Enhancing the Cardiovascular Safety of Hemodialysis Care: a Cluster-Randomized, Comparative Effectiveness Trial of Multimodal Provider Education and Patient Activation Interventions (Dialysafe)

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Protocol Amendments:
(Any modifications to the protocol should be annotated on the coversheet or in an appendix. The annotation should note the exact words that are changed, the location in the protocol the date the modification was approved, and the date it became effective.)

STATEMENT OF COMPLIANCE

The study will be carried out in accordance with Good Clinical Practice (GCP) as required by the following*:*

- United States (US) Code of Federal Regulations (CFR) applicable to clinical studies (45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56, and 21 CFR Part 312)
- PCORI Terms of Award
- University of Michigan Institutional Review Board (UM IRB-MED) regulations

All key personnel (all individuals responsible for the design and conduct of this study) have completed Human Subjects Protection Training.

SIGNATURE PAGE

The signature below constitutes the approval of this protocol and the attachments, and provides the necessary assurances that this trial 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.

Site Investigator:*

Signed: _____ Date: _____

Name
Title

** The protocol should be signed by the clinical site investigator who is responsible for the day to day study implementation at his/her specific clinical site; i.e., if Investigational New Drug (IND) study, the individual who signs the Form FDA 1572.*

TABLE OF CONTENTS

Table of Contents

LIST OF ABBREVIATIONS

CKD: Chronic Kidney Disease characterized by a gradual loss of kidney function over time (source: NKF). CKD occurs in 5 stages, with stage 1 being kidney damage with normal kidney function and stage 5 meaning kidney failure (or ESRD).

ESRD: End State Renal Disease is CKD stage 5, in which the kidneys no longer work on their own. People with ESRD require dialysis or a kidney transplant to survive. All patients in the study will be receiving hemodialysis therapy for ESRD.

FMCNA: Fresenius Medical Care of North America (FMCNA) is a large dialysis organization with over 2,000 dialysis facilities in the United States. FMCNA is a primary partner in the project under a facility services agreement that will be executed shortly. FMCNA is represented on both the Advisory Committee and Steering Committee. The intervention will take place in FMCNA clinics across the US, and is the source of data as outlined in the enclosed documents. *http://fmcna.com/*

IDH: Intradialytic Hypotension, or when a person experiences low blood pressure during a dialysis session.

IDWG: Interdialytic Weight Gain refers to weight that patients gain between dialysis sessions due to fluid accumulation. Because kidney failure leads to the body not being able to remove fluid efficiently, most weight gain between sessions is caused by fluid retention. Dialysis removes this excess fluid, with a goal of achieving a patient's ideal "dry weight."

KECC: The University of Michigan Kidney Epidemiology and Cost Center is located in the School of Public Health. It will house all of the data in the study. Executive UM-KECC faculty Rajiv Saran is Co-PI on the project. *http://kecc.sph.umich.edu/*

NKF: The National Kidney Foundation is a partner in the project. Their peer mentoring program will be adapted for the patient side of the intervention. NKF is represented in both the Advisory Committee and the Steering Committee. *https://www.kidney.org/*

PROTOCOL SUMMARY

Title:	*Enhancing the Cardiovascular Safety of Hemodialysis Care: a Cluster-Randomized, Comparative Effectiveness Trial of Multimodal Provider Education and Patient Activation Interventions*
Précis:	This project is a pragmatic, cluster-randomized comparative effectiveness trial through education of patients and healthcare providers, and the use of a checklist to heighten attention to patient clinical factors. The study compares a healthcare provider-focused to a patient-focused intervention in 20 hemodialysis facilities that are all part of the same parent organization. Facilities will be randomized in a 2x2 factorial design, such that 5 sites will receive the patient education intervention, 5 sites will receive the facility training and checklist intervention, 5 sites will receive both interventions, and 5 sites will receive neither intervention. The CRCT will compare the effectiveness of the two interventions for improving the primary outcome of HD session stability, operationalized as intradialytic hypotension (IDH). This outcome will be monitored for 12 weeks prior to the intervention, for 24 weeks during the intervention period and for 12 weeks after the intervention period (Aim 1). The interventions will also be assessed in terms of their effects on secondary outcomes, including patient symptoms, fluid adherence, dialysis adherence, quality of life, hospitalizations and mortality (Aim 2). We will also identify factors associated with successful implementation of the Dialysafe interventions, and ways in which implementation may influence intervention effectiveness (Aim 3).
Objectives:	We will compare two interventions to improve the cardiovascular/hemodynamic stability of HD care by pursuing the following specific aims: ● **Aim 1** Conduct a cluster-randomized controlled trial (CRCT) to test and compare the effects of the above HD facility-level interventions on the primary outcome of dialysis session stability over an intervention period of 24 weeks and a post-intervention follow-up period of 12 weeks. ● **Aim 2** Test and compare the effects of the two HD facility-level interventions on secondary patient-centered clinical outcomes, including: patient symptoms, fluid adherence, dialysis adherence, quality of life, hospitalizations and mortality over the same timeframe.

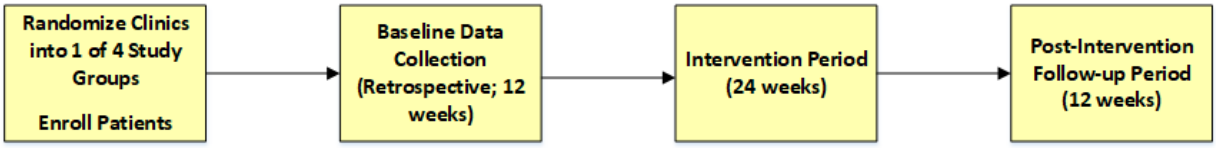
	● **Aim 3** Identify factors associated with successful implementation of the interventions, and ways in which implementation may influence intervention effectiveness.
Population:	1,200-1,440 patients, ages 21 and older, receiving in-center hemodialysis for chronic kidney disease
Phase:	IV
Number of Sites:	20
Study Duration:	21 months
Subject Participation Duration:	48 weeks/11 months
Description of Agent or Intervention:	Patient Intervention: ● 5 Educational Modules and Peer Mentoring Sessions delivered to patients via tablet computer Provider Intervention: ● 2 training sessions delivered to facility staff via online learning system ● 2 training sessions delivered to facility staff via online training sessions ● 1 training session delivered online for physicians, nurse practitioners and physician assistants ● 1 4-item checklist to be completed by facility nurse during every dialysis session
Estimated Time to Complete Enrollment:	17 months

***Schematic of Study Design:**

Treatment assignments will be as follows:

2 by 2 Factorial Design with Facility and Patient Sample Sizes - # Facilities (# Patients)			
	Patient Activation Intervention		**Total**
Provider Education	Yes	No	
Yes	5 (300)	5 (300)	10 (600)
No	5 (300)	5 (300)	10 (600)
Total	10 (600)	10 (600)	20 (1,200)

The sequence of activities in each study facility is as follows:



1 KEY ROLES

For questions regarding this protocol, contact *Tiffany Veinot at 734-615-8281 or tveinot@umich.edu.*

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2 INTRODUCTION: BACKGROUND INFORMATION AND SCIENTIFIC RATIONALE

2.1 BACKGROUND INFORMATION

2.1.1 NAME AND DESCRIPTION OF STUDY INTERVENTIONS:

I. Provider Education Intervention

Dialysafe IDH Checklist
Audience: Nurses, Patient Care Technicians (PCTs)
File Title: Provider Intervention (section 44 of IRB application)
A checklist application will be presented on provided tablet computers to nursing staff and PCTs at all clinics in the provider intervention arm. The checklist aims to identify patients at increased risk of intradialytic hypotension (IDH); it is to be completed by a nurse for each patient's dialysis treatment with verbal or documentation input from the PCT as indicated. The checklist has 4 items that may be associated with increased IDH risk: two pertaining to the past five treatments, and two regarding the date of the current session. The checklist is designed to focus nurse attention on clinical criteria related to IDH risk that change frequently. If any at-risk indication is selected in the checklist, a list of potential interventions to help prevent IDH will appear on the next screen of the checklist application.

See attached Checklist Application Overview.

Dialysafe Staff Training, part 1 of 4
Audience: Nurses, Patient Care Technicians, Dietitians, and Social Workers
File Title: Provider Intervention (section 44 of IRB application)
Staff training will begin by explaining the Dialysafe project goals and study design. Staff will refresh their knowledge on consequences of Intradialytic Hypotension (IDH) and the key role of fluid accumulation in the development of IDH. They will also identify their clinic's study group into which their clinic was randomized and training requirements related to their assigned study group. Finally, the role and responsibilities for each patient care staff member will be clearly defined.

Dialysafe Staff Training, part 2 of 4
Audience: Nurses, Patient Care Technicians, Dietitians, and Social Workers
File Title: Provider Intervention (section 44 of IRB application)
During part 2, staff will consider the most vulnerable points in time for cardiovascular instability, which includes intradialytic hypotension (IDH). The training will review principles of weight and blood pressure measurement per existing FMCNA policy, including orthostatic blood pressure to evaluate fluid volume status and risk for IDH. The audience will be introduced to how the nurse will use the Dialysafe IDH prevention checklist to systematically evaluate every patient for IDH risk early in the session. If patients are found to be at risk for IDH, nurses are encouraged to choose from a list displayed on the checklist of possible actions to prevent IDH. If the patient's

fluid removal goal is decreased as a result, nurses are encouraged to contact the physician if indicated by the nurse's assessment to discuss the possibility of following FMCNA policy to add extra time to that session or add an extra session to achieve fluid balance per the physician's order.

Dialysafe Staff Training, part 3 or 4
Audience: Nurses, Patient Care Technicians, Dietitians, and Social Workers
File Title: Provider Intervention (section 44 of IRB application)
Part 3 begins with staff reflecting on their experience with the Dialysafe IDH prevention checklist. They will also review actions for increasing cardiovascular stability and assessing need for additional actions for patients at higher risk of intradialytic hypotension (IDH). Finally, staff will review their role in IDH prevention through important actions like regular review of estimated dry weight. They will consider times when they might discuss with the physician if it is appropriate to extend treatment time or add an additional day of treatment, and when they should consider steps such as additional medication review beyond the usual standard medication review or cool dialysate per physician order for higher risk patients to prevent IDH.

Dialysafe Staff Training, part 4 of 4
Audience: Nurses, Patient Care Technicians, Dietitians, and Social Workers
File Title: Provider Intervention (section 44 of IRB application)
Fifteen multiple-choice questions to measure learning of the material covered in parts 1-3.

See attached Staff training modules.

Dialysafe condensed Provider training for physicians, NPs and PAs
Audience: Physicians, nurse practitioners, and physician assistants
File Title: Provider Intervention (section 44 of IRB application)
This training begins by introducing the Dialysafe study goals and design. Advanced practitioners will review the purpose of the Dialysafe IDH prevention checklist used by nurses for evaluating patients' risk for Intradialytic Hypotension (IDH). They will review their role in the Dialysafe Study by reviewing potential treatment changes that the nurse may discuss with the provider, based on systematic patient assessment and IDH risk.

See attached Physician, NP and PA training modules.

II. Patient Activation Intervention

Dialysafe Patient Activation Intervention: An Overview
Audience: Dialysis Patients Enrolled in the Intervention
File Title: Patient Education Sessions 1-5 (section 44 of IRB application)
The patient activation intervention occurs over the course of five sessions. These sessions will be digitally available on tablets shipped to patients for use at home, and are designed to be reviewed by patients at a time that is convenient for them. All content was created through the partnership between University of Michigan and National Kidney Foundation. Each session will be scheduled to occur roughly one week apart from one another, though patients will have the opportunity to complete their sessions on a compressed schedule in as little time as one week, pending patient and peer mentor availability. While each session is focused on a different aspect of preventing intradialytic hypotension, they all follow the same format:

Informational Slides

File Title: Patient Education Sessions 1-5 (section 44 of IRB application)
Content on slides provide patient education as part of the session. These slide decks will be transformed into video with voiceover for ease of patient accessibility, including patient visibility of the text of the slides and voiceover content.

