Peer mentorship to improve outcomes in patients on maintenance hemodialysis

PEER-HD

Protocol Number: 2018-01

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Sponsors: **Albert Einstein College of Medicine**

Vanderbilt University Medical Center

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*Acknowledgment that an earlier version (v1.0) employing different formatting was submitted and approved by the primary sponsor (Albert Einstein College of Medicine). This version reflects current activities as IRB approved at primary site and will serve as the protocol document for VUMC and any additional future AECOM updates.

CONFIDENTIALITY STATEMENT

This document is confidential communication. Acceptance of this document constitutes agreement by the recipient that no unpublished information contained herein will be published or disclosed without prior approval of the Principal Investigator or other participating study leadership and as consistent with the NIH terms of award.

Summary of Changes from Previous Version:

See section 10.4 for detailed description

Affected Section(s)	Summary of Revisions Made	Rationale	Date of Revision
Throughout Protocol	Remote consent procedure (telephone, email, or mail)	Re-opening of study after COVID crisis to accommodate social distancing	6/9/20
5.1	Inclusion Criteria (10) to include "or Spanish – Bronx, NY site)	Grammatical error	6/10/20
9.4.2	Analysis of the Primary Endpoints – ED Visit and Hospitalization Count language revision	Biostats review deemed revisions	6/10/20
9.4.3	Analysis of Secondary Endpoints & Feasibility Outcomes language revisions	Biostats review deemed revisions	6/10/20
9.4.5	Baseline Descriptive Statistics language revision	Biostats review deemed revisions	6/10/20
Throughout Protocol	Primary endpoint follow-up period from 18 months to 9 months (12 months observational)	Timeline revision due to COVID pandemic	4/30/21
6.1	Assignment of 3 mentees per mentor revised to 4 mentees	Mentee assignment revisions to meet timeline goals	4/30/21
7.2	T2 surveys administered at time of discontinuation	Established assigned discontinuation surveys	4/30/21

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STATEMENT OF COMPLIANCE

The trial will be conducted in accordance with International Council on Harmonisation Good Clinical Practice (ICH GCP), applicable United States (US) Code of Federal Regulations (CFR), and the NIDDK Terms and Conditions of Award. The Principal Investigator will assure that no deviation from, or changes to the protocol will take place without prior agreement from the funding agency and documented approval from the Institutional Review Board (IRB), except where necessary to eliminate an immediate hazard(s) to the trial participants. All personnel involved in the conduct of this study have completed Human Subjects Protection and ICH GCP Training.

The protocol, informed consent form(s), recruitment materials, and all participant materials will be submitted to the IRB for review and approval. Approval of both the protocol and the consent form(s) must be obtained before any participant is consented. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. All changes to the consent form(s) will be IRB approved; a determination will be made regarding whether a new consent needs to be obtained from participants who provided consent, using a previously approved consent form.

INVESTIGATOR'S SIGNATURE

The signature below constitutes the approval of this protocol and provides the necessary assurances that this study will be conducted according to all stipulations of the protocol, including all statements regarding confidentiality, and according to local legal and regulatory requirements and applicable US federal regulations and ICH guidelines, as described in the *Statement of Compliance* above.

Co-Principal Investigators:

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1 PROTOCOL SUMMARY

1.1 SYNOPSIS

Title:	Peer Mentorship to improve outcomes in patients on maintenance hemodialysis
Short Title:	PEER-HD
Grant Number:	R18DK118471
Study Description:	Pragmatic trial to test the effects and implementation of a low cost, educational, telephone-based, peer-mentor intervention on ED visits and hospitalizations among high-risk patients receiving hemodialysis.
Objectives:	Primary Objectives: 1) To perform a randomized controlled trial to evaluate the effects of a 3-month peer mentor intervention on a composite of ED visits and hospitalizations in patients on hemodialysis compared to usual care. 2) To test the feasibility of a dialysis peer training program. Secondary Objective: To evaluate the effect of peer mentoring intervention on dialysis adherence behaviors, dialysis knowledge, self-efficacy and perception of social support in intervention compared to control participants.
Endpoints:	Primary Endpoint: Composite count of ED visits and hospitalizations during 3 months of intervention and 15 months of follow up (18 months observation). Due to the covid pandemic and recommendations from the DSMB, after 4/30 all participants' post-activity period follow up will be limited to 9 months (12 months of observation), or truncated to the current observation period total of between 12 and 18 months. Secondary Endpoints: 1) Dialysis treatment adherence – mean missed minutes per month 2) Mean monthly inter-dialytic weight gain (%), serum albumin (g/dL); 3) Perceived self-efficacy, knowledge, perception of social support and quality of life. Feasibility Endpoints (intervention only): 1) number of telephone contacts per week; 2) content of telephone conversations; Feasibility of Peer Mentor Training: 1) attendance records for all sessions 2) change in pre-/post-knowledge assessments after training 3) content & descriptive evaluation of course evaluations

Study Population:	20 Mentor adult in-center hemodialysis patient participants 200 Adult in-center hemodialysis patient participants Enrolled from dialysis units in or near the Bronx, NY and Nashville, TN
Trial Type:	Pragmatic Randomized Trial
Description of Sites/Facilities Enrolling Participants:	Participants are enrolled from multiple dialysis units affiliated with Albert Einstein (AECOM) College of Medicine and Vanderbilt University Medical Center (VUMC). AECOM will serve as the coordinating center.
Description of Study Intervention:	Intervention will have 2 phases: 1) **Mentor training** • 4 Training sessions, 2 hours each covering topics in dialysis care, coaching and motivational interviewing techniques. • Refresher 2-hour session at 3-months and 10-months • Financial compensation by hour for training • Assessments of skills, role modeling & simulations, exit interviews 2) **Telephone based 3-month intervention** by mentors for mentees • Weekly phone contact with mentee (1-3 mentees per mentor) • Social mixers at the dialysis facility, or other group activities Usual care control group patient participants • Usual care as per facility procedures and protocols All participants: Provision of written educational material
Study Duration:	48 months
Participant Duration:	Mentors: up to 30 months Intervention or Control group participants: 12 to 18 months
Study Oversight:	National Institute of Diabetes and Digestive and Kidney Diseases / National Institutes of Health Project Scientist: Kevin Chan, MD Address: 2 Democracy Plaza 6707 Democracy Boulevard Bethesda, MD 20892-5458 Phone: 301-827-5251 Email: kevin.chan2@nih.gov
Data Safety & Monitoring Board:	Members [redacted]

Governing IRBs

Local IRBs for each clinical enrollment site:

- Albert Einstein College of Medicine
- Vanderbilt University Medical Center

1.2 SCHEMA

Figure 1. *Mentors* N~20

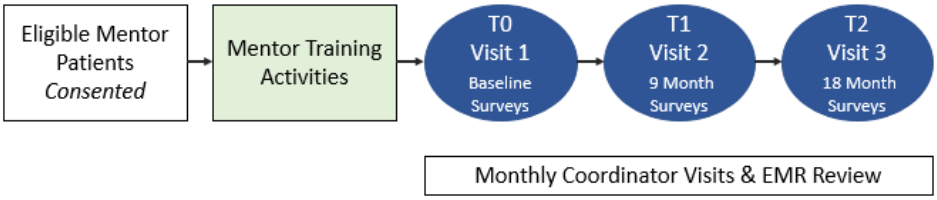
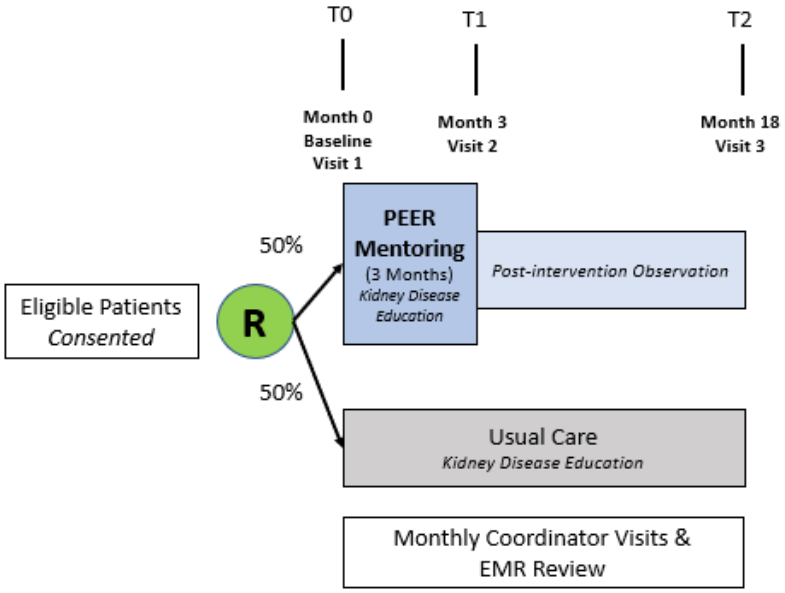


Figure 2. *Patient Participants* N=200 [All sites; Estimated enrollment AECOM=140; VUMC=60]



At the final study visit, all mentors and those randomized to the peer mentoring intervention will complete program evaluation interviews and surveys to gain feedback on the intervention.

Due to impact of the covid pandemic, the study DSMB recommended prioritizing enrollment and reduction of follow-up observational time. The recommendation is to limit total observation time to 12-months for intervention and control participants. Participants currently enrolled and who have passed the 12-month point will execute their T2 visit as soon as possible and truncate observation (13-18 months). For those whose observation time is less than 12-months, or any new enrolled participants, the T2 assessment will be moved to the 12-month time point. Mentors, may complete T2 at 18-months (Einstein site), or may complete T2 visit at 12-months if all other mentor activities have been completed at the site. Medical record monthly review will only occur for the observation period and will also be truncated at the time of the T2 visit. This alteration of the study design was approved by the DSMB and also the NIH program officer.

1.3 SCHEDULE OF ACTIVITIES

Table 1. Mentor and Patient participant study activities

Mentors	Pre-screening (Pre-consent)	Visit 1 – Day 1	Training 1-4; Within 6-8 Weeks after V#1	Each Month	~Month 3, Month 10, as needed	Visit 2-Month 9 ± 30d	Visit 3-Mon 18 ± 30d; between 12-18M or at 12M depending on date	Final visit Month 18 ± 30d between 12-18M or at 12M depending on date
Review Eligibility	x							
Informed Consent		x						
Demographics		x						
Clinical history		x						
Baseline assessments		x						
Mentors (continued)	Pre-screening (Pre-consent)	Visit 1 – Day 1	Training 1-4; Within 6-8 Weeks after V#1	Each Month; Quarterly	~Month 3, Month 10, as needed	Visit 2-Month 9 ± 30d	Visit 3-Mon 18 ± 30d between 12-18M or at 12M depending on date	Final visit Month 18 ± 30d between 12-18M or at 12M depending on date
Post training assessments (knowledge/formative/summative)			x					
Coordinator survey/check-in				x				
EMR Data Abstraction & Review				x				
Peer Mentor Refresher course (as needed)					x			
Optional social mixer or other group activity					x			
9-month follow-up assessments						x		
18-months follow up assessments							x	
Program evaluation interviews & field notes								x

Time of the start of the intervention activity with the first mentee will determine the start of when subsequent study visits (9-month; 18-month, or between 12-18-months) will occur for mentors.

Intervention or Control Participants	Pre-screening	Visit 1	Each Month	Every 3-4 Months, as needed	Visit 2 Month 3 ± 30d	Visit 3 Month 18 ± 30d between 12-18M or at 12M depending on date	Final visit Month 18 ± 30d between 12-18M or at 12M depending on date
Review Eligibility	x						
Informed Consent		x					
Demographics		x					
Clinical history		x					

Baseline assessment surveys		x					
Kidney Disease Educational Materials		x					
Coordinator survey/check-in			x				
EMR Data Abstraction & Review			x				
3-month follow-up assessments					x		
18-month follow-up assessments, or between 12-18-months as noted depending upon enrollment date						x	
Optional social mixer or group activity (intervention)				x			
Program evaluation interviews & field notes							x

Usual care group start time will begin at the time they receive the study kidney disease educational materials. Mentee group start time will begin at the time they receive their study phone and they are activated with their mentor.

2 INTRODUCTION

2.1 STUDY RATIONALE

The overarching goal of this research is to improve End Stage Kidney Disease (ESKD) related morbidity and mortality. The medical care of patients with ESKD is highly complex and expensive.[1,2] Hospitalizations drive up to 40% of the cost for ESKD care.[2-9] Cardiovascular disease and infections account for over 50% of ESKD-related hospitalizations and contribute to disproportionate mortality in this patient population.[10, 6, 11-22] We propose a pragmatic trial to test the implementation and impact on ED visit and hospitalization outcomes of a peer mentor led intervention designed to increase effective self-management in patients receiving hemodialysis, in a real-world setting with high potential for widespread dissemination.

Patients receiving hemodialysis who can self-manage their fluid status effectively, are adherent to their dialysis schedule and to their dietary plan are hospitalized less frequently and have lower morbidity and mortality than patients who are less adherent.[11, 14, 22-30] However, numerous impediments to dialysis self-management exist including facility, physician and patient-level barriers. The following are patient-level barriers to optimal self-management: 1) poor knowledge about the rationale and metrics of estimated dry weight (EDW), 2) poor knowledge about the metrics of urea clearance and nutritional parameters, 3) under-utilization of available hours for unscheduled dialysis, and 4) low self-efficacy leading to non-adherent schedule and dietary behaviors.[31-43] Dialysis self-management education is often not successful in improving patients' skills.[44] Educational tools from dialysis facilities and providers are didactic, have medical jargon and lack concrete steps to mitigate patient visits to emergency departments (ED) and subsequent hospitalizations.[4,4 45, 46] A culturally sensitive, easy to understand educational program that can increase hemodialysis self-management is critically needed.

