients who have previously consented to the DCS surveys at a clinic visit, along with their care partners, where available. The RC will provide a patient/care partner information sheet about the interviews and ask for permission to share contact information (for the patient and/or family/care partners) with the external research team for this purpose. If the patient and/or care partner assents, the RC will collect the contact information and share it with the central research team. Assent will be documented as an addendum to the ICF for the DCS surveys. The patient/care partner will be reminded that only a sample of patients/care partners who provide contact information will be contacted. See *Patient and Care Partner Information Sheet for Aim 2 Interviews, Addendum to Patient ICF — Contact Info* (Appendix).

Subsequently, if the patient or care partner is selected for longitudinal interviews or bereavement interview, ExPAND Team interviewers will contact the participant (patient or family/care partner) to invite them to participate. The process and interview content will be described, and any participant questions will be answered. For willing participants, an interview will be scheduled. At the beginning of the telephone or video call, the consent language will be read by the interviewer over the phone and verbal consent will be obtained both before and after the interview recording starts. A copy of the consent will be mailed to the participant if they wish to provide their street address or email. A thank-you card will be sent to the interview participant upon completion of the interview either via email or U.S. mail.

7.3.3 Screening

On a regular (e.g., weekly or biweekly) basis, an RC at each clinic will review the medical record of patients with upcoming clinic visits to identify eligible candidates. For eligible patients, the RC will notify the treating nephrologist/APP, who will determine final eligibility based on exclusion criteria. They will plan for research activities at the upcoming patient visit, potentially including discussion about treatment options, referral to KDE and/or recruitment for decision conflict surveys.

Patients who meet the eligibility criteria and attend the planned visit will be automatically enrolled for EHR data collection. We will seek a HIPAA waiver of authorization and a waiver of consent for this. EHR data will be collected for all patients who meet the primary eligibility criteria, including patients who lack decision-making capacity or do not speak English or Spanish.

7.3.4 Recruitment, Enrollment and Retention

Patients, family members and care partners

Intervention: Trial enrollment and randomization are at the site level. All patients at each site receive the intervention based on the approach in which the site is enrolled at the time.

Chart review: With a HIPAA waiver of authorization and a waiver of consent, the utilization outcomes will be collected on all eligible patients, with little missing data expected.

Participant level recruitment is applicable to patient and care partner reported outcomes collected via surveys and interviews as described below.

Decisional conflict surveys (DCS): The site RC will approach survey-eligible patients for the DCS at the enrollment visit or shortly thereafter. (May be up to 2 months later but not after post-enrollment KDE, if attended.) All eligible patients should be invited to take the surveys, including those who make a treatment decision at the enrollment visit and regardless of KDE referral status. For this co-primary outcome, we believe that the administration of the short (10-20 minute) survey on site during clinic visits will maximize participation rates. Ideally, the RC will approach eligible patients, explain the study, obtain written informed consent, and then immediately administer the survey. If needed, the RC may approach the patients by phone or email to obtain consent and administer the survey. We will pay an incentive for completion of DCS on the following schedule: $50 on completion of the first 2 surveys, additional $25 on completion of 3rd survey. We estimate that 35% of eligible patients will consent and 26% will complete the survey at all three time points. If the response rate is higher than expected, we will introduce random sampling to determine which patients are invited to participate.

Longitudinal and bereavement interviews (ATP patients/family/care partners): After patients choose an ATP, the RC will approach those patients who have previously consented to the DCS

surveys at a clinic visit, along with their care partners, where available. The RC will provide a patient/care partner information sheet about the interviews and ask for permission to share contact information (for the patient and/or family/care partners) with the external research team for this purpose. A patient may provide assent for his or ger own contact information even if the care partner chooses not to, and vice versa. If the patient and/or care partner assents, the RC will collect the contact information and share it with the central research team. Assent will be documented as an addendum to the ICF for the DCS surveys. The patient/care partner will be reminded that only a sample of patients/care partners who provide contact information will be contacted. See *Patient and Care Partner Information Sheet for Aim 2 Interviews* (Appendix).

Subsequently, if the patient or family/care partner is selected for longitudinal interviews, or if the patient dies, the ExPAND Team interviewers will contact the participant (patient or family/care partner) to invite them to participate. The process and interview content will be described, and any participant questions will be answered. For willing participants, an interview will be scheduled. At the beginning of the telephone or video call, the consent language will be read by the interviewer over the phone and verbal consent will be obtained both before and after the interview recording starts. A copy of the consent will be mailed to the participant if they wish to provide their street address or email. Participants will be paid $50 for each interview. We expect some drop out for the longitudinal interviews. Bereavement interviews are given only once.

Response rates

Although we will strive for higher response rates, we based our power calculations for the patient-reported outcomes on conservative projections of response rates. This conservative estimate aligns with our prior experience seeking to survey dialysis patients during the Pathways Project. This estimate is also consistent with the national response rate for the Consumer Assessment of Healthcare Providers and Systems In-Center Hemodialysis Survey (ICH CAHPS). The ICH CAHPS survey response rate, based on average response rates for all survey periods that have been completed as of Feb 2020, showed an expected response rate of 28% for mail only responses, 24% for telephone only responses, and 33% for mixed mode (mail and telephone).

To strengthen our response rate, we will incorporate evidence-based best practices for patient surveys, especially for vulnerable patients. Three key components that will be integrated into the survey instruments are brevity, clarity, and consistency. Keeping surveys short helps reduce burden and increase participation. An additional best practice we will employ is to offer multiple modality options such as in person, telephone, online. We will provide information about the study in multiple formats such as posters, flyers, and postcards. Finally, we will offer the surveys in English and Spanish.

The key to recruitment of patients will be at least one committed RC at each clinical site. The RC will be research personnel employed by the site who will have responsibility for 1) screening medical records and appointment lists to identify persons who meet the eligibility criteria for the study, 2) approaching eligible patients to explain the study and obtain their consent to

participate in the survey portion of the study, 3) administer the DCS surveys, 4) approach ATP patients and care partners to obtain permission to share contact information with the central research team, and 5) facilitate payment of incentives to participating patients.

We will pre-test these processes at one site. We expect to refine the recruitment process based on the pre-test experience and on input from the site planning group and National Advisory Council.

Clinical sites

Study Site Selection: The organizations providing the study sites were selected because their organizational leadership is invested in improving kidney supportive care, is willing to deliver the interventions, has sufficient research infrastructure, and has sufficient number of CKD patients. These organizations manage over 70,000 patients with kidney disease at more than 70 offices and satellite practice sites, of which 28 sites will participate in the project (to allow for site drop-out over course of the study to attain a final analysis sample of 24 sites.) These nephrology organizations are "real world" settings operating under the regulatory and financial conditions and constraints typical for nephrology clinical practice, which will bolster generalizability of the results. The patient population served across all sites includes rural, suburban, and urban populations, patients from diverse races and ethnicities, and a wide range of economic circumstances. The organizations identified the specific participating sites based on size (at least 1,000 CKD patients), staffing levels, presence of a nephrologist or NP "champion" to be lead at the site, and availability of research infrastructure.

One of the key ways we will retain clinical sites is to meaningfully engage their leadership in the project. One mechanism for engagement will be a Clinical Site Council of the participating practices. Each practice site will designate a representative to serve on the council, which will provide input especially into questions around adaptation of the interventions for implementation based on local conditions. The council will consult with the investigators on barriers and problems that arise during the project as well as identify innovations in practice that facilitated implementation through incorporation in routine workflows.

It is possible that sites will drop out of the study over the five years for reasons beyond the control of the research project, such as sale of the practice, closure of offices, or other major reorganizations. We have prepared for 15% dropout by recruiting more sites than needed for final analysis sample. We think it highly unlikely that site attrition will exceed 15%, since the nephrology organizations we are partnering with are stable practices, with deep track records in clinical care as well as renal research.

Clinical staff participants

The intervention is at the clinic level, and supervisors at each clinic will decide which employees will be asked to participate in training and implementation. Recruitment applies to feedback provided by employees to the research team via surveys. Members from the ExPAND team will

provide an online link for the training evaluation survey, and reminders including the survey link will be emailed to participants.

Avoiding undue influence or coercion in recruitment:

Patients: Patients, family members, and care partners will be informed that participation is voluntary and that all patients, regardless of their participation status, will continue to receive standard care. They will be informed that they may stop participating at any time without penalty. Research staff will not provide final lists of participants to the nephrology center providers or staff. In some cases, research staff may include nurses who have had human subjects research training. Otherwise, in general, the people delivering patient care will not be aware of whether an individual patient participated.

Staff: The intervention is at the clinic level, and supervisors at each clinic will decide which employees will be asked to attend training and participate in implementation. Participation in the evaluation of the training is voluntary. Participants will be informed that their employment will not be affected in any way by their participation status and that they may stop participating at any time without penalty. In summary reports to sites, we will not identify study participants; however, due to the small sample sizes, it is possible that participant identities may be inferred in some cases.

7.3.5 Study Visits

See section 7.3.1 for study schedule.

7.3.6 End of Study and Follow Up

Enrollment of patients into the study will stop on February 29, 2028.

Follow-up of patients, including bereavement interviews of family members/care partners will stop on June 30, 2028.

7.3.7 Removal of Subjects

No subjects will be removed from the EHR data collection (with HIPAA waiver) unless it is determined that they were added in error, i.e., they did not meet the eligibility criteria.

Consented participants who request to be withdrawn from the study in writing will be removed for purposes of further data collection, but data already collected may be used. We will not publish any quotations or individual-level data for these participants.

Consented participants who drop out or are lost to follow-up will not be removed from the study and data collected may be used.

7.4 Statistical Method

7.4.1 Statistical Design

UPDATES:

1. The statistical design and power calculations described below were based on earlier sample size projections (N = 2,800) based on 21 clinics in the final analysis sample. We now anticipate having approximately 24 clinics; however, we still aim to enroll an analysis sample of N = 2,800. The additional sites provide us with a buffer, which we believe is prudent given the high risk of attrition in these types of studies and the limited information available upon which to base our estimates of enrollment rates.
2. We originally planned to perform advance care planning chart audits on a random sample of enrolled patients (n = 264) as described in this section. For simplicity, we now plan to perform the chart audit for all enrolled patients.
3. We originally planned to have WVU interviewers conduct a separate telephone interview of a sample of patients. We have now decided to include the shared decision-making questions that were going to be part of the telephone interview (SQM-Q-9, CollaboRATE) into the second DCS survey and the decision regret question into DCS-3.
4. The question regarding decisional regret in DCS-3 was changed from a yes/no question to a 5 point Likert scale with 1 being “no regret at all” and 5 being “a lot of regret”.

Effectiveness (Aim 1)

To compare which mode of improving SDM and access to ATP is more effective, we will use a repeated cross-sectional stepped wedge (SW) design with randomization at the practice site level. Each clinic will be randomly assigned to one of three sequences. Each sequence consists of four 10-month time periods during which patients are accrued and followed for study outcomes. To minimize contamination in the primary analysis, we will exclude patients recruited during the 4 months before each sequence moves to Approach 2 (see white squares in Figure 5.1). These patients will be included in a sensitivity analysis. In the 4th study period, accrual of new patients will stop at 10 months, allowing a closing 4-month follow-up period to collect primary outcomes at the end of the study, (see Figure 5.1). All practice sites begin by implementing Approach 1 (Educate and Engage). Practice sites then add Approach 2 (Kidney Supportive Care Program) at the assigned period based on their sequence. With 24 clinics participating, we have prepared for 15% drop-out of sites, leaving 21 sites in the final analysis sample. Patients will receive the intervention based on the approach (condition) in which the site is enrolled at the time of accrual. When a practice site begins implementation of Approach 2, referral to the supportive care clinic will become standard care at that site. All patients still alive who chose ATP in the prior period will be offered the option of receiving care from the newly organized supportive care program. Ethics require offering existing ATP patients the new care option once it is implemented, even though this may greatly reduce the number of patients who die during Approach 1 care, thereby limiting our ability to compare Approach 1 and Approach 2 on EOL outcomes (Aim 2b).

There are several advantages to a cluster randomized stepped wedge (SW) design vs. standard cluster randomized trial. First, SW gives every practice the opportunity to implement both

approaches, which is something that the physician practice leaders have told us they value. Second, SW means that from the patient perspective, they will be receiving the standard care delivered by the practice site at that time, and there is no need for patients to opt in or out of a trial to receive this improved access to best practice care.

Prior to implementation of Approach 1, we will measure the proportion of patients who choose each treatment option. We will also retroactively assess hospital EOL utilization and proportion of ATP patients who begin dialysis within 30 days of death.

Patient and family/care partner experience using ATP (Aim 2)

To describe the patient/family experience of ATP care through the end of life, we will monitor utilization patterns for all ATP patients and conduct chart audits at end of life, survey a subset of ATP patients periodically throughout the course of care, and interview bereaved family members. A panel of patients who have chosen an ATP and family members/care partners will be interviewed every 4 months to develop a description of experience over time. A sample of bereaved family members/care partners will be interviewed 4 months after a patient's death. Mixed methods, including thematic analysis, will be used to explore themes about quality of life during receipt of ATP, concordance of end-of-life experience with patient goals, family/care partner experience of caregiving and at EOL, and utilization patterns, especially change to other treatment modes and hospitalizations.

Exploratory comparison of patients who receive EOL care in Approach 1 vs Approach 2 will be conducted, especially through qualitative themes emerging during interviews. The study may not have sufficient power to detect differences in the quantitative measures because the number of patients receiving Approach 1 who are projected to die is expected to be small. Nevertheless, the qualitative interviews will reveal themes that illuminate the effects of the two approaches. We expect that Approach 2, which provides more care management and more advance care planning, will lead to lower EOL intensity scores, fewer initiations of standard dialysis within 30 days of death, and care more concordant with known patient wishes as reported by family. **(**See *Flowchart of Study Activities and Outcomes* (Appendix) for schematic flow of Aim 2 clinical processes and data collection points.)

7.4.2 Sample Size Considerations

UPDATE: See Section 7.4.1 for changes made since the power calculations below were performed.

Sample Size and Power (Aims 1 and 2)

Detailed assumptions for sample size targets are shown in the table below. Sample sizes will vary by outcome, e.g., medical record derived outcomes should be available for all eligible patients, while survey-based outcomes will need to exclude patients who do not consent to complete the surveys. Aim 2 outcomes are only relevant to patients choosing ATP. Because the two approaches are delivered under SW design and the number of accruable eligible patients at

each practice site during the study period are largely beyond the control of the study, the choice of the number of participating practice sites is key for planning adequate power.

Table 7.4.2.A Assumptions for Sample Size and Power Projections

Assumption	**Rationale/Data Source/Calculation**	**Resulting N**
AIM 1: Impact of approaches on patient treatment decisions		
21 practice sites; 2,000 patients average per clinic	Data from first 13 practice sites agreeing to participate 2,000*21 practice sites = 44,000 patients	44,000 CKD patients, all stages, all ages
Annually, 117 patients per practice reach eGFR <= 20 (75 patients new to practice site + 42 moving from stage 3 or early stage 4)	Data from first 13 practice sites agreeing to participate 117*21*(32/12) months = 6,552 patients (rounded to 6,550)	6,550 patients reach eGFR <=20 during 32 months of recruiting
- 60% of patients with eGFR <20 are age 65+ - 75% of age 65+ are not transplant recipients - 95% of non-transplant have decision-making capacity.	Data from first 13 practice sites and US Renal Data System website 6,550*0.60*0.75*0.95 = 2,800 patients	**2,800 patients added to study for EHR data collection (1,400 per approach)**

- 35% of patients consent to Decisional Conflict survey offered onsite at 1st office visit. - 75% of these complete 2nd survey at 2nd office visit.	Prior experience of team, including My Way project (40% response rate of patients approached for participation) 2,800*.35*.75=735 participants	735 for Aim 1 Decisional Conflict survey (367 each approach)
Target n is 300. Includes oversample to obtain sufficient numbers of Black and Hispanic patient responses.	The detectable effect sizes range from medium to large.	300 telephone survey responses. (150 each approach)
Randomly sample patient deciders for chart audit	99% power to detect a difference of 35% vs. 10%, alpha = .05, estimated rates based on My Way project experience.	264 chart audits (132 each approach)
AIM 2: Patient and family experience during ATP care and at end of life		
# patients who will choose ATP: Approach 1: 5% AMCWD, 0% TLT or palliative dialysis, 5% DND = 10% ATP. (SIHD = 10% home dialysis, 80% in-center dialysis) Approach 2: 15% AMCWD, 5% TLT, 5% palliative dialysis, 5% DND = 30% ATP.	Approach 1: Expert opinion Approach 2: Canadian, Australian, UK experience: 20% of older patients choose AMCWD. We have assumed a lower rate as the Approach 2 programs may need time to get established and gain the trust of providers and patients.	560 patients choose ATP (AMCWD, TLT, palliative dialysis, DND) Approach 1: 140 patients Approach 2: 420 patients

(SIHD = 15% home dialysis, 55% in-center dialysis)	1,400*0.10 = 140 patients added in Approach 1 1,400*0.30 = 420 patients added in Approach 2	
# patients who switch back to dialysis	Expert opinion. Canadian, Australian, UK experience — very few AMCWD patients switch to dialysis.	560 for denominator (all ATP)
Randomly sample ATP patients to invite for qualitative interviews. 25% will agree to interview.	Prior experience of team, including My Way project and Pathways project. Difficult to reach patients for phone interview; many patients too tired or sick for phone interview.	About 40 patients will be interviewed
25% of ATP patients anticipated will die yearly (.02 person/month)	This is more conservative than actual experience in Australian and Canadian programs to allow for possibility that patients will be choosing ATP earlier in disease progression and thus living longer	173 deaths* (Approach 1: 35 Approach 2: 138)
Contact family member/care partner for all ATP patients who die. Will not have contact information for some proportion. 25% will agree to interview.	Survey data will be examined for missing items, and any patterns will be reported qualitatively and be used to qualify the interpretation of findings, e.g., "families under	About 20 family members/care partners may be reachable and agree to interview. Complete one bereavement interview per family member/care partner.

	more apparent stress were less likely to complete certain of the quality-of-life items.	