Quiz
File Title: Patient Education Sessions 1-5 (section 44 of IRB application)
After viewing the informational slides, an optional quiz will allow patients to test their knowledge. Correct answers will be displayed after the quiz is submitted, but "passing" the quiz will not be required.

Patient Story Videos
See section 31 of IRB application.
Several patients told their stories to Dialysafe study coordinators through webcast. These stories were divided into short (less than 5 minute) videos relevant to each session topic. Each session contains 1-4 patient story videos, which can be viewed after the main educational content is reviewed.

Goal Setting Module
File Title: Patient Education Sessions 1-5 (section 44 of IRB application)
After viewing each session, patients will be directed to a goal setting module. This will ask a set of questions to help the patient select a S.M.A.R.T. goal for behavior change (specific, measurable, attainable, realistic, and timely) for the IDH prevention-related material they viewed.

Supplementary PDF Resources
File Title: Patient Education Sessions 1-5 (section 44 of IRB application)
Additional resources will be available for patients interested in more information related to the content they watched in each session. These resources include NKF handouts, tracking forms, and suggested apps for supporting dialysis patients in a healthy lifestyle.

Peer Mentoring Discussion Guide
File Title: Patient Education Sessions 1-5 (section 44 of IRB application)
Each session includes this guide to support mentors as they review session content and S.M.A.R.T. goals with their mentee during a 20-60 minute video call. Each guide includes probing questions to help the mentee think through the material and goal, as well as, encouraging statements for the mentor to choose from. To encourage patients, peer mentors will also role model positive behavior change where applicable.

Action Plan
File Title: Patient Education Sessions 1-5 (section 44 of IRB application)
After each mentoring session, the mentor will complete this summary of the session and email it to the mentee as a reference. This summary includes patient identified goal and values, patient stated action plan, identified barriers and steps to overcome barriers, and patient identified support system.

Individual sessions focus on five areas related to IDH prevention, as follows:

Patient Education Session 1: Getting Enough Dialysis
Module 1 covers how dialysis helps patients feel better by removing fluid and preventing fluid overload. Target behaviors for this module are attending regularly-prescribed hemodialysis sessions and remaining at the treatment for the full prescribed length of the session; also, helping the patient to understand benefits of attending lengthened or supplemental hemodialysis

sessions as needed. Session 1 also includes a value-setting module, in which patients will select values that will help them set goals for the rest of the intervention.

Patient Education Session 2: Feeling Better with Less Salt/Sodium
Module 2 covers why people on dialysis need a low-sodium diet. Slides display high sodium foods to avoid and low sodium foods to choose, as well as reading a food label. Target behaviors for this module are maintaining a diet that is low in sodium so as to reduce thirst and fluid retention; reading food labels to assess sodium content; and tracking sodium intake.

Patient Education Session 3: Making Fluid Restrictions Work for You
Module 3 covers why people on dialysis need to limit fluid intake. Slides offer ways to decrease thirst and strategies to keep track of fluid intake. Target behaviors for this module are maintaining a level of fluid intake that will optimize interdialytic weight gain; tracking fluid intake; becoming aware of usual interdialytic weight gain; discussing symptoms of fluid overload with the dialysis team; and discussing the possible need for a longer or extra sessions with the dialysis team if experiencing fluid overload symptoms.

Patient Education Session 4: Feeling Better on Dialysis and Having Easier Sessions
Module 4 covers strategies to prevent low blood pressure and other symptoms of fluid removal. Patients learn what to do if symptoms occur, steps to correct low blood pressure, and why it is helpful to check blood pressure at home. Target behaviors for this session include recognizing their symptoms of IDH, reporting symptoms to staff; tracking blood pressures at home; tracking and reporting episodes of IDH to their healthcare team; and notifying staff of changes in weight.

Patient Education Session 5: Getting More Involved in Your Care
Module 5 covers the patient's role and responsibilities as a member of the healthcare team. Patients also review the roles and responsibilities of the other dialysis team members. Target behaviors for this session include actively participating in decisions with providers regarding fluid removal targets, ultrafiltration rates, and treatment times. Also, patients should ask questions of their dialysis team relevant to session stability, share concerns related to health and care, as well as emotional well-being, with the dialysis team, and share with clinicians symptoms, ER trips, medication changes, and upcoming procedures.

See attached Patient activation intervention materials, including Patient Story Videos (by peer mentoring session; uploaded separately in IRB application per instructions) and content from five peer mentoring sessions (Overview, Educational Module Peer Mentoring Discussion Guide, Quiz, Goal Setting Module, Supplemental Materials).

See attached Peer Mentor Training Materials: videos and slide sets by session.

2.1.2 PRIOR STUDIES RELEVANT TO THE TRIAL:

I. Checklists and team training for prevention of treatment complications:

Patient safety interventions are typically "multifactorial and complex,"[1] built from several interacting components.[2] Thus the provider education intervention, which aims to prevent a common complication of hemodialysis, will include a checklist, education, team training, and procedures for intervention implementation. A recent Agency for Healthcare Research and Quality (AHRQ)-sponsored systematic review concluded that checklists are a strongly encouraged strategy for the improvement of healthcare quality and safety.[3] Furthermore, a 2014

systematic review of use of checklists in surgery showed a 37% relative risk reduction and number-needed-to-treat of 27 for surgical complications. Another systematic review specifically of implementation of World Health Organization checklists showed a 41% relative risk reduction for surgical complications.[4] Checklists can prevent errors and improve care quality.[5] Checklists codify and support organizational routines,[6] and are compatible with hemodialysis care because they reduce cognitive effort in complex, tiring and stressful work situations.[7] Co-PI Saran's experience with an infection control trial in hemodialysis care using checklists, [8, 9] and a recent Canadian pilot project underscore the suitability of checklists for hemodialysis care.[10] Successful checklist implementation is facilitated by educational sessions and ongoing support.[11]

As for team training, the aforementioned AHRQ systematic review encourages team training for improvement of healthcare quality and safety.[3] A systematic review of this approach across industries found a moderate effect size ($\rho = 0.39$) between training and team performance (work quality, quantity, accuracy, efficiency and effectiveness).[12] A 2014 review of team training in healthcare also concluded that there is moderate-to-high quality evidence that team training can positively affect team performance and patient outcomes.[13] Furthermore, the review concluded that the intervention approach planned in our study, team training combined with tools such as checklists, had the largest effect sizes in relation to team effectiveness.[13] One notable study cited in that review found that there was a large (50%) reduction in patient mortality at Veteran's Health Administration facilities that received a surgical team training intervention compared to those facilities that did not receive the training.[14]

II. Peer-based interventions for behavior change

Our intervention uses peer mentoring, which has proven successful in health behavior change interventions.[15-17] Research by an advisory member of our team, the National Kidney Foundation of Michigan, showed the effectiveness of peer mentoring in hemodialysis patients for initiating advanced directives and registering for non-kidney organ donation.[18-20] Peer mentoring also proved successful in populations similar to hemodialysis patients, including older adults[21] and people with a vulnerable health status,[22-24] including cardiovascular disease.[25] The approach can be effective for health disparity populations such as African Americans and Hispanics,[26] two groups overrepresented in the hemodialysis patient population.[27] While not previously applied to patient involvement in dialysis session stability, it can provide the education, support and motivational enhancement that has been missing from patient safety involvement initiatives.[28-30]

A systematic review of peer-based interventions showed a pooled small-to-moderate effect size on health behavior,[22] and a systematic review of telephone-based peer support in particular found a pooled significant improvement (Standardized Mean Difference=0.19) in self-management behavior among patients with vascular diseases.[31] Furthermore, a recent telephone peer mentoring randomized controlled trial with a similar patient population found a moderate effect size on health *outcomes*. Specifically, average HbA1c levels fell from 9.8% to 8.7%, while it fell by 0.01% in the control group.[23]

2.1.3 CLINICAL AND EPIDEMIOLOGICAL BACKGROUND TO STUDY:

Chronic kidney disease (CKD) was the tenth leading cause of death in the United States (US) in 2020.[1] The most advanced stages of CKD often lead to end-stage renal disease (ESRD), when dialysis or transplantation is required to stay alive. In 2019, 492,096 Americans (61.1% of

ESRD patients) received outpatient, facility-based hemodialysis (HD), while 239,413 (29.7%) had a kidney transplant and 74,518 (9.2%) were on peritoneal dialysis or home hemodialysis.[2] The ESRD patient population increased by 34.5% since 2009, with 114,432 starting HD in 2019.[2] Transplants may not be an option for many HD patients due to health status and limited organ supply.[2] The leading causes of ESRD in the US are diabetes and hypertension;[2] hence, *most ESRD patients have multiple chronic conditions, particularly cardiovascular (CV) disease.* For example, 40% of dialysis patients have had heart failure.[4] Sudden cardiac death, the leading cause of death in HD patients, accounts for death in up to one-quarter of this population.[5] The annual mortality rate is 17.5%, with half from cardiovascular (CV) causes.[2] HD patients also suffer low quality of life,[6] and considerable pain, fatigue, social restrictions, and distress.[7-10] There is significant public expenditure on ESRD care: Medicare funds the majority of US ESRD care, spending $51 billion in 2019, or 7.2% of its budget.[2]

Hemodialysis session instability is an important source of cardiovascular harm and patient suffering.

Most hemodialysis patients receive therapy sessions thrice weekly, typically for 12 hours per week. The stability of sessions varies, with an average of 20% becoming unstable—most commonly from intradialytic hypotension (IDH); this affects half of all hemodialysis patients.[45-48] IDH may prompt cramping, dizziness, vomiting, fainting, and fatigue.[40, 49, 50] Serious unstable sessions lead to hospitalization or even death on days in which dialysis was received [51-53]. The chief cause of unstable hemodialysis sessions is rapid removal of large volumes of fluid; this is driven by both patient-level and facility-level factors.[48] Indeed, there are wide facility-level variations in IDH rates after controlling for patient characteristics,[48] 20% of the variation in IDH is predicted at the patient level.[54]

Hemodialysis session instability is associated with repetitive and cumulative cardiovascular and other organ system injury.[55-57] Large volumes of fluid (3 liters or more) may be removed at higher than desired ultrafiltration rates during a typical HD session due in part to high interdialytic weight gains. In the face of pre-existing diminished cardiovascular reserves, this may result in HD instability and repeated myocardial hypoperfusion with resultant wall-motion abnormalities, an event called “myocardial stunning”.[55-57] Emerging evidence shows it may be responsible for injury resulting from hypoperfusion in other microcirculatory beds, including in the central nervous system (e.g., repetitive neurological injury leading to cognitive dysfunction).[58]

The most common form of hemodialysis session instability, IDH, predicts low quality of life, hospitalization and mortality.[47, 59] Our team[60] and others[17, 18] have shown that a care process directly linkable to IDH onset, the ultrafiltration rate (i.e. rate of fluid removal) greater than10 ml/h/kg bodyweight, is linked to elevated mortality risk. Of note, the FMCNA UFR goal is <13 ml/kg/hr. We have also shown that the thrice-weekly schedule paradigm is associated with significantly higher mortality earlier in the week, potentially due to the long interdialytic interval over the weekend, which leads to a greater need for fluid removal early in the week.[61] Negative symptoms may result in session shortening by patients or providers.[62] A national survey found that 90% of hemodialysis providers had witnessed sessions stopped due to patient status in the three months prior.[63]

2.1.4 IMPORTANCE OF THE STUDY:

While improvements in care procedures and enhanced patient involvement in safety may improve hemodialysis session stability, this has not been systematically addressed. *Hemodialysis session instability is preventable in some cases.* Session stability is determined by the interplay of multiple factors, many of which are modifiable. At a patient level, these include patient decisions regarding sodium and fluid consumption, timing of antihypertensive medication and of eating, and skipping or shortening sessions.[64] Moreover, because early intervention in an IDH episode is important to prevent worsening, patients can notify providers of related symptoms, such as nausea, vomiting, dizziness or muscle cramping, facilitating prompt provider-based interventions such as placing the patient in Trendelenburg position.[65] Clinician practice patterns influencing session stability include the physician's decisions regarding the patient's target post dialysis weight and prescribed treatment time, and how often these are revisited. Modifiable within-session decisions made primarily by nurses and technicians include assessment of fluid status and setting a patient's ultrafiltration rate (rate of fluid removal).[66] Physician decisions such as session length, thresholds for ultrafiltration rates and consideration toward adding an extra session per week for specific patients are also potentially modifiable factors.