Peer mentorship has been used effectively to enhance self-efficacy and self-management behaviors in patients with chronic disease.[47-60] A single study of peer mentorship for ESKD patients found that peer mentors improved adherence and satisfaction with care among mentees.[61] This strategy has high potential to improve the factors that drive hospitalizations among this high-risk patient group. The goal of this research is to implement a peer mentor training program to increase patients' knowledge about the metrics of hemodialysis, enhance self-management to meet EDW, nutritional and adherence goals, and to enhance self-efficacy in mentees.[38] The peer-mentor intervention is based on the information, motivation, behavior (IMB) model of health behavior and the Chronic Disease Self-Management Program.[22, 44, 62-68] We will test the feasibility of implementation of this program and the efficacy of it to reduce hospitalizations in a pragmatic trial comparing the peer mentor intervention on mentees to a control group assigned to usual care. *We hypothesize that a structured peer mentor telephone*

intervention will be more effective than usual care in increasing hemodialysis related knowledge, self-management adherent behaviors and in decreasing ED visits and hospitalizations in ESKD.

2.2 BACKGROUND

2.2.1. *Excessive hospitalization rates in patients treated with hemodialysis*

There are over 400,000 ESKD patients in the United States and they constitute one of the most clinically complex and expensive patient groups.[1] Patients treated with hemodialysis comprise 1% of the Medicare population but account for close to 9% of the total expenditures.[2] Hospitalizations drive up to 40% of the cost for ESKD care.[1-3, 69] Patients receiving hemodialysis are hospitalized, on average, 2 times per year and over 35% of these patients are re-hospitalized within 30 days of discharge.[3, 6, 8, 9, 70] During hospitalizations, patients' nutritional status and mobility deteriorate, and the risk for infectious complications increases, all of which add to short-term morbidity and mortality.[6, 14, 71, 72]

2.2.2. *Hospitalizations are avoidable in patients treated with hemodialysis*

Cardiovascular disease is the most common cause of hospitalizations in patients on hemodialysis, followed by infections and vascular access complications.[2, 3, 10, 12, 17, 75] In the U.S., the rate of hospitalization for fluid overload is 40 per 100 person year with a risk of 30-day re-hospitalization of 38%.[10, 16] Fluid overload presenting as heart failure is the most common reason for ED visits in the U.S. and Canada.[22, 76] Chronic fluid overload is common in patients treated with hemodialysis, is related to EDW achievement for each treatment, dialysis adherence and IDWG, and contributes to excessive and avoidable hospital resource utilization. In a study examining the types of US claims used for fluid related ESKD hospitalizations, heart failure was the primary diagnosis in 83% of episodes, average cost was $6,372 per episode, and importantly total costs were more than $266 million per year.[17] Patients on hemodialysis rarely demonstrate understanding of the metrics of EDW and IDWG that are important for patients' ability to set goals, problem solve and understand their symptoms.[44, 77] Complications related to low dialysis adherence contribute to avoidable hospitalizations in other ways and include infection risk, uremia related malnutrition and cognitive decline.[36, 37, 78-81] Dialysis adherence and recognition of vascular access malfunction are important to prevent low dialysis clearance and malnutrition.[33, 39, 82] Patients are given monthly reports of dialysis parameters but they infrequently recognize its relation to uremia, access dysfunction, associated symptoms, and to outcomes.[83-85] Poor patient self-management is associated with: 1) low dialysis adherence, 2) lack of self-examination of access and 3) dietary non-adherence to IDWG limits leading to fluid overload, and malnutrition.[86-89] These behaviors, in turn, lead to chronic and maladaptive clinical changes such as ventricular dysfunction and vascular calcification which increase the risk of hospitalizations in part attributed to self-referral to the ED because of poor understanding of and communication about fluid related symptoms by the patient to their clinician.

2.2.3 Avoidable hospitalizations: opportunities for intervention

Most cardiovascular hospitalizations in patients on hemodialysis are secondary to either cardiac or pulmonary disease related to chronic volume overload or to episodes of pulmonary edema manifesting as shortness of breath.[4, 11, 17, 75] Patients who are adherent and can regularly achieve accurately prescribed EDWs do not develop complications of acute or chronic volume overload.[22, 27, 29, 90-92] Up to 50% of patients on hemodialysis are chronically fluid overloaded.[12, 13, 75] Patients receiving dialysis skip 8% and shorten 20% of their treatments on a regular basis which increases the risk of not meeting EDW goals.[32, 33] Patient with high IDWG have a 35% higher risk for death, and those with chronic fluid overload have a greater than 2 times greater hazard ratio for mortality.[13, 22] Relative IDWG greater than 4% of body weight is associated with hospitalizations and IDWG >5.7% of body weight is associated with mortality.[16] In a national database study, 34% of patients skipped treatments.[33] Those patients who skipped at least one or more sessions per month or shorten at least one treatment per month had a

significantly higher HR for increased short-term, fluid related, hospitalizations (HR 1.13) and a 25% higher risk for mortality.[33, 39, 93]

Uremia and non-adherence to dialysis are associated with malnutrition and inflammation, both of which are strongly associated with hospitalizations in patients with ESKD.[3, 36-39, 94] Dialysis facility education focuses on isolated patient behaviors such as IDWG and dietary phosphorus intake. Education about the contribution of vascular access type and function, dietary and dialysis non-adherence to uremia, malnutrition and infection risk is not systematically undertaken by facility staff. Patients do not universally recognize or attribute the symptoms of uremia or IDWG to poor self-management behaviors.[31, 34, 45, 77, 84, 89, 95-100] Uremia is not routinely diagnosed by staff because the urea reduction ratio (URR) metrics do not consider mean monthly urea and dialysis access recirculation is not factored into the majority of monthly reports.[101] With regards to infection and sepsis related hospitalizations: 80% of patients start dialysis with a dialysis catheter and up to 20% of prevalent patients use catheters as their permanent vascular access.[102-104] Patients with catheters have up to a 7 fold increase in infectious complications requiring hospitalizations as compared to patients who start dialysis with a fistula.[102-104] Fluid mismanagement, dialysis and dietary non-adherence, and catheter use are associated with cardiovascular and infectious morbidity, and resultant hospitalizations and mortality. These conditions are opportunities for a preventive intervention that can mitigate poor outcomes. With education, patients on hemodialysis are in a unique position to self-diagnose fluid overload, uremia and access dysfunction based on their symptoms, where dialysis facility and nephrologist metrics may fall short.

2.2.4 Patient level barriers to prevent avoidable hospitalizations

The barriers to hemodialysis self-management to prevent hospitalizations are multifactorial and related to 1) facility level barriers, 2) physician level barriers and 3) patient level barriers. Patient level barriers to self-management include 1) lack of knowledge, 2) negative attitudes about self-management and 3) low self-efficacy. Dialysis facility staff offer patients educational material on diet and fluid self-management but the uptake of this material by patients is limited. Lack of knowledge among patients about the relationship between behaviors and outcomes limits adoption of concrete skills to improve outcomes. Forty three percent of patients on dialysis have limited health literacy and most patients have limited understanding of EDW and dietary principles pertaining to IDWG, urea clearance and nutrition.[84, 105-109] More than 25% of patients are unsure of their EDW and most patients do not attribute cramping or dyspnea to fluid management or realize that EDW varies with time and is adjustable.[77, 109] Most patients are unaware of the option to use extra dialysis to achieve EDW.

Attitudes about self-management including fear of failure and anxiety about obtaining necessary skills are common in ESKD. Self-management describes the process by which the patient becomes an active participant in his/her treatment.[108, 110-111] Self-management by select patients on hemodialysis is successful as demonstrated by self-cannulation, home hemodialysis programs and newer programs wherein patients monitor and control their own in-center dialysis treatments using a computer interface.[25] These patients had high self-care agency (self-efficacy) scores and quality of life.[30] Most patients on hemodialysis have poor self-management skills and depend on dialysis facility staff.[34, 35, 111-113] A poor sense of the chronicity of ESKD, the adverse effects of non-adherence and mistrust of dialysis facility staff, are common negative attitudes in those with poor self-management skills.[43, 114-116]

Low self-efficacy (the ability of an individual to set goals and the belief that s/he can achieve those goals) is common in dialysis patients and is directly related to suboptimal self-management behaviors.[43, 66, 67, 117-120] Self-efficacy is a mediator of self-management behaviors.[66, 67, 111, 112] Patients with low self-efficacy comprise up to 1/3 of the dialysis population, are more likely to shorten or skip dialysis treatments, have high IDWG, and experience frequent hospitalizations.[13, 33, 39, 82, 84] Low self-efficacy in dialysis patients is related to psychological, social and educational background.[121-124] Lack of social support is a mediator of

low self-efficacy and non-adherence behaviors.[40-42] One third of patients on hemodialysis have poor social support.[125] Low perception of social support is associated with morbidity, hospitalizations and mortality in patients on hemodialysis independent of clinical variables.[42] Some patients treated with hemodialysis have low social support, have low self-efficacy and poor self-management behaviors.

2.2.5 Improving self-efficacy can improve self-management skills

Self-management skills in chronic disease include goal setting, problem solving, communicating, resource utilization and self-tailoring.[126-129] Self-efficacy is an important mechanism by which self-management improves outcomes.[66, 67, 111, 114, 127] Relevant self-management skills in patients on hemodialysis are setting dietary, treatment adherence and IDWG goals, communicating symptoms of fluid overload, cramping, uremia, and vascular access dysfunction to caregivers, and using available resources in dialysis facilities and vascular access centers to problem-solve. Patients' reported self-efficacy is more consistently associated with self-management behavior than demographic or clinical characteristics.[46] Most patients treated with dialysis desire to understand numbers pertaining to their care and when furnished with knowledge and motivation, many patients are willing to extend treatments or to add extra sessions per week to attain optimal EDW.[77, 109] The use of contextually sensitive interventions that improve social support and self-efficacy improve IDWG and dialysis treatment adherence.[61, 121]

2.2.6 Peer mentorship to enhance self-management in patients treated with hemodialysis

Peer mentorship has been effective in chronic diseases such as diabetes mellitus, depression, AIDS, and ESKD.[52, 56, 57, 60, 130-137] Peer mentors are recruited members of a community that share similar health circumstances and thus have concrete and pragmatic knowledge derived from personal experience.[133, 138] In this way mentors act as knowledgeable equals by their target population and are not part of the healthcare system.[44, 138] In fact, attainment of too much formal knowledge is detrimental to this status and runs the risk of transformation from a peer to a para-professional.[48] Peer based interventions improve health related behaviors and self-management.[55, 134] Self-efficacy can be increased by mastering performance, social modeling, interpretation of symptoms and social persuasion, all of which are supported by peer mentors. Peer mentors provide the following types of support to mentees: 1) emotional (increasing perception of social support/motivation), 2) affirmation and encouragement to persist in problem solving (increase self-efficacy/motivation) and 3) knowledge acquisition relevant to the practical aspects of self-management.[134, 138] By providing emotional and affirmation support, peers encourage performance mastery, as role models, peers provide social persuasion and model effective behaviors, and by providing practical knowledge peers improve interpretation of symptoms and communication of those symptoms to caregivers. Peer mentor interventions in patients on hemodialysis have shown success in improved goals of care discussions, treatment adherence and quality of life parameters.[61, 139, 127, 140, 141] Peer mentors in dialysis facilities are in a unique position to facilitate perceived social support.[61, 129, 139] The Michigan state ESKD program and the National Kidney Foundation both have peer mentorship programs.[60, 140] In other chronic disease states, a variety of peer mentorship models have shown variable success in the attainment of certain concrete outcomes. Targeted, specific and contextually appropriate peer-mentor models are the most effective.[60, 131, 139, 142] Peer interventions for patients on dialysis, however, have not defined a consistent and structured program to increase performance mastery, nor have they examined outcomes such as hospitalizations.

2.3 RISK/BENEFIT ASSESSMENT

2.3.1 KNOWN POTENTIAL RISKS

For **mentors**, the risks of the study include: 1) inconvenience of attending training sessions, 2) discomfort with assessments during training, 3) discomfort with ongoing weekly telephone based

interventions with mentees throughout the study, 4) confidentiality issues associated with research and health data, 5) conflicts or emotional distress with intervention with some of the mentees. These risks will be discussed with the potential participants during the informed consent process.

Inconvenience of attending training session. This study requires training sessions of peer mentors conducted at dialysis facilities for 2 hours weekly over 4 weeks. This requires that the mentors come to the facility, or participate in a web-based version, outside of their regularly scheduled dialysis times and participate in training.

Discomfort with assessments during training. We will use validated and novel tools to measure knowledge at baseline and after training about dialysis and kidney disease. We will keep scores on these evaluations confidential and will not discuss them with other mentors.

Discomfort with weekly telephone-based intervention with mentees. During the informed consent process the expectations for each mentor will be discussed. Mentors will be compensated for carrying out the expected mentor activities. There will be frequent opportunities for mentors to discuss with the research team any concerns. There will be explicit criteria for potential withdrawal as a mentor if they do not fulfil their expectations. If mentors drop out because of clinical illness or inability to continue we will substitute their position from the pool of trained mentors.

Confidentiality issues associated with research and health data. Because of the collection of personal health information and formative assessments, we will enter personal information in a de-identified manner according to a study ID. All paper documents linking study ID and personal identifiers will be recorded in one location (electronic or hard copy) under the supervision of the site-PI. Participants will sign an agreement to not disclose personal or health information about other participants.

Conflicts or emotional distress arising between mentor/mentee pairs, or from one member dying during the intervention. If conflicts arise between mentor/mentee pairs, or if one of the parties decide to drop out of the study, the remaining member of the pair will be given the choice to continue in the study with a different mentor/mentee. Reasons for conflict will be recorded as process outcomes. If one member of a pair dies during the intervention grief counseling will be provided by the dialysis facility social worker and study staff will offer connections with additional counseling services as requested.

For **patient participants**, the risks of the study include: 1) discomfort with being identified as a high-risk patient during screening, 2) discomfort with receiving telephone calls by mentors, 3) discomfort with getting assessments at study visits, 4) confidentiality issues associated with research and health data, and 5) conflicts or emotional distress with intervention mentors (if applicable). These risks will be discussed with the potential participants during the informed consent process.

Discomfort with being identified as a high-risk patient during screening. Because identifying patients as high risk to qualify as a mentee recruit may be associated with stigma in the dialysis facility, we will ensure all study staff are aware and receive communication training regarding this concern. This will include discretion as part of the training.