* The number of deaths was calculated for each period using a 25% annual mortality rate and the number of ATP patients alive (under each approach) at the beginning of the period. Note that some patients accrued under Approach 1 will die under Approach 2.

A series of stepped wedge (SW) power analyses were conducted, where the following parameters were varied: number of clusters, steps, periods, within-cluster intraclass correlation (ICC)s, effect sizes, the expected number of patients with usable data at each cluster-period, and desired power. Besides power, the following were considered: a greater number of practice sites allows 1) confidence in generalizability of findings, 2) more opportunity to explore site/ population characteristics associated with approach differences in outcomes, and 3) more precise estimates of effect sizes which are essential for policy decisions. Consequently, the optimal design was 21 practice sites, 3 sequences, each stepping 7 practices from Approach 1 to Approach 2 after a 4-month transition. This would entail 4 periods, each with 6 or 10 months of patient accrual. The last period has 6 months of accrual to allow complete 4-month follow-ups. (See Figure 5.1.) Although the power analyses and design assume 21 practice sites, we have recruited 24 practice sites (plus 2 more for pilot testing) as allowance for practice sites who might drop out for unforeseen reasons.

Table 7.4.2.B Power for Comparing Approach 1 and Approach 2 Outcomes

#	Outcome	n	Effect Size, Power		
#	Outcome	n	Smaller Effect	Medium Effect	Larger Effect
Aim 1 (all patients making treatment decision)					
1	Proportion of patients choosing ATP	2,800	P_1=.10, P_2=.15 Power = .46	P_1=.10, P_2=.20 Power = .96	P_1=.10, P_2=.25 Power = .99

2	Decisional conflict score at return nephrology visit	735	d=.20 Power = .40	d=.35 Power = .89	d=.50 Power = .99
3, 4	Patient-reported experience of SDM (SDM-Q-9, CollaboRATE)	300	d=.40 Power =.65	d=.50 Power =.83	d=.60 Power =.94
5	Patient reported decision regret (proportion regretting decision)	300	P_1=.25, P_2=.15 Power = .26	P_1=.25, P_2=.10 Power = .54	P_1=.25, P_2=.05 Power = .84
6	Advance care planning documentation	2,800	P_1=10., P_2=.15 Power = .57	P_1=10, P_2=.25 Power = .99	P_1=.10, P_2=.35 Power = .99
Aim 2a (only includes patients initially choosing ATP)					

7	Proportion of ATP patients who change to dialysis <1 month before death	n_1=140, n_2=420	P_1=.40, P_2=.30 Power = .26	P_1=.40, P_2=.25 Power = .52	P_1=.40, P_2=.20 Power = .79
8	Advance care planning documentation	n_1=140, n_2=420	P_1=.10, P_2=.30 Power = .88	P_1=.10, P_2=.35 Power = .96	P_1=.10, P_2=.40 Power = .99

Notes. P_1, P_2 are proportions choosing the outcome for Approach 1 and 2, respectively. Where unequal n's are expected under the 2 approaches, n_1 andn_2 are number of patients expected under each Approach 1 and 2, respectively; otherwise, the n's are expected to be equal. d is Cohen's d (standardized effect size).

Table 7.4.2.B summarizes minimum sample size expectations and power estimates for key outcomes. Actual power will be lowered by unequal sample sizes per practice site but increased if more than 21 practice sites remain in the study. The total sample size of 2,800 for Outcome 1 is based on data from the first 13 sites agreeing to participate, as described in Table 7.4.2.A. The survey-based sample size (Outcome 2) is much lower because patient consent and availability is required, and the telephone survey (Outcomes 3, 4, 5) will be based on a pre-planned sampled subset of the surveyed sample. Power calculations used R package swCRTdesign version 3.3. (28) ICCs currently listed in the CLOUD Bank (29) for SW studies in health care settings average about .03, and therefore a slightly more conservative ICC=.05 was incorporated into calculations. Alpha (two-sided) is set at .025 for the 2 co-primary Aim 1 outcomes, and at .05 for the remaining outcomes.

For Outcome 1, an increase from 10% choosing an ATP under Approach 1 to 20% under Approach 2 would be substantial enough to be considered important (30) (31) and we believe an increase to 25% or 30% is highly plausible. This is based on personal communication with US nephrologists regarding the present number of CKD patients wanting AMCWD and on reports from AMCWD programs in the UK, Australia, and Canada. (32) (33) (34) The moderate effect (change from 10% to 20% choosing ATP) is detectable with .96 power.

For Outcomes 2, 3, and 4, the standardized effect sizes detectable with .80 or higher power range from about .35 to .60 in magnitude. Power calculations for those outcomes assume a pre-post r=.50, which increases power. (35) Power for Outcome 5 (decision regret) will be weaker, only reaching power >.80 if the there is a very large difference between the 2 approaches. For Outcome 6 (ACP documentation) power should be excellent (.99) for detecting plausible differences based on experience from the My Way study, where the rates were 4% at baseline, 18% in the enhanced control and 33% among CKD patients who received ACP coaching. (36)

For the Aim2a Outcome 7, although we expect a large effect of Approach 2 in reducing change to dialysis 1 month before death (detectable with power of .79), a more modest effect would have weak power. Therefore, a non-significant result would need to be interpreted cautiously, with an emphasis on descriptive statistics and confidence intervals. For Outcome 8, (ACP documentation), we are assuming stronger Approach 2 effects in this population of patients choosing an ATP, and therefore statistical power should be excellent.

7.4.3 Planned Analyses

7.4.3.1 Primary Analyses

Aim 1 and 2

For all primary outcomes as well as most secondary quantitative outcomes, statistical hypotheses concern the contrast between patients accrued under Approach 1 and 2. The intent-to-treat principle will be followed for all primary outcomes. Treatment choice, unless otherwise defined, refers to the treatment preference recorded 4 months (+/- 2 months) after enrollment. Differences between the two approaches will be tested through a generalized linear mixed effect model, which can accommodate the random cluster effects inherent to the SW design and handle outcomes that are binary, normally distributed, etc. Analyses will include age and gender as fixed effect covariates, and cluster as a random effect. For the survey-based outcomes, the Decisional Conflict Score assessed at the first nephrology visit will also be included as a covariate. The telephone survey analyses (Outcomes 3, 4, and 5), which involve data from a stratified sample of patients by race, will include race as a covariate and a test of effect modification through inclusion of a Race x Approach interaction term. Racial/ethnicity categories will be decided based on observed frequencies in the survey. In SW designs, time is a potential confounder but is expected to be minimal.

Sensitivity Analysis: For the deciding not to decide (DND) treatment choice, we will not be able to reliably distinguish between a conscious shared decision to postpone deciding and simply not deciding. Therefore, we define DND as not making a treatment choice within the 10 ½ months of follow-up. To measure the impact of including this population among patients who choose an ATP, we will conduct a sensitivity analysis excluding patients who do not make a treatment decision within the 10 ½ months of follow-up.

Heterogeneity of Treatment Effects: It is hypothesized that for Outcomes 1 and 2, there will be a more pronounced effect for patients who are over age 80, frail, or have heart disease. Although

pre-specified tests are described here, they will be interpreted as secondary analyses because of uncertainties regarding power. As a pre-specified analysis, this will be tested by adding Approach x Age Group, Approach x Frailty Group, and Approach x Heart Disease Group terms to the regression model, which would also include the main effect variables (age group, frail group, and heart disease group as indicator variables). Because these subgroups are likely to have considerable overlap leading to possibly high multicollinearity of variables, the 3 interaction terms will first be tested together as a set with an omnibus test. A significant p-value result (< .05) would be followed by testing the regression coefficients for each of the separate terms (with significance at $p<.05$), which would determine, say, whether the heart disease group was more affected by Approach 2 after controlling for the other interaction effects. For Outcomes 3, 4, and 5, an Approach x Race term will be included in those models. For Outcome 1, as an exploratory analysis, heterogeneity in approach effect across clinics will be tested through inclusion of a Site x Approach interaction random effect. Practice site differences in Approach effects will also be examined through descriptive and graphical methods. Any strong patterns observed will then be compared with known characteristics of each practice site to gather plausible explanations of any important Approach effect differences among the clinics. Currently, this is the only exploratory interaction test planned. If any later heterogeneity tests are conducted, these will be tested through an interaction term added to the model; however, any publication describing those results will state clearly that these are exploratory and therefore those results are highly tentative.

Preliminary analyses: Internal consistency reliability will be assessed for scale scores. Because the SW design partly confounds treatment and time, we will examine de-identified patient demographic and diagnostic trends across the study period to identify any that may confound or limit study interpretation. For example, shifts in outcomes under either study condition may occur due to secular external trends, new legislation or rules, etc., as well as changes due to greater staff experience. As an indicator of secular trends, we will monitor the proportion of older adults (80+ years) starting dialysis in the national data reported annually by the USRDS and include this information in the interpretation of results. Missing data. For the outcome of choosing ATP, data will be available for all participants via chart audit. Survey-based outcomes will only be available for participants who consent and complete the survey. This may introduce a selection bias, e.g., if participants under Approach 2 feel more motivated to complete the survey. A preliminary analysis will therefore examine whether there is a difference in study participation rate between the 2 study conditions. If there is an important difference, then the survey-based results will be subjected to sensitivity analyses to identify whether the conclusions would differ under various reasonable missing data scenarios. Practice dropout. If any practice sites drop out of study participation after randomization, a judgment will be made by the PI as to whether any patient study data collected from patients by those sites can reasonably be considered missing completely at random, and therefore included in the analysis, or whether it likely represents an important bias (e.g., a practice site largely non-adherent on staff education required for the study) and will be excluded from analysis, or whether to do a sensitivity analysis on the effect of that practice site's data on study results.

Exploratory analyses: Although a primary outcome is choosing any ATP, the range of specific ATPs or standard dialysis options chosen will be examined descriptively. For example, one of the approaches may lead to greater or less use of home dialysis as a sub-type of SIHD. Other analyses will examine practice site characteristics as predictors of outcomes as a multi-level model e.g., stronger Approach 2 effects for clinics with higher staff/patient ratios.

7.4.3.2 Analysis of Subject Characteristics

Subject characteristics (e.g., age, gender, race, etc.) will be collected, summarized, and regularly reported (overall and by site) at DSMB meetings. Subject characteristics will be reported in all publications.

7.4.3.3 Interim Analysis (if applicable)

No interim analysis of outcomes is planned as the interventions pose minimal risk.

7.4.3.4 Health economic evaluation, if applicable

NA

7.4.3.5 Other

NA

7.4.4 Subsets and Covariates

Subgroups of patient population (older patients (≥ 65 years) with stage 4 or 5 CKD (eGFR < 30) being cared for at a participating practice site):

- Patients who are frail, based on the Clinical Frailty Scale (39)
- Patients who are 80+ years old
- Patients with heart disease: ICD-10 I20-I52
- (Exploratory only) Patients with diabetes
- (Exploratory only) Black patients
- (Exploratory only) Hispanic patients
- (Exploratory only) socioeconomic status, based on zip code

The following covariates will be included in models for the outcomes specified:

- Age (in models for all Outcomes)
- Gender (in models for all Outcomes)
- Decisional Conflict Score (in models for survey Outcomes)
- Race (in models for Outcomes 3, 4, 5)

7.4.5 Handling of Missing Data

Missing data. For the outcome of choosing ATP, data will be available for all participants via chart audit. Survey-based outcomes will only be available for participants who consent and complete the survey. This may introduce a selection bias, e.g., if participants under Approach 2 feel more motivated to complete the survey. A preliminary analysis will therefore examine whether there is a difference in study participation rate between the 2 study conditions. If there is an important difference, then the survey-based results will be subjected to sensitivity analyses to identify whether the conclusions would differ under various reasonable missing data scenarios.

Practice site dropout. If any practice sites drop out of study participation after randomization, a judgment will be made by the PI as to whether any patient study data collected from patients by those sites can reasonably be considered missing completely at random, and therefore included in the analysis, or whether it likely represents an important bias (e.g., a practice site largely non-adherent on staff education required for the study) and will be excluded from analysis, or whether to do a sensitivity analysis on the effect of that practice site's data on study results.

8. Trial Administration

8.1 Ethical Considerations: Informed Consent/Assent and HIPAA Authorization

This is benign behavioral intervention and a minimal risk study.

HIPAA waiver of authorization and waiver of consent

To answer the research questions (effect of interventions on number of patients who attend kidney disease education, choose alternative treatment plans, have advance care planning documentations in the chart), we need to have the information for all eligible patients. Obtaining informed consent would introduce selection bias and reduce power to evaluate the effects of the intervention. It might also undermine our ability to evaluate the effect of the intervention on subgroups (race, comorbidities, etc.). With a HIPAA waiver of authorization and waiver of consent, we will collect data from the medical record that are protected (PHI), but not highly sensitive. Most of the information we will collect will be completely deidentified, but we need to collect dates of services to reliably keep track of time intervals and of which services take place under each intervention approach. Because some patients will be followed as the clinic moves from Approach 1 to Approach 2, we need to measure the duration of exposure to each approach, and to know whether certain activities occurred during the baseline period, Approach 1, or Approach 2. We will not collect date of birth but will collect year of age to be able to evaluate whether effects differ by age. We will also collect provider name (to evaluate reach of intervention), zip code as a means to assess the impact of social determinants of health and whether we see disparities by zip code. Non-PHI to be collected include demographic information, clinical information (e.g., comorbidities), kidney failure treatment decision, and healthcare utilization (clinic visits, hospital visits, etc.)

We expect that the waiver will not directly affect the participants in any way. No research data will be added to the patients' permanent medical records. The data collected will be used only for the purposes of the research, and we will take appropriate measures to minimize the potential for a breach of confidentiality (8.3, 8.9). We will destroy the identifiable information and code link when this research and any approved follow-up research are complete, as described in section 8.10.

Information collected with consent

After providing informed consent, some patients will participate in surveys and interviews. Recruiting and consenting procedures, including measures taken to avoid coercion, are described in sections 7.3.2 and 7.3.4. When describing the study to patients, we will use general language without specific descriptions of the differences between the two intervention approaches. The reason is to avoid introducing bias by influencing treatment decisions or perceptions about care that are reported in patient-reported outcomes (surveys and interviews). For example, a patient in Approach 1 who might otherwise consider AMCWD, who learned that other clinics were providing a kidney supportive care program while their own clinic was not,

might conclude that they would not receive adequate support and decide to choose dialysis after all; or the same patient might have negative perceptions about the care they received if they imagined that patients in the other approach were receiving better care.

HIPAA waiver of documentation of consent

To reduce the burden on site RCs, some surveys and interviews will be administered remotely by ExPAND Team interviewers . For these interviews, the site RC will obtain permission from patients and/or family members/care partners to share their contact information with the research team outside the local clinic. With patient/care partner permission, this contact information will be stored in REDCap and made available to the remote interviewers. The remote interviewers will be responsible for describing the research procedures and verbally consenting the patients, as described in sections 7.3.2 and 7.3.4. We will request a HIPAA waiver of documentation of consent for these activities. The reason we ask for waiver of documentation of consent is to reduce the burden on the local RC (to obtain consent) or on the participant (to return a signed consent form in the mail). It will also facilitate maximal participation, which will provide more statistical power and reduce selection bias.

Payments to participants

Participants (patients and family members/care partners) will receive the following payments for participation in surveys and interviews:

- Decision conflict survey ($50 after second survey, $25 after third survey)
- Longitudinal interviews ($50 per interview)
- Bereavement interviews ($50 per interview)

As part of consent, patients may choose to receive the payment in the form of a debit card, electronic wire transfer, or paper check delivered via US mail. We believe these amounts will express our appreciation and provide an incentive to participate while not being so significant as to be coercive.

Family members/care partners who participate in a longitudinal or bereavement interview will receive a gift card upon completion. During the interview, the family member/care partner may choose to receive the gift card either via email or US mail.

8.2 Institutional Review Board (IRB) Review

Central IRB / IRB of Record

Advarra will serve as the Central IRB (also known as the IRB of Record).

The protocol will be submitted to the Central IRB for review and approval. Approval of the protocol must be obtained before initiating any research activity. Any modification to the protocol will be approved by the Central IRB before implementation.

Continuing review requests will be submitted to the Central IRB annually, and a study closure report will be submitted after all research activities have been completed.

Other study events (e.g., data breaches, protocol deviations) will be reported as described in this protocol and per the Central IRB's policies.

Relying Institutions

Each participating practice will formally cede their IRB review to the Central IRB using a fully executed reliance agreement (known as an IRB authorization agreement or IAA).