To provide a better foundation for decisions about volume management, a 2014 consensus statement from Medical Directors of US hemodialysis facilities called for trials of methods for improving patient fluid management[67]; we address this call in our proposed research.

Preventing treatment complications has been a nationwide priority since publication of a key Institute of Medicine (IOM) report more than a decade ago,[68] although the majority of progress has been in inpatient settings. For example, advances in the field[3] include successful implementation of strategies to decrease central-line associated bloodstream infections, [69-71] use of checklists to improve surgical safety [72] and workflow "bundles" that decrease healthcare-associated infections.[73] As a reflection of this predominant inpatient focus, a 2011 systematic review (SR) concluded that no interventions to prevent treatment complications have been credibly shown to improve safety in outpatient settings.[74] Our proposed study is designed to fill this critical gap in knowledge by testing interventions that have been successful in inpatient settings and chronic disease care within an outpatient hemodialysis context.

National and international stakeholder organizations have advocated for greater patient involvement in the prevention of treatment complications and healthcare provider errors.[68, 75-77] It is argued that patients should be engaged in this since they are present at every treatment, can provide important information, and are motivated to reduce risk of harm.[78] However**,** a 2013 systematic review found knowledge gaps in patient involvement in the prevention of treatment complications and errors, and thus prioritized research in this area.[78] No studies to date have examined the potential for patient involvement in dialysis session stability.[75, 78] Patient involvement is particularly promising in the context of hemodialysis because *patients already make daily decisions such as how much sodium and fluid to consume and whether to shorten or skip hemodialysis sessions. Patients often make appropriate and well-informed decisions, but some may make choices without realizing the corresponding implications for dialysis session stability.*

Our research aims to improve care and outcomes in the outpatient hemodialysis healthcare sector. There are over 7,982 outpatient hemodialysis facilities in the US in 2019, the majority

(approximately 89%) of which are freestanding facilities.[27] A smaller proportion of outpatient hemodialysis care is delivered in hospital-based dialysis units (approximately 7%), with the remainder in other settings.

The cardiovascular stability of hemodialysis is vitally important to patients. IDH is linked to negative symptoms such as cramping, dizziness, vomiting, fainting, and fatigue,[40, 49, 50, 79] and increased risk of other outcomes important to patients including cardiovascular disease,[80] hospitalization[81] and mortality.[82-84] IDH is a top-10 priority outcome (of 33 ranked) for dialysis patients.[85] Patients express concern about the receipt of insufficient dialysis and/or administration of fluids in cases of IDH.[79]

The *enhancement of the cardiovascular/hemodynamic stability of hemodialysis is a critical concern for clinicians* as they become increasingly aware of the complications of hemodialysis session instability,[65, 86] and hear vociferous calls for reform in fluid management practices in hemodialysis care.[87-90] The consensus statement from Medical Directors of US dialysis facilities reflects the significant concern among clinicians.[67] With a lack of clear guidance, approaches to cardiovascular/hemodynamic stability in dialysis care are variable. Indeed, there are also *wide facility-level variations in IDH rates*, demonstrating the ability for practice patterns to influence cardiovascular session stability. For instance, IDH prevalence varied between 11.1 and 25.8% in a study of 13 US facilities.[91] Facility was also a significant predictor of IDH with odds ratios between 0.608 and 1.468 after adjustment for patient characteristics.

Our evidence-based approach contends that to prevent unstable hemodialysis sessions, fluid management must be at the forefront of typical care practices. In line with a growing body of evidence, we support gentle adjustment of post-hemodialysis target weights and consideration for longer treatment time prescriptions when appropriate, regular assessment of patient fluid/volume status, lower ultrafiltration rates (preferably < 10-12ml/kg/hour), and early intervention if a patient begins to show signs or symptoms of low blood pressure. We do so while continuing to emphasize lower interdialytic weight gain and a low-sodium diet to reduce thirst and thus fluid intake.[60, 92-96] To facilitate this fluid management-focused practice, our intervention translates successful interventions from inpatient and chronic disease care settings, respectively, to the outpatient hemodialysis context.

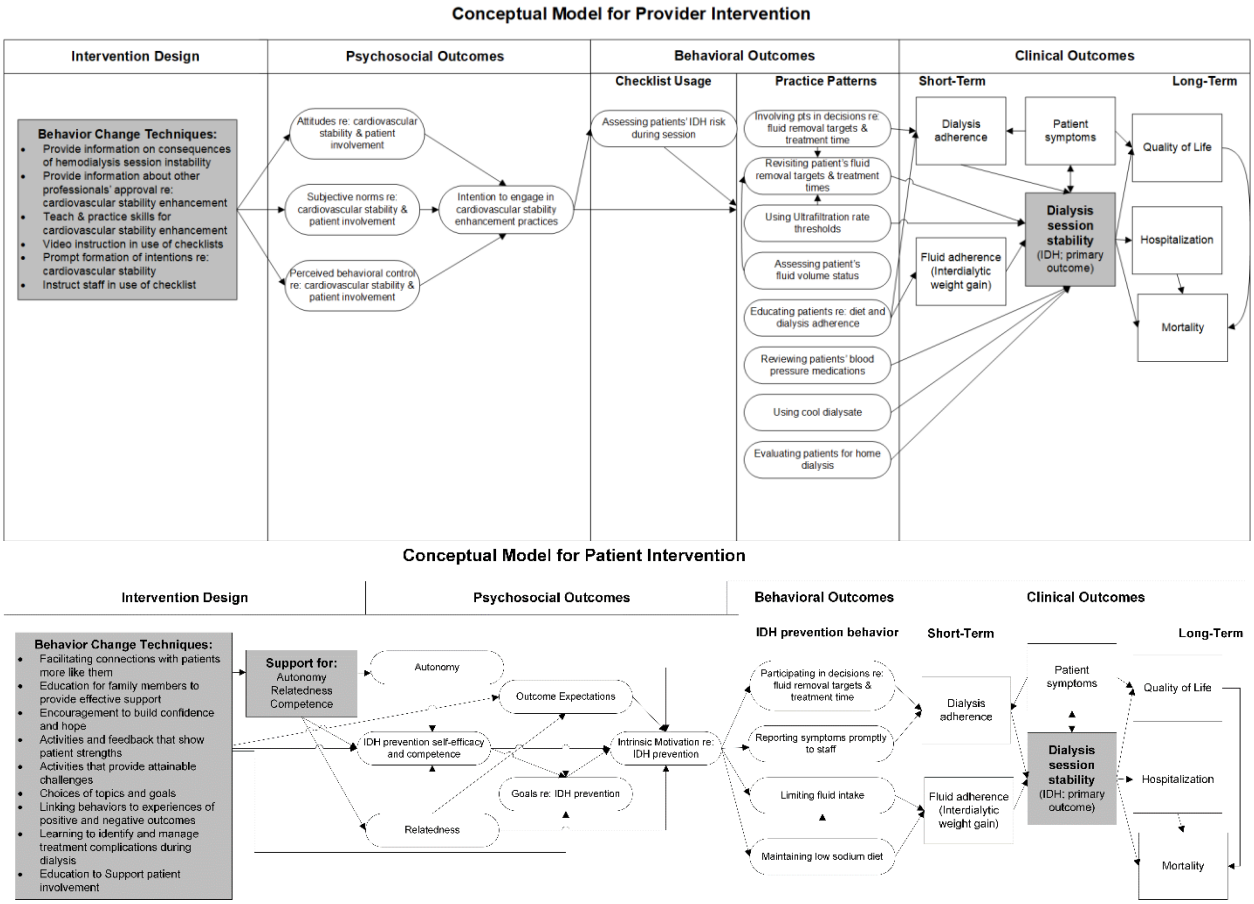
2.2 RATIONALE

2.2.1 JUSTIFICATION OF BEHAVIORAL INTERVENTION METHODS

As Figure 1 shows, we have two facility-level interventions, one focusing on the HD provider care team, and one on patients. Both are posited to directly influence the cardiovascular stability of hemodialysis. See section 2.1.B for summaries of evidence regarding the effectiveness of checklists, team training, and peer mentoring in inpatient settings and chronic disease care.

With regard to specific behavioral intervention methods, Figure 1 illustrates how the interventions will address the cardiovascular stability of hemodialysis. Two theoretical approaches with strong empirical support in evidence-based interventions have guided development of the conceptual model.

Figure 1



I. Patient Activation Intervention

Socio-cognitive theory (SCT), [97-99] is the key framework underlying the patient intervention. SCT emphasizes the predictive power of *self-efficacy*, or confidence in one's ability to perform an action, in the likelihood of performing that action. SCT has informed successful peer-based chronic disease interventions.[100, 101] Further, peer mentors will use *motivational interviewing (MI)*[102] principles that involve encouragement, exploration of feelings and personalized goal setting. MI is robust across clinical contexts,[103-108] including peer mentoring focused on behavior change.[19, 20] After influencing motivation and self-efficacy, we posit that the intervention will influence patient session instability prevention behavior, which will in turn influence fluid and HD adherence, both which predict HD session stability. As Figure 1 shows, we posit a direct relationship between patients' behavioral involvement in session instability prevention activities and HD session stability. As Figure 1 shows, for patients, the behavioral outcomes (involvement in instability prevention activities) to be encouraged as part of the intervention (as well as post-intervention) include:

i. *maintaining a diet that is low in sodium* so as to reduce thirst and fluid retention;
ii. *maintaining a level of fluid intake that will lead to optimizing interdialytic weight gain, thereby resulting in a reduced need for excessive fluid removal* during hemodialysis (fluid adherence);
iii. *attending regularly-prescribed hemodialysis sessions and remaining at the treatment for the full prescribed length (*dialysis session adherence);
iv. on an as-needed or continual basis, *understand the importance of be agreeable to attending lengthened or supplemental hemodialysis sessions* so as to ensure that treatments can be conducted at a lower ultrafiltration rate (<13 ml/kg/hour) (i.e., attention to session length/*treatment time* and *ultrafiltration rate*);
v. *actively participating in decision-making* with their physicians and nurses regarding fluid removal targets (and achievement of appropriate post-hemodialysis target weight) and treatment times, with a goal of maximizing their cardiovascular stability; and
vi. *recognizing and reporting their symptoms of dialysis session instability* / intradialytic hypotension (IDH) (e.g., dizziness, cramping, etc.) as soon as they begin to occur and *promptly notifying facility staff* so that appropriate interventions can be implemented (e.g., placing the patient in the Trendelenburg position) early.