Discomfort with receiving telephone calls by mentors. While responding to telephone calls is optional and while patients can ignore telephone calls made to them by mentors, the design of the intervention depends on successful telephone contact between pairs. This will be reviewed with all mentees during the informed consent process. All subjects will be given the choice to opt out or to drop out of the study at any point. The enrolled participants will have frequent opportunity to discuss concerns with the research coordinator and provide feedback on the intervention/mentor.

Discomfort with study visits. Mentees will undergo assessments using validated instruments to determine self-efficacy, perception of social support, health literacy and quality of life. These assessments will be scheduled at a time that is convenient for the subjects.

Confidentiality issues associated with research and health data. We will collect demographic, clinical, behavioral and outcome data on all mentees and controls. We will explain this during the informed consent process. All data will be collected from institutional electronic health records and will be recorded in REDCap as de-identified. All paper documents linking study ID and personal identifiers will be recorded in one location (electronic or hard copy) under the supervision of the site-PI.

Conflicts or emotional distress arising between mentor/mentee pairs, or from one member dying during the intervention. If conflicts arise between mentor/mentee pairs, or if one of the parties decide to drop out of the study, the remaining member of the pair will be given the choice to continue in the study with a different mentor/mentee. Reasons for conflict will be recorded as process outcomes. If one member of pair dies during the intervention grief counseling will be provided by the dialysis facility social worker and study staff will offer connections with additional counseling services as requested.

2.3.2 KNOWN POTENTIAL BENEFITS

A peer mentorship intervention that can reduce ED visits and hospitalizations, may be a novel low-cost program that has major implications not just in the ESKD population, but also in other complex chronic diseases. The model shifts the focus of healthcare interventions towards patients' education and self-management. Process measures that define easily reproducible implementation outcomes will have a major impact on the structure of accountable care.
The following is a list of potential benefits gained from this study:

1) Paradigm Shift: **The proposed research study will use peer mentorship to increase dialysis self-management as an efficient intervention to reduce morbidity, mortality and cost.** This proposal has implications for major provider stakeholders including dialysis facilities, dialysis physicians, Accountable Care Organizations including ESKD seamless care organizations (ESCOs) and payers. The intervention will integrate a curriculum focused on self-management into ESKD education and serve as a model for future educational programs. This will shift the paradigm of care to supporting patient self-management directly through explicit partnerships with peer leaders derived from the local community.

2) Educational Program**: We will implement a structured, reproducible training program with participation by a multi-disciplinary team, including patients, and a curriculum that includes concrete self-management skills.** For training peer mentors, we will develop a resource guide based on the chronic disease self-management program (CDSMP) framework that will be available for use by dialysis facilities.[131 143] The CDSMP is a program developed at Stanford University to help patients better manage chronic conditions and their quality of life. The study design allows measurement of intensity, frequency and duration of effect of the peer-mentor intervention, to inform future scalability.[48 55 131 134 144]

3) Cost savings**: Peer mentorship can translate into savings that exceed program costs by a ratio of 5:1**.[145 146] The Institute of Medicine and the World Health Organization state that enhancing support for patient self-management is a top priority for improving healthcare in the U.S.[131] Peer support as a tool to increase mentee self-efficacy and self-management, is less expensive than traditional case management models and is promising for providers and health systems with budgetary constraints.

4) Addressing health disparities: **Peer mentorship includes a culturally sensitive approach to increase self-management behaviors by minority groups who are at risk because of health care disparities.** Health disparities affect minority patients undergoing hemodialysis in lower socio-economic neighborhoods.[147 148] We will test peer mentorship process measures in our facilities across the Bronx,

where most of our patients are black and Hispanic, and in Nashville, with a black majority ESKD population, to understand the differential effects of peer mentorship across population groups.

5) Improving dialysis facility outcomes: **Improving patients' dialysis self-management may reduce hospitalizations which is a measure used to determine reimbursement rates.** Reducing hospitalizations and improving adherence to dialysis may improve reimbursement for facility fees. Increased communication by patients through a cooperative/participatory framework may improve job satisfaction of dialysis staff.

2.3.3 ASSESSMENT OF POTENTIAL RISKS AND BENEFITS

Overall, the risks to both mentor and mentee participants are no more than minimal above usual clinical practice and there are substantial potential benefits to intervention participants' clinical outcomes, as well as improvements in the efficiencies of delivery of dialysis care.

Protection of confidentiality. Participant confidentiality will be carefully protected. Facility staff will not be allowed access to trial data (single-blinded design). All research staff will complete the Collaborative Institutional Training Initiative computer-based training program which includes a module on privacy and confidentiality. All study documents will include participants' ID rather than personal names and these include survey documents and assessments. Only one form will link participants' names and study IDs and this will be stored in a password protected and encrypted file overseen by the site PI. Publication of study results will not reveal any identifiable information.

3 OBJECTIVES AND ENDPOINTS

Table 3.

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS	PUTATIVE MECHANISMS OF ACTION
Primary			
To test the effects of a telephone-based peer mentor intervention on hospital resource utilizations	Composite count of ED visit and hospitalizations at the conclusion of the 12 to 18-month (T2) observation period comparing mentee group to usual care group.	Some visits made by patients on hemodialysis to the ED and subsequent hospitalizations may be avoidable with better outpatient care coordination and patient engagement. Peers may be best suited to provide support for patient activation.	Improvements in patient knowledge, self-efficacy, and skills related to self-care and connecting with their dialysis care team.
Secondary			
1) To test the effects of a mentor peer training program on the uptake of: a) dialysis knowledge and b) mentorship skills.	a) Change in scores on knowledge assessments after training (BL, 9M, 12-18M) b) Uptake of skills involving	a) Knowledge in mentors is important to then disseminate to mentees through the peer intervention. These skills are in the causal pathway related to adherence behaviors.	Coaching skills by mentors to improve mentee knowledge, self-efficacy, communication skills and perceived social

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS	PUTATIVE MECHANISMS OF ACTION
	motivational interviewing, emotional support, non-judgmental listening and self-efficacy promotion in role playing exercises	b) An established method of training program evaluation includes assessments by the trainer during role playing of mastery of skills by the trainee.	support are hypothesized to increase activation to success in dialysis self-care.
2) To test the effects of a telephone-based peer mentor intervention on adherence behaviors, perception of self-efficacy, perception of social support and overall nutrition as possible mediators in the association of this intervention with primary outcomes	<u>Month 3 & M-12 to 18 (T2)</u> *Intervention compared to UC* a) Mean weekly missed minutes of dialysis; b) Mean monthly IDWG; c) Serum Alb; d) Self-efficacy; e) Social support; f) Knowledge	The effects of the peer intervention on adherence behaviors and perception of social support may alter the causal pathway(s) of high hospitalization rates in hemodialysis. Studies have shown an association between lack of patients' engagement and social support and adherence behaviors in patients on hemodialysis. Further studies have established the strong association between adherence behaviors and incidence of hospitalizations in this population.	Low perception of social support and low self-efficacy are associated with adherence behaviors and hospitalization outcomes.
Tertiary/Exploratory			
To test the feasibility and fidelity of a peer training program on mentor uptake	a. Attendance records of training sessions; b. Formative assessments of each training session	To inform future dissemination by characterizing the structural elements of the training program methods	n/a
To test the feasibility of the telephone-based intervention on mentees assigned to the intervention group	a) number and duration of telephone contact made by mentor/mentee; b) self-recorded content of mentor/mentee conversations;	Telephone records serve as the primary data to determine total dosing of intervention (minutes), as well as pattern of contact over the 3-month period	n/a

4 STUDY DESIGN

4.1 OVERALL DESIGN

The goal of this study is to test the effects of a peer mentorship program on hospital utilization among high risk patients on hemodialysis as compared to a usual care control group. This is a two-arm pragmatic, randomized at the patient-level controlled trial. Exploratory analyses within the intervention arm will also be performed. Patients will be randomized in a 1:1 allocation and blinded to the research team until the disclosure of the randomization assignment. There will be enrollments in groups until each mentor has been randomly allocated their maximal number of mentees. Randomization will be computer generated and assigned by the coordinating center research team.

This is a multi-site trial, including dialysis units in Bronx, NY and Nashville, TN areas. The collaborating organizations include Albert Einstein College of Medicine (Coordinating Center) and Vanderbilt University Medical Center.

Intervention: Hemodialysis peer mentoring training and telephone coaching program.

The control group will receive kidney disease education about dialysis treatment adherence and access care in alignment with standard of care. Usual care will be at the discretion of the participant's clinical care team.

No interim analyses are planned.

4.2 RATIONALE FOR STUDY DESIGN

Patient-level randomization. We decided against cluster randomization because the threat of contamination of the intervention in this study with usual care is low. Additionally, dialysis facility location and culture is a potential confounding variable since the receptivity of the staff to patient requests and provision of care in response to patient self-management enhancement may be different between units.[154] We also decided against this method because of feasibility and power considerations.

Single blinded randomization. Limitations to single blinding include patients speaking to staff and among themselves about their involvement with the study will be accounted for in the final analysis by tracking and adjusting for this variable through patient report. Using sequential multiple assignment randomization would enable better understanding of the different elements of the treatment on outcomes as this design assigns one element of an intervention only to those patients that have not responded to first in a series of interventions. We decided against using this method of randomization because of feasibility and the lack of rigorous evidence available to inform sequential program delivery.

4.3 JUSTIFICATION FOR INTERVENTION

Why peer mentor design? Peer mentoring increased the completion of advanced directives among African Americans on hemodialysis highlighting demographic differences in its impact. [139] Peer mentorship also improved patient dialysis adherence and quality of life scores.[61] Peer mentorship is effective in reducing anxiety, increasing perception of social support and self-efficacy through modeling and empathic listening, and is well suited to a dialysis population with a fixed schedule.[52, 150]

Why telephone intervention? The use of a telephone had the advantage of being less expensive, easy to use and available to most patients on dialysis unlike interventions that require the use of the internet.[60, 138] Furthermore there are advantages such as confidentiality and immediacy of response as compared to

the use of email or internet which may make telephone interventions palatable to patients.[133] We also felt that some maintenance of privacy through the use of telephone was important for the development of trust between the mentor/mentee pairs.[52] Potential downfalls to use of telephone include no guarantee that a connection will be made, and the risk of losing contact because of frequent telephone number changes. Study telephones will be provided.

A participant is considered to have completed the study if he or she has completed the baseline assessment, and the assessments at 3 months of intervention and 12-18 months of follow-up. An intention-to-treat approach will be considered in the analyses; however, an as-treated analysis will require a minimum of 60 minutes of telephone time during the 3-month intervention period between mentor/mentee pair.

4.4 END-OF-STUDY DEFINITION

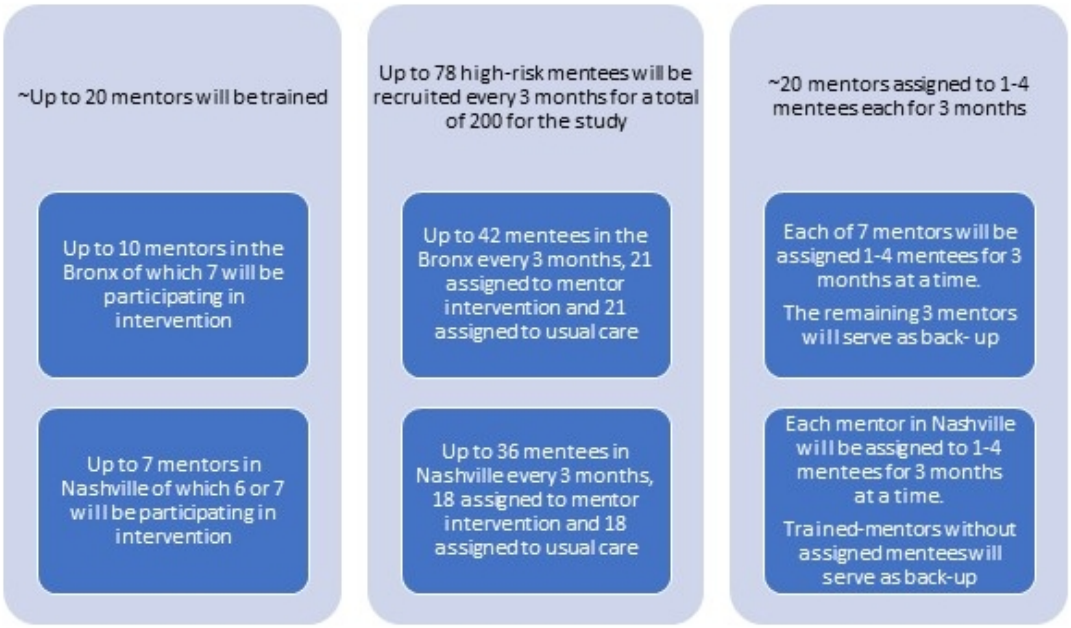
The end of the study for participants is defined as completion of the 12 to 18-month follow-up assessment shown in the Schedule of Activities (SoA), **Section 1.3**. The study will monitor participants' EHR for 30 days after completion of the 12 to 18-month (T2) visit to assess for serious adverse events (SAEs).

5 STUDY POPULATION

Subjects for this study will be selected from a population of patients with ESKD on maintenance hemodialysis who receive treatment in one of affiliated dialysis facilities in the Bronx and Nashville. The study population is comprised of dialysis patient Mentors and Mentees or Usual Care.

The study population will consist of approximately 17 mentors (7 in Nashville and 10 in the Bronx) who will be trained by the study team using the developed mentor training modules (Figure 3). We will make it clear during the consent process that not all mentors may participate in the intervention phase. After mentor training, each mentor will be assigned to 1-4 intervention mentees for 3-month periods. Patient participants will be recruited to try to achieve balance in the 1:1 allocation to intervention or usual care groups during study periods. There may remain differences in the counts in each group during each period depending upon randomization allocation.

Figure 3. Schema summary of mentor and patient group participants.