Study documents approved by the Central IRB, including initial and modified protocols, consent forms, and others, will be sent to the relying institutions per Central IRB protocol. Reports and other communications with the Central IRB will be reported to relying institutions, if relevant.

8.3 Subject Privacy, Confidentiality & Data Management

Protection of data confidentiality:

We will maintain all standard processes for maintaining data in a secure manner:

- Identifiable data will be stored only in secure REDCap research database at GWU or other secure platform approved for regulated data (e.g., GW Box). (A copy of site-specific study data may be housed securely at each participating site.)
- Access to the secure database will be limited to specified research staff.
- All enrolled patients will be assigned a unique study identification number. All data collected will be identified only by these study identification numbers. Where it is necessary to collect direct identifiers (e.g., for contact and payment of survey participants), these will be kept in separate databases from other data collected. A site-specific link between each study identification number and participant name will be kept in a password-protected file on a password protected computer at each participating site.
- Research personnel at the clinical sites may temporarily use paper documents for participant tracking and data collection. Data will be transcribed to REDCap in a timely manner. Paper documents will be secured in a locked cabinet at the clinical site until they are no longer needed. Then they will be shredded.
- Only completely de-identified data will be provided to others outside the study team as needed for data analysis.
- No medical records or protected health information (collected for the patient participants only) shall be re-disclosed, unless required by law.

- Data and code links will be destroyed after the period for maintaining data has elapsed, in accordance with this protocol and Central IRB's policies, (see section 8.10).

Oversight of research personnel to maintain research participant protection and rights:

For GWU and all subaward organizations, all research personnel will have up to date training in the conduct of human subjects research, such as Collaborative Institutional Training Initiative (CITI) or Association of Clinical Research Professionals (ACRP) coursework. Research personnel will meet either the GW IRB requirements for training, or the requirements of their home institution.

At clinical sites (participating nephrology practices), RCs (aka "study coordinators") employed by the sites will have responsibility for 1) screening medical records to identify persons who meet the eligibility criteria for the study, 2) conducting chart reviews to obtain data on treatment decision, advance care planning and service utilization (e.g. hospitalizations at end of life), 3) entering study data into REDCap, 4) maintaining a code link, 5) approaching eligible patients to explain the study and obtain their consent to participate in the survey portion of the study, 6) administering the DCS surveys, 7) providing contact information to ExPAND Team interviewers of patients who give permission, and 8) facilitating incentive payments to participating patients. We will also provide project specific videoconference training for the site research personnel on the study protocol, best practices for involving patients from diverse backgrounds, and best practices for maintaining privacy, confidentiality and protection of research participants and data collected.

For personnel involved in the study in roles *other than research* (for instance, nurse practitioners who lead the kidney supportive care clinics) but do not obtain data from the chart or from patients for research purposes, we will provide an overview of research ethics and procedures as part of the orientation to the overall project. Clinical personnel who provide information to patients about the clinical services being studied under each approach are not considered to be engaging in research and will not be tracked as to whether they have appropriate training in the conduct of human research. We will also clearly delineate between patient *assent* processes (giving assent to provide contact information to the research team) — for which research training is not required — and *consent* processes (being informed about risks and benefits, asking questions, and providing consent to use data). Consent will only be obtained by personnel who have appropriate research training.

8.4 Deviations/Unanticipated Problems

Protocol Deviations

This is a minimal risk study, and we do not expect protocol deviations to impact participant safety. In the unlikely event that a protocol deviation occurs that may impact participant safety, it will be reported to the IRB and the DSMB within 48 hours of the Principal Investigator becoming aware of the event. Other protocol deviations will be logged and reported to the IRB and DSMB as part of periodic reports and continuing review requests. The log will be maintained by the

Project Manager and will include date, description of deviation, impact on participants, and remediation actions. Examples of protocol deviations that could occur in this study are:

- Enrollment of an ineligible participant
- Failure to obtain informed consent
- Data collection outside study windows
- Mishandled data

Unanticipated problems

Unanticipated problems are defined as any incident, experience, or outcome that meets **all** of the following criteria:

- Unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the IRB-approved research protocol and informed consent document; and (b) the characteristics of the participant population being studied
- Related or possibly related to participation in the research. Possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research
- Suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized

Unanticipated problems will be reported to the IRB and the DSMB within 48 hours of the Principal Investigator becoming aware of the problem. They will be logged by the Project Manager, as for protocol deviations, and included in periodic reporting to the IRB, DSMB, and PCORI.

8.5 Data Collection

Code link and separate storage of data

To better ensure confidentiality, patient research data will be stored in several separate secure REDCap databases:

1. The first database will contain patient PHI and other information collected from the medical record under a HIPAA waiver of authorization and a waiver of consent. This database will include indirect identifiers, as described in section 8.1.
2. The second database will contain patient survey data. No identifying information will be stored in this database.
3. The third database will contain information needed by the Advarra payment system to pay participant incentives. This includes direct identifiers.

4. The fourth database will contain patient/family/care partner contact information for use in administration of remote surveys and interviews.
5. The fifth database will contain data from the ExPAND Research Team interviewers. This includes interview completion status, interviewer/interviewee information, and date of the interview.

All enrolled patients will be assigned a unique study identification number. All data collected will be identified only by these study identification numbers, which will be used to link patient and care partner data between the REDCap databases. A site-specific link between each study identification number and participant name will be kept in a password-protected file on a password protected computer at each participating site. (More information about secure management of the code link and data can be found in sections 8.3, 8.9, and 8.10.)

Collection of patient and care-partner information

See section 7.3 for study procedures including schedule of study activities.

- Chart audit and participant tracking data (with indirect patient identifiers, mainly dates) will be entered by site RC directly into REDCap database 1.
- DCS survey data (completely deidentified) will be entered into a REDCap database 2 by the RC or directly by the patient (for patients who choose to take the survey electronically).
- Information needed for payment of patient incentives (including direct identifiers) will be entered by site RC directly into REDCap database 3.
- Patient/family/care partner contact information will be entered by the RC into REDCap database 4, to keep identifying information separate from deidentified survey responses and partially deidentified medical record data.
- For the ATP patient and family/care partner telephone interviews, the ExPAND Team interviewers will enter information pertaining to interview completion status into REDCap database 5.
- All recordings and transcripts of the longitudinal and bereavement interviews will be kept in the GW Box.
- De-identified interview transcripts will be imported to GWU's NVivo for thematic analysis.

Alternatively, the RC may use paper documents temporarily for participant tracking and data collection. In that case, data will be transcribed to GW Box in a timely manner. Paper documents will be secured in a locked cabinet at the clinical site until they are no longer needed and then shredded.

Collection of clinic employee information

- Employee survey data will be stored on GW Box or other platform approved for regulated data by GWU.

Collection of baseline chart audit data

Prior to the beginning of the intervention (Approach 1), or as soon as possible thereafter, local RC will conduct a retrospective chart audit to assess key outcomes at baseline (prior to intervention Approach 1). Patients seen in the clinic between 1/1/2023 and 1/31/2024 will be retrospectively screened for study eligibility using the same criteria as for the main study. The charts of eligible patients will be reviewed from the date of eligibility to six months later. The following outcomes will be recorded: referral to KDE (y/n, eGFR at referral), attendance at KDE (y/n), advance care planning documentation (y/n), treatment decision (choice), start of treatment, if applicable (y/n, treatment, number of days after eligibility), death or loss to follow-up (number of days after eligibility). For patients who chose an alternative treatment plan, the follow-up period will be through July 31, 2024 for the following addition outcomes: death (number of days after eligibility), place of death, dialysis start (number of days after eligibility, setting). In addition to the outcomes data, the RC will record the patient's age, gender, race, ethnicity, whether the patient has decision-making capacity, and the most recent eGFR at the time of eligibility. All data will be completely deidentified: ages > 90 years will be recorded as 90, and all dates will be reported as the number of days from becoming eligible. Deidentified data will be entered into REDCap.

8.6 Data Quality Assurance

With the use of video-conferencing and instructional documents, site RCs will be trained in study protocol and data collection procedures. In addition, the data management team will correspond regularly with site RCs to answer questions and solve problems.

Data will be entered into REDCap, which has built-in mechanisms to minimize typos, encourage data entry in the correct format, flag missing data, and apply customized data quality checking in real time. Data will be regularly monitored by the data management team using human assessment as well as customized software to check for missing, improperly formed, or implausible data in the context of the study. Data quality reports will be sent regularly to the data collection personnel at the clinical sites, who will work with the data management team to correct missing and erroneous data.

8.7 Study Records

The following study records will be maintained by the ExPAND Project Manager

- Regulatory documents (IRB applications and approvals, approved documents)
- Reports to the funder (PCORI)
- Reports to and from the DSMB

- Study protocol

The following study records will be maintained by the RC at each clinical site

- Consent forms
- Code link

The following study records will be maintained in REDCap or on GW Box by the ExPAND data management team

- Case report forms
- Patient data collected from the medical record
- Patient contact and payment information (with permission)
- Survey responses (with written or verbal consent)
- Interview completion status (REDCap)
- Interview recordings and transcripts (GW Box)

8.8 Access to Source

Data will be collected from four sources:

1. Patient medical record: collected by site RC and entered into REDCap
2. Patient surveys
    a. DCS survey responses collected by RC and entered into REDCap, or entered directly by participant (if taking the survey electronically)
3. Employee surveys
    a. Surveys: responses entered directly into REDCap or U.S. mailed to central data management team
4. Semi-structured interviews: recorded by interviewers, transcribed, and stored securely on GW Box or another GWU-approved platform approved for regulated data

8.9 Data or Specimen Storage/Security

Most study data will be stored on a GWU-approved REDCap server. REDCap (Research Electronic Data CAPture) is a mature, secure, web-based application for building and managing online surveys and databases. Security measures include both electronic (encryption) and physical (monitored, restricted access) measures. It is the database platform of choice for all NIH Clinical and Translational Science Award (CTSA) awarded institutions and for other

institutions who want to collect and store health-related research data securely. REDCap is HIPAA compliant.

Some study data, including semi-structured interview data, may be stored on another platform that has been approved by GWU for regulated data, such as the password-protected GW Box.

See section 8.3 for other information on how we will maintain data security and confidentiality.

8.10 Retention of Records

After this study, we would like to do a follow-up study to see what happens with patients' health for up to 5 years after the end of the current study. If we obtain funding and approval for the follow-up study, we will retain the study records (listed in 8.7) until the completion of the follow-up study, including data analysis and dissemination of results.

At the completion of the follow-up study, or sooner if no follow-up study is done, we will completely deidentify the study patient data and add the deidentified data to a shared data repository, as required by PCORI. The code links at each participating nephrology practice site will then be destroyed (electronic records deleted). At the completion of the follow-up study, the clinic staff data will not be shared to the data repository and will be destroyed.

After completion of the studies, deidentified data, consent forms, and research records will be maintained for the period required by the Central IRB. Consents documents will then be shredded.

8.11 Study Monitoring

Ongoing study progress is reported at least annually to the ExPAND Clinical Site Council, ExPAND National Advisory Council, ExPAND Data Safety and Monitoring Board, the Central IRB, and PCORI.

Mandatory reporting to PCORI occurs at least quarterly for pre-specified study milestones. Enrollment reports are submitted to PCORI monthly.

8.12 Data Safety Monitoring Plan

The study will empanel a Data and Safety Monitoring Board (DSMB) to act in an advisory capacity to the PIs and to evaluate the progress of the study, including periodic assessments of data quality and timeliness, participant recruitment, accrual and retention, participant risk versus benefit, performance of trial sites, and other factors that can affect study outcomes. The DSMB will make recommendations to the PIs concerning the continuation, modification, or conclusion of the trial.

The DSMB will have multidisciplinary representation, including physicians from relevant medical specialties, biostatisticians, ethicists, clinical trialists, patients, and a person expert in racial and ethnic inequities in healthcare. The DSMB members shall be free of significant conflicts of interest (i.e., financial, intellectual, professional, or regulatory). A DSMB Charter for the study

will be developed by the study team and approved by the DSMB members. Further details are in the attached *DSMB Charter* and *Data Safety Monitoring Plan* (Appendix).

The DSMB will meet in person or by Zoom:

- prior to recruitment to review and approve the study protocol
- every 12 months, at a minimum, to review study progress
- after the end of data collection

The Principal Investigators will attend these meetings, and minutes and any recommendations will be documented. The DSMB will review enrollment and attrition rates and advise the PIs on any potential risks as well as on any risk mitigation plans. The DSMB recommendations will be discussed with the PIs. All data will be reviewed for protocol adherence, including a data verification check that the appropriate outcome measures are given at the appropriate time points.

8.13 Study Modification

Any modification to the protocol will be approved by the Central IRB before implementation. The IRB-approved revised protocol and other revised documents will be sent to the relying institutions per Central IRB protocol.

Modifications which increase risk for participants (not anticipated) will be brought to the Data Safety Monitoring Board for review.

Any major changes in overall research plan (as contrasted to changes in procedures) will be submitted to PCORI for approval.

8.14 Study Discontinuation

Any decision about study discontinuation will be made in conjunction with the DSMB.

8.15 Study Completion

After the last patient is enrolled for EHR data collection (with HIPAA waiver), chart data will be collected for up to six months. During this time, final surveys and interviews will be collected.

The data will then be analyzed, and the results reported to participants (unless they opted out during consent), stakeholders, and the public, via conferences and peer-reviewed journals. We have found that dissemination can take up to two years or more.

Study data, including data stored at GWU and code links maintained at each site, will be retained, shared (deidentified data only), and eventually destroyed as described in section 8.10.

At this point, final reports will be made to the IRB and DSMB, and the study will be closed.

8.16 Conflict of Interest Management Plan

The independence of this study from any actual or perceived influence, such as by the dialysis industry, is critical. Therefore, any actual conflict of interest of persons who have a role in the design, conduct, analysis, publication, or any aspect of this trial will be disclosed and managed. Furthermore, persons who have a perceived conflict of interest will be required to have such conflicts managed in a way that is appropriate to their participation in the trial. The study leadership in conjunction with the appropriate conflict of interest review committee has established policies and procedures for all study group members to disclose all conflicts of interest and will establish a mechanism for the management of all reported dualities of interest.

Any investigator who has a conflict of interest with this study (patent ownership, royalties, or financial gain greater than the minimum allowable by their institution, etc.) must have the conflict reviewed following the procedure outlined in the George Washington University Conflict of Interest Policies. A conflict management plan will be established according to GW policy and reviewed by appropriate Dean and approved by the study sponsor prior to participation in this study. All investigators will follow the applicable conflict of interest policies. As needed, the PI's will consult with the GW Office of Ethics, Compliance, and Risk for guidance on any conflict of interest issues.

8.17 Funding Source

This study is funded through a contract from the Patient Centered Outcomes Research Institute (PCORI).

Contract title: Expanding Patient Choice in Kidney Failure Treatment, Contract #: IHS-2022C2-27678

8.18 Publication Plan

Abstracts for Scientific Meetings of Professional Societies

1. Abstracts will be submitted to annual scientific meeting of the American Society of Nephrology and the spring clinical meeting of the National Kidney Foundation
2. Abstracts with palliative medicine outcomes will be submitted to the annual assembly of the American Academy of Hospice and Palliative Medicine
3. Abstracts will be submitted to the annual American Nephrology Nurses Association National Symposium

Possible papers resulting from unique research challenges of ExPAND

1. Effectiveness of implementation science approach of creating a core function/form matrix and intervention table to facilitate flexible multisite trial with multiple nephrology practices. (Appropriate for Kidney360 Innovative Technology and Methodology article type.)

2. Process with stakeholder input for 1) choice of patient-centered, patient-friendly Kidney Disease Education and patient decision aid for shared decision-making; and 2) recruitment approach to increase patient KDE participation-appropriate for Medical Decision Making or Patient Education and Counseling. (If patient recruitment for KDE is substantially higher than previously reported, then it could be appropriate for CJASN or AJKD.)
3. Communication skills training to increase SDM-Q-9 scores of ExPAND participants. (If successful, appropriate for CJASN, AJKD, Kidney360, Kidney Medicine, Medical Decision Making or Patient Education and Counseling.)
4. Role of nurses or social workers in implementing shared decision-making for nephrology practices and delivering KDE and presenting patient decision aids. (Nephrology Nursing Journal or the Journal of Nephrology Social Work)

Main Papers with Results

1. Results paper comparing number/percentage of patients choosing ATP and decisional conflict, SDM-Q-9, and CollaboRATE scores in approach 1 vs approach 2. (Appropriate for CJASN or AJKD. If really successful, could be appropriate for Ann Intern Med or JAMA Intern Med.)
2. Separate paper analyzing ATP selections (to our knowledge, no one has studied the extent to which patients choose a time-limited trial or deciding not to decide when explicitly informed of possibility. (Depending on strength of results potentially appropriate for CJASN, AJKD, Kidney 360 or Kidney Medicine.)
3. Possible brief communication article type on stability of preference paper comparing approach 1 to approach 2 regarding planned and unplanned dialysis starts. (Depending on strength of results, could be appropriate for CJASN, AJKD, Kidney 360 or Kidney Medicine.)