The intervention extends the peer mentoring program offered by the National Kidney Foundation (NKF), a patient-driven organization on our team. Peer Mentors are trained ESRD patients who volunteer to support other patients. Mentors can speak from experience about the challenges of life on hemodialysis; thus patients often view mentors as credible and accessible information sources.[100, 109-111] Mentors can role model health behavior change as they share their experiences.[110]

II. Provider Education Intervention

The provider intervention is informed by the Theory of Planned Behavior (TPB), commonly used in practice change interventions for clinicians,[112, 113] including patient safety checklist adoption.[114] The TPB provides a model for predicting behavior based on behavioral intentions.[115, 116] In the TPB, three belief-based constructs predict intention: (1) **attitude** toward the behavior; (2) **subjective norms**, i.e., the level of social pressure the person experiences to perform it; and (3) **perceived behavioral control (PBC)**, i.e., how easy the person thinks it would be to do. In a meta-analysis of healthcare providers behavior studies, there was a frequency-weighted mean correlation between TPB constructs and intention of $R^2 = 0.59$, and between intentions and behavior of $R^2 = 0.31$.[113] The model posits that changes PBC and behavioral intentions will change providers' fluid management practice patterns, which will in turn reduce rates of dialysis session instability (Figure 1). The behavioral outcomes (fluid management practice patterns) to be encouraged among providers are also depicted on Figure 1. They include:

vii. *revisiting patients' fluid removal targets and treatment time;*
viii. *involving patients in decisions regarding their fluid removal targets and treatment time;*
ix. *focusing more on patients* who are having difficulties with IDH so as to address these problems*;* and
x. *assessing patients' fluid volume status.*

Various frontline staff members are engaged with the checklist intervention. While the checklist will be completed by the nurse, the checklist is designed as a tool to coordinate the involvement of multiple team members (please see attachment for full checklist content). For example, the checklist may involve obtaining information from the PCT for a data point which they typically gather ("Drop in SBP >=20 mmHg from sitting to standing?") and will involve obtaining information from the patient ("Pt says he or she had symptoms of low BP?") Furthermore, if implemented, the treatment considerations mentioned on the decision support component of the checklist also spark engagement with other staff members for their implementation. For example, the actions "place patient in modified Trendelenburg position," and "more frequent BP measurement" will typically be implemented by PCTs. The dietitian (and often the nurse) is engaged with the following treatment consideration: "Reinforce dietary salt and fluid limits - seek dietitian input." The social worker may also be engaged with the following action: "Stay on full prescribed time; do not miss treatments." Physicians are also engaged with the following treatment consideration: "Review medications that affect blood pressure & consult MD as needed."

2.2.2 SELECTION OF STUDY POPULATION

To accomplish rapid dissemination, and in keeping with the comparative effectiveness paradigm, this is a pragmatic trial; thus the effectiveness of the interventions will be assessed under the usual conditions in which they will be applied.[117] The trial will take place as part of routine hemodialysis care, with low-intensity patient follow-up and use of outcome data already gathered routinely by facilities.[118] Pragmatic intervention studies are most suited to support for healthcare-related decision making.[117]

Facility inclusion criteria include: (1) outpatient HD facilities, (2) at least 70 adult patients (≥>=21 years of age) who are permanent patients at the study facility (i.e., not from an outside clinic to receive isolation at the study facility or a visitor), (3) not involved in other Frenova research, (4) facilities with two to five stars in CMS's Dialysis Facility Compare; (5) not in immediate jeopardy in previous two years; (6) not a facility in which the entire facility has been designated for isolation of patients with suspected or confirmed COVID-19; and (7) not a Kaiser Permanente facility. Dialysis facility staff will not be subjects in the research. These criteria were chosen to: protect the sample size (at least 70 adult patients), will not have its attention and resources devoted to other matters rather than the study (involvement in other research, one-star facilities, immediate jeopardy), and will not have a high proportion of patients suspected of having, or diagnosed with, COVID-19. Kaiser Permanente facilities are also excluded due to their additional administrative requirements. Randomization was stratified based on region (Midwest, Northeast, Southeast, Southwest), and the socio-economic status of the facility's geographic area neighborhood (determined by the poverty rate in the county in which the facility is located; these were stratified into low/medium/high poverty levels) to account for potential differences in facilities.

We aim to include all non-vulnerable in-center patients at participating dialysis facilities. The trial is designed so as not to exclude anyone, including women and minorities to the extent they are represented at the dialysis facilities from the ages of 21 and older. We will only exclude vulnerable patients: those under 21 years of age; prisoners; those with a cognitive barrier (poor cognition or cognitive impairment); those deemed vulnerable by the Clinical Manager, Medical Director, and/or Social Worker (see Table 3: Screening for Patient Vulnerable Status), and those who are unable to comprehend the patient information sheet due to lack of facility in

English or Spanish. This will counter selection bias by ensuring that participants are representative of the full spectrum at a given facility. Selection bias is a risk in a peer mentoring intervention for a seriously ill population because patients who are comparatively less sick, and more motivated to manage their health actively, may be more likely to participate. The difficulty with such selection bias is that the study participants could be part of a subgroup of people who may have improved on their own, without the intervention. Therefore, improvements in outcomes may be erroneously attributed to the intervention. Our planned approach minimizes the likelihood of such mistaken conclusions. With regard to peer mentoring only, we will randomly select patients who are not vulnerable or have not opted out of the study in succession, until approximately a maximum of 30 patients in a facility finish peer mentoring (with partial data on at least 6 patients who start but do not finish). That is, every time a patient declines to participate, we will choose another patient randomly until the enrollment target is reached. Due to limited availability of peer mentors fluent in languages other than English, only English-speaking patients will be offered peer mentoring.

2.2.3 STUDY HYPOTHESIS

Our main study hypothesis is that hemodialysis session stability will significantly improve with either multimodal provider education or patient activation interventions, and that multimodal provider education will show a larger improvement. This hypothesis is based on our expectation that some hemodialysis patients might refuse or be unable to participate in peer mentoring, potentially leading to greater penetration of the provider intervention. We will test this main hypothesis and explore this potential explanation of any differential improvement as part of our planned sensitivity, mediation and moderation analyses.

2.3 RISKS AND BENEFITS

2.3.1 Potential Risks

This study has low risk to patients. The study uses current, accepted ways to prevent low blood pressure during dialysis. There is a very low risk that any patient's health data could be seen by people other than the research team. Sensitive patient information, such as medical information and medical history, will be collected as part of the study. Medical history includes conditions such as diabetes, high blood pressure, Hepatitis B or C, history of substance use, and mental health. The study is not collecting information about HIV or AIDS. However, there is a small risk that a diagnosis of HIV or AIDS will be included in the study data (see next paragraph). The study will collect information about COVID-19 diagnoses to examine the condition as a possible rival explanation for primary and secondary outcomes, and to account for patient absences from their home facility (e.g., in the context of dialysis adherence measures as a secondary outcome). All study data will be linked to a patient identifier and the researchers will make no attempt to link the information collected as part of the study to a patient's name or identity. Every effort will be made to keep patient information private. There are no known risks to the broader public or community.

As noted in the Data Elements List, FMCNA will provide medical diagnoses and the associated ICD codes extracted from the EHR. Information on co-morbidities will be extracted from the patient diagnosis section of the medical record. HIV/AIDS diagnoses will be excluded on the

basis of ICD9 and ICD10 codes provided by University of Michigan, with the list updated annually before October of each year. Although the risk of disclosure of HIV/AIDS diagnoses is minimal using this process, inadvertent disclosure may occur if this approach fails to identify all potential HIV/AIDS related diagnoses or if conditions associated with HIV/AIDS are included in the limited data set. In the event of inadvertent disclosure, such information will have been delivered to UM-KECC within a limited data set and will not be linked to any direct patient identifiers by the University of Michigan nor will it be included in any analyses. The patient information sheet will also include a statement regarding risk of disclosure of HIV/AIDS status. Additionally, sensitive diagnoses such as Hepatitis B, substance use, and mental health will be included in the limited data sets. The patient diagnoses will include additional diagnoses not included in the primary analysis, UM-KECC will restrict the diagnoses to medical co-morbidities of interest, including COVID-19.

2.3.2 Known Potential Benefits

If the research is beneficial, describe in detail any physical, psychological, social, legal, economic, or any other benefits to subjects that the PI foresees.
Note: Payment to subjects, whether as an inducement to participate or as compensation for pain and inconvenience, is not considered a "benefit."

Study results will determine whether a provider education or a patient activation intervention can reduce the occurrence of a common complication of hemodialysis, intradialytic hypotension. This will inform hemodialysis care providers on whether to pursue these provider-focused or patient-focused interventions, both, or neither. People on hemodialysis will also have information to help them decide whether to become engaged in dialysis session stability, and the intervention will help them learn how to do so.

Peer-based healthcare approaches as trials have shown benefits in health outcomes[23, 119-121] and behavior[15-17]—including complex health behaviors such as diet change.[23, 24] Therefore, through an *innovative* application of peer mentoring, we aim to support the cardiovascular stability of hemodialysis by helping patients become more actively engaged in treatment and self-care decisions that affect their cardiovascular well-being. We will address patients' lack of information to help them meaningfully participate in cardiovascular stability-related decisions such as fluid removal targets, session length and frequency. Our preliminary studies showed that some patients already try to influence their treatment targets and speed so as to reduce distressing symptoms, and that ESRD patients share strategies for making hemodialysis more tolerable.[122]

3 OBJECTIVES

3.1 STUDY OBJECTIVES

We will compare two interventions to improve the cardiovascular/hemodynamic stability of HD care by pursuing the following specific aims:

- **Aim 1** Conduct a cluster-randomized controlled trial (CRCT) to test and compare the effects of the above HD facility-level interventions on the primary outcome of dialysis session stability over an intervention period of 24 weeks and a post-intervention follow-up period of 12 weeks.
- **Aim 2** Test and compare the effects of the two HD facility-level interventions on secondary patient-centered clinical outcomes, including: patient symptoms, fluid adherence, dialysis adherence, quality of life, hospitalizations and mortality over the same timeframe.
- **Aim 3** Identify factors associated with successful implementation of the interventions, and ways in which implementation may influence intervention effectiveness.

3.2 STUDY OUTCOME MEASURES

3.2.1 Primary Outcome Measures

Dialysis session stability (primary outcome, Aim 1).
We define a dialysis session as unstable based on direct blood pressure measures that are routinely gathered during hemodialysis care. Secondary measures of the primary outcome include: (1) additional direct blood pressure measures; and (2) hospitalization or death on day in which dialysis was received.

Primary measure. The primary indicator of IDH based on direct blood measures after session start will be sitting Systolic blood pressure (SBP) falling below 100 mmHg (using lowest SBP during session) if starting SBP ≥100.

Secondary measures of primary outcome. Secondary measures of IDH based on direct blood pressure measures will include: the lowest (minimum) valid SBP below 100 mmHg during the session if starting SBP is ≥100, the number of SBP measurements <100 mmHg (using raw blood pressure measures, time of blood pressure measure, and starting SBP) if starting SBP is ≥100, and whether the sitting SBP falls below 90 mmHg (using lowest SBP during session) if starting SBP ≥100.

Hospitalization or death on a day in which dialysis was received will be determined based on matching the date of cardiovascular or fluid-related hospitalization or death with the date/time of the administered dialysis session, and assessing the hospital discharge diagnosis or primary cause of death based on FMCNA records.