At some dialysis facilities a HIPAA waiver form may be required to be signed by a potential participant prior to screening. This will depend upon individual facility requirements. A verbal consent may also be required by site-specific IRB processes or local regulations to proceed with screening.

5.1 INCLUSION CRITERIA

Mentors

Mentor participants must meet all of the following inclusion criteria:

1. Provision of signed and dated informed consent form
2. Stated willingness to comply with all study procedures and availability for the duration of the study
3. Males and females; Age > 21 years
4. Diagnosis of ESKD and treatment with in-center hemodialysis for at least 1 year at the time of recruitment
5. Dialysis treatment at one of the participating dialysis units
6. No hospitalizations in the prior 6 months
7. No unexcused absence or shortening (2 or more x 10 minutes per treatment) of dialysis treatments in the past 6 months
8. Use of an AV fistula or graft as dialysis access
9. Serum albumin 3.5 g/dL or greater in the month prior to enrollment
10. Fluent in English (or Spanish – Bronx, NY site)

Patient Participants [Intervention or Usual Care]

Patient participants must meet all of the following inclusion criteria:

1. Provision of signed and dated informed consent form
2. Stated willingness to comply with all study procedures, including randomization, and availability for the duration of the study
3. Males and females; Age > 21 years
4. Dialysis treatment at one of the participating dialysis units
5. One of the following criteria:

a. Diagnosis of ESKD and treatment with in-center hemodialysis for less than 90 days
b. One or more hospitalizations in the prior month
c. One or more ED visits in the prior month
d. More than 1 unexcused missed dialysis treatments in the prior month
e. 2 or more shortened (more than 10 minutes) dialysis treatments in the prior month
f. Use of a catheter for dialysis access
g. An average of more than 4% IDWG in any week during the prior month
h. Serum albumin less than 3.5 mg/dL in the prior month

6. Fluent in English (or Spanish – Bronx, NY site)

5.2 EXCLUSION CRITERIA

Patients without ability to give informed consent, who opt out of being approached by staff after initial screening and who are actively recruited to another research study will not be approached for recruitment. All patients meeting eligibility criteria will be considered for inclusion.

Mentors

Any individual who meets any of the following criteria will be excluded from participation as a mentor:

1. Severe cognitive impairment or psychiatric illness as determined by clinical provider
2. Less than 6-month life expectancy as determined by clinical provider
3. Active substance use, excluding cannabinoids
4. Enrolled in another peer support or educational dialysis research study (discretion of study team)

Patient Participants

Any individual who meets any of the following criteria will be excluded from participation as a patient participant (intervention or usual care):

1. Severe cognitive impairment or psychiatric illness as determined by clinical provider
2. Less than 6-month life expectancy as determined by clinical provider
3. Active substance use, excluding cannabinoids
4. Enrolled in another peer support or educational dialysis research study (discretion of study team)

5.3 LIFESTYLE CONSIDERATIONS

N/A

5.4 SCREEN FAILURES

Screen failures are defined as participants who consent to participate in this study but are not subsequently assigned to the study intervention or entered in the study. Mentor screen failures will be kept on a reserve list from which to consider if one of the study mentors drops out. Patient participant screen failures due to participation in another study, may be considered in the future. Rescreened participants will be assigned the same participant number as for the initial screening.

5.5 STRATEGIES FOR RECRUITMENT AND RETENTION

Additional details are provided in the study manual of procedures. This protocol section includes an overview of the approaches to recruitment and retention of all study participants including mentors and patient participants. Mentors and patient participants will be recruited separately. While mentors will aim to be recruited at the start of the study, it is possible that new mentors during the study period will be needed if there is a loss of mentors due to illness, relocation, or withdrawal. Special populations will not be included in this research, including children. The affiliated dialysis units do not care for children, and children have different support needs warranting separate dedicated scientific investigation.

Mentors

Screening will include all adult patients on hemodialysis at study affiliated dialysis units. The study team will inform dialysis unit staff (administrators, physicians, physician-extenders, nurses and technicians) about the study objectives and criteria during a group meeting, by flyers, by email or during individual conversations. The dialysis staff will be asked to refer patients who they think may be good mentors to the study team. The study team will then assess the patient for eligibility, after any required HIPAA waiver or other verbal consent by the patient is obtained including for evaluation of medical records if required. If this initial screening meets eligibility criteria the patient will be approached to inform them about the study, inform them about the mentor role, further assess eligibility and offer participation if eligible. Potential participants may be approached in the dialysis facility or other mutually agreed location, by phone, by video research visit depending upon patient preference.

As this will predominantly be a referred participant role, we anticipate screening approximately 2-3 times our enrollment target at each site for mentors. There are no exclusions based on sex, race or age. The study will aim to include diverse representation across the enrolled group of mentors.

Retention

Mentors will be in close contact with the study coordinator to promote continual feedback and support for the duration of the study. This will include at a minimum monthly check-ins. There will also be opportunities to connect with other mentors during refresher training sessions. All efforts will be made by the study team to ensure the mentors understand the activities and time commitments for participating in this important role at the beginning of their involvement and throughout the study. The study will also disseminate to the mentors various brief thank you notes or cards spontaneously to show them appreciation for their efforts in addition to the study compensation plan.

Patient participants: Mentees and Usual Care

A target of 200 eligible patients will be enrolled in the study and randomized in a 1:1 allocation to either the mentee peer support intervention group or the usual care group. We anticipate screening 3-4 times the target enrollment number to (up to 600-800 patients) from across affiliated dialysis units to identify those who are eligible and invite them to participate. There are no criteria based on sex, race or age. We anticipate that the enrollment will reflect the overall demographic characteristics of each region with both approximately equal in sex distribution, New York with almost 40% Latino/Hispanic, 45% Black and Tennessee 50% Black and 50% non-Hispanic White.

Several strategies will be employed to recruit patient participants from affiliated dialysis units. All strategies will be IRB approved. This will include referrals from usual clinical care providers to the study, informational flyer/handouts for patients, as well as screening of patient clinic rosters for potential eligibility. The study team will assess the patient for eligibility, after any required HIPAA waiver or other verbal consent by the patient is obtained including for evaluation of medical records if required. If initial review of medical record confirms potential eligibility, the patient will be approached in person at the dialysis unit or other mutually agreed location, by phone or by video research visit. If eligibility is confirmed, the patient will be informed about the study activities and expectation, invited to participate and if they agree proceed with informed consent. The informed consent process may be executed in-person, by telephone or video procedures, or by electronic eConsent (RedCap). The dialysis facility staff will not be explicitly informed about the randomization assignment of patient participants.

Retention

Retention will be enhanced by 1) conducting research assessments by the mode preferred by the participants and this may include on-site in dialysis facilities or another agreed location in-person, by phone, video research visit or electronic survey, 2) close tracking of participant contact information 3) monitoring of telephone contact between mentor/mentee pairs, and 4) reimbursement for study activities (see next section). This level of reimbursement is standard for clinical research conducted at

our sites and is not considered undue inducement for participation. There will be opportunities for participants to provide feedback to the research team and participate in group activities. The study team will send thank you notes throughout the study to show appreciation for participation.

There will be a procedure in place for both mentors and mentees to report to the study team concerns about the matching or fit of the pair. If these concerns are not amenable to resolution, then a new matching will be performed for the mentee to complete the remaining activities of the planned intervention period. This will be recorded in the study record.

Incentives for mentors: Peer mentors will be compensated $10 for each hour of attended training session (2 hours each), for travel back and forth and $15/hour for time spent on the telephone while mentoring. Partial time for calls will be offered at the following rate: 3-30 minutes $7.50 and >30 min $15. Similar compensation for any 2-hour refresher courses after the initial training with the same incentives will be offered. Attempts to contact mentees at least four times during a week at different days and times will be compensated $12/week, unless a successful call is performed. While mentor participants will each get a phone they will be given instructions on their use for study purposes only. The telephone will be returned at the end of the study. For the assessments completed at baseline, 9 months and at 12 to 18 months, mentors will receive $50 for each visit. Sites may also provide compensation for travel costs if customary, included in the consent and IRB approved.

Incentives for patient participants: For the assessments completed at baseline, 3 months and at 12 to 18 months, patient participants will receive $50 for each visit and may be offered transportation costs if customary, included in the consent and IRB approved. Participants assigned to the intervention will receive a study telephone for the duration of 3 months with specific instructions to use the telephone only for study purposes. The phone will be returned at the conclusion of the intervention period. Intervention participants will also be offered compensation for time spent successfully on the phone with their mentor. This will be compensated at $15/hour. Partial time for calls will be offered at the following rate: 3-30 minutes $7.50 and >30 min $15. The study will support a maximum of 2 hours per week per mentee for mentor calls.

6 STUDY INTERVENTION(S) OR EXPERIMENTAL MANIPULATION(S)

6.1 STUDY INTERVENTION(S) OR EXPERIMENTAL MANIPULATION(S) ADMINISTRATION

6.1.1 STUDY INTERVENTION OR EXPERIMENTAL MANIPULATION DESCRIPTION

Mentor Training

All enrolled mentors will participate in mentor training. Details of this training are described in the 'Mentor Training Manual' and also the 'PEER Mentor Training Manual' (for the Trainer). A brief summary and overview is provided here.

We will train enrolled mentors over 4 weekly sessions, 2 hours each at preferentially in person group format at dialysis facility conference rooms, or other research location. An alternative for group training will be by webinar format. The training program is informed by the chronic disease self-management program (CDSMP), developed by Dr. Katie Lorig at Stanford University, to a dialysis population. Additionally, the Information Motivation Behavior (IMB) health behavior framework serves at the basis to inform the key topics focused on during the mentor training and deployed during the telephone peer support intervention.[68] (Figure 1)

We will use motivational interviewing, non-judgmental listening and boundary setting curricula adapted from programming provided by the Albert Einstein School of Medicine Division of General Internal Medicine for peer mentorship studies of opioid use, and programming in peer support of diabetes from the University of Michigan (Dr. Michele Heisler). The training focuses on maintaining and attaining a healthy EDW, understanding uremia, clearance, dialysis access and their relation to infection, and effectively self-advocating with a dialysis care team. The following skills will be included: a) confidentiality and setting boundaries with mentees, b) motivational interviewing, c) non-judgmental listening, d) emotional support, e) assistance with tailored goal setting and problem solving, f) increasing perception of self-efficacy and g) modeling self-management behaviors. The format of the training will include didactic teaching sessions from a clinician instructor with content expertise, role playing exercises, group discussion of cases, and independent study. Although group training is preferred, if this is not possible for an enrolled mentor then individual training by the instructor may also be provided to complete the four core sessions either in-person or using webinar/zoom format.

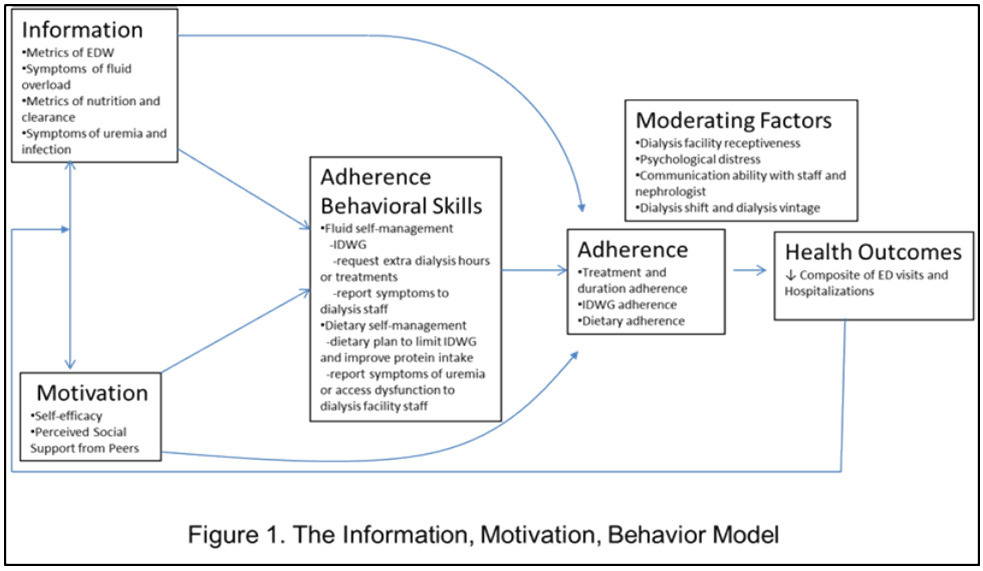


Figure 1. The Information, Motivation, Behavior Model

Refresher courses will be offered periodically, at approximately 3 months and 10 months after initial training or as needed for individual mentor's re-training. This will be at the discretion of the study team depending upon the information gathered during monthly and quarterly coordinator assessments of mentors (or mentee feedback). These refresher sessions will be approximately 2 hours, and be delivered in person, individually or in a group, or by video/webinar.

Trained mentors will receive a manual with all of the materials provided during training and this will serve as a reference for them throughout the study. There will be explicit support from the research team. It is possible that not all trained mentors will serve as intervention mentors and some may be assigned as 'back-up' mentors in the event an intervention mentor is not able to fulfil their role. Mentor selection will be discussed during training. The priority is optimizing the matching criteria between mentor/mentee pairs (sex, race (Hispanic, Black, White), age group (± 15 years), and language). Selection criteria is not based on mentor performance during training. If matching criteria are not applied, then random selection of mentor assignments will be employed.

Assessments during the training will provide information both about feasibility and efficacy of the training on the desired knowledge, attitude and skill outcomes among mentors (See Section 8).

Mentee Telephone PEER Support Program group

The mentor telephone PEER support intervention includes a trained mentor, who is assigned 1-4 mentees. The mentees each will participate in telephone support for a 3-month period. Study telephones will be assigned to mentors and required to be used for all study activities and offered to mentees for use during the program. Intervention mentees will be offered a study supplied phone, or

permitted to use their own device with the understanding they will be responsible for any incurred costs on their own device.

Pairing mentors and mentees
As noted above, the priority criteria for matching pairs includes and prioritized as: language, sex, age group, and race. Additionally, schedule availability and preferences by mentees will be considered.