Final Report to PCORI

LIST OF TABLES

LIST OF CHARTS

REFERENCES

1. USRDS Annual Data Report USRDS Annual Data Report. Chapter 1: Incidence, Prevalence, Patient Characteristics, and Treatment Modalities. United States Renal Data System 2018; 42. URL: https://www.usrds.org/2018/download/v2_c01_IncPrev_18_usrds.pdf.

2. Chandna, Shahid M. Da Silva-Gane, Maria Marshall, Catherine Warwicker, Paul Greenwood, Roger N. Farrington, Ken. Nephrology Dialysis Transplantation Survival of elderly patients with stage 5 CKD: Comparison of conservative management and renal replacement therapy. 2011; 5:1608 - 1614. doi: 10.1093/ndt/gfq630.

3. Saeed F, Ladwig SA, Epstein RM, Monk RD, Duberstein PR.. Dialysis Regret: Prevalence and Correlates. CJASN 2020; 15 (7):957-963. doi: 10.2215/CJN.13781119.

4. Murtagh, Authors Fliss E M Burns, Aine Moranne, Olivier Morton, Rachael. Clin J Am Soc Nephrol Comprehensive Conservative Care in End-Stage Kidney Disease. 2016; 10:1909 - 191411.

5. Renal Physicians Association (RPA). Clinical Practice Guideline on Shared Decision-Making in the Appropriate Initiation of and Withdrawal from Dialysis, Second Edition. 2010; URL: https://www.renalmd.org/store/ViewProduct.aspx?id=7014408.

6. Davison, Sara N. Clinical journal of the American Society of Nephrology : CJASN End-of-life care preferences and needs: perceptions of patients with chronic kidney disease.. 2010; 2:195 - 204. doi: 10.2215/CJN.05960809. URL: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2827591&tool=pmcentrez&rendertype=abstract http://cjasn.asnjournals.org/content/5/2/195.

7. Morton, R L Tong, A Howard, K Snelling, P Webster, a C. BMJ (Clinical research ed.) The views of patients and carers in treatment decision making for chronic kidney disease: systematic review and thematic synthesis of qualitative studies.. 2010; 7742:350. doi: 10.1136/bmj.c112. URL: http://www.bmj.com.proxygw.wrlc.org/content/bmj/340/bmj.c112.full.pdf.

8. Wong, Susan P. Y. McFarland, Lynne V. Liu, Chuan-Fen Laundry, Ryan J. Hebert, Paul L. O'Hare, Ann M.. JAMA Internal Medicine Care Practices for Patients With Advanced Kidney Disease Who Forgo Maintenance Dialysis. 2019; 3:305. doi: 10.1001/jamainternmed.2018.6197. URL: http://archinte.jamanetwork.com/article.aspx?doi=10.1001/jamainternmed.2018.6197.

9. Celine Foote, Sradha Kotwal, Martin Gallagher, Alan Cass, Mark Brown, Meg Jardine . Survival outcomes of supportive care versus dialysis therapies for elderly patients with end-stage kidney disease: A systematic review and meta-analysis . Nephrology (Carlton) 2016 Mar; 241-53. doi: 10.1111/nep.12586. PMID: 26265214.

10. Shahid M Chandna, Maria Da Silva-Gane, Catherine Marshall, Paul Warwicker, Roger N Greenwood, Ken Farrington. Survival of elderly patients with stage 5 CKD: comparison of conservative management and renal replacement therapy. Nephrology Dialysis Transplantation 2011 May; Volume 26, Issue 5:1608-14. doi: 10.1093/ndt/gfq630. PMID: 21098012.

11. Ying-Ying Seow, Yin Bun Cheung, Li Min Qu, Alethea Chung Pheng Yee. Trajectory of quality of life for poor prognosis stage 5D chronic kidney disease with and without dialysis. Am J Nephrol 2013; 231–238. doi: 10.1159/000347220. PMID: 23467046.

12. Louise Engelbrecht Buur, Jens Kristian Madsen, Inge Eidemak, Elizabeth Krarup, Thomas Guldager Lauridsen, Lena Helbo Taasti & Jeanette Finderup . Does conservative kidney management offer a quantity or quality of life benefit compared to dialysis? A systematic review . BMC Nephrology 2021 Sep 11; doi: 10.1186/s12882-021-02516-6. PMID: 34507554.

13. Supakanya Wongrakpanich, Paweena Susantitaphong, Suramath Isaranuwatchai, Jirat Chenbhanich, Somchai Eiam-Ong, Bertrand L Jaber. Dialysis Therapy and Conservative Management of Advanced Chronic Kidney Disease in the Elderly: A Systematic Review. Nephron November 2017; Volume 137, Issue 3:178–189. doi: 10.1159/000477361. PMID: 28538218.

14. Murphy E, Burns A, Murtagh FEM, Rooshenas L, Caskey FJ. The Prepare for Kidney Care Study: prepare for renal dialysis versus responsive management in advanced chronic kidney disease. Nephrology Dialysis Transplantation 2021; 36(6):975-982. doi: 10.1093/ndt/gfaa209.

15. O'Connor, Annette M.. Medical Decision Making Validation of a Decisional Conflict Scale. Med Decis Making 1995; 1:25 - 30. doi: 10.1177/0272989X9501500105. URL: https://doi.org/10.1177/0272989X9501500105.

16. Koch-Weser S, Kennefick K, Tighiouart H, Wong JB, Gordon EJ, Isakova T, Rifkin D, Rossi A, Weiner DE, Ladin K. Development and Validation of the Rating of CKD Knowledge Among Older Adults (Know-CKD) With Kidney Failure. Am J Kidney Dis 2023 Dec 7:S0272-6386(23)00944-7:doi: 10.1053/j.ajkd.2023.09.024. PMID: 38070590.

17. O'Connor AM. User Manual - Stage of Decision Making [document on the Internet]. Ottawa: Ottawa Hospital Research Institute 2000 [modified 2003]; URL: http://decisionaid.ohri.ca/docs/develop/User_Manuals/UM_Stage_Decision_Making.pdf.

18. Kriston L Scholl I Hölzel L Simon D Loh A Härter M. The 9-item Shared Decision Making Questionnaire (SDM-Q-9). Development and psychometric properties in a primary care sample.. Patient education and counseling 2010 Jul; 1873-5134 (Electronic):PMID: 19879711.

19. Elwyn, Glyn Barr, Paul James Grande, Stuart W. Thompson, Rachel Walsh, Thom Ozanne, Elissa M. Developing CollaboRATE: A fast and frugal patient-reported measure of shared decision making in clinical encounters. Patient Education and Counseling 2013; 93 (1):102 - 107. doi: 10.1016/j.pec.2013.05.009. URL: http://dx.doi.org/10.1016/j.pec.2013.05.009.

20. Cohen SR, Mount BM, Strobel MG, Bui F. The McGill Quality of Life Questionnaire: a measure of quality of life appropriate for people with advanced disease. A preliminary study of validity and acceptability. Palliative Medicine 1995; 9 (3):207-219. doi: 10.1177/026921639500900306.

21. Engelberg, Ruth Downey, Lois Curtis, J. Randall. Journal of Palliative Medicine Psychometric Characteristics of a Quality of Communication Questionnaire Assessing Communication about End-of-Life Care. 2006; 5:1086 - 1098. doi: 10.1089/jpm.2006.9.1086. URL: http://www.liebertpub.com/doi/10.1089/jpm.2006.9.1086.

22. Wong, Susan P, Kreuter, William, O'Hare, Ann M.. Treatment Intensity at the End of Life in Older Adults Receiving Long-term Dialysis. Arch Intern Med 2012; 172 (8):661-2.

23. Earle, C, Neville B, Landrum MB, Ayanian, J, Block, S, Weeks, J. Trends in the aggressiveness of cancer care near the end of life. J Clin Oncology 2004; 22 (2):315-21.

24. Kurella TM, Holdsworth L, Stedman M, Aldous A, Asch SM, Han J, Harbert G, Lorenz KA, Malcolm E, Nicklas A, Moss AH, Lupu DE. Implementation and Effectiveness of a Learning Collaborative to Improve Palliative Care for Seriously Ill Hemodialysis Patients. Clin J Am Soc Nephrol 2022; 17(10):1495-1505. doi: 10.2215/CJN.00090122. PMID: PMC9528276.

25. Enola Proctor, Hiie Silmere, Ramesh Raghavan, Peter Hovmand, Greg Aarons, Alicia Bunger, Richard Griffey, Melissa Hensley. Outcomes for implementation research: conceptual distinctions, measurement challenges, and research agenda . Adm Policy Ment Health 2011 Mar; 38:65-76. doi: 10.1007/s10488-010-0319-7. PMID: 20957426.

26. Kathryn Louise Reilly, Sarah Kennedy, Gwenndolyn Porter, Paul Estabrooks. Comparing, Contrasting, and Integrating Dissemination and Implementation Outcomes Included in the RE-AIM and Implementation Outcomes Frameworks . Front. Public Health 02 September 2020; Volume 8:doi: 10.3389/fpubh.2020.00430. URL: https://www.frontiersin.org/articles/10.3389/fpubh.2020.00430/full.

27. Russell E Glasgow, Samantha M Harden, Bridget Gaglio, Borsika Rabin, Matthew Lee Smith, Gwenndolyn C Porter, Marcia G Ory, Paul A Estabrooks . RE-AIM Planning and Evaluation Framework: Adapting to New Science and Practice With a 20-Year Review. Front Public Health 2019 Mar; Volume 7:doi: 10.3389/fpubh.2019.00064. PMID: 30984733.

28. Emily C Voldal, Navneet R Hakhu, Fan Xia, Patrick J Heagerty, James P Hughes. swCRTdesign: An RPackage for Stepped Wedge Trial Design and Analysis . Comput Methods Programs Biomed 2020 Nov; Volume 196:doi: 10.1016/j.cmpb.2020.105514. PMID: 32554025.

29. Elizabeth Korevaar, Jessica Kasza, Monica Taljaard, Karla Hemming, Terry Haines, Elizabeth L Turner, Jennifer A Thompson, James P Hughes, Andrew B Forbes. Intra-cluster correlations from the CLustered OUtcome Dataset bank to inform the design of longitudinal cluster trials . Clin Trials . 2021 Oct; Volume 18, Issue 5:doi: 10.1177/17407745211020852. PMID: 34088230.

30. Fahad Saeed, Jane O Schell . Shared Decision Making for Older Adults: Time to Move Beyond Dialysis as a Default . Ann Intern Med 2023 Jan; 129-130. doi: 10.7326/M22-3431. PMID: 36534979.

31. Keren Ladin, PhD, MSc, Hocine Tighiouart, MS, Olivia Bronzi, BA, Susan Koch-Weser, ScD, John B. Wong, MD, Sarah Levine, BA, Arushi Agarwal, BA, Lucy Ren, BA, Jack Degnan, MPH, Lexi N. Sewall, BS, Brianna Kuramitsu, MSW, Patrick Fox, BS, Elisa J. Gordon, PhD, MPH, Tamara Isakova, MD, MMSc, Dena Rifkin, MD, MS, Ana Rossi, MD, and Daniel E. Weiner, MD, MS. Effectiveness of an Intervention to Improve Decision Making for Older Patients With Advanced Chronic Kidney Disease : A Randomized Controlled Trial . Ann Intern Med . January 2023; 29-38. doi: 10.7326/M22-1543. PMID: 36534976.

32. Rachael L Morton, Angela C Webster, Kevin McGeechan, Kirsten Howard, Fliss E M Murtagh, Nicholas A Gray, Peter G Kerr, Michael J Germain, Paul Snelling. Conservative Management and End-of-Life Care in an Australian Cohort with ESRD. Clin J Am Soc Nephrol 2016 Dec 7; doi: 10.2215/CJN.11861115. PMID: 27697783.

33. Rachel C. Carson, Maciej Juszczak, Andrew Davenport, and Aine Burns. Is Maximum Conservative Management an Equivalent Treatment Option to Dialysis for Elderly Patients with Significant Comorbid Disease? . Clin J Am Soc Nephrol. 2009 Oct; 1611–1619. doi: 10.2215/CJN.00510109. PMID: 19808244.

34. Fliss E M Murtagh, Aine Burns, Olivier Moranne, Rachael L Morton, Saraladevi Naicker. Supportive Care: Comprehensive Conservative Care in End-Stage Kidney Disease . Clin J Am Soc Nephrol American Society of Nephrology 2016 Oct 7; 1909-1914. doi: 10.2215/CJN.04840516. PMID: 27510453.

35. Steven Teerenstra, Sandra Eldridge, Maud Graff, Esther de Hoop, George F Borm. A simple sample size formula for analysis of covariance in cluster randomized trials . Stat Med 2012 Sep 10; 2169-78. doi: doi:10.1002/sim.5352. PMID: 22495809.

36. Dale E. Lupu Annette Aldous Elizabeth Anderson Jane O. Schell Hunter Groninger Michael J. Sherman Joseph R. Aiello Samuel J. Simmens. Advance Care Planning Coaching in CKD Clinics: A Pragmatic Randomized Clinical Trial . Am J Kidney Dis . VOLUME 79, ISSUE 5:P699-708. doi: 10.1053/j.ajkd.2021.08.019. PMID: 34648897.

37. T Rhodes, G V Stimson, C Fitch, A Ball, A Renton. Rapid assessment, injecting drug use, and public health . Lancet 1999 Jul 3; 65-8. doi: 10.1016/S0140-6736(98)07612-0. PMID: 10406380.

38. Randall C. Gale, Justina Wu, Taryn Erhardt, Mark Bounthavong, Caitlin M. Reardon, Laura J. Damschroder & Amanda M. Midboe . Comparison of rapid vs in-depth qualitative analytic methods from a process evaluation of academic detailing in the Veterans Health Administration . Implementation Science 01 February 2019; 14:doi: 10.1186/s13012-019-0853-y.

39. Kenneth Rockwood, Xiaowei Song, Chris MacKnight, Howard Bergman, David B. Hogan, Ian McDowell, Arnold Mitnitski. A global clinical measure of fitness and frailty in elderly people. CMAJ 173 (5):489-495. doi: 10.1503/cmaj.050051.

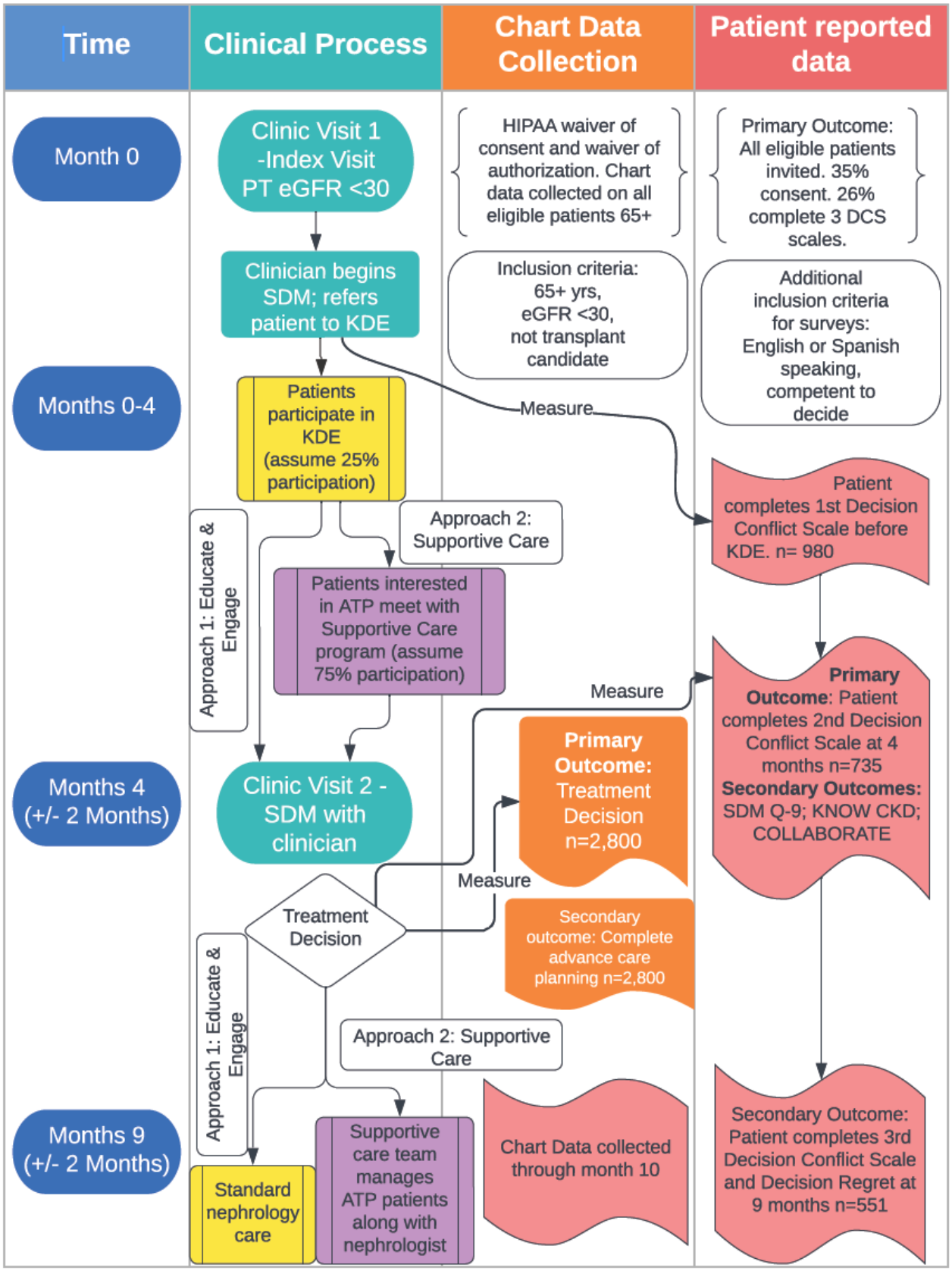
APPENDICES

#	Title	Section	Topic
1	Flowchart of Study Activities and Outcomes	Synopsis	Study Flow Chart (Optional)
2	ExPAND Adverse Event Reporting Guidelines	7 Methods	7.2.3 Adverse Events Definition and Reporting
3	Informed Consent Form for Patient DCS Survey	7 Methods	7.3.2 Informed Consent
4	Recruitment Letter/Email to Patients for DCS Survey	7 Methods	7.3.2 Informed Consent
5	eConsent REDCap Script	7 Methods	7.3.2 Informed Consent
6	Patient and Care Partner Information Sheet for Aim 2 Interviews	7 Methods	7.3.2 Informed Consent
7	Addendum to Patient ICF – Contact Info	7 Methods	7.3.2 Informed Consent
8	Data Safety Monitoring Plan	8 Trial Administration	8.12 Data Safety Monitoring Plan
9	DSMB Charter	8 Trial Administration	8.12 Data Safety Monitoring Plan