Justification of primary outcome. Our primary outcome is hemodialysis session stability, defined as intradialytic hypotension (IDH). The primary indicator of IDH based on direct blood measures after session start will be sitting Systolic blood pressure (SBP) falling below 100 mmHg (using lowest SBP during session) if starting SBP ≥100. A fall of Systolic BP to less than 100mmHg signals a clinically important event during dialysis, with a higher probability of (patient-reported) symptoms[123] which equates to overtly suboptimal patient experience during dialysis. For example, in Meredith's 2015 study an SBP <100 mmHg and/or reduction in SBP of 20% of baseline were the thresholds that maximized the probability that a session would result in an intervention (which typically occurs in response to symptoms).[123] Furthermore, the threshold of SBP<100mmHg was also shown to be detrimental both by Flythe et al.[82] and Chou et al.[84] Furthermore, intervention at this threshold, even when asymptomatic, has the potential to prevent repetitive multi-organ tissue ischemia (e.g., a recent pilot study that studied cerebral

ischemia using noninvasive monitoring during hemodialysis).[124] Intervention at this SBP level is also likely prevent further decline to dangerously low levels of SBP<90mmHg.[81, 82]

3.2.2 Secondary Outcome Measures

Secondary Outcomes (Aim 2):
Fluid adherence. Interdialytic weight gain, a fluid intake measure, predicts stability; it is routinely recorded by facilities at each session.
Dialysis adherence. Data regarding dialysis adherence[125] are routinely collected by all hemodialysis facilities at each session. We will use three measures: number of minutes of prescribed dialysis time missed per week, number of missed sessions per week and total missed session time.
Patient symptoms. We will create a Patient Symptom Burden measure combining: symptom frequency and severity for each of the following symptoms that are often indicative of IDH, if they occur during or after the dialysis session (not pre-dialysis): nausea, vomiting, abdominal pain, dizziness, muscle cramps, headache, chest pain, shortness of breath, palpitations, diaphoresis, and blurred vision (as listed in the digital Chairside symptom module that is completed every session by the nurse. Symptoms listed on the KDQOL survey (see below) will be added to the patient symptom burden measure to supplement the scores obtained from the symptom module. We will also calculate the proportion of sessions with each symptom using date and time of session.

The nurse does a nursing assessment of the patient at each dialysis session and records symptoms (which are by definition reported by the patient) in the Chairside documentation system using structured fields and free text fields as needed. The structured fields include options for the nurse to record the location, duration, and severity of the symptom (including cramping) based on patient complaints. Symptom frequency and severity will be stated by the patient and recorded by the nurse during the assessment.

Additionally, after consultation with FMCNA's patient advisory committee and our patient partners, we have created a survey question to assess recovery time that builds on past research. [126]

The patient recovery time measure is based on a question to be posed by the patient care technician or nurse on a weekly basis (not occasionally). This question, which will appear in the Chairside documentation system as part of the intake screen, is as follows:

> After your last dialysis session, how long did it take you to recover enough to do the things you normally do on a non-dialysis day?
> a. Within minutes
> b. By the time I returned home
> c. After a short nap (30 minutes or less)
> d. After a long nap (over 30 minutes)
> e. By bed time
> f. By the next morning
> g. Before the next scheduled dialysis session
> h. Did not recover before the next scheduled dialysis session
> i. Patient unable or declined to answer

Furthermore, the Chairside system will require completion of this question once a week before the staff member begins the dialysis session. The patient care technicians and nurses will be trained prior to study start to record these data.

Responses to this variable will also be used as a secondary outcome for patient symptoms, alone and in combination with the patient symptom burden measure described above. This question will be asked once per week of every patient in the study.

Quality of life. Quality of life is a patient-reported outcomes, which is "any report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else."[127] PRO instruments can be interviewer-administered, self-administered, computer-administered or interactively administered.[127] We will use the 36-item Kidney Disease Quality of Life (KDQOL™-36 Version 1) ,[128, 129] which has good internal consistency based on alpha scores.[129] This instrument is required annually for US hemodialysis patients.[130] The quality of life survey, the Kidney Disease Quality of Life (KDQOL™-36 Version 1), is intended to be completed on at least an annual basis. KDQOL results will be provided twice for each patient from surveys available as follows: 1) The latest survey within 12 months prior to the start of the study intervention and 2) the earliest survey within 12 months after the start of the intervention. As is current procedure at FMCNA, the measure of quality of life is based on a self-administered survey by providing a paper copy to the patient to complete during treatment or at home. If a patient needs assistance, the Social Worker will assist patients during treatment or via phone in completion of the survey as needed or desired.

Hospitalization. These data will be gathered from FMCNA records for all patients. Hospitalizations within the study period will be calculated. Secondary analyses of this outcome will assess hospitalizations by cause using hospital discharge diagnosis (e.g., fluid-related or cardiovascular causes, COVID-19), number of hospitalizations per patient, and length of hospitalization.

Mortality. These data will be gathered from FMCNA patient records.

3.2.3 Behavioral Outcomes (Behavior Change Measures)

Patient session instability prevention behavior. Once per week, the patient care technician or nurse will also record data regarding patient participation in their fluid removal goals for a specific session. The question, which has already been incorporated into FMCNA's Chairside documentation system for study purposes, is as follows:

"Did the patient make a request today regarding their fluid removal goal?

- o No
- o Yes, requested more than the recommended fluid removal goal
- o Yes, requested less than the recommended fluid removal goal"

Using these data, we will create a patient-level measure of instability prevention behavior that sums the number of requests regarding fluid removal made by each patient, along with weighting based on the appropriateness of the request. Appropriateness of the patient request will be determined based on the "direction of patient request" combined with assessment of clinical factors.

Fluid practice patterns measure. We will create a patient-level measure of fluid management practice patterns that combines the frequency of the following behaviors: (1) Number of times a patient's post-dialysis target weight was changed, (2) patient average treatment time delivered, (3) patient average session ultrafiltration rate, (4) number of changes in number and categories of BP medications patient is taking, (5) use of cool dialysate (based on average dialysate temperature for the session), and (6) whether the patient switched to home dialysis (peritoneal dialysis or home hemodialysis, using treatment modality change) during study period. These are practices that could change as a result of the interventions that may explain intervention effects in the primary and secondary outcomes.

3.2.4 Importance of secondary outcomes, and their role in the analysis and interpretation of study results

We will analyze the impact of the interventions on each of the secondary outcomes; thus, the effectiveness of the interventions will be assessed in relation to both the primary and the secondary outcomes. The study has the following patient-centered secondary outcomes:

Interdialytic weight gain. Interdialytic weight gain, a measure of fluid gains between dialysis sessions, which is measured every session. This outcome is important to patients as high fluid gains are linked to unpleasant symptoms such as bloating and shortness of breath.[131] High fluid gains are associated with fluid overload, which is a leading cause of hospitalization in dialysis patients.[132, 133] High fluid gains are also associated with mortality risk, particularly from cardiovascular causes.[134, 135] Interdialytic weight gain is a top-20 priority outcome (of 33 ranked) for dialysis patients.[85]

Patient symptoms during the dialysis session based on patient reports of their physical experiences and sensations. This is a priority outcome for patients.[136] This is further justified since HD patients are burdened by negative symptoms. Patients report severe fatigue in 50% of HD sessions, and cramping in 30%.[40]

Patient symptoms after the session in the form of recovery time, which represents both post-dialysis fatigue and functioning. More than 40% of patients feel that they have not fully recovered even after returning home after HD.[40] As an indicator of both fatigue/energy and dialysis-free time, this is one of the most important outcomes to hemodialysis patients (1st and 4th of 33 ranked), and more important to patients than healthcare providers.[85, 137]

Health-related quality of life, a patient-reported outcome which will be measured before and after the intervention which has been provided as a key example of a patient-centered outcome by PCORI.[138] HRQOL is a longer-term measure that reflects symptom patterns and other key life dimensions including physical functioning, emotional well-being, pain, and energy levels.[139] The human suffering represented by low HRQOL predicts outcomes that matter to patients, including hospitalizations[140] and mortality.[140, 141]

Hospitalizations, which represent a period of heightened symptoms and lost functioning among patients; patients describe hospitalizations as extremely distressing, and hospitalizations are a top-21 priority outcome for dialysis patients (of 33 ranked).[85]

Mortality, which has been provided as a key example of a patient-centered outcome by PCORI.[138]

4 STUDY DESIGN

4.1 Description and Justification of Study Design

I. Cluster-Randomized Controlled Trial

The study is a cluster randomized controlled trial. The cluster-randomized controlled trial design[142] is most appropriate to our goal of improving health care systems—that is, routine dialysis care. A cluster-randomized controlled trial design is needed because the interventions are, by nature, facility-level strategies. For example, team-based provider education and checklist implementation are geared towards all care team members in hemodialysis facilities. Similarly, peer mentoring is ultimately meant to be offered to a randomly-selected group of patients within a hemodialysis facility. See attached Script for UM Study Coordinator to use when calling patients to offer them Peer Mentoring.

Furthermore, a cluster-randomized controlled trial design is most appropriate for optimizing pragmatic trial designs, of which our trial is an example.[143] Finally, a cluster-randomized controlled trial design minimizes the potential problem of contamination.[144] We considered contamination likely given the nature of the interventions: it would be difficult for trained providers who are accustomed to using checklists to change their practice patterns depending on the patient to whom they are providing care. Moreover, peer mentoring will be given to patients based on their home facility. Because hemodialysis is typically administered in a shared location, patients might learn about others' peer mentoring interactions through conversation, which could be seen as a design problem. Accordingly, individual patients not randomized to receive peer mentoring could indirectly receive aspects of it through changes in other patients' attitudes and/or behavior. However, this effect could actually become an advantage within a cluster-randomized controlled trial, because patients who do not directly receive the intervention could nonetheless benefit from it via passive exposure.

II. Factorial Design

Our 2X2 factorial design trial is a comparative effectiveness trial that is uniquely positioned to answer multiple treatment comparison questions (see below), including *"What is the comparative effectiveness of patient mentoring versus provider education?"*

This design is a *superior choice* in our circumstance to a simple two-arm trial design (i.e., provider education vs. patient activation intervention only) because it provides a control group for testing each intervention. An aim of the project is to translate effective interventions from other settings into the setting of outpatient hemodialysis care. Therefore, there is an inherent need to validate the effectiveness of both interventions in this new environment and patient population (see treatment comparison questions i and ii below), while also comparing their relative magnitudes of effect (see treatment comparison question iii below) and their potentially synergistic or antagonistic effects (see treatment comparison question iv below). If we were to conduct a simple two-arm trial (provider education vs. patient activation only), we would only be able to answer treatment comparison question iii below.

Table 1 - 2 by 2 Factorial Design with Facility and Patient Sample Sizes - # Facilities (# Patients)			
	Patient Activation Intervention		**Total**
Provider Education	Yes (N_2)	No	
Yes (N_1)	**A** - 5 (300)	**B** - 5 (300)	10 (600)
No	**C** - 5 (300)	**D** - 5 (300)	10 (600)
Total	10 (600)	10 (600)	20 (1,200)

Therefore, we have designed a trial to answer the following **four treatment comparison questions (see Table 1)**:

i. Provider education vs. no provider education (assumes no interaction between interventions)
   a. Cells ((A+B) vs. (C+D)) – F test comparison

ii. Peer mentoring vs. no peer mentoring (assumes no interaction between interventions)
   a. Cells ((A+C) vs. (B+D)) – F test comparison

Note that all data are re-used in the comparisons for i and ii. This shows a key advantage of the 2x2 design: it allows testing two interventions for the "price of one". Furthermore, if an interaction is seen (question iv below), then the effect of one intervention can be estimated at each level of the other intervention.

iii. Comparative effectiveness of provider education alone vs. peer mentoring alone
   a. Cell B vs. C – F test comparison. The head-to-head comparison of the magnitude of effect for the two interventions is **actually comparing only the interventions alone, in the absence of the other ones.**

One problem with limiting the focus of this trial to only this comparison (as in a simple two-arm trial) is that if the two interventions were found to be equally effective, there would be no way to determine whether either represented an improvement over standard care. Without a control group, changes in the intervention groups compared to baseline could be attributed to secular trends. Because we have a control group in our design, we can rule out (or confirm) secular trends; therefore, when paired with tests i and ii above, we are able to determine simultaneously that one intervention is both: 1) better (or not) than standard care, and 2) equivalent (or not) to the other intervention.

iv. Are there synergistic or antagonistic effects between the provider education and peer mentoring interventions?
   a. The purpose of this test is to determine whether the effect of one intervention differs depending on the presence of the other intervention. The test compares:
   - [Cells ((A-C) – (B-D))] – F test comparison to examine the effects of provider education intervention with and without the presence of the patient activation intervention.
     - This is equivalent to ((A-B) – (C-D)), which examines the patient activation intervention with or without provider education.