Mentor telephone support
Mentors are expected to call each mentee once a week, with a goal of talking for an average of 20 minutes. Call durations of at least 3 minutes will be considered complete. Mentors are asked to make a minimum of four attempts to reach mentees by phone on different days and times throughout the week. Both mentors and mentees are offered compensation based on the time executed for study calls. Mentors and mentees are asked to record in a log a record of their calls including notes on discussions. Mentors will also be given a study digital recorder. They are expected to randomly record calls with mentees for fidelity and content review, approximate 3-4 over the intervention period for each mentee. Mentor and mentees are informed that telephone billing records will be reviewed for characterization of attempts and contacts between mentors and mentees. Communication between mentors and mentees after conclusion of the 3-month period is not expected but will be permitted. Mentors will continue to use their assigned study phone for all calls.

Optional social mixers, or other similar group gathering (in-person or virtual) will be offered for all mentor and mentee participants. This will provide an opportunity for mentors and mentees to provide informal feedback to each other, as well as an opportunity for informal interactions with the study team. A study newsletter for mentors to share knowledge and encourage retention may be used.

The frequency and the mean duration will be measured, the content of the call recorded in a notebook by each member of the team after contact. During mentor training, a schedule of suggested themes and discussion content for calls will be provided. In general, the focus of the first 4 weekly calls will be to increase knowledge of the mentee, and the last 8 weekly calls will focus on motivational interviewing, emotional and affirmation support. The structure will be flexible to the needs of individual mentees.

If one member of the pair dies, then the study team will meet with the other member, provide counseling, engage the clinical provider, and offer being paired with another mentor/mentee.

All intervention mentees will also be provided kidney disease educational materials: 1. Kidney School: Follow Your Treatment Plan; and 2. National Kidney Foundation: Hemodialysis Access. They will also receive study-specific educational materials that are also provided to mentors. This includes: Mentor Training Manual Appendix documents 1 (EDW information), 2 (Skills checklist for fluid), 4 (Uremia information), 5 (What to do for uremia), 6 (Information card), and 18 (Action Planning).

Usual Care control group
The usual care control group will be under the clinical care of the usual providers. The study will provide two kidney educational documents to the patient: 1. Kidney School: Follow Your Treatment Plan; and 2. National Kidney Foundation: Hemodialysis Access. They will also receive study-specific educational materials that are also provided to mentors. This includes: Mentor Training Manual Appendix documents 1 (EDW information), 2 (Skills checklist for fluid), 4 (Uremia information), 5 (What to do for uremia), and 6 (Information card).

6.1.2 ADMINISTRATION AND/OR DOSING

Mentor Training
As above, full details in training manual documents. The training will be delivered by clinician experts in dialysis care and patient-centered communication. Trainings include 4 core sessions, and refresher

modules. Additional individual re-training of mentors by study clinicians may also be provided. Attendance records will determine completion or dosing of mentor training.

Mentor PEER Phone Support

Mentors will contact their mentees at least once a week for a total of 12 weeks. The mentees will also be given the option to contact their mentees should the need arise at any point during the 3-month intervention. Phone billing records will be reviewed to determine the total dose of intervention (call minutes with mentor) total for the period, monthly average, and weekly average. The distribution of the range of call duration for each mentee will also be described. A minimum of 3 minutes completed is required to count as a completed call.

Additional in-person, or video interactions between mentors and mentees will be self-reported by mentors in their contact logs, or as observed by study team during social mixers. These interactions will be included in the dose calculation of the intervention.

The quality of the mentor/mentee interactions will be evaluated using content analysis of recordings and the contact logs of mentors and mentees. Additional information of the quality will be evaluated by the study coordinator in the monthly or quarterly surveys of mentors and mentees.

6.2 FIDELITY

6.2.1 INTERVENTIONIST TRAINING AND TRACKING

The mentors are the interventionists in this study. Initial training will be evaluated and confirmed using knowledge surveys, and evaluations by the trainer of skills during training. During the intervention program monthly and quarterly surveys by the study team will be used to identify problems with delivering the intervention as planned. As described above, phone records will also be used to evaluate frequency and dosing of attempts and successful calls. These records will be reviewed as frequently as monthly, but not less than every four months. Less than 10 minutes total of contact time between mentor and mentee in one month will prompt addressing barriers to executing the intervention for both mentor and mentee by the study team.

6.3 MEASURES TO MINIMIZE BIAS: RANDOMIZATION AND BLINDING

We will randomize enrolled patient participants after completion of informed consent and the baseline visit utilizing a random number generator. As each subject is enrolled we will select envelopes with the random assignment to either the intervention or the usual care control group (1:1). The randomization will occur in blocks of between 28 to 42 depending upon the number of mentor and planned assigned mentees at the site. The goal is to have approximately equal total number of enrolled participants within each ~3-month intervention period. There may be staggering of the window and timeline depending upon enrollment pacing.

The mentee assignments will be blinded to usual care nephrologist and dialysis staff, but not to study subjects and mentors, because of the nature of intervention. The research team additionally will not be blinded to group assignment. While this may be preferred, it is not feasible in this pragmatic trial. Enrolled participants will be encouraged to complete visit surveys on their own, to limit interactions with study staff in the process of data collection.

Trial randomization codes will be stored in a single file maintained by the data coordinating center. They will be shared with the research team as described above for patient participant assignment. Should accidental unblinding occur prior to completion of a baseline visit for a participant, the PI will be notified and this will be documented as a protocol deviation.

No change in study activities will occur in the event that it is identified that a usual care provider is unblinded to study assignment of their patient.

6.4 STUDY INTERVENTION/EXPERIMENTAL MANIPULATION ADHERENCE

Adherence of mentees to the peer support intervention will be monitored by the research team including monthly surveys with the mentee asking about the calls with their mentors, as well as review of phone records (See Section 6.2.1). For mentees not participating in calls with mentor the study team will attempt to identify and address the barriers to participation. If pairs want to disengage, we will give the option of pairing with another mentor/mentee from the pool.

Attendance records and notes for participation in any social mixers (in-person or video) will also be maintained and reviewed for assessment of mentee participation in the intervention, including engagement with mentors.

Although all activities are intended and preferred, mentees will not be withdrawn for not participating in the intervention. They will be included in the primary study analysis as intention-to-treat. Secondary analyses may include an adjustment variable considering the dose delivered of the intervention.

6.5 CONCOMITANT THERAPY

N/A

6.5.1 RESCUE THERAPY

N/A

7 STUDY INTERVENTION/EXPERIMENTAL MANIPULATION DISCONTINUATION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

7.1 DISCONTINUATION OF STUDY INTERVENTION/EXPERIMENTAL MANIPULATION

Conflicts or emotional distress may rise between mentors and paired mentees. The study team will get information from both mentor and mentee and determine the nature and severity of the conflict. If there are any concerns regarding emotional or physical safety of participants this will be recorded as an adverse event, reported to the DSMB and the participant(s) withdrawn from the intervention. The participant(s) may also be considered for withdrawal from the study overall depending upon the nature and severity of the event(s).

A mentor may decide to discontinue the study in case of clinical illness, inability to commit to the intervention schedule, or for any other personal reason. Participants may withdraw from the intervention at any time by notifying the study personnel. Mentors may be withdrawn from the intervention due to acute or temporary illness, but may be reconsidered for reactivation if agreed upon by the mentor and the study investigator. Mentors may be discontinued from the intervention if the study team is unable to reach them or they do not fulfil their mentor responsibilities. Mentors who receive a kidney transplant may continue as mentors, but EMR data specific to dialysis will not be collected by the study. Other study visit activities including surveys will be collected.

A mentee may decide to discontinue the study in case of severe illness, conflict, or inability to participate. The PIs at each site will maintain a record of these events and drop-outs and report them to the DSMB or IRB as required.

The PIs at each site will maintain a record of all adverse events, unanticipated problems, protocol

deviations or error. A summary of these will be reported to the IRB. These events will all be reviewed as potential reasons for discontinuation of the intervention (mentor or mentee), or withdrawal from the study overall. The PIs will be primarily responsible for this decision, however this will be reviewed by the DSMB, and if recommended an experienced clinician external to the study team.

If a clinically significant finding is identified (including, but not limited to changes from baseline) after enrollment, the investigator or qualified designee will determine if any change in participant management is needed. Any new clinically relevant finding will be reported as an adverse event (AE).

The data to be collected at the time of study intervention discontinuation will include the following:

- The reason(s) for discontinuing the participant from the intervention and the date the intervention ceased will be recorded in the subject's research file
- Study assessments including visits for survey completion and EMR review will continue as per the usual assigned scheduled throughout the duration of the overall study period

7.2 PARTICIPANT DISCONTINUATION/WITHDRAWAL FROM THE STUDY

Participants are free to withdraw from participation in the study at any time upon request.
An investigator may discontinue a participant from the study for the following reasons:

- Lost-to-follow up; unable to contact subject (see **Section 7.3, Lost to Follow-Up**)
- Any event or medical condition or situation occurs such that continued collection of follow-up study data would not be in the best interest of the participant or might require an additional treatment that would confound the interpretation of the study
    - Death
    - illness requiring institutionalization or a change in their dialysis unit
    - illness of a mentor that leaves them unable to fulfil their mentor role in any way
- The participant meets an exclusion criterion (either newly developed or not previously recognized) that precludes further study participation such as:
    - Receipt of a kidney transplant (patient participant mentee or usual care)
    - Change in mentation or cognition rendering the participant unable to participate, including suicidality
    - A change in the willingness of the participant to continue
    - A safety altercation between the paired participants
    - Verbal abuse or threats of physical abuse of any kind
- If the participant is to be discontinued but is medically able and willing, the T2 surveys will be administered at the time of discontinuation. Monthly EMR review will also end at the time of the T2 survey completion or date of discontinuation as determined by the PI.

The reason for discontinuation or withdrawal will be recorded on the withdrawal study form. Subjects who sign the informed consent form and are randomized, but do not receive the study intervention may be replaced. Subjects who sign the informed consent form, and are randomized and receive the study intervention, and subsequently withdraw, or are discontinued from the study, will not be replaced.

7.3 LOST TO FOLLOW-UP

A participant (either mentor or mentee) will be considered lost to follow-up if he or she fails to return for 2 or more scheduled study visits and study staff are unable to contact the participant after at least 6 attempts. We will minimize loss to follow up by inquiring with the dialysis facility about the participant's whereabouts if mentors miss 2 or more training sessions, 2 or more scheduled weekly calls to mentees and/or 2 or more telephone calls from study staff; or as mentees or usual care group if they miss 1 or more study visits, and do not return calls from study staff.

The following actions must be taken if a participant fails to return to the clinic for a required study visit:

- The site will attempt to contact the participant, reschedule the missed visit within 14 days of scheduled visit, counsel the participant on the importance of maintaining the assigned visit schedule and ascertain if the participant wishes to and/or should continue in the study
- Before a participant is deemed lost to follow-up, the investigator or designee will make every effort to regain contact with the participant (where possible, 6 telephone calls and, if necessary, a certified letter to the participant's last known mailing address). These contact attempts will be documented in the participant's study file.
- Should the participant continue to be unreachable, he or she will be considered to have withdrawn from the study with a primary reason of lost to follow-up

8 STUDY ASSESSMENTS AND PROCEDURES

8.1 ENDPOINT AND OTHER NON-SAFETY ASSESSMENTS

Refer to Section 5 for details regarding recruitment for mentors and patient participants for screening procedures to evaluate for eligibility, including execution of a HIPAA waiver prior to screening if required by local site regulations. Scoring for surveys is detailed in the PEER HD Survey Scoring guide.

Screening & Enrollment

Mentors. Potential participants will first undergo a screening of their EMR and the information will also be confirmed by interview with the patient prior to enrollment (RedCap: 'Mentor Eligibility Questionnaire From EMR'). This includes questions about the inclusion/exclusion criteria.

Patient Participants. Potential participants will first undergo a screening of their EMR and the information will also be confirmed by interview with the patient prior to enrollment (RedCap: 'Mentee Eligibility Questionnaire From EMR'). This includes questions about the inclusion/exclusion criteria.

Mentor Training Assessments

Mentors will be evaluated by *post-training* assessments. This will include the following:

- Fluid Training Survey (Module 1; 6 items)
- Uremia & Infection Training Survey (Module 2; 6 items)
- Mentor Role Training Survey (Module 3; 5 items)
  Each of these survey items has one correct answer. Score will be reported as % correct overall.
- Mentor Role Play Self-Assessment (Modules 3 & 4; 'Confident' Likert-type responses; 11 items)
- Formative Assessment after each module (Strongly agree to Strongly disagree; 11 items)
- Summative Assessment at the conclusion of core training (open ended questions; 5 items)

Refresher training events will only include formative and/or summative post-training assessments.

Baseline Visit, 3-Month (Patient participants), 9-Month (Mentor), 12 to 18-Month (T2; All)

Surveys will be completed for all visits by both mentors and patient participants, unless otherwise specified. Mentors will complete baseline surveys prior to participating in training activities.

Baseline visit. Include the following assessments:

- Demographics, health literacy, behaviors, and ED/Hospitalization self-reported use
- Self-report of medical history and access to care

All visits. Include the following assessments:

- Quality of Life (RAND SF-36)
- Depressive symptoms (CESD-10)
- Dialysis Self-management Self-efficacy (PDialSMS)

- Kidney Disease Self-Management Behaviors Index (KDBI)
- Multidimensional Scale of Perceived Social Support (MSPSS)
- Dialysis-specific Social Support Survey
- Brief Kidney-COPE Survey
- Chronic Hemodialysis Knowledge Survey (CHeKs)
- CHeKs PLUS Survey
- Communication Assessment Tool (CAT)

Mentee group only – 3-Month Visit. Include the following assessments:

- Health Care Climate Questionnaire (HCCQ) Long Form
- Checklist for Mentee Assessment of Mentors

Monthly all participants. Include the following assessment:

- Self-report of ED visits and/or hospitalizations

Monthly & Quarterly Intervention Survey (Mentor)

Study personnel will contact all mentors to monthly and perform the 'Study Staff Monthly Mentor Check-in Survey'. Additionally, mentors will perform a quarterly self-assessment.