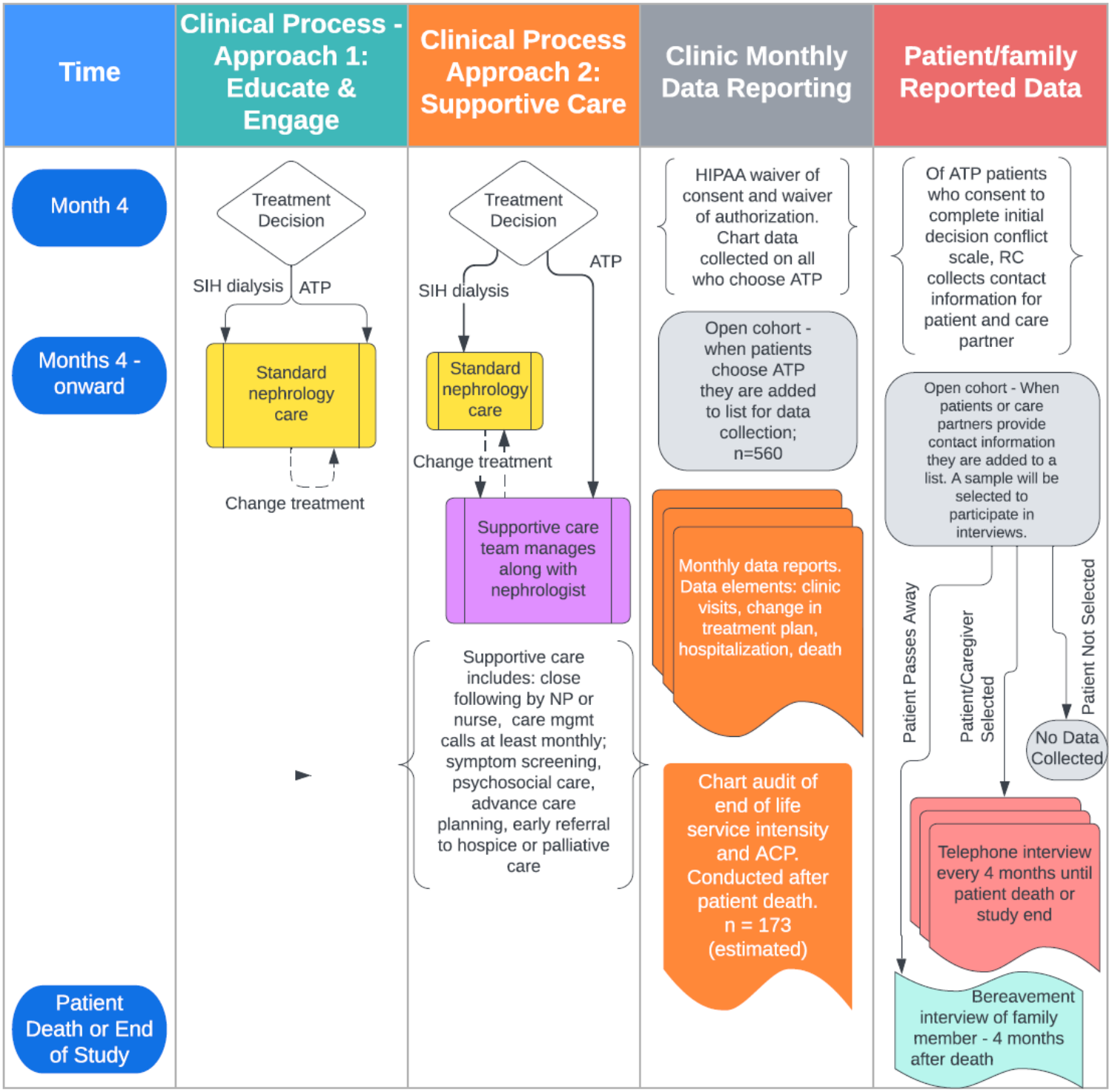
Appendix 1

Flowchart of Study Activities and Outcomes

Aim 1 - Intervention and data collection in stepped wedge randomized trial



Aim 2 - Intervention and data collection in descriptive and qualitative observation of patients who choose ATP or Deciding not to Decide



Key: SIH= Standard in-center or home dialysis; ATP= alternative treatment plans

Appendix 2
ExPAND Adverse Event Reporting

ExPAND Working Instructions:

Adverse Event and Serious Adverse Event Reporting

Version 3.0 – 11/1/2024

- This document must be kept within the Site Investigator File
- Updates will be sent to centers periodically

Amendment History

Version no.	Date issued	Details of changes made
1.0	9/20/2023	
2.0	3/22/2024	Prompt reporting requirement changed from unexpected or related SAE to unexpected and related SAE.
3.0	11/2/2024	Reporting requirement changed from reporting all AEs in REDCap to reporting only AEs **related** to the intervention or research procedures.

1. Safety reporting overview

No serious adverse events related to this minimal risk study are anticipated. However, to be comprehensive in our monitoring of adverse events, we have developed detailed policies and processes for monitoring and reporting adverse events. The key feature is distinguishing between adverse events that may be related to the study interventions from adverse events that are likely to happen in the study population but are unrelated to the study interventions. Local site PI's will assess all serious events and all unexpected events to determine whether or not they are related to study participation.

Due to the nature of advanced CKD and its treatment, especially in multi-morbid frail older people, SAEs would be expected to occur frequently throughout the course of the disease. These expected SAEs include:

- Abnormal electrolyte and hematological laboratory results that can be explained directly or indirectly by their advanced CKD
- Hospital admissions – elective and emergency – that can be explained directly or indirectly by their advanced CKD or comorbidities
- Hospice admissions – planned and emergency – that can be explained directly or indirectly by their advanced CKD or comorbidities
- Infections and cardiovascular events, including fluid overload and swelling, that can be explained directly or indirectly by their advanced CKD or comorbidities
- Commencement of dialysis
- Death that can be explained directly or indirectly by their advanced CKD or comorbidities

Given the high frequency of SAEs expected, the ExPAND trial utilizes the following risk-adapted safety reporting approach.

Prompt Reporting: These AEs must be reported on the AE form to the Principal Investigator within 24 hours of when the site becomes aware of the event:

- SAEs categorized as **causally related** to the intervention or research procedures.
- AEs (whether serious or not) categorized as **unexpected *and* causally related** to the intervention or research procedures.

Other Reporting: These will be regularly reviewed by the study team, the IRB, the Data Safety Monitoring Board, and the sponsor.

- All AEs (whether serious or not) categorized as **causally related** to the intervention or research procedures should be reported in REDCap.

2. Definitions

Adverse Event (AE)

Any untoward medical occurrence in a participant, including occurrences which are not necessarily caused by or related to the intervention or to participation in research. AEs include both physical and psychological harms.

Serious Adverse Event (SAE)

A serious adverse event is any untoward medical occurrence that:

- results in death
- is life-threatening (actually, not hypothetically)
- requires inpatient hospitalization or prolongation of existing hospitalization
- results in persistent or significant disability/incapacity

Other 'important medical events' may also be considered serious if they jeopardize the participant or require an intervention to prevent one of the above consequences.

3. Collection and classification of AE data

Sites are requested to conduct an assessment of whether hospitalizations, deaths, and other AEs are expected and of whether they are causally related to the study procedures or treatment. These assessments need to be conducted by site PI. Guidance on conducting these assessments is provided in the remainder of this document.

Information on AEs and SAEs categorized as **causally related** to the intervention or research procedures should be reported in REDCap. This includes:

- Hospitalizations
- Deaths
- Other AEs

Within REDCap, sites should document their assessment of the event's expectedness and of its relatedness (to the study procedures or treatment).

Related events

Events are related if they resulted from administration of any of the procedures required by the ExPAND protocol. Relationship is described using the following categories:

- Definitely related
- Probably related
- Possibly related
- Unlikely to be related
- Not related

Events that are expected to occur in people with advanced CKD (see below) may be categorized as "Not related" to the research procedures unless there is reason to believe otherwise.

Expected events

Events are expected if they are listed in the protocol (7.2.3) as an expected AE.

Appendix 1 sets out a more detailed breakdown of events that are expected to occur in people with advanced CKD to assist in the classification of whether an event is expected.

This list is not meant to be exhaustive, but rather illustrative of the types of events that are expected. If an event is not listed in Appendix 1, please seek advice from the trial team and principal investigator before a decision is made.

4. What events need prompt reporting as an AE or SAE?

- **Any inpatient stay in hospital or death classified as definitely, probably, or possibly related to the intervention or the research procedures.**
- **Any AE classified as definitely, probably, or possibly related and unexpected.**

All other **research-related** AEs are collected in the REDCap database.

Due to the benign nature of the study, study-related and unexpected SAEs are likely to be rare. An example would be psychological harm or distress related to participation in the trial, for example as a result of decision conflict, resulting in hospitalization or death.

5. Reporting procedures for promptly reportable AEs

- AEs occurring from the time of consent until 30 days after the end of the trial must be reported
- Central trial team must be notified within **24 hours** of site being made aware
- Document the AE in REDCap
- Send an email to the study Principal Investigator and Study Manager notifying them of the event and providing the study ID of the patient.
- **Email (marked URGENT) to: Dale Lupu (dlupu@gwu.edu) and Matthew Ryan (m.ryan@gwu.edu)**
- **Receipt will be confirmed. Please follow up for confirmation if not received.**
- Any change of condition or other follow-up information relating to a previously reported AE should be documented in REDCap as soon as available. Study Principal Investigator and Study Manager should be notified.
- Events must be followed up until the event has resolved or a final outcome has been reached.

Appendix 1. An illustrative list of events that would be considered as expected SAEs due to advanced CKD and common comorbidities

Death or admission to hospital related to:

Cardiac/Cardiovascular	**CKD and Dialysis-Related†**	**Endocrine/Metabolic**
Diagnoses Hypertension Angina Chest pain, MI ruled out Acute myocardial infarction (MI) Cardiac arrest/sudden death Congestive heart failure Cardiomyopathy Valvular heart disease Atrial fibrillation Other arrhythmia Pericarditis &/or tamponade Hypotension *Procedures* Cardiac catheterization Coronary angioplasty Coronary bypass graft (CABG) Valve repair or replacement Cardioversion Cardiac defibrillator placement Pacemaker placed Pericardial procedure	*Diagnoses* Hyperkalemia Fluid overload PD peritonitis† Peritoneal catheter complication† *Procedures* Extra dialysis treatment† Peritoneal catheter insertion/ removal†	*Diagnoses* Hyperparathyroidism Diabetes complication (e.g., DKA) Thyroid disease Hypercalcemia Hypothyroidism *Procedures* Parathyroidectomy
Eye, Ear, Nose, Throat	**Gastrointestinal**	**Health investigation**
Diagnoses Diabetic retinopathy Cataract Glaucoma Blindness Epistaxis *Procedures* Retinal laser surgery Cataract extraction	*Diagnoses* GI bleed Gastritis/Peptic ulcer disease Gastroenteritis Abdominal pain Diarrhea Bowel obstruction Diverticulitis Malnutrition/cachexia Nausea/vomiting Other *Procedures* OGD (upper GI endoscopy) ERCP Colonoscopy Gastric surgery Hernia repair Colectomy/colon surgery Appendectomy Parenteral nutrition	*Procedures* Diagnostic Tests unrelated to the HD/ HDF process
Hematologic	**Infectious Diseases**	**Liver, Biliary, Pancreas**
Diagnoses Anemia	*Diagnoses* Pneumonia	*Diagnoses* Viral hepatitis

Procedures Blood transfusion Bone marrow biopsy	Septicemia Endocarditis AIDS/HIV Urinary Tract Infection Wound Infection Abscess Meningitis Cellulitis/soft tissue infection Osteomyelitis Viral infection Fungal infection Fever or chills, source unknown *Procedures* Abscess Drainage	Liver Failure Ascites Pancreatitis Gall bladder disease *Procedures* Liver biopsy Liver surgery Gall bladder surgery Pancreas surgery
Musculoskeletal *Diagnoses* Carpal tunnel syndrome Dialysis amyloidosis (B2-microglobulin deposition) Infectious arthritis *Procedures* Carpal tunnel release (surgical)	**Neoplastic/Cancer** *Diagnoses* Benign tumor Cancer, non-metastatic Cancer, metastatic Multiple myeloma Lymphoma/leukemia *Procedures* Surgical resection Chemotherapy Radiation therapy	**Neurologic/Cerebrovascular** *Diagnoses* Seizure Dementia Mental status change/ confusion TIA Stroke (CVA) – hemorrhagic Stroke (CVA) – ischemic Stroke (CVA) – type unknown Subdural hematoma *Procedures* Carotid revascularization Carotid endarterectomy Evacuation of hematoma
Obstetric/Gynecologic/Breast *Diagnoses* Abnormal bleeding Breast disease Other *Procedures* Breast Biopsy Hysterectomy	**Orthopedic** *Diagnoses* Hip Fracture Other fracture Herniated intervertebral disk Other *Procedures* Fracture repair Hip replacement Other joint replacement	**Psychiatric/Mental Health** *Diagnoses* Depression * Suicide attempt * anxiety disorder * Alcohol abuse Substance abuse Psychosis
Pulmonary *Diagnoses* Chronic Obstructive Pulmonary Disease Asthma Bronchitis Pneumonia Hemoptysis Pleural effusion Pulmonary oedema Respiratory Failure/ Arrest Shortness of breath	**Skin** *Diagnoses* Psoriasis Cellulitis/Skin infection Calciphylaxis Rash	**Social/Rehabilitation** *Diagnoses* Placement issues Failure to thrive Fall Rehabilitation Hospice/palliative care

Pulmonary embolism *Procedures* Ventilator-assisted breathing Bronchoscopy Thoracentesis		
Transplant-Related *Diagnoses* Transplant evaluation Other *Procedures* Kidney transplant Transplant nephrectomy	**Trauma/Injury** *Diagnoses* Death Other *Procedures* Laparotomy Skin graft	**Urologic** *Diagnoses* Hematuria Renal cysts Kidney stone Other *Procedures* Cystoscopy Prostate surgery Nephrectomy
Vascular *Diagnoses* Claudication/Rest pain Ulcer of extremity Gangrene Aortic aneurysm Deep vein thrombosis Other *Procedures* Angiogram Arterial bypass surgery Amputation Aortic aneurysm repair Wound debridement	**Vascular Access** *Diagnoses* Clotted access† Infected access† Aneurysm† Failing access† Access bleeding† Other *Procedures* Salvage procedure† Revision procedure† New access creation† Access removal† Catheter placement†	
Other/Miscellaneous *Diagnoses* Drug reaction/allergy		

* Unless thought to be related to participation in the trial.

† Dialysis related

Appendix 3

Informed Consent Form for Patient DCS Survey

Informed Consent for Participation in a Research Study

For Patients

Sponsor / Study Title:	**Patient-Centered Outcomes Research Institute (PCORI) / "Expanding and Promoting Alternative Care and Knowledge in Decision-Making: The ExPAND Study (Improving Shared Decision-Making and Access to Non-Dialytic Treatment for People with Kidney Disease)"**
Principal Investigator:	**«PiFullName»**
Telephone:	**«IcfPhoneNumber»**
Address:	**«PiLocations»**

Key Information

We invite you to take part in a research study. About 20-30 kidney care offices across the United States are taking part. Around 3000 participants are expected to be enrolled. The purpose of this study is to find better ways for providers and patients with kidney disease to make decisions about treatment. As part of this study, our office is enhancing discussions about options for treating advanced kidney disease. To help us learn how patients feel about these enhanced discussions, we invite you to complete three short surveys, one now and two later. The surveys ask how clear you are about your treatment choices, how you feel about your decision, and your conversations with your provider. The total amount of time you will spend is about 30-45 minutes over the next nine months. Taking part in these surveys is voluntary, which means it is your choice. Your treatment will be the same either way.

The main reason you might choose to volunteer for these surveys is to help us learn how to provide better care for people with chronic kidney disease.