This interaction test will provide power to detect strong synergistic or antagonistic effects.

The use of factorial designs in clinical trials is widely accepted, and is discussed, for example, in a well-known book on clinical trials.[145] Two particular advantages of factorial designs mentioned in this book are the **gain in efficiency** (the ability to test two treatments using the same number of subjects ordinarily used to test a single treatment) and the **ability to test for interaction** between treatments. This statistically efficient approach is valuable for health care interventions, where rigorous evaluation is typically expensive.[146]

One wrinkle in the analysis of factorial designs is that interaction effects must be assumed to be null in order to test the main effects, but interaction effects are often of interest and are generally tested. Much has been written about this issue in the statistical literature; in practice, main effects are presented in the absence of a (statistically or clinically) significant interaction. When a statistically and clinically significant interaction is present, then the effect of each intervention is presented in the presence and absence of the other. Note that no other design can even test the presence of an interaction, so the simplicity gained by other analyses is at the cost of ignoring the possibility of interaction.

After the 12-week baseline period we plan to track outcomes for 36 weeks (24-week intervention period and 12-week post-intervention period). The parallel design with a 24-week intervention period, in assessing a post-intervention follow-up period, will generate valuable information related to the extent to which the intervention can sustain effects beyond an intensive implementation period. This meets the need for longer-term effectiveness studies of patient safety checklists,[147] This will also help clinics to understand an optimal schedule for intervention implementation.

III. Trial phase

The study is designed to be a cluster-randomized, pragmatic comparative effectiveness trial. As such, the trial will take place as part of routine HD care, with low-intensity patient follow-up and use of outcome data already gathered routinely by facilities.[118] As such, this trial leverages unobtrusive existing electronic health record data to collect data regarding outcomes with the addition of two new data collection items to be collected through the electronic health record.[148]

IV. Multi-center trial

The study will take place in 20 outpatient hemodialysis facilities operated by FMCNA. FMCNA has provided one site Principal Investigator for the complete study, since all sites are part of the same organization. All data from each of these facilities will be provided by FMCNA through its central corporate data warehouse, which aggregates data across FMCNA's digital documentation system. FMCNA will submit an IRB Authorization Agreement to cede IRB review and oversight to the University of Michigan.

V. Study Arms

There are four study arms: (1) patient activation intervention only; (2) provider education intervention only; (3) both patient activation and provider education interventions; and (3) no intervention.

Table 1 - 2 by 2 Factorial Design with Facility and Approximate Patient Sample Sizes - # Facilities (# Patients)		
	Patient Activation Intervention	**Total**

Provider Education	Yes	No	
Yes	5 (300)	5 (300)	10 (600)
No	5 (300)	5 (300)	10 (600)
Total	10 (600)	10 (600)	28 (1,200)

VI. Participant Enrollment and Participation

In this protocol, enrollment refers to the period in which patients are given a patient information sheet and given the opportunity to opt out of having their data used as part of the study, and from being offered peer mentoring. See the attached patient information sheet and patient information sheet distribution script. Detailed procedures are provided in the Opt Out Process Attachment. The approximate time to complete initial participant enrollment will be one month per study facility, followed by a period in which new patients who enter the study facilities will be enrolled in the study (i.e., given a patient information sheet and given an opportunity to opt out) until 8 weeks prior to the end of the intervention period. Patients who enter the facility 1-7 weeks before the intervention period ends will not be enrolled since this would not give patients enough time to participate in the patient activation intervention if randomly-selected to do so (assuming time for opting out, offering peer mentoring, intake, matching, and scheduling five sessions was meant to happen approximately weekly). As shown in Table 2 below, the enrollment period will be approximately 4.5 months in all facilities, with two facility groups taking 7.5 months due to staggering of enrollment and intervention delivery over the holidays.

Table 2 - Patient Enrollment and Participation Summary

	Patient Enrollment				**Patient Participation**		
Facilities/Implementation Group	**Initial Enrollment Start (Estimated)**	**Initial Enrollment Ends (Estimated)**	**New patients enrolled until (Estimated)**	**Total Enrollment Period**	**Data Collection Begins (Estimated)**	**Data Collection Ends (Estimated)**	**Total Data Collection Period per Facility**
1-4 (Group 1)	January 1, 2023	January 31, 2023	May 2022	4.5 months	October 1, 2022 (Retrospective)	September 30, 2023	11 months
5-8 (Group 2)	February 1, 2023	February 28, 2023	June 2023	4.5 months	November 1, 2022 (Retrospective)	October 31, 2023	11 months
9-12 (Group 3)	October 1, 2023	January 31, 2024	May 2024	7.5 months (staggered over holidays)	July 1, 2023 (Retrospective)	September 30, 2024	12 months
13-16 (Group 4)	October 1, 2023	January 31, 2024	May 2024	7.5 months	July 1, 2023	September 30, 2024	12 months

				(staggered over holidays)	(Retrospective)		
17-20 (Group 5)	February 1, 2024	February 28, 2024	June 2024	4.5 months	November 1, 2023 (Retrospective)	October 31, 2024	11 months

VII. Trial Periods

As Table 2 shows, implementation of the trial study facilities is staggered such that four facilities, each randomized to one of the treatment arms, begin the trial simultaneously. Each such set of four facilities is referred to as an "implementation group." There are a total of five implementation groups, such that group one begins the trial first, and group five is the last to launch. Each facility participates for 11 months, during which patient data is collected for the trial. This 11-month period includes: (1) a 12-week baseline data collection period; (2) a 24-week intervention period; and (3) a 12-week follow-up period.

The "phased introduction/implementation" strategy adopted in this study is an established approach to clinical trial design that is warranted in situations in which there are "practical, logistical or financial constraints that mean the intervention can only be implemented in stages."[149] Accordingly, one of the main drivers that justify the staggered recruitment and rollout for our trial is logistical feasibility. In addition, our planned patient involvement approaches will benefit from a staggered implementation structure. We do not believe that this will pose difficulties in our analyses since our trial design accounts for the temporal variability introduced by staggered implementation.

VIII. Intervention Description

Patient Activation Intervention

The patient activation intervention occurs over the course of five sessions. These sessions will be digitally available on tablets provided to participating dialysis clinics. All content was created through the partnership between University of Michigan and National Kidney Foundation. While each session, scheduled to occur roughly one week apart from one another, is focused on a different aspect of preventing intradialytic hypotension, they all follow the same format:

- Informational Slides
- Quiz
- Patient Story Videos
- Goal Setting Module
- Supplementary PDF Resources
- Peer Mentoring Discussion Guide
- Action Plan

The topics of these five sessions are as follows:

- Session 1: Getting Enough Dialysis
- Session 2: Feeling Better with Less Salt/Sodium
- Session 3: Making Fluid Restrictions Work for You
- Session 4: Feeling Better on Dialysis and Having Easier Sessions
- Session 5: Getting More Involved in Your Care

We now provide more information about the peer mentoring program.

Peer mentoring model. NKFs telephone/videoconference-based peer mentoring model for ESRD patients is flexible and compatible with rigorous HD schedules. The mentor's previous role was to provide social support to other patients; this is expanded in the intervention to include teaching and motivation with appropriate training and multimedia support. Peer mentoring sessions will incorporate behavior change techniques drawn from SCT,[150] including providing information about CV complications related to HD, teaching skills, encouragement, and role modeling (Figure 1). To enhance motivation, mentors will use MI techniques, including exploration of feelings and personalized goal setting. *Peer Mentor Selection.* Peer Mentors must: (1) have dialysis experience, and (2) not have an active substance use disorder, disorders with psychotic features, or suicidal ideation.[151]

Peer mentor-mentee matching. Mentees will undergo an intake procedure with NKF staff to understand the patient's characteristics, interests, illness experiences/challenges; these data will be used to match compatible mentors with them.

Peer mentor training. The training manual is adapted from NKF's existing curriculum in consultation with peer mentors and the Advisory Committee. There will be multiple training cycles over the course of the project. Training will be nine hours long, divided into six teleconference based sessions lasting 90 minutes each. Training will include information on (1) the role of the peer mentor, (2) CV stability, (3) listening and communication skills, including MI techniques, (4) sharing experiences and strategies; (5) confidentiality and boundaries, and (5) program protocol/logistics such as using multimedia tools, intervention fidelity and record-keeping (see Figure 1). Peer mentors will be trained to refer patients with obvious symptoms of depression or other mental health issues to NKF staff. Trainers for the peer mentor program training will consist of NKF staff and peer mentors; they will receive recorded training on motivational interviewing (MI) from Dr. Kenneth Resnicow, a leading expert on MI. To ensure mentors have gained needed skills, each mentor will be assessed during role plays. The fidelity of training sessions will be tracked with the use of checklists.

Peer mentor supervision/support. Mentors will receive ongoing support via monthly phone calls from NKF staff. An e-community will be available to peer mentors, developed with input from the focus groups. Within the e-community, peer mentors will have access to a communication tool with which to speak with one another, records of their progress, and educational materials. The e-community will be developed using Basecamp, a collaboration platform already used by NKF volunteers and staff. No patient data will be entered into Basecamp.

Peer mentor motivation and burnout prevention. Current demographics and interest levels in the NKF program shed predictive insight into the future engagement of Dialysafe peer mentors.

Reflecting on NKF statistics from June 2018, we are encouraged by the likelihood of high peer mentor motivation and low mentor burnout.

Of all of National Kidney Foundation's currently trained peer mentors, 56% have hemodialysis experience. As participation in Dialysafe requires that peer mentors to have this experience, we have looked further into this population in order to assess the time generally spent in clinics for their own hemodialysis treatment. Importantly, of the peer mentors with hemodialysis experience, only 17% are currently undergoing dialysis treatment. The remaining 83% have been on hemodialysis previously, but currently have a working kidney transplant or another modality that does not require in-center treatment. Thus, less than 10% of all NKF peer mentors are currently visiting a dialysis clinic for hemodialysis therapy. Not only are few peer mentors currently undergoing hemodialysis, but the team has also found reassurance in the overall engagement and interest in the NKF peer mentoring program. As of June 2018, there were five times more applicants to be peer mentors than could be trained and active in the program. This means that for every peer mentor in the NKF program, five have applied in hopes of joining the program soon.

Answers to application questions also provide insight into the dedication of those who want to be peer mentors. A look into application responses provides virtually endless descriptions behind applicant motivations. When asked, "why do you want to become a peer mentor?" real example answers include "*hopes of lessening [other patients'] fears and improving their lives,"* "*I never felt like I had anyone to talk to and I know others must feel the same*," and, "*I learned a long time ago that a few kind words can go a long way."* A majority of applicants mention that they want to share their experience. As one applicant said, *"There is so much to be said for someone who has been through it all... and I have been through it ALL."* It is apparent that potential mentors are highly motivated to help other patients.