Intervention recordings & logs & phone billing record review

Phone billing records for all mentor and mentee phones will be reviewed. All calls will be abstracted including: phone number called, date, time, and duration. A summary of weekly minutes between mentor and mentee pairs will be generated for characterization of intervention dosing as well as evaluation of execution of mentor and mentee responsibilities. If the mentor uses his/her own personal telephone to contact the mentees, the study staff may ask to review the pertinent personal telephone records with that mentor to ascertain the time spent mentoring.

Random recordings of calls will be submitted to the study team for qualitative review of content. Call logs by mentors and mentees will also be reviewed, coded and characterized for content notes.

Medical Record Review

All records reviewed will be from clinical care. All participants will provide HIPAA authorization as part of informed consent to request this information and permit its inclusion in the study. Additional permission for records requests from external health systems may be provided by the participant to the study.

A review of medical records will be performed at baseline for all participants during their active study period. This will include insurance type, comorbidity evaluation, date of first dialysis ever, information from Form 2728 about pre-dialysis care, medications, dialysis schedule. ED visits and hospitalizations.

Monthly medical record review will include dialysis treatment duration prescribed and delivered, interdialytic weight gain mean (%) for the month, serum albumin, ED visits and unplanned hospitalizations.

8.2 SAFETY ASSESSMENTS

There are no dedicated safety assessments in this study given no more than minimal risk related to the intervention. However, all participants have a serious chronic medical condition (ESKD requiring dialysis). Coordinators will be trained to report any unexpected events to study PIs. Planned evaluations include feedback about the intervention to report concerns, or suggestions for improvements.

8.3 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

8.3.1 DEFINITION OF ADVERSE EVENTS

Due to the nature of the intervention this study is considered no more than minimal risk to participants. However, monitoring for adverse events will be included as described below given the study population is medically complex and at high risk for health events independent of the study.

This protocol uses the definition of adverse event from 21 CFR 312.32 (a): any untoward occurrence associated with the use of an intervention in humans, ***whether or not considered intervention-related***. Examples may include emotional distress, or study related anxiety.

- The adverse events for mentors associated with this study include:
  - Distress related to curriculum training duration and skills assessments
  - Distress related to telephone conversations with assigned mentees
- The adverse events for patient participants, including intervention mentees, include:
  - The embarrassment and/or stigma of being identified as a high-risk patient
  - Distress related to concern for loss of privacy of health information by mentor disclosure
  - Distress related to telephone conversations with mentors

8.3.2 DEFINITION OF SERIOUS ADVERSE EVENTS

A *serious adverse event* (SAE*)* is any AE that is:

- fatal or results in death
- life-threatening
- requires or prolongs hospital stay
- results in persistent or significant disability or incapacity
- an important medical event*

  *Important medical events are those that may not be immediately life threatening but are clearly of major clinical significance.

8.3.3 CLASSIFICATION OF AN ADVERSE EVENT

8.3.3.1 SEVERITY OF EVENT

All adverse events (AE), including serious adverse events (SAEs) will be assessed by the principal investigator, using the following defined grading system. For any events deemed to be severe, and related to the intervention, a report will be written and submitted to the IRB as well as to the DSMB for further evaluation.

- **Not serious** – Events require minimal or no treatment and do not interfere with the participant's daily activities.
- **Serious** – Events that result in a low level of inconvenience or concern with the therapeutic measures. Moderate events may cause some interference with functioning.
- **Life-threatening** – Events interrupt a participant's usual daily activity and may require treatment. Severe events are usually potentially life-threatening or incapacitating. Of note, the term "severe" does not necessarily equate to "serious".
- **Fatal**

8.3.3.2 RELATIONSHIP TO STUDY INTERVENTION/EXPERIMENTAL MANIPULATION

The study site PI, an expert nephrology clinician, will review the events and determine relatedness with the study intervention. If the determination is not clear, the site PI will engage the DSMB to additionally review a de-identified version of the case and determine related-ness to the study intervention.

The PI and/or DSMB will grade the causality of the adverse event to any element of the study using the following categories.

- **Definitely Related** – The AE is known to occur with the study procedures, there is a reasonable possibility that the study procedures caused the AE, or there is a temporal relationship between the study procedures and the event. Reasonable possibility means that there is evidence to suggest a causal relationship between the study procedures and the AE.
- **Probably Related** – There is evidence to suggest a causal relationship, and the influence of other factors is unlikely. The clinical event, occurs within a reasonable time after administration of the study procedures, is unlikely to be attributed to concurrent disease or other drugs.
- **Potentially Related** – There is some evidence to suggest a causal relationship (e.g., the event occurred within a reasonable time after administration of study procedures). However, other factors may have contributed to the event (e.g., the participant's clinical condition, other concomitant events). Although an AE may rate only as "possibly related" soon after discovery, it can be flagged as requiring more information and later be upgraded to "probably related" or "definitely related", as appropriate.
- **Unlikely to be Related** – There is not a reasonable possibility that the study procedures caused the event, there is no temporal relationship between the study procedures and event onset, or an alternate etiology has been established.

8.3.3.3 EXPECTEDNESS

A clinician with appropriate expertise in nephrology/dialysis will be responsible for determining whether an adverse event (AE) is expected or unexpected. An AE will be considered unexpected if the nature, severity, or frequency of the event is not consistent with the risk information previously described for the study procedures. As described previously some discomfort to mentors during training and their mentoring activities is expected. Some conflicts may also arise between the mentor/mentee pairs which are to be expected as well. These occurrences will be considered "expected".

The following serious adverse events are anticipated in the hemodialysis population and are not considered "unexpected" or Unanticipated Problems. Note that the designation as "Anticipated" does *not* imply that the event is not an SAE but relates to the regulatory definition of Unanticipated Problems as provided in Section 8.4.

- Death
- Coronary Ischemia including:
  - Unstable angina
  - Acute MI
  - Coronary revascularization
- Heart failure hospitalization or exacerbation
- Cardiac arrest
- Cardiac arrhythmia (ventricular or atrial)
- Peripheral vascular revascularization
- Amputation
- Hypotension
- Hypertension
- Nausea or vomiting
- Vascular Access Events including:
  - Catheter exchange, removal or thrombolysis
  - Arteriovenous graft or fistula complications

  - Thrombosis
  - Stenosis
  - Revascularization
  - Infection
- Infections including:
  - Pneumonia
  - Bacteremia
  - Hemodialysis vascular access infection

8.3.4 TIME PERIOD AND FREQUENCY FOR EVENT ASSESSMENT AND FOLLOW-UP

The occurrence of an adverse event (AE) may come to the attention of study personnel during study visits and interviews of a study participant presenting for medical care, or review by a study monitor. All AEs, not otherwise precluded per the protocol, will be captured on the Adverse Event Log Form. Information collected includes event description, time of onset, clinician's assessment of severity, relationship to study procedures (assessed only by those with the training and authority to make a diagnosis), assessment of expectedness, and time of resolution/stabilization of the event. All AEs will be followed to adequate resolution.

Any medical or psychiatric condition that is present at the time that the participant is screened will be considered as baseline and not reported as an AE. Changes in the severity of an AE will be documented to allow an assessment of the duration of the event at each level of severity to be performed. Documentation of onset and duration of each episode will be maintained for intermittent AEs.

In this study, ED visits and hospitalizations, including reasons for these encounters, are collected as solicited events as they serve as the primary outcome. Vascular access use are solicited, and satisfaction with the intervention will be solicited monthly.

The study PIs, with the help of the research assistants, will record adverse events with start dates occurring any time after informed consent is obtained until 7 (for non-serious AEs) or 30 days (for SAEs) after the last day of study participation. At each study visit, the investigator will inquire about the occurrence of AE/SAEs since the last visit. Events will be followed for outcome information until resolution or stabilization.

8.3.5 ADVERSE EVENT REPORTING

All AEs will be assessed by a principal investigator, using the above protocol defined grading system. Disease-related events common in the study population are described in 8.3.3.3. All AEs will be documented on the AE Study Log Form and also in the individual participant research record. If the AE meets the criteria for an SAE it will be documented accordingly and reported to the PIs, DSMB and IRB if indicated (Unexpected and Probably or Definitely related to the Intervention). Events that meet criteria for reporting to the IRB, this will occur within 10 business days and also summarized in the continuing review. If the event is unexpected probably or related to the intervention and results in death, the event will be reported to the IRB within 3 days and also summarized at the continuing review, or as required by the local IRB.

8.3.6 SERIOUS ADVERSE EVENT REPORTING

SAEs will be evaluated as described previously and recorded on the Adverse Event Study Log Form. This include information about if the study intervention was discontinued, the reason why the event is classified as serious, and the assessment of relatedness to the intervention. Any additional records for evaluation will be requested as needed and continue until the event is resolved. AE forms may be completed by research coordinators, but must be reviewed and signed by a site investigator. SAEs that

are ongoing at the end of the trial will be followed to determine the final outcome. SAEs will be reported as per the timeline and requirements for AEs (Section 8.3.5).

8.3.7 REPORTING EVENTS TO PARTICIPANTS

Study findings, including an aggregated report about AEs and SAEs will be available to study participants in publicly available online sources (clinicaltrials.gov), scientific literature and any associated reports, and potentially websites of the investigators, or their organizations.

8.3.8 EVENTS OF SPECIAL INTEREST

N/A

8.3.9 REPORTING OF PREGNANCY

N/A

8.4 UNANTICIPATED PROBLEMS

8.4.1 DEFINITION OF UNANTICIPATED PROBLEMS

This protocol uses the definition of Unanticipated Problems as defined by the Office for Human Research Protections (OHRP). OHRP considers unanticipated problems involving risks to participants or others to include, in general, 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 protocol-related documents, such as the Institutional Review Board (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); and
- 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.

Examples may include events such as loss of study equipment with private information, or complaints by participants, family or staff members.

8.4.2 UNANTICIPATED PROBLEMS REPORTING

The investigator will report unanticipated problems (UPs) to the reviewing Institutional Review Board (IRB) and to the DSMB and lead PI. The UP report will include the following information:

- Protocol identifying information: protocol title and number, PI's name, and the IRB project number
- A detailed description of the event, incident, experience, or outcome
- An explanation of the basis for determining that the event, incident, experience, or outcome represents an UP
- A description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the UP

To satisfy the requirement for prompt reporting, UPs will be reported using the following timeline:

- UPs that are serious adverse events (SAEs) will be reported to the IRB and to the DCC/study sponsor/funding agency within 10 days of the investigator becoming aware of the event. However,

if the UP is classified as probably or related to the intervention and results in death the IRB will be notified within 3 calendar days, or as required by the local IRB.

- If the unanticipated problem is unrelated to the intervention it will be documented on the Adverse Event Study Log Form and summarized and reported to the DSMB as part of continuing review.

8.4.3 REPORTING UNANTICIPATED PROBLEMS TO PARTICIPANTS

Reporting of UPs to participants will depend on the nature of the UP. This may include:

- Modification of informed consent documents to include a description of newly recognized risks
- Provision of additional information about newly recognized risks to previously consented/enrolled participants.

9 STATISTICAL CONSIDERATIONS

9.1 STATISTICAL HYPOTHESES

- Primary Endpoint:
  The primary objective is to determine the effectiveness of a peer support telephone intervention compared with usual care to reduce a composite of ED visits and hospitalizations among patients receiving in-center hemodialysis for ESKD. The null hypothesis is that the count of composite events at the end of the study period between intervention and usual care are the same. The alternative hypothesis is that the count of composite events at the end of the study period are different.

- Secondary Endpoint(s):
  - To determine the effectiveness of a peer support phone intervention compared to usual care to improve:
    - dialysis self-management including:
      - Dialysis treatment schedule adherence (mean minutes missed per month)
      - Inter-dialytic weight gain (IDWG) (mean monthly %)
    - nutritional status (serum albumin)
    - dialysis knowledge
    - dialysis self-management self-efficacy
    - social support (general and dialysis-specific)
    - coping skills
    - quality of life
    - communication with providers

  The null hypothesis is that the secondary endpoint values at the end of the study period between intervention and usual care are the same. The alternative hypothesis is that the secondary endpoint values at the end of the study period are different.
- Feasibility endpoint(s):
  - To determine the feasibility of a structured, multicomponent, multiple session peer mentor training program at two sites. There is no specified hypothesis.
  - To determine the acceptance of peer mentor phone intervention by patients. There is no specified hypothesis.

Table 4. Scientific Questions to be Addressed with the Trial

Scientific question	Outcome(s)	Analysis
1. Does phone peer support improve outcomes at 18-months (*12 to 18-months)?	• Primary: composite endpoint count of ED visit and hospitalization events • Secondary: Various as listed above	Poisson regression with two random intercepts. Random intercepts account for clusters by (1) mentor; (2) dialysis unit See Section 9.4.2 (Primary); 9.4.3 (Secondary)
2. Is a peer mentor training program feasible?	• Attendance records • Pre- and Post-knowledge test scores • Satisfaction with training • Summative assessment	Paired t-tests Descriptive summaries and content analysis of qualitative data
3. Is a peer mentor training program accepted by patient receiving hemodialysis	• Satisfaction with intervention • Communication rating of mentors	Descriptive Content analysis of qualitative data

9.2 SAMPLE SIZE DETERMINATION

For evaluation of the primary endpoint, estimates are based on local dialysis unit hospitalization events in the past 12 months. For the control group, we expect 0.27 events per month (100 prevalent patients and 27 composite events per month). With 73 patients per group (after 25% drop-out), our study has >80% power to detect 20% reduction (i.e. a reduction of 0.054 visits per person-month) at type 1 error level 0.05.[155] We will recruit at least 100 patients per group over the course of the study.

9.3 POPULATIONS FOR ANALYSES

For the primary endpoint comparison, an intention-to-treat analysis will be used, including all available data on randomized participants. It is expected that up to 20% of randomized participants may discontinue from the study prior to the end point. These participants will be included in the primary analysis and data from the monthly outcome ascertainment up until the last available time point will be used. As preparation for the follow-up period modification, events to date were evaluated at one site (Einstein) and were found to be more frequent than initial estimates. This informed the request for reduction in the follow-up period.