The reasons you might choose not to take part are you might by too busy, or you might feel uncomfortable answering the survey questions. You may skip any questions you do not want to answer. We will make every effort to keep your information confidential, but we cannot guarantee this. Later in this form, we describe the ways we keep your information safe.

You can get more information about this study by contacting the study investigator using the contact information on the first page of this form.

What is this study about?
The purpose of this research program is to find better ways for kidney care providers and patients to make healthcare decisions together. We want to know how to explain all of the treatments so that patients can make decisions based on what is most important to them.

Patients have choices about what to do when their kidneys are no longer working well. The offices in this study are training their staff members in better ways to help all patients make these choices. The staff members are learning:

- To give information about all the choices.
- To ask patients about what is important to them.
- To support patients in the choices they make.

If you take part in the surveys, you will:

- Take a short survey today about your decision about your future kidney treatment and your conversations with your provider. The survey will take about 10-20 minutes.
- Take the survey again in about 4 months. You can choose to do this follow-up survey in person, on the telephone, or online.
- Take the survey again about 9 months from now. Again, you can choose how you want to take the survey.

The total amount of time you will spend on these surveys is about 30-45 minutes. You may skip any of the survey questions, and you may stop taking part in this study at any time.

We will gather some limited and de-identified information about your health and the healthcare services you receive from the kidney office's electronic medical record. This shortens the time you would need to spend taking the survey because we can get some basic information from the medical record (such as your age, sex, whether you have been in the hospital recently, and when you last visited your kidney doctor) rather than asking you additional questions.

What are the costs?
There will be no charge to you for your participation in this study.

Will I get paid for taking part?
«Compensation»

You will receive payments after the second and third short surveys as a thank you. After the second survey, the payment will be $50. After the third survey, the payment will be $25. The total amount you will receive is $75.

The research team will use a system called Advarra (formerly known as FORTE) Participant Payments to manage payments to research participants. The system offers 3 payment options:

1. Reloadable debit/credit card. With this option, funds are available on the same business day. There may be some restrictions on the use of the card. You can see these in the cardholder agreement.
2. Electronic deposit into your bank account. If you choose this method, we will email you a link where you will provide your bank account information. If all the information is provided correctly, the funds are available within 3 business days.
3. Paper check mailed to you. If you choose this method, we will email you a link where you will provide your mailing address. If all your

information is entered correctly, a paper check takes 3 days to process plus delivery time.

All three options require the collection of your name and date of birth. If you choose payment option 2 or 3, you will need to provide your email address to the research team.

If you choose a reloadable card, Advarra Participant Payments may share information about the card or the purchases you make. They would only do this for the reasons below:

- Where it is needed for completing transactions,
- To verify the existence and condition of the card for a third party, such as a merchant,
- To follow government agency, court order, or other legal or administrative reporting requirements,
- If you consent by giving us your written permission,
- To our employees, auditors, affiliates, service providers, or attorneys as needed, or
- To fulfill our obligations under the card holder agreement (provided separately).

What are the risks of taking part?
You might feel uncomfortable answering the survey questions. You may skip any questions you do not want to answer. We will make every effort to keep your information confidential, but we cannot guarantee this. Later in this form, we describe the ways we keep your information safe.

What are the benefits of taking part?
It is possible that answering the survey questions might help you think about your decision. You may also learn more about kidney disease. We hope that other people with kidney disease will benefit in the future. This could happen if kidney care teams learn better ways of helping patients make decisions based on what is important to them in their care.

Will my answers be kept private?
Only the research team or people who are required to review the study will have access to your information. Your kidney care team will not see your answers.

We will keep your information on a secure, password protected computer. Any personally identifiable information collected will be coded using a unique study ID. The coded lists are only accessible to the research coordinator at your kidney doctor's office. The information that has your personally identifiable information will be kept separately from the rest of your data.

After this study, we would like to do a follow-up study to see how you are doing after the end of this study. We may keep your information for the follow-up study. At the end of the follow-up study, or sooner if no follow-up study is done, we will remove any information that could be used to identify you. Then, your de-identified study data may be shared on data repositories for future research studies. While every effort will be made to protect the confidentiality of your information, absolute confidentiality cannot be guaranteed.

How will the findings of this study be shared?
A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

We plan to report the findings of this research study in journals and at scientific meetings. It can take several years to publish the final results. You will not be named or identified.

During the study, we plan to send you a newsletter about how the study is going. These may come out once or twice a year. At the end of the study, we will provide you a summary of the main findings. Later in this form, you can tell us whether you want to receive this information.

Whom to contact about this study
During the study, if you have questions, concerns or complaints about the study such as:

- Payment or compensation for being in the study, if any;
- Your responsibilities as a research participant;
- Eligibility to participate in the study;
- The Investigator's or study site's decision to withdraw you from participation;

Please contact the Investigator at the telephone number listed on the first page of this consent document.

An institutional review board (IRB) is an independent committee established to help protect the rights of research participants. If you have any questions about your rights as a research participant, contact:

- By **mail**:
  Study Subject Adviser
  Advarra IRB
  6100 Merriweather Dr., Suite 600
  Columbia, MD 21044
- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00078064.

New findings
Any new important information that is discovered during the study and which may influence your willingness to continue participation in the study will be provided to you.

Alternatives to participation
This research study is for research purposes only. The only alternative is to not participate in this study.

Voluntary participation / Withdrawal
Your decision to participate in this study is voluntary. You may choose to not participate or you may withdraw from the study for any reason without penalty or loss of benefits to which you are otherwise entitled and without any effect on your future medical care. However, please note that any information collected up to the point of your withdrawal will not be removed from the study.

The Investigator or the sponsor can stop your participation at any time without your consent for the following reasons:

- If you fail to follow directions for participating in the study;
- If it is discovered that you do not meet the study requirements;
- If the study is canceled; or
- For administrative reasons.

Signature
By signing below, you agree that the above information has been explained to you and you have had the chance to ask questions. Your signature documents your permission to take part in this research.

_____
Printed name of participant

_____ _____
Signature of participant Date

Check one payment method:
☐ Reloadable debit/credit card
☐ Electronic deposit into my bank account
☐ Paper check delivered by US mail

Check one:
☐ I do not want to receive newsletters and other information about the study.

☐ I give my permission for you to send me emails with newsletters and other information about the study.

_____ _____
Signature of participant Date

WITNESS SIGNATURE FOR SUBJECTS WHO CANNOT READ
The study participant has indicated that he/she is unable to read. The consent document has been read to the participant by a member of the study staff, discussed with the participant by a member of the study staff, and the participant has been given an opportunity to ask questions of the study staff.

_____
Printed Name of Impartial Witness

_____ _____
Signature of Impartial Witness Date

Please keep a copy of this form in case you want to read it again.

Appendix 4

Recruitment Letter/Email to Patients for DCS Survey

Dear _____

At <clinic name>, we always look for ways to improve our care. Research is one way we do this. We have joined with a team of researchers for a study. It is called ExPAND. This letter is to tell you about it.

We are testing ways to talk about treatments for kidney disease. We want patients to understand all their choices. Also, we want to listen to what matters most to patients. The goal is to help patients make decisions they feel good about.

We invite you to be a part of this study. We ask you to take a short survey now and two more times over the next few months. Each survey takes about 10-20 minutes. They are about the decision for the type of treatment you want for kidney disease. We will pay you $75 for the three surveys.

We have attached a form to this <letter/email>. We encourage you to read it. Please think about whether you would like to take part. You may want to discuss it with family or friends. If you have questions, we will be happy to answer them. Call or email <RC name> at <phone number> or <email address>.

What will happen next?

The research coordinator will call you. <She/he> will answer any questions you have. If you would like to take part, <she/he> will ask you how you want to answer the survey questions. You can answer them on the phone. Or <she/he> can send you an email link. You can click on the link and answer the questions.

You do not have to take part in ExPAND. You will receive the same care either way. If you do not want the research coordinator to call you, let us know. You can call our office <phone number> or reply to this email.

Thank you for reading about the ExPAND study. It is our pleasure to provide your kidney care.

Sincerely,

<signature>

Appendix 5

eConsent REDCap Script

Informed Consent for Participation in a Research Study

This form gives you important information you need to know about the ExPAND study before you decide if you want to take part. The research coordinator will talk to you about the study and answer all of your questions.

We encourage you to discuss this study with your family and anyone else you trust before making your decision. It's important that you have as much information as you need and that all your questions are answered.

This is a placeholder for the content of the informed consent for participation in a research study for patients.

The electronic ICF(s) will be a complete and exact copy of the current, site-specific, IRB approved study consent document(s) and will be updated to match IRB-approved revisions.

Signature

By signing below, you agree that the above information has been explained to you and you have had the chance to ask questions. Your signature documents your permission to take part in this research.

First name of adult participant

_____

Last name of the adult participant

_____

Check one payment method:

- ◯ Reloadable debit/credit card
- ◯ Electronic deposit into my bank account
- ◯ Paper check delivered by US mail

Enter email address:

_____

Advarra will send you an email at this address to set up payment.

Do you want to receive newsletters about the study? other Check one:

- ◯ I do not want to receive newsletters and information about the study.
- ◯ I give my permission for you to send me emails with newsletters and other information about the study.

Please enter the identification code provided to you by the research coordinator:

_____

Electronic signature of participant

Please type your full name:

_____

(For example, Mary Smith)

Date and time of signature

_____

(Click the 'NOW' button to enter the time and date automatically)

AFFIDAVIT OF PERSON OBTAINING CONSENT:

I certify that I have explained to the above individual the nature and purpose of the study, possible risks, and potential benefits associated with participation in this study.

I have answered any questions that have been raised.

Name of the person obtaining consent:

- ◯
- ◯ _____

CKD clinic (office) where patient seen:

Clinic A
Clinic B

Electronic signature of the person obtaining consent. Please type your full name in the box to the right.

Date and time of signature:

(Click the 'NOW' button to enter the time and date automatically)

Appendix 6

Patient and Care Partner Information Sheet
for Aim 2 Interviews

Information Sheet for Patient and Care Partner Interviews

Thank you for being a part of the ExPAND research study!

We are trying to improve the way providers support patients in making healthcare decisions.

As part of the study, we would like to interview a small group of patients and their care partners. A care partner is a close friend or family member who is involved with the patient's healthcare. It may be the person who brings the patient to the clinic. We want to learn how patients and care partners feel about the healthcare they have received.

With your permission, we would like to provide your contact information to interviewers from the ExPAND Research Team. If you are selected, they will contact you to tell you more.

What is the purpose of the interviews?

We want to learn about the experiences of patients who choose a treatment plan that is not standard dialysis. We also want to learn about the experiences of the people who are close to them. The treatment plan could be active medical care (conservative care). It could also be a time-limited trial or waiting a while to decide. We want to understand patient and care partner views and experiences of health and healthcare after the treatment decision.

Will we interview everyone?

No. The study will last about 4 years. We expect over 500 patients to choose an alternative treatment plan. We will interview about 40 patients and about 35 care partners.

How will we choose people to interview?

We will invite a few people from each of the kidney care practices in the study. We will choose people of different ethnicities and cultural backgrounds. We want all the patients and care partners in the study to be represented.

Why are we interviewing care partners?

Care partners are closely involved in the patient's healthcare. We want to learn how they are affected by the patient's experience. If a patient passes away during the study, we would like to talk to their care partners about how things went at the end of life and how they are doing now.

What if a patient doesn't have a care partner? Or if their care partner does not want to give permission?

We will interview some patients without care partners. We will also interview some care partners without patients. Patients and care partners can each choose whether to share their own contact information.

What will the interviews be like?

The interviewers will talk to participants on the phone. Some people will be asked to take part in a single interview. Others will be invited to take part in a few interviews. Each interview will last about 40 minutes. The questions will be about the health and healthcare experiences of the patient and the care partner.

How much will people be paid for taking part?

Patients and care partners will receive $50 for each interview.

If you are selected, when will you be contacted?

You may be contacted at any time during the study. The study will last for about 4 years.

If you are selected, do you have to take part?

No. If you are selected to take part, the interviewers will contact you. They will provide more information. Then you can choose whether you want to take part.

Appendix 7

Addendum to Patient ICF – Contact Info

INFORMED CONSENT FORM ADDENDUM

PERMISSION TO SHARE CONTACT INFORMATION

Sponsor / Study Title:	**Sponsor Name / "Protocol Title"**
Protocol Number:	**Protocol Number**
Principal Investigator: (Study Doctor)	**«PiFullName»**
Telephone:	**«IcfPhoneNumber»**
Address:	**«PiLocations»**

Purpose of this Addendum.
When you joined this research study, you signed an Informed Consent Form. You agreed to take a series of three short surveys. This addendum contains information about an extra study activity. We would like to interview a small group of patients and their care partners. We want to learn about their healthcare experiences over time.

Please read this form carefully. Ask the study staff as many questions as you would like. They can explain words or information you do not understand. Everything in the consent form you signed before still applies to this study.

We are not asking you to take part in the new study activity right now. We are just asking for your permission to share your contact information. If you give us permission, we will share it with the interviewers. The interviewers are from the ExPAND Research Team. If you are selected to take part, they will contact you and provide more information.

New Study Activity.
We would like to interview a small group of patients and their care partners. We want to learn about their healthcare experiences over time. The interviewers are from the ExPAND Research Team. We are asking for your permission to share your contact information with them. If you do, they may contact you later to provide more information.

What is the purpose of the interviews?
We want to learn about the experiences of patients who choose a treatment plan that is not standard dialysis. We also want to learn about the experiences of the people who

are close to them. The treatment plan could be active medical care (conservative care). It could also be a time-limited trial or waiting a while to decide. We want to understand patient and care partner views and experiences of health and healthcare after the treatment decision.

Will we interview everyone?
No. The study will last about 4 years. We expect over 500 patients to choose an alternative treatment plan. We will interview about 40 patients and about 35 care partners.

Why are we interviewing care partners?
Care partners are closely involved in the patient's healthcare. We want to learn how they are affected by the patient's experience. If a patient passes away during the study, we would like to talk to their care partners about how things went at the end of life and how they are doing now.

What if a patient doesn't have a care partner? Or if their care partner does not want to give permission?
We will interview some patients without care partners. We will also interview some care partners without patients. Patients and care partners can each choose whether to share their own contact information.

If you are selected, when will you be contacted?
You may be contacted at any time during the study. The study will last for about 4 years.

If you are selected, do you have to take part?
No. If you are selected to take part, the interviewers will contact you. They will provide more information. Then you can choose whether you want to take part.

Whom to contact about this study
During the study, if you have questions, concerns, or complaints about the study such as:

- Payment or compensation for being in the study, if any;
- Your responsibilities as a research participant;
- Eligibility to participate in the study;
- The Investigator's or study site's decision to withdraw you from participation;

Please contact the Investigator at the telephone number listed on the first page of this document.

An institutional review board (IRB) is an independent committee established to help protect the rights of research participants. If you have any questions about your rights as a research participant, contact:

- By **mail**:
  Study Subject Adviser
  Advarra IRB
  6100 Merriweather Dr., Suite 600
  Columbia, MD 21044
- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00078064.

CONTACT INFORMATION FOR PATIENT

If you are selected to take part in the study, interviewers from the ExPAND Research Teamwill use the information you provide below to contact you. They will only use the information to schedule and conduct the interviews and to send reminders about the interviews. They will not share the information with anyone else.

How may they contact you? Check all the apply:

☐ Home address: _____

_____

☐ Email address: _____

☐ Phone number: _____

May they send text messages for reminders and to identify themselves before they call?
☐ Yes ☐ No Phone number for text messages: _____

May they leave voice messages?
☐ No messages ☐ Short messages ☐ Messages including private information

Best times to call: _____

_____

_____

PATIENT ASSENT STATEMENT

I have read this Addendum, and its contents have been explained. I give permission for my contact information to be shared for the purposes listed above. I understand that I may or may not be contacted at some point during the study. If I am contacted, I can decide whether I want to take part in interviews at that time. I will receive a signed copy of this Addendum for my records.

I am not giving up any of my legal rights by signing this form. Nothing in this form is intended to change applicable federal, state, or local laws.

_____ ____/____/____

Signature of Research Subject Date

_____

Printed Name of Research Subject

CONTACT INFORMATION FOR CARE PARTNER

If you are selected to take part in the study, interviewers from the ExPAND Research Team will use the information you provide below to contact you. They will only use the information to schedule and conduct the interviews and to send reminders about the interviews. They will not share the information with anyone else.

Name of care partner: _____

Relationship to patient: _____

How may they contact you? Check all the apply:

☐ Home address: _____

_____

☐ Email address: _____

☐ Phone number: _____

May they send text messages for reminders and to identify themselves before they call?
☐ Yes ☐ No Phone number for text messages: _____

May they leave voice messages?
☐ No messages ☐ Short messages ☐ Messages including private information

Best times to call:-

_____
_____
_____

CARE PARTNER ASSENT STATEMENT

I have read this Addendum, and its contents have been explained. I give permission for my contact information to be shared for the purposes listed above. I understand that I may or may not be contacted at some point during the study. If I am contacted, I can decide whether I want to take part in interviews at that time. I will receive a signed copy of this Addendum for my records.

I am not giving up any of my legal rights by signing this form. Nothing in this form is intended to change applicable federal, state, or local laws.