As an additional source of motivation, the study has incentives. Patients who join the peer mentoring program will receive a blanket after completing their first peer mentoring sessions. Patients frequently bring blankets to their dialysis sessions, so this incentive may also generate interest in the program among other patients (see "Mentee Blanket Note" for the letter that will be enclosed with the blanket). Further, a proportion of the total project budget is allocated to a subcontract with the National Kidney Foundation (NKF). This subcontract budget includes stipends for peer mentors at a level of compensation deemed fair, $100 per patient with whom a mentor completes all five mentoring sessions, or a prorated amount based on the number of sessions completed, paid upon completion of the peer mentoring sessions with each patient. Peer mentoring satisfaction surveys, $15 per person. (See attached documents: Peer Mentee Satisfaction Survey and Peer Mentor Satisfaction Survey). NKF will administer these incentives. The study will also provide mentees with a payment of $120 for the completion of the full peer mentoring program, with payment on a per-session basis at an escalating rate ($10 for session 1, $15 for session 2, $20 for session 3, $25 for session 4, and $50 for session 5 and completion of the final peer mentoring satisfaction survey). Participants may only receive incentives upon completion of each task. These incentives are offered to compensate for the time spent on the intervention, in order to show that the patient's time is valued.

The ratio of peer mentors to mentees will also aid in preventing peer mentor burnout, particularly among any mentors currently undergoing in-center hemodialysis therapy. As described in the project budget, the National Kidney Foundation will train a minimum of 150 peer mentors in the Dialysafe program. In each of the 10 clinics where peer mentoring will be offered, we estimate that up to 30 patients will receive at least one peer mentoring session and

up to 22 will complete all 5 sessions, totaling 300 mentees over the course of the study. A maximum of 30 will finish peer mentoring in each clinic with peer mentoring. This results in a ratio of slightly less than three mentees per mentor over the course of the complete study. Note that this number is variable and driven by the peer mentor: some may only want to mentor one patient, and some may be very involved and want to mentor more than three. In both cases, this ratio allows the peer mentor to accept the number of mentees that they wish without pressure of taking on more mentees than their schedule allows. In the case that most mentors prefer only one mentee, more peer mentors can be trained, as the study has allocated for the training of up to 300 peer mentors.
Family involvement. We have created information sheets for family caregivers that describe peer mentoring and detail what caregivers can do to support patients' cardiovascular/hemodynamic stability (e.g., ensuring patients' access to low-sodium foods). Family members will receive the information sheet in one of three ways:

1) Inclusion in a mailing from NKF, if patients indicate they want materials from NKF mailed to them
2) Email from the peer mentoring management system to patient's email
3) Available for review on the peer mentor management system at any time; patients can email forward it from the application to anyone they wish

Management of peer mentoring program. NKF will hire a full-time Project Coordinator, who will be responsible for overall management of the peer mentoring program, including working with the University of Michigan to develop a system to track and manage the mentors and mentees. The system will be similar to that which NKF is already using for its existing Peer mentoring program (with some updates for this project), which includes an online platform created for the program. The online platform tracks program participants (mentors/mentees), sends alerts about actions that need to be taken by the NKF Project Coordinator on an ongoing basis, and automates scheduling of calls between mentors and mentees. NKF will also hire a Project Assistant to ensure that they have adequate staff support for the training, matching and supervision of peer mentors as part of the project.

The NKF Project Coordinator and the NKF Project Assistant will communicate with all potential/actual mentors and mentees throughout the course of the project on an ongoing basis, utilizing the online platform described above to automate reminders and communications when possible. The Project Coordinator will work with the University of Michigan to develop the online platform and ensure that it meets the needs of the project. The online community will also be a moderated environment in which mentors can access project-related materials and support one another and problem-solve together as they mentor patients as part of the project. This online community is part of our plan for facilitating ongoing learning and feedback among peer mentors.

Emergency procedures (See attachment entitled: Dialysafe Peer Mentor Emergency Procedures). In the case that a patient has a medical emergency during a peer mentor **session,** the peer mentor will encourage the patient to call for/get the attention of a clinic nurse. The peer mentor will then end the videoconference; that is, the peer mentor will not continue the Dialysafe project-related discussion once an incident has occurred. The peer mentor will report any incomplete session discussions through the peer mentor view of the Dialysafe peer mentor management system (PMMS), which will be visible to the Peer Mentoring Program Coordinator at the National Kidney Foundation. Interrupted sessions will be rescheduled, if possible.

In the case that a patient indicates that they may be of danger to themselves or others, peer mentors are obligated to share this information with the Peer Mentoring Program Coordinator at the National Kidney Foundation. Should the program coordinator not be available, there will be a backup coordinator who can be contacted. While peer mentors must keep strict confidentiality with all mentees, the peer mentor training will explicitly state that this rule does not apply to suicidal or homicidal ideation. Mentors who have reason to believe that a mentee is suicidal or homicidal will inform the mentee that they are concerned about them and cannot keep what was shared confidential. The peer mentor will then contact the Peer Mentoring Program Coordinator by email or phone. This will then be followed up by the Peer Mentoring Program Coordinator, who will communicate directly with the mentee about whom the concern was expressed. The mentee will be assessed for suicidal/homicidal ideations and their intentions/plan, as well as an assessment of the patient's support system in place at the time. The mentee will be referred back to their clinic social worker as well. The program coordinator will also be responsible for notifying the clinic manager or designated appointee at the dialysis facility, who in turn will notify the attending physician responsible for the care of the patient.

Role of patients post intervention. At each study facility, the trial includes a baseline 12-week period of data collection, a 24-week intervention phase, and a 12-week post-intervention phase. Data collection in each facility will conclude at the end of the post-intervention phase. Therefore, there is no explicit 'non-intervention phase' after study completion, i.e., we do not envisage active patient involvement in study activities after the 24-week trial implementation concludes at the participating facilities. However, the University of Michigan or NKF will make efforts to recognize and appreciate patients' involvement in the trial after it is officially over in their facility. Specifically, patients who completed the patient activation intervention will be awarded a certificate of recognition for their participation. The University of Michigan will also provide opportunities for patients to follow the study as it progresses. At the end of the intervention in their facility, patient participants will be given access to a study Web site (https://dialysafe.si.umich.edu/) that will provide updates about the trial's progress.

Finally, at the end of data collection in each study facility, facilities will be verbally encouraged, using positive messages, by study staff to continue the behaviors that they have learned as part of the intervention, if they find them helpful. There is also an important role for patients to play in the longer-term dissemination and implementation of study results. First, patient representatives on the Steering Committee will be given an opportunity to co-present findings at meetings and conferences, and to serve as co-authors on manuscripts. Second, our project includes a dissemination partner, the 5-Diamond Patient Safety program. The program is a national initiative that includes 12 regional dialysis care quality improvement networks; each of these networks involves dialysis patients in liaison and/or advisory roles. Thus if the trial shows positive results from the interventions, 5-Diamond will engage its participating networks, which involve patients, in dissemination of the intervention to hemodialysis facilities across the country. Furthermore, our implementation partner, the National Kidney Foundation, is a national, patient-driven organization that is interested in wider implementation of the patient activation intervention if study results are positive.

Provider Education Intervention

The provider education intervention has two main components: (1) a checklist that aims to identify patients at elevated risk of intradialytic hypotension (IDH); and (2) team training.

Team training.

The team training has several components. Staff in the facility (nurses, patient care technicians, dietitians and social workers) will receive:

- 2 training sessions delivered to facility staff via online learning system
- 2 training sessions delivered to facility staff via videoconference (facility earns 5-Diamond credit for this training)

Physicians, nurse practitioners and physician assistants, who typically round in multiple facilities, will be offered:

- 1 training session delivered online

For the live videoconference training, our intervention will follow the 5-Diamond Patient Safety Program format, including slides, speaker notes, tools and resources. The 5-Diamond program includes a choice of several modules which facilities who wish to obtain 5-Diamond Status can complete, of which our completed training will be one after the trial implementation in the 20 study facilities is complete. Our training module will follow the 5-Diamond format of slides, which includes facility engagement, procedures for implementation of the education and attendance sheets. Additionally, self-learning modules delivered through the existing FMCNA LMS (Learning Management System) will be used to expand upon the current 5-Diamond format; this expansion has already been approved by 5-Diamond. In order to receive 5-Diamond certification, facilities must complete 4 training modules, earning a “diamond” for the two completed synchronous modules. Facilities that choose to implement our module will earn a “diamond” towards their 5-Diamond certification.

In line with the aforementioned evidence, the staff training will be implemented on a team basis within the facilities. The training itself will involve a mixture of material for presentation, discussion and online modules to complete independently. The training will be implemented by the University of Michigan Project Coordinator(s). A “Study Champion,” ideally a Clinic Manager or Staff Nurse, will attend a train-the-trainer session with other Study Champions prior to intervention start at their sites. At the training sessions, there will be facilitated discussions regarding checklist implementation so that the facility staff can evaluate how to make checklist implementation fit into their workflows

Checklist. A checklist application will be presented on provided tablet computers to nursing staff at all clinics in the provider intervention arm. The checklist aims to be completed by a nurse for each patient’s dialysis treatment. The checklist promotes: (1) systematic identification of patients who may be at increased risk of having IDH; and (2) considerations for preventive interventions to reduce IDH rates in hemodialysis clinics. To accomplish these aims, the checklist is designed to enhance: (1) critical thinking regarding factors which place patients at risk for IDH; and (2) increased focus on IDH prevention in routine hemodialysis care. The checklist has two main parts: (1) four questions to be answered with “yes,” “no,” or “data not available;” and (2) A list of potential treatment considerations for interventions, which are presented as reminders/prompts if any of the answers to the questions are “yes”. In line with the value of team training for patient safety,[152] training will be provided to the care team, and to individuals through a self-study online curriculum. This holds promise for stimulating both collective ownership and for influencing providers’ subjective norms.

The checklist will be made available as an application on an Android tablet computer; the tablet computer, with the checklist application preloaded, will be provided to clinics as part of the

study. The tablet computer will be placed in a protective case that can withstand cleaning with bleach and facility staff will follow existing policies for disinfection. The checklist will not identify the patient or the staff member, but it will automatically log the facility, date, time, items displayed, and items clicked on a HIPAA-compliant server. The tablet will not need to be connected to the Internet to function; it will synchronize with the remote server when the Internet is available. If any screen other than the home screen is idle for more than 2 minutes, the system will revert to the home screen, which contains a blank checklist.

IX. Randomization and Stratification

To be in the study, facilities have been randomly selected. Randomization was stratified based on region, and the socio-economic status of the facility's geographic area neighborhood (determined by the poverty rate in the county in which the facility is located; these were stratified into low/medium/high poverty levels) to account for potential differences in facilities.

The 20 HD facilities will be randomized to the four intervention combinations of the 2x2 factorial design, assigning 5 facilities to each of the 4 combinations (both provider education and patient activation using peer mentoring; provider education alone; patient activation alone; and neither intervention). Facilities will be stratified by geographic region and possibly socio-economic status to ensure treatment balance on those factors.