The characteristics of those who do not complete all study activities will be compared to those with complete follow-up to examine for potential biases introduced by differential follow-up among the two groups. These will be considered ancillary analyses.

Secondary analyses will examine additionally an as-treated population. This will group any intervention patient who did not participate in more than 20 minutes total of the intervention during the three-month period to be classified as the usual care group.

9.4 STATISTICAL ANALYSES

9.4.1 GENERAL APPROACH

Descriptive statistics will be used to provide for each variable: number of observations, mean, standard deviation, median, minimum and maximum for continuous variables; frequencies and proportions for categorical variables. Results will be reported in accordance with the extended CONSORT guidelines for pragmatic clinical trials using two-sided statistical tests and confidences intervals. For all analyses, the overall level of significance will be set at 0.05. All analyses will be adjusted for site. Adjustment variables will be pre-specified in the following sections. All analyses will be performed using SAS v9.4 (SAS Institute, Cary, NC), STATA (College Station, Tx), or R (currently 3.6.1; *https://cran.r-project.org/*).

Analyses of qualitative data will include content analysis, novel code generations as applicable, interpretation and descriptive reporting.

9.4.2 ANALYSIS OF THE PRIMARY ENDPOINT(S)

ED Visit and Hospitalization Count

Each month all enrolled patients will be evaluated for ED visit or hospitalization encounters by both self-report and medical record review. The events will be tabulated each month up to an 18-month period of follow-up. The rates of the composite event will be determined as event per patient-month and compared between the intervention and usual care group using Poisson regression with two random intercepts. In the regression model, the composite counts of ED visits and hospitalization during up to 18-months follow-up is the outcome variable and the intervention assignment of the mentees is the primary binary predictor. The log of follow-up time will be included as offset. The random intercepts will account for the correlation between mentees who share a common mentor as well as the correlation between mentees who are from a common dialysis facility (out of seven facilities). As a randomized controlled trial, we do not anticipate the need for covariate adjustment. However, if evaluation of patient characteristics by group identifies a failure of randomization and imbalance in key characteristics as an example including age, gender, comorbidity, race, or dialysis vintage they will be considered as adjustment variables in the analysis. We will control for type 1 error at 0.05. An exploratory analysis will consider the comparison between the groups but at 3-months of observation after the conclusion of the intervention delivery.

We will perform residual analysis for the mixed effects models. For mixed effects models, we will examine marginal residuals to check linearity and within-subjects covariance matrix and conditional residuals to check outliers as well as normality and homoscedasticity of the residual errors. In case Pearson residual analyses indicate overdispersion in the Poisson mixed effects model, we will perform quasi-Poisson model. We will use robust sandwich estimator in the presence of misspecification of the covariance matrix (i.e. random effects structure).

All data analyses will be preceded by extensive data checking and verification to identify and resolve the reasons for missing values, inconsistencies, and out-of-range values. Although, we anticipate less than 15% missing data, we will carefully examine whether missingness is completely at random (MCAR), at random (MAR) or informative (MNAR). Models proposed for analysis can handle incomplete data (i.e. entire subject is not deleted if missing data at one time point), but do require at least that missingness be at random. Modelling will consider using multiple imputation techniques of covariates to reduce potential biases.

9.4.3 ANALYSIS OF THE SECONDARY ENDPOINT(S)

The primary evaluation will be at the end of the study period (12 to 18-months) using all available data regardless of the period end for participants, and comparisons at 3M will be secondary. For the primary evaluation, we will test the longitudinal effect of a peer mentor led telephone intervention on mentee self-management skills including 1) dialysis adherence (mean number of outpatient dialysis hours per month), 2) mean monthly inter-dialytic weight gain (IDWG), and 3) mean monthly albumin levels. We

will compare the rate of change over time of the monthly secondary endpoints between two intervention groups using linear mixed effects regression model. In the regression model, the secondary endpoint (e.g. monthly mean dialysis hours) is the outcome variable with two main effects (the intervention assignment and months from baseline) and the interaction term between the main effects. The interaction term (i.e. the difference in slopes between two groups) is the primary predictor of interest. There will be three random intercepts to account for mentor effect, facility effect (out of seven facilities) and subject effect (to account for within correlation from repeated measurements). We will evaluate differences in baseline variables identified in Table 6 and if they are different between the groups, we will adjust for them as confounders.

For the secondary evaluation at 3M, we will perform Wilcoxon rank-sum test to compare the 3-months change of secondary endpoints between the intervention mentee and control mentees. To account for confounders, we will also fit linear regression model with two random intercepts. In the regression model, the 3 months-change of secondary endpoint is the outcome variable and the intervention assignment of the mentees is the primary binary predictor. The random intercepts will account for the correlation between mentees who share a common mentor as well as the correlation between mentees who are from a common dialysis facility.

Below, each endpoint is described including its source, scoring and planned analysis approach. Additional details for scoring of surveys is provided in the PEER HD Survey Scoring guide document. Within group (mentors) for change in outcomes over time will also be evaluated.

Outcomes derived from clinical EHR records

Dialysis treatment schedule adherence (mean minutes missed per month)

This outcome will be summarized as total minutes prescribed per month, minutes delivered per month and the missed minutes is the prescribed minus the delivered minutes. There will be no value less than zero (eg. no accounting for additional minutes).

This is a repeated end-point with values for each month of the observation period (Months 1 through up to 18). The value itself is interval (0 – 240, or higher).

Inter-dialytic weight gain (IDWG) (mean monthly, %)

This outcome will be summarized each month as the mean IDWG for the month prior in kilograms. The value will include all intervals regardless of time between treatments (2-days, 3-days or other), and will be calculated as the pre-weight minus the prior treatment post-weight. Prescribed dry weight will also be collected monthly to permit an average calculation of % of dry weight. This value is interval.

Nutritional status (serum albumin g/dL)

The serum albumin collected for monthly labs will be collected. If there are multiple values in one calendar month, then the last value of the month will be collected. This is an interval variable.

Outcomes derived from patient-reported measures

Dialysis knowledge {CHeKS; CHeKS PLUS]

See scoring guide for full detail. These are multiple choice knowledge questionnaires where there is only one correct answer. The score will be % correctly answered of the total. Missing responses are scored as incorrect. At least 75% of the items must have answer to be scored.

Dialysis self-management self-efficacy

The PDialSMS is collected at three times during the study. It is an interval value ranging from 8 to 40.

Social support

This is measured with the 12 item Multidimentional Scale of Perceived Social Support (MSPSS). The total score is the sum across the 12 items (each 1-7) divided by 12. There are also 3 subscales (significant other, family, and friends) each composed of 4 items. This value is interval.

A dialysis-specific social support survey is also collected to characterize the frequency of interactions between the participant and other dialysis patients. There are six items (range 1-5) and the total score is the mean of the six items.

Quality of life

This is measured with the RAND SF-36. Responses are standardized to a 0 to 100 scale and then averaged together to derived 8 subscale scores. Four of these then contribute to the physical component score (PCS), and four contribute to the mental component score (MCS). All values are interval.

For the perception of social support and self-efficacy we will use linear regression with two random intercepts to compare the scores on the PKDSMS, social support survey and quality of life surveys between the intervention mentee and control mentees at the various time points. The outcome variable for the regression is the assessment scores and the predictor of interest is the binary indicator of intervention groups.

Coping skills

This is measured with the Brief K-COPE a kidney-oriented adaptation of the Brief COPE survey. It has 28 items score 1 to 4. There are 14 subscales composed of 2 items each. The score for each subscale is the sum of the two individual items that compose that scale (2-8).

Communication with providers

This is measured with the Communication Assessment Tool (CAT). There are 14 items with a response ranging from 1 to 5. The total score is the average of the 14 items. Question 15 is descriptive and not included in the overall score of the CAT.

Feasibility Outcomes: We will perform Wilcoxon rank sum test to test the difference in pre-and post-training knowledge assessments in the mentors (Baseline CHeKS; PLUS vs. 9M and 12 to 18M). The outcome variable for the regression is the difference between pre-and post-training scores and the parameter of interest is the intercept. We will test if the intercept is zero.

For qualitative data, we will review the content of the individual surveys and develop a novel coding scheme to characterize the content including common themes identified. We will also provide descriptive results of the HCCQ survey characterizing mentees' ratings of mentor communication.

9.4.4 SAFETY ANALYSES

Adverse events will be descriptively tabulated and included in the analysis report of the study.

9.4.5 BASELINE DESCRIPTIVE STATISTICS

All baseline variables will be summarized by treatment group using descriptive statistics (sample size, mean, standard deviation, median, minimum, and maximum) for continuous variables and by the number and percentage of patients for categorical variables. We will test the success of randomization by examining differences in the two treatment groups by performing two-sample Mann-Whitney non-parametric test for continuous variables, and chi-square test for the categorical variables.

This will also include an evaluation of the degree of concordance between mentors and mentees for variables considered for pairing. This includes: sex, race/ethnicity, language, age category and schedule preferences.

9.4.6 PLANNED INTERIM ANALYSES

No planned interim analyses.

9.4.7 SUB-GROUP ANALYSES

Potential effect modification will be examined by including interaction terms between the intervention and patient characteristics such as sex, race/ethnicity, age, health literacy, numeracy, and depressive symptoms. For baseline factors with statistically significant interactions, intervention effects will be reported by subgroups. This will be applied to all endpoints (primary and secondary).

9.4.8 TABULATION OF INDIVIDUAL PARTICIPANT DATA

Data will be tabulated as de-identified, without site or patient identifiers.

9.4.9 EXPLORATORY ANALYSES

In exploratory analyses, we will examine the dose of intervention (total minutes; average minutes per week), and the degree of concordance between mentor and mentee characteristics as a mediator or moderator of the impact of the intervention.

10 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1 REGULATORY, ETHICAL, AND STUDY OVERSIGHT CONSIDERATIONS

10.1.1 INFORMED CONSENT PROCESS

We will obtain informed consent from mentors and mentees separately. Recruitment procedures include screening for eligibility. Verbal consent will be provided by the participant for proceeding with screening. In some sites, a HIPAA consent form may be required prior to initiating any recruitment procedures, including screening for eligibility. We will comply with NIH Human Research Protections Program policies and procedures. The investigator will also comply with applicable regulatory requirements (45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56) and will adhere to the ICH-GCP. All of the informed documents are approved by the institutional review boards of each participating site.

10.1.1.1 CONSENT/ASSENT AND OTHER INFORMATIONAL DOCUMENTS PROVIDED TO PARTICIPANTS

All documents, including recruitment scripts (in-person, virtual, phone or email/letter), will be IRB approved prior to use in this study. They will be available in English, and may be available in Spanish (site specific). Consent forms describing in detail the study intervention, study procedures, and risks will be given to the participant and written documentation of informed consent, or alterations in the procedure if IRB approved and described in the following section, will be completed prior to starting the study.

10.1.1.2 CONSENT PROCEDURES AND DOCUMENTATION

Participants identified by the study recruitment strategies and who are deemed to be eligible for participation will provide informed consent. This may be performed according to local IRB approvals including the provision of written consent after an in-person discussion about the study with the research team. A copy of this written consent will be provided to the participant, stored in their research record, and many also be stored in their medical record, if required. Alterations of the consent process may also be performed if approved by local IRB. This may include a virtual research consent visit where the participant and study team have a video visit to discuss the study. The consent form will be provided ahead of time to the participant by mail, email (if provided by the participant and requested) or picked up at a clinic location if permitted. The patient may then return a signed copy of the consent to the research team. It will be stored as above. A phone consent process may also be performed similar to a virtual consent visit. A final option may be the execution of an electronic version of the consent form through RedCap. In this case, the participant will still have either a phone or virtual visit with the

coordinator to discuss the study. In place of a paper copy of the consent form, an electronic exact content copy will be sent to the patient by email link for their review and electronic signature. This will be stored in RedCap. A copy will be printed, if possible, and stored in the participant's research file and/or medical record if required. Study materials may provide a web address or QR code to the study's econsent if permitted by local IRB. Consent forms will be available in English, and may be available additionally in Spanish (site specific).

All participants currently active in the study after 4/30 amendment approval, and any new enrollments, will execute the revised version of the informed consent document describing the revised study timeline.

10.1.2 STUDY DISCONTINUATION AND CLOSURE

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to study participants, investigator, funding agency, and regulatory authorities. If the study is prematurely terminated or suspended, the Principal Investigator (PI) will promptly inform study participants, the Institutional Review Board (IRB), and sponsor/funding agency and will provide the reason(s) for the termination or suspension. Study participants will be contacted, as applicable, and be informed of changes to study visit schedule.

Circumstances that may warrant termination or suspension include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to participants
- Insufficient compliance to protocol requirements
- Data that are not sufficiently complete and/or evaluable
- Unforeseen circumstances, including natural disasters, that preclude safe execution of study activities

The study may resume once concerns about safety, protocol compliance, and data quality are addressed, and satisfy the funding agency, sponsor, or other relevant regulatory or oversight bodies (DSMB).

10.1.3 CONFIDENTIALITY AND PRIVACY

Participant confidentiality and privacy is strictly held in trust by the participating investigators, their staff, the safety and oversight monitor(s), and the sponsor(s) and funding agency. This confidentiality is extended to the data being collected as part of this study. Data that could be used to identify a specific study participant will be held in strict confidence within the research team. No personally-identifiable information from the study will be released to any unauthorized third party without prior written approval of the sponsor/funding agency.

All research activities will be conducted in as private a setting as possible. The study monitor, other authorized representatives of the sponsor or funding agency, representatives of the Institutional Review Board (IRB), or regulatory agencies, may inspect all documents and records required to be maintained by the investigator, including but not limited to, medical records for the participants in this study. The clinical study site will permit access to such records.

The study participant's contact information will be securely stored at each clinical site for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for as long a period as dictated by the reviewing IRB, Institutional policies, or sponsor/funding agency requirements.