_____ ____/____/____
Signature of Care Partner Date

_____
Printed Name of Care Partner

Appendix 8

Data Safety Monitoring Plan

Data Safety and Monitoring Plan

Study Title: Improving Shared Decision-Making and Access to Non-Dialytic Treatment for People with Kidney Disease (the ExPAND study)

Sponsor: Patient-Centered Outcomes Research Institute (PCORI)

Contract Number: IHS-2022C2-2678

Principal Investigator: Dale E. Lupu, PhD, MPH, Alvin H. Moss, MD, FACP, FAAHPM

Site Investigator: Dale E. Lupu, PhD, MPH

Institutions: George Washington University, West Virginia University

Version 2 – 11-01-24
Submitted to PCORI for Approval
Approved by the DSMB

Brief Description of Interventions

The interventions being studied are Approach 1: Educate and Engage and Approach 2: Educate and Engage + Kidney Supportive Care in older patients with advanced chronic kidney disease. Approach 1 provides kidney disease education covering both dialysis and non-dialysis options in an unbiased way using a shared decision-making (SDM) approach and patient decision aids while Approach 2 includes these as well as the creation of a kidney supportive care program for patients who choose alternative (non-dialysis) treatment plans (ATPs).

Specific Aims

Aim 1. Compare the effectiveness of two approaches: 1) improved kidney disease education (KDE) and SDM or 2) improved KDE and SDM plus the creation of a kidney supportive care program in a) increasing proportion of patients choosing ATP and b) reducing patient decisional conflict.

Aim 2. Compare the patient and family/care partner experience of an ATP between Approach 1 and Approach 2, with particular emphasis on TLT and AMCWD in terms of quality of life, services used, and end-of-life experience through medical record review and interviews with a sample of bereaved family members/care partners. Aim 2a will focus on experience while patients are receiving an ATP (several months to several years). Aim 2b will describe the end-of-life experience.

Aim 3. In order to evaluate implementation of each intervention (Approaches 1 and 2), the ExPAND research team will cooperate with a separate tandem evaluation conducted by an independent evaluation team based at NORC. The implementation evaluation is a mixed-methods design based on the expanded Reach, Effectiveness, Adoption, Implementation, Maintenance (RE-AIM) framework. The implementation evaluation will consist of staff surveys, interviews, and site visits conducted by the NORC evaluation team. Regulatory oversight of AIM 3 will be handled by the NORC IRB.

Brief Description of Project Design

This will be a repeated cross-sectional stepped wedge cluster-randomized trial (SW-CRT) with randomization at the nephrology clinic level. Twenty-five clinics will be randomly assigned to one of three sequences. Each sequence consists of four 10-month time periods during which patients are accrued and followed for study outcomes. To minimize contamination in the primary analysis, we will exclude patients recruited during the 4 months before each sequence moves to

Approach 2. These patients will be included in a sensitivity analysis. In the 4th study period, accrual of new patients will stop at 10 months, allowing a closing 4-month follow-up period to collect primary outcomes at the end of the study.. All practices begin by implementing Approach 1 (Educate and Engage). Practices then "step" into Approach 2 (Kidney Supportive Care Program) at the assigned time based on their sequence. We have prepared for 15% drop-out of sites, leaving 21 sites in the final analysis sample. We expect to recruit approximately 2800 patients (1400 under Approach 1 and 1400 under Approach 2). Patients at least 65 years and with eGFR recently having dropped below 30 will be included in the study.

We will also recruit 35 family members/care partners of patients who chose ATP to be interviewed about their experiences.

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1.0 PARTICIPANTS SAFETY

This study includes three types of participants: *patient* participants, *care partner* participants, and nephrology *clinic employee participants*. Any mention of medical information below only applies to the *patient* participants. Caregiver participants and clinic employee participants are not the target of the intervention, and the study team will not be collecting any sensitive information about them.

1.1. Potential Risks and Benefits for Participants

1.1.1. Potential risk and protections against risks

Patients: Because this study is implementing recommended best practices in the care of older patients with advanced chronic kidney disease, there are no anticipated major risks associated with it. Clinicians will employ recommended communication approaches and ask for permission to provide information about the patient's kidney disease and possible treatment options before doing so. Nonetheless, some patients might experience distress once informed that they have advanced chronic kidney disease if they were not previously aware of it. This distress is comparable to that experienced by patients in routine clinical practice who receive bad news. This study may differ from standard care in that patients might become better informed and more aware of the range of treatment options they have. Also, in taking the Decisional Conflict Scale and other surveys, they might realize more clearly that they don't know 1) what are the benefits of treatment that matter most to them, 2) what risks and side effects are most troublesome to them, and 3) overall, what treatment option is best for them. Interviewers will be trained to watch for indications of emotional distress and will be trained in how to respond calmly and empathetically. If the situation persists or worsens, the interview will be terminated, and the incident will be reported within 24 hours to the patient's treating clinician, who will develop a plan for supporting the patient including referral for further mental health services, as indicated.

Care partners and clinic employees: The main risk to these participants is loss of confidentiality of research data. Specific steps to minimize these risks are described below.

Before data collection starts, all study personnel will be required to undertake appropriate Collaborative Institutional Training Initiative (CITI) coursework, including Human Subjects Research and Health Information Privacy and Security training. All staff will complete an IRB approved training program developed by the study PIs. This training will include modules covering: (1) study overview, (2) recruitment procedures, (3) study arm procedures, (4) collection and management of study data, and (5) adverse event reporting and managing emergencies. The trial will be registered on ClinicalTrials.gov and the George Washington University (GWU) IRB will be the IRB of record. Participant recruitment will begin at each site only after that site's clinical trials office (or equivalent) has approved the study materials containing IRB-approved protocol, surveys, and data collection instruments. The following sections provide a detailed overview of our specific efforts to minimize risks including risks to privacy and confidentiality:

1) The majority of patient and care partner participant information collected for this project will be stored in a GW REDCap database, GW Box, or other GWU platform approved for regulated data. An additional copy of the site-specific study data may be housed securely at each participating site.
2) Patient chart data collected from the EMR under a HIPAA waiver of consent will only be shared with CITI-trained researchers from GWU, and will be stored securely at GWU as described above.
3) All enrolled patients will be assigned a unique study identification number. All data collected will be identified only by these study identification numbers. This will minimize risks regarding breach of confidentiality with respect to the study data. A site-specific link between each study identification number and participant name will be kept in a password-protected file on a password-protected computer at each participating site.
4) Before any patient is invited to participate in surveys or interviews, the patient's treating nephrologist or advance practitioner will have the opportunity to opt-out the patient. Reasons for exclusion include insufficient decision-making capacity, lack of proficiency with English or Spanish language, anticipated loss to follow-up, or if otherwise contra-indicated for the patient's health. The research assistant may also opt-out a patient if similar information is available in the EMR.
5) Printed forms with identifiable participant data, e.g., signed consent forms, will be stored in separate file folders in locked filing cabinets at each clinic site.
6) No medical records or protected health information (collected for the patient participants only) shall be re-disclosed, unless required by law.
7) After completion of the study, the completely deidentified research data from this project will be deposited with the digital repository, the Patient-Centered Outcomes Data Repository (PCODR), of the Inter-university Consortium for Political and Social Research (ICPSR), University of Michigan to ensure that the research community has long-term access to the data. This is required by PCORI and included in consent forms.

Avoiding undue influence or coercion in recruitment**:**

Patients and care partners: Information from the electronic medical record (EMR) will be collected on all eligible patients with a HIPAA waiver of consent. Participation in surveys and interviews is voluntary. Patients, family members, and care partners will be informed that participation is voluntary and that all patients, regardless of their participation status, will continue to receive standard care. They will be informed that they may stop participating at any time without penalty. Research staff will not provide final lists of participants to the nephrology center providers or staff. Therefore, in general, the people delivering patient care will not be aware of whether an individual patient or care partner participated.

Clinic employees: The intervention is at the clinic level, and supervisors at each clinic will decide which employees will be asked to attend training and participate in implementation. Participation in the evaluation of the training is voluntary. Participants will be informed that their employment will not be affected in any way by their participation status and that they may stop participating at any time without penalty. In summary reports to sites, participants will not be identified; however, due to the small sample sizes, it is possible that participant identities may be inferred in some cases.

1.1.2. Potential benefits

Because this study mirrors recommended best clinical practices such as the use of shared decision-making, patient decision aids, and kidney supportive care to address unmet palliative care needs in the population of older patients with advanced chronic kidney disease, the investigators believe that there will be significant benefits for the participants. These include being aware that they have a choice about treatment to make, being fully informed of all treatment options, participating as a co-equal in treatment decisions and the development of a treatment plan, being offered the opportunity to participate in advance care planning, being routinely assessed for symptoms and being treated for them, and being referred to palliative care and/or hospice in a timely manner as appropriate.

2.0 ADVERSE EVENT AND SERIOUS ADVERSE EVENT COLLECTION AND REPORTING

No serious adverse events related to this minimal risk study are anticipated. However, to be comprehensive in our monitoring of adverse events, we have developed detailed policies and processes for monitoring and reporting adverse events. The key feature is distinguishing

between adverse events that may be related to the study interventions from adverse events that are likely to happen in the study population but are unrelated to the study interventions. Local site PI's will assess all serious events and all unexpected events to determine whether or not they are related to study participation. Specific reporting timetables for reporting events are detailed in the appendix.

2.1. AE/SAE definitions and expected events

Adverse Event (AE): Any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign, symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research (modified from the definition of adverse events in the 1996 International Conference on Harmonization E-6 Guidelines for Good Clinical Practice). AEs encompass both physical and psychological harms. AEs are assessed in terms of seriousness, expectedness, and relatedness.

Serious Adverse Event (SAE): An AE that meets any of the following conditions:

- results in death
- is life-threatening (actually, not hypothetically)
- requires inpatient hospitalization or prolongation of existing hospitalization
- results in persistent or significant disability/incapacity
- Other 'important medical events' may also be considered serious if they jeopardize the participant or require an intervention to prevent one of the above consequences.

Related Adverse Event: An AE is "possibly related" to the research procedures if, in the opinion of the investigator, the research procedures may have caused the harm.

Unexpected Adverse Event: An AE is "unexpected" when its nature, severity or frequency is inconsistent with risk information previously reviewed and approved by the IRB in the context of the study population.

Expected SAEs: Due to the nature of advanced CKD and its treatment, especially in multi-morbid frail older people, SAEs would be expected to occur frequently throughout the course of the disease. These expected SAEs include:

- Abnormal electrolyte and hematological laboratory results that can be explained directly or indirectly by their advanced CKD or comorbidities
- Hospital admissions — elective and emergency — that can be explained directly or indirectly by their advanced CKD or comorbidities
- Hospice admissions — planned and emergency — that can be explained directly or indirectly by their advanced CKD or comorbidities
- Infections and cardiovascular events including fluid overload and swelling that can be explained directly or indirectly by their advanced CKD or comorbidities
- Commencement of dialysis
- Death that can be explained directly or indirectly by their advanced CKD or comorbidities

Expected study-related AEs: Because of the nature of this minimal risk study, no physical harms are expected. It is possible that patients might suffer psychological distress. Some patients may become emotionally upset when thinking about their disease progression or the decisions they are making about their treatment. In standard CKD patient care, patients also need to make decisions about what treatment they want. This study may differ from standard care in that patients might become better informed and more aware of the range of treatment options they have. Also, in taking the Decisional Conflict Scale and other surveys, they might realize more clearly that they don't know 1) what are the benefits of treatment that matter most to them, 2) what risks and side effects are most troublesome to them, and 3) overall, what treatment option is best for them. Interviewers will be trained to watch for indications of emotional distress and will be trained in how to respond (see 7.1.5 of the study protocol).

2.2. AE/SAE Documentation and Reporting

Detailed guidance will be provided to the Site Principal Investigator and research coordinator about AE/SAE reporting (see Appendix 2). **The Site Principal Investigator will assess the severity, expectedness, and relatedness of the AE, which will be reported accordingly**.

Prompt reporting: The Site Principal Investigator will report the following events to the study Principal Investigator within 24 hours of becoming aware of the event. The study Principal Investigator will report the AE to the Institutional Review Board (IRB) within 48 hours of becoming aware of the event.

- SAEs that are **causally related** to the research procedures
- AEs, including SAEs, that are both **unexpected and causally related** to the research

Other reporting: All adverse events categorized as **related** to the research procedures will be recorded in Research Electronic Data Capture (REDCap) by the research coordinator (date, description, severity, expectedness, relatedness, and management/remediation of AE). The central data management team will assemble a list and summary of AEs, which will be reported to the IRB, DSMB, study sponsor, and site principal investigators as part of periodic reporting.

3.0 DATA AND SAFETY MONITORING

Data quality: The site research coordinator, under the supervision of the site PI, is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported. Participant tracking and survey data will be entered directly into electronic case report forms in REDCap, and clinical data will be entered directly from the source documents (EMR) into REDCap. REDCap includes password protection and internal quality checks, such as automatic range checks, to identify data that appear inconsistent, incomplete, or inaccurate. Data will be regularly monitored by the data management team using human assessment as well as customized software to check for missing, improperly formed, or implausible data in the context of the study. Data quality reports will be sent regularly to the data collection personnel at the clinical sites, who will work with the data management team to correct missing and erroneous data.

The study will empanel a Data and Safety Monitoring Board (DSMB) to act in an advisory capacity to the PIs and to evaluate the progress of the study, including periodic assessments of data quality and timeliness, participant recruitment, accrual and retention, participant risk versus benefit, performance of trial sites, and other factors that can affect study outcomes. The DSMB will make recommendations to the PIs concerning the continuation, modification, or conclusion of the trial.

3.1. Frequency of Data and Safety Monitoring

A Data and Safety Monitoring Board (DSMB) will be appointed to provide additional oversight of the trial and will meet prior to recruitment to review the study protocol and at the end of data collection. The PIs will attend these meetings, with minutes and any recommendations documented. The DSMB will consist of nine members, including geriatric nephrologists, a health equity specialist, biostatisticians, a CKD patient, a CKD patient's family member, a nurse practitioner, and an ethicist. A DSMB Charter for the study will be developed by the study team and approved by the DSMB members. The DSMB will then meet by Zoom to review study progress at minimum, every 12 months throughout the project. The DSMB will review enrollment and attrition rates and advise the PIs on any potential risks as well as on any risk mitigation plans. The DSMB recommendations will be discussed with the PIs. All data will be reviewed for

protocol adherence, including a data verification check that the appropriate outcome measures are given at the appropriate time points.

APPENDICES

EXPAND
Expanding and Promoting Alternative Care and Knowledge in Decision-making
Expanding choice for people with kidney disease

Appendix 1. Adverse Event Log

Adverse Event Type	Relatedness to Study Intervention Relationship	Expected	SAE	Outcome of Event
1. Emergency room visit 2. Hospital admission 3. Other medical emergency 4. Other medical event (non-emergency) 5. Psychological 6. Death 7. Hospice admission 8. Other	1 = Definitely related 2 = Possibly related 3 = Not related	1 = Yes 2 = No	1 = Yes 2 = No	1 = Resolved, 2 = AE still present- no treatment 3 = AE still present- being treated 4 = Unknown 5 = Death 6 = Other

Participant Study ID	Age	Sex	Adverse Event (Description)	Adverse Event Type	Start Date	Relatedness to Study Intervention	Expected	SAE	Response/ Remediation (Description)	Outcome of Event	PI Initials & Date

Appendix 2. ExPAND Working Instructions: Adverse Event and Serious Adverse Event Reporting

ExPAND Working Instructions:
Adverse Event and Serious Adverse Event Reporting
Version 3.0 – 11/1/2024

- This document must be kept within the Site Investigator File
- Updates will be sent to centers periodically

Amendment History

Version no.	Date issued	Details of changes made
1.0	9/20/2023	
2.0	3/22/2024	Prompt reporting requirement changed from unexpected or related SAE to unexpected and related SAE.
3.0	11/2/2024	Reporting requirement changed from reporting all AEs in REDCap to reporting only AEs **related** to the intervention or research procedures.

6. Safety reporting overview

No serious adverse events related to this minimal risk study are anticipated. However, to be comprehensive in our monitoring of adverse events, we have developed detailed policies and processes for monitoring and reporting adverse events. The key feature is distinguishing between adverse events that may be related to the study interventions from adverse events that are likely to happen in the study population but are unrelated to the study interventions. Local site PI's will assess all serious events and all unexpected events to determine whether or not they are related to study participation.

Due to the nature of advanced CKD and its treatment, especially in multi-morbid frail older people, SAEs would be expected to occur frequently throughout the course of the disease. These expected SAEs include:

- Abnormal electrolyte and hematological laboratory results that can be explained directly or indirectly by their advanced CKD
- Hospital admissions – elective and emergency – that can be explained directly or indirectly by their advanced CKD or comorbidities
- Hospice admissions – planned and emergency – that can be explained directly or indirectly by their advanced CKD or comorbidities
- Infections and cardiovascular events, including fluid overload and swelling, that can be explained directly or indirectly by their advanced CKD or comorbidities
- Commencement of dialysis
- Death that can be explained directly or indirectly by their advanced CKD or comorbidities

Given the high frequency of SAEs expected, the ExPAND trial utilizes the following risk-adapted safety reporting approach.