Study participant research data, which is for purposes of statistical analysis and scientific reporting, will be transmitted to and stored at the study data coordinating center. This will not include the participant's contact or identifying information. Rather, individual participants and their research data will be identified by a unique study identification number. The study data entry and study management systems used by study sites will be secured and password protected. At the end of the study, all study databases will be de-identified and archived at the data coordinating center, and shared with data repositories or other investigators as may be required or agreed upon for additional research.

Measures Taken to Ensure Confidentiality of Data Shared per the NIH Data Sharing Policies

It is NIH policy that the results and accomplishments of the activities that it funds should be made available to the public (see *https://grants.nih.gov/policy/sharing.htm*). The PI will ensure all mechanisms used to share data will include proper plans and safeguards for the protection of privacy, confidentiality, and security for data dissemination and reuse (e.g., all data will be thoroughly de-identified and will not be traceable to a specific study participant). Plans for archiving and long-term preservation of the data will be implemented, as appropriate.

Certificate of Confidentiality

To further protect the privacy of study participants, the Secretary, Health and Human Services (HHS), has issued a Certificate of Confidentiality (CoC) to all researchers engaged in biomedical, behavioral, clinical or other human subjects research funded wholly or in part by the federal government. Recipients of NIH funding for human subjects research are required to protect identifiable research information from forced disclosure per the terms of the NIH Policy (see *https://humansubjects.nih.gov/coc/index*). As set forth in 45 CFR Part 75.303(a) and NIHGPS Chapter 8.3, recipients conducting NIH-supported research covered by this Policy are required to establish and maintain effective internal controls (e.g., policies and procedures) that provide reasonable assurance that the award is managed in compliance with Federal statutes, regulations, and the terms and conditions of award. It is the NIH policy that investigators and others who have access to research records will not disclose identifying information except when the participant consents or in certain instances when federal, state, or local law or regulation requires disclosure. NIH expects investigators to inform research participants of the protections and the limits to protections provided by a Certificate issued by this Policy.

10.1.4 FUTURE USE OF STORED SPECIMENS AND DATA

Data collected for this study will be analyzed and stored at the Albert Einstein College of Medicine. A de-identified dataset may also be shared with study investigators at Vanderbilt University Medical Center. After the study is completed including completion of analyses and publication of study results, the de-identified, archived data may be transmitted to and stored at the NIH/NIDDK repository, for approved use by other researchers including those outside of the study. Permission to share data will be included in the informed consent. Additional requests by investigators may be made to the coordinating center for consideration of sharing of the de-identified dataset for IRB approved research.

There will be no storing of biosamples for this study.

10.1.5 KEY ROLES AND STUDY GOVERNANCE

This is a multi-site with shared responsibilities in a Multi-PI governance. There is no pre-identified medical monitor or independent study monitor given the no more than minimal risk of the intervention of this study. The safety of participants and execution of the study is overseen by a DSMB (See Section 10.1.6)

Principal Investigator (Contact)	**Co-PI**	**Co-PI**
Ladan Golestaneh, MD MS *Professor of Medicine*	*Michal Melamed, MD MHS* *Associate Professor of Medicine*	*Kerri Cavanaugh, MD MHS* *Associate Professor of Medicine*
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10.1.6 SAFETY OVERSIGHT

Safety oversight will be under the direction of a Data and Safety Monitoring Board (DSMB) composed of individuals with the appropriate expertise, including care of patients on hemodialysis and behavioral clinical research. Members of the DSMB will be independent from the study conduct and free of conflict of interest. The DSMB will meet at least semiannually to assess safety and efficacy data from each arm of the study. The responsibilities of the DSMB include: 1) to review the feasibility and safety of the study protocols; 2) to review feasibility and safety of training materials for mentors; 3) to approve any adaptation of the protocols or training material; and 4) to review enrollment, study procedures and any events during the course of the study. A template of the DSMB report is available and includes descriptions of study activities by site, including enrollment, data collection and any AEs. The DSMB will provide its input to the study team, the site IRBs, and the National Institutes of Diabetes and Digestive and Kidney Diseases/National Institutes of Health.

The DSMB will be comprised of 3 individuals from Albert Einstein College of Medicine who are unaffiliated with the study and who have appropriate expertise. They will meet and vote on the approval of the protocol prior to initiation and the minutes of the meeting will be submitted to the IRB. The DSMB will review trial progress and will offer advice with respect to study continuation, modification and/or termination. Case reports about any adverse events or protocol violations will be sent to the group, in addition to the IRB, at least every six months. The DSMB will meet every 6 months and as needed via conference call/video meeting.

10.1.7 CLINICAL MONITORING

Each site Principal Investigator will be responsible for overseeing the safety of the study at his/her site. This safety monitoring will include careful assessment and appropriate reporting of adverse events as described in **Section 8**. Medical monitoring will include a regular assessment of the number and type of serious adverse events. Additionally, the study will be overseen by an Independent Data and Safety Monitoring Board (DSMB) (Section 10.1.6).

Clinical site monitoring on-going by the site PIs and by the DSMB (2-3 meetings annually) will be conducted to ensure that the rights and well-being of trial participants are protected, that the reported trial data are accurate, complete, and verifiable, and that the conduct of the trial is in compliance with the currently approved protocol/amendment(s), with International Council on Harmonisation Good Clinical Practice (ICH GCP), and with applicable regulatory requirement(s).

10.1.8 QUALITY ASSURANCE AND QUALITY CONTROL

Quality control and assurance measures will be implemented throughout the study starting with the development of this detailed study protocol and manual of operations. The availability of these documents will standardize screening, recruitment, physical and laboratory measurement and data entry. All study staff will be trained in the protocols for this study and will be observed for fidelity to protocol and retrained as needed while working on the study. Peer mentors will be trained on proficiency with phones and intervention schedule and retrained as needed. To assure data integrity, a REDCap database will be developed for the study that will include limits for inputs and pull-down menus for quality control during data entry. In addition, 20% sample of questionnaires will be double entered to check for errors. If a significant number of errors are found, all data will be double entered by two different personnel.

Each clinical site will perform internal quality management of study conduct, data collection, documentation and completion. All sites will follow a common quality management plan.

Quality control (QC) procedures will be implemented as follows:

Informed consent --- Study staff will review both the documentation of the consenting process as well as a percentage of the completed consent documents. This review will evaluate compliance with GCP, accuracy, and completeness. Feedback will be provided to the study team to ensure proper consenting procedures are followed.

Source documents and the electronic data --- Data will be initially captured on source documents (see Section 10.1.9) and will ultimately be entered into the study database. To ensure accuracy site staff will compare a sample of source data against the database, targeting key data points for review.

Intervention Fidelity — Consistent delivery of the study interventions will be monitored throughout the intervention phase of the study. Procedures for ensuring fidelity of intervention delivery are described in Section 6.2.1.

Protocol Deviations – The study team will review protocol deviations on an ongoing basis and will implement corrective actions when the quantity or nature of deviations are deemed to be at a level of concern. This will be reported to the DSMB and IRB as required.

Should independent monitoring become necessary, the PI will provide direct access to all trial related sites, source data/documents, and reports for the purpose of monitoring and auditing by the sponsor/funding agency, and inspection by local and regulatory authorities.

10.1.9 DATA HANDLING AND RECORD KEEPING

Only approved trained study personnel will have access to data collection and management. Data will be maintained locally at each site secured in study research folders, or electronically secured. The data collected from enrolled participants will be entered into a secure RedCap database overseen by the data coordinating center (Albert Einstein). Only approved study personnel will be granted access to the study RedCap database. Authorized representatives of the NIH, sponsor, and regulatory agencies will be approved to examine (and when permitted by applicable law, to copy) clinical records for the purposes of quality assurance reviews, audits, and evaluation of the study safety, progress, and data validity.

10.1.9.1 DATA COLLECTION AND MANAGEMENT RESPONSIBILITIES

All data collected will be as described in earlier sections of this protocol. This will include data derived from patient report, observations by the research team, medical records from varying sources, and phone billing records. Recordings of calls between mentor/mentee participants will be digital files, stored on a secure server at the site accessible to only study personnel. Any transcriptions or recordings

will be de-identified and stored electronically. Logs and diaries submitted by participants will be scanned as electronic files and any hard copies maintained in the research record.

Preferentially all data will be entered into the secure online database RedCap at the data coordinating center. When required, paper versions of the data collected or de-identified source documentation (medical records) will be stored in the participant's research record. Participants may respond to surveys electronically, when they will directly enter the data and there will be no paper copy in the research file. This will be noted by the study coordinator. Similarly, if a phone interview is performed by a study coordinator, data may be directly entered into the RedCap database.

Instructions for completing forms will be additionally detailed in the MOP. A scoring guide for surveys will be included as part of the study data dictionary.

The data coordinating center will perform a review of data every 4 months including evaluating the degree of missingness of forms or data points. This will be described by site and included for review by the DSMB.

Data collection will be the responsibility of the clinical trial staff at the site under the supervision of the site investigator. The investigator will be responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported. All source documents, when applicable, will be completed in a neat, legible manner to ensure accurate interpretation of data.

Clinical data (including adverse events (AEs), and clinical laboratory data will be entered into RedCap, a 21 CFR Part 11-compliant data capture system provided by the Data Coordinating Center. The data system includes password protection and internal quality checks, such as automatic range checks, to identify data that appear inconsistent, incomplete, or inaccurate. Clinical data will be entered directly from the source documents.

10.1.9.2 STUDY RECORDS RETENTION

Clinical Center investigators will retain study documents, including participant files and regulatory forms for at least 5 years after the close of the study, or longer depending on site institutional requirements. No records will be destroyed without the written consent of the sponsor/funding agency, if within 3 years of the submission of the Federal Financial Report to the NIH by the coordinating center. It is the responsibility of the sponsor/funding agency to inform the investigator when these documents no longer need to be retained.

10.1.10 PROTOCOL DEVIATIONS

This protocol defines a protocol deviation as any noncompliance with the clinical trial protocol, International Council on Harmonisation Good Clinical Practice (ICH GCP), or Manual of Procedures (MOP) requirements. A protocol deviation is considered to be any change or alteration of the IRB-approved study protocol without advanced IRB approval. A protocol exception is a one time, intentional change or alteration to the IRB-approved protocol that is approved by the IRB prior to execution.

Major deviations will be consider as any change that has the potential to adversely affect the rights, welfare or safety of participants, or adversely affect the integrity of the research data.

This may include: failure to obtain informed consent prior to research activities, use of an invalid consent form, enrollment of a participant who is ineligible, performing research not included in the protocol, failure to report AEs to the DSMB and/or IRB, use of recruitment procedures that are not IRB approved, or enrolling more participants than IRB approved.

Minor deviations may be those that do not have the potential to affect the rights, welfare or safety of participants, or the integrity of the research data. This may include execution of a study visit beyond the

protocol define window. These deviations will be recorded and reported to the DSMB and IRB as a part of continuing review.

As a result of deviations, corrective actions will be developed by the site and implemented promptly.

It will be the responsibility of the site investigator to use continuous vigilance to identify and report major deviations within 7 working days of identification of the protocol deviation. All deviations will be addressed in study source documents, reported to NIDDK Program Official, DSMB and IRB. Protocol deviations will be sent to the reviewing Institutional Review Board (IRB) per their policies. The site investigator will be responsible for knowing and adhering to the reviewing IRB requirements.

10.1.11 PUBLICATION AND DATA SHARING POLICY

The PIs of the study will be responsible for developing publication procedures and resolving authorship issues. The study must comply with:

- The *NIH Public Access Policy*, the *NIH Policy on the Dissemination of NIH-Funded Clinical Trial Information*, *Clinical Trials Registration and Results Information Submission*,
- The *NIH Data Sharing Policy* (if applicable),
- The *NIH Data Sharing Policy and Implementation Guidance*,
- Any other relevant policies (e.g., NIH IC-specific data sharing or publication policy)

National Institutes of Health (NIH) Public Access Policy, which ensures that the public has access to the published results of NIH funded research. It requires scientists to submit final peer-reviewed journal manuscripts that arise from NIH funds to the digital archive PubMed Central upon acceptance for publication.

This study will comply with the NIH Data Sharing Policy and Policy on the Dissemination of NIH-Funded Clinical Trial Information and the Clinical Trials Registration and Results Information Submission rule. As such, this trial will be registered at ClinicalTrials.gov, and results information from this trial will be submitted to ClinicalTrials.gov. In addition, every attempt will be made to publish results in peer-reviewed journals. Data from this study may be requested from other researchers after publication of the primary study results by contacting the data coordinating center. Additionally, a de-identified dataset may be placed in the NIDDK data repository.

10.1.12 CONFLICT OF INTEREST POLICY

All investigators are required to report all financial conflicts of interest on an annual basis as per site institutional and NIH policies. All conflicts of interest will be reported in manuscripts. If conflicts of interest arise during the conduct of the study, the sponsor organizations will review and make determinations regarding any necessary management.

10.2 ADDITIONAL CONSIDERATIONS

10.3 ABBREVIATIONS AND SPECIAL TERMS

AE	Adverse Event
AECOM	Albert Einstein College of Medicine
CFR	Code of Federal Regulations

COC	Certificate of Confidentiality
CONSORT	Consolidated Standards of Reporting Trials
DCC	Data Coordinating Center
DSMB	Data Safety Monitoring Board
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
ICH	International Council on Harmonisation
IRB	Institutional Review Board
ISM	Independent Safety Monitor
MOP	Manual of Procedures
NCT	National Clinical Trial
NIH	National Institutes of Health
NIH IC	NIH Institute or Center
OHRP	Office for Human Research Protections
PI	Principal Investigator
QC	Quality Control
SAE	Serious Adverse Event
SOA	Schedule of Activities
SOC	System Organ Class
UP	Unanticipated Problem
US	United States
VUMC	Vanderbilt University Medical Center

10.4 PROTOCOL AMENDMENT HISTORY

Version	Date	Description of Change	Brief Rationale
2.2	6/17/20	Grammatical revisions, formatting revisions, language updates to Biostats section	Protocol Amendment from v2.1
3.0	4/30/21	Revisions include grammatical, formatting, timeline endpoints, mentee assignment, and discontinuation surveys	Protocol Amendment from v2.2

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