Prompt Reporting: These AEs must be reported on the AE form to the Principal Investigator within 24 hours of when the site becomes aware of the event:

- SAEs categorized as **causally related** to the intervention or research procedures.
- AEs (whether serious or not) categorized as **unexpected *and* causally related** to the intervention or research procedures.

Other Reporting: These will be regularly reviewed by the study team, the IRB, the Data Safety Monitoring Board, and the sponsor.

- All AEs (whether serious or not) categorized as **causally related** to the intervention or research procedures should be reported in REDCap.

7. Definitions

Adverse Event (AE)

Any untoward medical occurrence in a participant, including occurrences which are not necessarily caused by or related to the intervention or to participation in research. AEs include both physical and psychological harms.

Serious Adverse Event (SAE)

A serious adverse event is any untoward medical occurrence that:

- results in death
- is life-threatening (actually, not hypothetically)
- requires inpatient hospitalization or prolongation of existing hospitalization
- results in persistent or significant disability/incapacity

Other 'important medical events' may also be considered serious if they jeopardize the participant

or require an intervention to prevent one of the above consequences.

8. Collection and classification of AE data

Sites are requested to conduct an assessment of whether hospitalizations, deaths, and other AEs are expected and of whether they are causally related to the study procedures or treatment. These assessments need to be conducted by site PI. Guidance on conducting these assessments is provided in the remainder of this document.

Information on AEs and SAEs categorized as **causally related** to the intervention or research procedures should be reported in REDCap. This includes:

- Hospitalizations
- Deaths
- Other AEs

Within REDCap, sites should document their assessment of the event's expectedness and of its relatedness (to the study procedures or treatment).

Related events

Events are related if they resulted from administration of any of the procedures required by the ExPAND protocol. Relationship is described using the following categories:

- Definitely related
- Probably related
- Possibly related
- Unlikely to be related
- Not related

Events that are expected to occur in people with advanced CKD (see below) may be categorized as "Not related" to the research procedures unless there is reason to believe otherwise.

Expected events

Events are expected if they are listed in the protocol (7.2.3) as an expected AE.

Appendix 1 sets out a more detailed breakdown of events that are expected to occur in people with advanced CKD to assist in the classification of whether an event is expected.

This list is not meant to be exhaustive, but rather illustrative of the types of events that are expected. If an event is not listed in Appendix 1, please seek advice from the trial team and principal investigator before a decision is made.

9. What events need prompt reporting as an AE or SAE?

- **Any inpatient stay in hospital or death classified as definitely, probably, or possibly related to the intervention or the research procedures.**
- **Any AE classified as definitely, probably, or possibly related and unexpected.**

All other **research-related** AEs are collected in the REDCap database.

Due to the benign nature of the study, study-related and unexpected SAEs are likely to be rare. An example would be psychological harm or distress related to participation in the trial, for example as a result of decision conflict, resulting in hospitalization or death.

10. Reporting procedures for promptly reportable AEs

- AEs occurring from the time of consent until 30 days after the end of the trial must be

reported

- Central trial team must be notified within **24 hours** of site being made aware
- Document the AE in REDCap
- Send an email to the study Principal Investigator and Study Manager notifying them of the event and providing the study ID of the patient.
- **Email (marked URGENT) to: Dale Lupu (dlupu@gwu.edu) and Matthew Ryan (m.ryan@gwu.edu)**
- **Receipt will be confirmed. Please follow up for confirmation if not received.**
- Any change of condition or other follow-up information relating to a previously reported AE should be documented in REDCap as soon as available. Study Principal Investigator and Study Manager should be notified.
- Events must be followed up until the event has resolved or a final outcome has been reached.

Appendix 1. An illustrative list of events that would be considered as expected SAEs due to advanced CKD and common comorbidities

Death or admission to hospital related to:

Cardiac/Cardiovascular	**CKD and Dialysis-Related†**	**Endocrine/Metabolic**
Diagnoses Hypertension Angina Chest pain, MI ruled out Acute myocardial infarction (MI) Cardiac arrest/sudden death Congestive heart failure Cardiomyopathy Valvular heart disease Atrial fibrillation Other arrhythmia Pericarditis &/or tamponade Hypotension *Procedures* Cardiac catheterization Coronary angioplasty Coronary bypass graft (CABG) Valve repair or replacement Cardioversion Cardiac defibrillator placement Pacemaker placed Pericardial procedure	*Diagnoses* Hyperkalemia Fluid overload PD peritonitis† Peritoneal catheter complication† *Procedures* Extra dialysis treatment† Peritoneal catheter insertion/ removal†	*Diagnoses* Hyperparathyroidism Diabetes complication (e.g., DKA) Thyroid disease Hypercalcemia Hypothyroidism *Procedures* Parathyroidectomy
Eye, Ear, Nose, Throat	**Gastrointestinal**	**Health investigation**
Diagnoses Diabetic retinopathy Cataract Glaucoma Blindness Epistaxis *Procedures* Retinal laser surgery Cataract extraction	*Diagnoses* GI bleed Gastritis/Peptic ulcer disease Gastroenteritis Abdominal pain Diarrhea Bowel obstruction Diverticulitis Malnutrition/cachexia Nausea/vomiting Other *Procedures* OGD (upper GI endoscopy) ERCP Colonoscopy Gastric surgery Hernia repair Colectomy/colon surgery Appendectomy Parenteral nutrition	*Procedures* Diagnostic Tests unrelated to the HD/ HDF process

Hematologic	Infectious Diseases	Liver, Biliary, Pancreas
Diagnoses Anemia	*Diagnoses* Pneumonia	*Diagnoses* Viral hepatitis
Procedures Blood transfusion Bone marrow biopsy	Septicemia Endocarditis AIDS/HIV Urinary Tract Infection Wound Infection Abscess Meningitis Cellulitis/soft tissue infection Osteomyelitis Viral infection Fungal infection Fever or chills, source unknown *Procedures* Abscess Drainage	Liver Failure Ascites Pancreatitis Gall bladder disease *Procedures* Liver biopsy Liver surgery Gall bladder surgery Pancreas surgery
Musculoskeletal *Diagnoses* Carpal tunnel syndrome Dialysis amyloidosis (B2-microglobulin deposition) Infectious arthritis *Procedures* Carpal tunnel release (surgical)	**Neoplastic/Cancer** *Diagnoses* Benign tumor Cancer, non-metastatic Cancer, metastatic Multiple myeloma Lymphoma/leukemia *Procedures* Surgical resection Chemotherapy Radiation therapy	**Neurologic/Cerebrovascular** *Diagnoses* Seizure Dementia Mental status change/ confusion TIA Stroke (CVA) – hemorrhagic Stroke (CVA) – ischemic Stroke (CVA) – type unknown Subdural hematoma *Procedures* Carotid revascularization Carotid endarterectomy Evacuation of hematoma
Obstetric/Gynecologic/Breast *Diagnoses* Abnormal bleeding Breast disease Other *Procedures* Breast Biopsy Hysterectomy	**Orthopedic** *Diagnoses* Hip Fracture Other fracture Herniated intervertebral disk Other *Procedures* Fracture repair Hip replacement Other joint replacement	**Psychiatric/Mental Health** *Diagnoses* Depression * Suicide attempt * anxiety disorder * Alcohol abuse Substance abuse Psychosis

Pulmonary	Skin	Social/Rehabilitation
Diagnoses Chronic Obstructive Pulmonary Disease Asthma Bronchitis Pneumonia Hemoptysis Pleural effusion Pulmonary oedema Respiratory Failure/ Arrest Shortness of breath	*Diagnoses* Psoriasis Cellulitis/Skin infection Calciphylaxis Rash	*Diagnoses* Placement issues Failure to thrive Fall Rehabilitation Hospice/palliative care

Pulmonary embolism *Procedures* Ventilator-assisted breathing Bronchoscopy Thoracentesis		
Transplant-Related *Diagnoses* Transplant evaluation Other *Procedures* Kidney transplant Transplant nephrectomy	**Trauma/Injury** *Diagnoses* Death Other *Procedures* Laparotomy Skin graft	**Urologic** *Diagnoses* Hematuria Renal cysts Kidney stone Other *Procedures* Cystoscopy Prostate surgery Nephrectomy
Vascular *Diagnoses* Claudication/Rest pain Ulcer of extremity Gangrene Aortic aneurysm Deep vein thrombosis Other *Procedures* Angiogram Arterial bypass surgery Amputation Aortic aneurysm repair Wound debridement	**Vascular Access** *Diagnoses* Clotted access† Infected access† Aneurysm† Failing access† Access bleeding† Other *Procedures* Salvage procedure† Revision procedure† New access creation† Access removal† Catheter placement†	
Other/Miscellaneous *Diagnoses* Drug reaction/allergy		

* Unless thought to be related to participation in the trial.
† Dialysis related

Appendix 9

DSMB Charter

Data Safety and Monitoring Board (DSMB) Charter

Study Title: Improving Shared Decision-Making and Access to Non-Dialytic Treatment for People with Kidney Disease (the ExPAND* study)

Sponsor: Patient-Centered Outcomes Research Institute (PCORI)

Contract Number: IHS-2022C2-2678

Principal Investigators: Dale E. Lupu, PhD, MPH, Alvin H. Moss, MD, FACP, FAAHPM

Site Principal Investigators: Dale E. Lupu, PhD, MPH

Institutions: George Washington University, West Virginia University

Version 1.0 February 12, 2024 – Approved by DSMB

*__Ex__panding and __P__romoting __A__lternative Care and K__n__owledge in __D__ialysis Care (EXPAND) Trial

Version 1.0 February 12, 2024 – Approved by DSMB

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Abbreviations

COI	Conflicts of Interest
DSMB	Data Safety and Monitoring Board
DSMP	Data Safety and Monitoring Plan
ExPAND	Improving Shared Decision-Making and Access to Non-Dialytic Treatment for People with Kidney Disease Study
IRB	Institutional Review Board
PCORI	Patient-Centered Outcomes Research Institute
PO	Program Officer

The Data and Safety Monitoring Board (DSMB) will act in an advisory capacity to the Patient-Centered Outcomes Research Institute (PCORI) to monitor participant safety, data quality and study progress of “Improving Shared Decision-Making and Access to Non-Dialytic Treatment for People with Kidney Disease (the ExPAND study)”, contract number IHS-2022C2-2678 by PI Dale Lupu (George Washington University).

DSMB Responsibilities

The DSMB responsibilities are to:

At the initial meeting,

- Review the entire IRB-approved study protocol, regarding data/participant safety including recruitment, randomization, intervention, data management, quality control and analysis and the informed consent documents.

- Recommend changes to the protocol related to data/participant safety and the informed consent forms, when applicable.

- Identify the relevant data parameters (including those related to adverse events (AEs), serious AEs (SAEs) and unanticipated problems (UPs)) and the format of the information to be regularly reported.

- Recommend participant recruitment be initiated after receipt of a satisfactory protocol. If the need for modifications to the protocol, consent forms, Data Safety and Monitoring Plan (DSMP) or any other study document is indicated by the DSMB, the DSMB will postpone its recommendation for the initiation of participant recruitment until after the receipt of a satisfactory revised protocol(s) or other study documents.

During the study meetings,

- Review masked (if masking is feasible) and unmasked data. These data can be related to safety, recruitment, randomization, retention, protocol adherence, trial operations, data completeness, form completion, intervention effects on primary endpoints, gender and minority inclusion.

- Identify needs for additional data relevant to safety issues and request these data from the study investigators.

- Propose additional analyses.

- At each meeting, consider the rationale for continuation of the study, with respect to progress of recruitment, randomization, retention, protocol adherence, data management, safety issues, and outcome data (if relevant) and make a recommendation for or against the trial's continuation.

- Review and make recommendations on proposed protocol changes, and/or new protocols proposed during the trial. The DSMB may recommend to PCORI to appoint a blinded working group of the DSMB to review the proposed protocol changes and make recommendations to PCORI on whether to approve the requests.

- Provide advice on issues regarding data discrepancies found by the data auditing system or other sources.

- DSMB members with expertise in a particular area may be asked to contribute their thoughts regarding the conduct of the ExPAND trial (e.g. asked Review manuscripts of trial results if requested).

The DSMB will discharge itself from its duties when the study is complete.

Membership

The DSMB consists of nine members that have been appointed by the study investigators. Members are completely independent of the study investigators and have no financial, scientific or other conflict of interest with the trial. The DSMB members and their expertise are as follows:

- Geriatric Nephrologist: **Ann O'Hare, MD**
- Geriatric Nephrologist: **Vanita Jassal, MD**
- Health Equity Nephrologist: **Vanessa Grubbs, MD**
- Biostatistician: **Denise Esserman, PhD**
- Biostatistician: **Jonathan Yabes, PhD**
- Patient: **Patrick Gee**
- Nurse Practitioner: **Suzanne Ward, NP**
- Ethicist: **Donna Chen, MD, MPH**
- Patient Family Member: **Melissa Tolzien**

Dr. Ann O'Hare will serve as the Chairperson and is responsible for facilitating the meetings, reviewing the first draft of the meeting notes and any decision making in the case of a tie vote. The Chair will act as the official contact for the DSMB. At each DSMB meeting, the Chairperson will prepare a formal summary of the DSMB's recommendations regarding continuation or termination of the study as well as any other changes requested by the DSMB. The GWU School of Nursing will provide the logistical management and support for the DSMB.

Meetings

Meeting Format

Meetings of the DSMB will be held at a minimum every 12 months after the protocol is approved by the DSMB, including: 1) prior to data collection to approve the study protocol and 2) within three months of the completion of data collection. An emergency meeting of the DSMB may be called at any time by the DSMB Chair, should participant safety questions or other unanticipated problems arise.

A quorum will require 5 DSMB members including the chair and a statistician. Meetings will be held in-person, by telephone conference, or a combination of the two.

DSMB meetings will consist of open, closed, and optional executive sessions, all closed to the public because discussions may address confidential participant data.

The **open session** is attended by study PIs, key staff members, including the study biostatistician, and DSMB members. Discussions at these sessions focus on the review of the aggregate study data, conduct and progress of the study, including participant accrual, protocol compliance, and problems encountered. Data by treatment group are not presented in the open session.

The **closed session** will be attended by the DSMB members and the unblinded study biostatistician. The primary objective of the closed sessions is to review safety-related outcomes, adverse events and serious adverse events data by study group, and recommend any safety-related protocol changes required to the study team.

If necessary, an **executive session** may be requested by the DSMB and will be attended only by voting DSMB members.

Meeting Agenda

The DSMB Chair or the Principal Investigators will prepare the meeting agenda that usually includes the following:

1. **Welcome and introduction** – study team and DSMB members
2. **Open session** (review study protocol and its amendments, consent form, open study report, etc.) - study team and DSMB members
3. **Closed session** (review closed session report, including unmasked safety data, etc.) – DSMB members, study team if invited
4. **Executive session** (optional, upon DSMB request) – DSMB members, PCORI staff if invited

5. **Debriefing** (optional, upon DSMB request, time permitting) - study team and DSMB members

The DSMB may modify its processes and procedures at any time as needed.

Meeting Materials

DSMB interim report templates developed by the study staff for both the open and closed sessions and plans for interim analyses will be reviewed and either approved at the initial DSMB meeting or changes requested. Upon DSMB request, reports could be modified at any time during the study.

Part 1 - Open Session Reports. Open session reports will include administrative reports that describe participants (screened, enrolled, completed), fidelity to study procedures, as well as baseline characteristics of the study population that is not grouped by treatment. Other general information on study status may also be presented. Listings of adverse events and serious adverse events, and unanticipated problems will also be presented (also not grouped by treatment). See DSMB Report Template.

Part 2 – Closed Session Reports. Closed session reports will present the same information but additionally summarized by treatment group. The Closed Session Report is considered confidential and should be destroyed at the conclusion of the meeting.

Meeting Minutes

The minutes will be taken by the DSMB support staff. Minutes will be circulated to all DSMB members for approval.

Reports from the DSMB

The DSMB Chair will prepare the report based on the meeting minutes from the open session and any recommendations from the closed and executive session and circulate the report to the DSMB members for feedback and revision. After DSMB review and approval of the minutes, the DSMB chair will forward the report to the study PIs.

The report will contain the recommendations for continuation or modification of the study. As stated above, each meeting must include a recommendation to continue the study made by a formal DSMB majority or unanimous vote. Should the DSMB decide to issue a termination recommendation, the full vote of the DSMB is required. In the event of a split vote, majority vote will rule, and a minority report should be appended. The DSMB Chair provides the tie-breaking vote in the event of a 50-50 split vote.

A recommendation to terminate the study may be made by the DSMB at any time by majority vote. If this recommendation was made during the DSMB's Executive session, the Chair should notify PCORI immediately by telephone and email.

The study PIs will ensure that a summary of recommendations based on the report is sent to all participating Institutional Review Boards (IRBs) after each DSMB meeting.

Confidentiality

All materials, discussions and proceedings of the DSMB are completely confidential. Members and other participants in DSMB meetings are expected to maintain confidentiality.

Conflicts of Interest

Each member of the DSMB will complete a COI form before attending the first DSMB meeting. The DSMB Chair will be responsible for deciding whether any disclosed COIs materially affect their objectivity on the DSMB. Members of the DSMB will be responsible for notifying the DSMB Chair of any changes in conflicts of interest. Members will be polled at the beginning of each DSMB meeting to disclose whether status has changed. Members of the DSMB who develop potential or significant perceived conflicts of interest will be asked to resign from the DSMB.