X. Primary and Secondary Outcomes

- Primary Outcome:
    - Dialysis session stability (Intradialytic hypotension)
- Secondary outcomes:
    - Fluid adherence (Interdialytic Weight Gain)
    - Dialysis adherence
    - Patient symptoms
    - Quality of Life
    - Hospitalization
    - Mortality
- Behavioral Outcomes
    - Patient Involvement in Dialysis Session Stability
    - Fluid Management Practice Patterns Measure (Providers)

XI. Data Collection Methods

Please refer to the attachment entitled "Data Elements List" for a detailed list.

a) Data for the following outcomes **are gathered as part of the standard workflow at hemodialysis facilities**, and will be electronically transferred from FMCNA to UM's Kidney Epidemiology and Cost Center for analyses:

- Intradialytic hypotension (primary outcome)
- Interdialytic weight gain
- Patient symptoms during the dialysis session based on patient reports of their physical experiences and sensations, recorded in the digital Chairside documentation system
- Health-related quality of life

- Hospitalizations
- Fluid practice patterns measure components: post-dialysis target weights, treatment time delivered, ultrafiltration rate, patient medications, use of cool dialysate
- Mortality
- Change in treatment modality for a patient

The FKC ID1 and FKC ID2 unique patient identifiers will be used to link data clinical patient and session data, and data from peer mentoring received from the peer mentoring management system (PMMS).

3) Data for the following outcome is not part of the standard workflow at hemodialysis facilities, but **will gathered electronically (via 2 questions added to the FMCNA Chairside application) by staff as part of the routine workflow while facilities are in the study** (these data will also be electronically transferred):

- Patient symptoms after the session in the form of recovery time
- Patient fluid removal goal requests

Dialysis session and patient electronic health record-based data will be transferred by FMCNA to the UM-KECC on a scheduled basis using a unique random identifier for each patient that is generated by FMCNA (FKC ID1). Peer mentoring records will be generated in a report with the University of Michigan School of Information-managed Peer Mentoring Management System; this report will be sent to FMCNA using FKC ID2, second a unique patient ID given to each patient for the purposes of peer mentoring only. The report will include FKC ID2 along with peer mentoring data. FMCNA will then replace each patient's FKC ID2 with FKC ID1 in the peer mentoring dataset, and send it to UM-KECC for analyses (please see attached document entitled, *Data relinking process*).
UM-KECC has an extensive data security infrastructure to ensure secure data transfer and storage. Codebooks will be generated to document the data set and calculated scales.

4) Intervention implementation data will be gathered and shared at the facility level. This includes data on training completion, checklist completion, and patient intervention completion. Data collected on intervention implementation will be gathered from study tools as follows:

- Checklist Completion Data will be gathered via a tablet computer, and completion data will be stored on a database on a secure, HIPAA-compliant server at the University of Michigan Medical School (identifiable by a Facility ID) and then transferred to a secure research server at the University of Michigan School of Information (UMSI). Data will then be used to calculate completion rates by facility using a program such as SPSS or Excel. Checklist completion metrics by facility will be transferred to UM-KECC for analysis (e.g., checklist completion rate by facility over specific time points; proportion of checklist sessions in which patients are identified as being at risk of IDH; and prevalence of reasons why patients were identified as being at risk of IDH). See the attached Staff Incentive Plan for Checklist and Study Completion for incentives tied to monthly checklist completion and the completion of the entire study.
- Live videoconference Training Attendance Records by facility and staff role (staff names will not be provided) will be emailed from the Clinical Manager to the University of Michigan Study Coordinator, via an FMCNA email account and then transferred to an Excel or Word document (identifiable by a Facility ID) and stored on a secure research server at the University of Michigan School of Information (UMSI). Training completion metrics by facility will be transferred to UM-KECC for analyses (e.g., proportion of staff

by role who completed each training session, tracked by facility; average proportion of training elements completed; proportion of training sessions in which all training elements completed).

- Learning Management System online Training Records, will be provided by FMCNA to UMSI by facility and staff role (staff names will not be provided) by placing these records in SharePoint, a secure computing environment to share research data with UMSI). Data from SharePoint will be stored on a secure research server hosted by Fresenius Medical Care (FMCNA). UMSI staff will be granted limited access to SharePoint by FMCNA and will sign an attestation indicating that they understand the security procedures and limitations of SharePoint (see section 44, "FMC SharePoint use by External Partners Attestation"). Training completion metrics by facility will be transferred to UM-KECC for analyses (e.g., proportion of staff by role who completed each training session, tracked by facility; average proportion of training elements completed; proportion of training sessions in which all training elements completed).
- Patient Intervention Completion Data – Tablet-based Educational Modules. Data will be gathered regarding patient interactions with the digital educational modules. Data will be stored on the PMMS stored on secure, HIPAA-compliant server at the University of Michigan Medical School. These data will be analyzed at the UM School of Information. Metrics include: average number of mentoring sessions completed per patient; patient retention rates across all five peer mentoring sessions; average peer mentoring session length; education module completion rates by topic and section; quiz completion rates; average time spent on each educational module section; average proportion of peer mentoring session components completed by session; proportion of peer mentoring sessions in which all session components completed; and mentor-specific peer mentoring completion rates. In addition to analysis by UM, these data may be used by NKF for training and supporting mentors.

XI. Centralization of Study

All data analyses for Aims 1 and 2 will take place at UM-KECC. Dialysis session and patient electronic health record-based data will be transferred by FMCNA on a scheduled basis to UM-KECC using a unique random FKC ID 1 for each patient. UM-KECC has an extensive data security infrastructure to ensure secure data transfer and storage. Codebooks will be generated to document the data set and calculated scales.

Data will be transmitted electronically to UM-KECC via secure password-protected file transfer protocols. Fidelity data regarding checklists will be retrieved from data entered via tablets, and online training data will be securely made available to UM-KECC, and placed in a database at UM-KECC.

Aim 3 analyses will take place at the UM School of Information, under the direction of the study's Principal Investigator.

XI. Interim Analysis Plans

The study team will produce interim analyses every year of the trial implementation period, or as requested by the DSMB. We currently anticipate reporting annually to the DSMB blinded data on IDH and mortality rates in each treatment arm. The study has no stopping rules.

XII. Structure for Safety Oversight

The study will have a Data and Safety Monitoring Board (DSMB).

4.2 SUBSTUDIES (IF APPLICABLE)

N/A

5 STUDY ENROLLMENT AND WITHDRAWAL

The sample size for the overall study will be 20 outpatient hemodialysis clinics with approximately 1,200-1,440 patients in total. For the peer mentoring intervention, sample size will be 30 patients at each of 10 clinics randomized to receive the peer mentoring (n=300).

5.1 SUBJECT INCLUSION CRITERIA

We aim to include all non-vulnerable in-center patients at the 20 participating hemodialysis facilities. The trial is designed so as not to exclude anyone, including women and minorities to the extent they are represented at the dialysis facilities from the ages of 21 and older.

5.2 SUBJECT EXCLUSION CRITERIA

We will only exclude those who have opted out of the study and vulnerable patients: those under 21 years of age, prisoners, those with poor cognition or cognitive impairment, and those deemed vulnerable based on cognitive impairment by the Clinical Manager, Medical Director, and/or Social Worker (see Table 3: Screening for Patient Vulnerable Status), and those who are unable to comprehend the patient information sheet due to lack of facility in English or Spanish (patients whose primary spoken language is not English or Spanish). Due to limited availability of peer mentors fluent in languages other than English, only English-speaking patients will be offered peer mentoring.

5.3 STRATEGIES FOR RECRUITMENT AND RETENTION

In order to recruit facilities, the FMCNA Project Manager has approached/will approach regional management (regional vice presidents, RVPs) at FMCNA to educate them regarding the study process. After screening of facilities by FMCNA based on inclusion criteria and random selection by UM from the pool of eligible facilities, these RVPs were/will be approached and their approval sought, on a voluntary basis. At that time, RVPs have assessed/will assess whether facilities were/are adequately staffed to participate in the study and have considered/will consider the level of staff effort required in the context of other ongoing FMCNA and CMS initiatives. RVPs have management authority over their regional clinics and were/will be able to facilitate clinic recruitment. The RVP or the FMCNA Project Manager has approached/will approach the medical director of the randomly-selected facilities, and each facility's management body (called Governing Body) will approve study participation.

If a facility declines to participate, we will approach the next randomly-selected facility until the recruitment goal for the region is reached. Once recruited, facilities will also be randomized into study arms. If a facility drops out of the trial, the UM team will select another eligible facility to participate in the trial according to the clinic inclusion criteria and recruitment process used for the initial clinics.

We plan to include all non-vulnerable patients at participating dialysis facilities who do not opt out of the study. The study population of patients enrolled in this trial will be representative of the general adult hemodialysis population in the United States with respect to age and health status (e.g., typically with multiple comorbid conditions, including diabetes, hypertension, and cardiovascular disease). Our target subject sample is approximately 1,200-1,440 patients across the 20 facilities will be enrolled in the study (see attached Performance Site Listing). It is anticipated that there will be more than adequate representation by minorities as these are typically over represented in the dialysis population and also because of the geographic diversity of participating sites (e.g., Michigan, Ohio, California, Alabama, Massachusetts and Connecticut). Health care providers will not be study subjects.

As is described in this IRB application, we are seeking Institutional Review Board approval for a waiver of consent and waiver of HIPAA authorization based on the study's minimal risk to patients. There will be an opt out process for the Dialysafe Study to meet ethical obligations to patients, including respect for patient decision-making and a patient-centered approach to research. Thus, each patient will have the opportunity to **opt out of having their data used in the study, and from being offered peer mentoring if their facility is randomized to the intervention and if they are randomly selected to be offered an opportunity to participate in the patient activation intervention**. The University of Michigan is responsible for the opt out process for patients, although it will be implemented by FMCNA staff. Under the direction of, and with remote support from, a UM study coordinator, each patient will be given an information sheet by FMCNA staff, using a script to be approved by the IRB. The UM study coordinator will be available for further explanation of the study and to answer questions, and will monitor and check messages at, the toll-free number included in the patient information sheet. Facility staff will record that each patient has received the information sheet, and if they have verbalized a decision to opt out of the study. The information sheet will also provide a 1-800 telephone number to call in order to learn more about the study and opt out of the study if desired (see attached Help Line scripts). Any patient opt outs received through the toll-free number while the UM coordinator is off-site will be securely transferred to FMCNA. A master list will be maintained of all patients informed about the study, and those who have opted out. One week will pass to allow patients an opportunity to opt out before starting the study. Thereafter, patients may opt out at any time. Enrolled (patients who do not opt out) will have study data shared with UM-KECC along with the FKC ID1 unique identifier. If patients do not opt out, no further action is required from patients to have their data used in the study.

A randomly-selected subset of patients in facilities randomized to the patient activation intervention arm will be offered the opportunity to participate in the intervention. A list of patients who have not opted out of the study will be provided by FMCNA to UM School of Information staff in a secure computing environment, SharePoint. This list will include only the information needed to contact patients (first/last name, sex, clinic name/clinic ID, treatment day/shift, primary/alternate phone). Patients who are randomly selected will be contacted by a UM Study Coordinator on a non-dialysis day by phone to offer them the opportunity to participate using a designated script. If the UM Study Coordinator cannot reach the patient after 5 calls, they will ask the Study Champion to follow up with the patient to gauge interest. In the event that a

patient is interested in joining the peer mentoring program but does not have regular access to a phone to contact UMSI study staff and/or NKF, a pre-paid cell phone will be provided for the patient to use. The phone will be shipped to the patient's home address with a limited number of minutes pre-loaded for their use. At the end of the study, the phone may be discarded, or the patient may choose to purchase more minutes and retain the phone as a personal device. The pre-paid phone is not considered an incentive because it will not be preloaded with enough minutes to be used for personal use. The estimated value of the phone without minutes is $25. Neither study nor clinic staff will have the ability to track the phone's use after it has been activated by the patient.

Patients may also be contacted by a "patient advocate," a current in-center dialysis patient who will be identified by their clinic staff as a potential advocate for the peer mentoring program who is already enrolled in the peer mentoring program. As in the Operations Committees, clinic staff will identify potential advocates. UMSI staff will contact potential patient advocates using the contact information they have for the peer mentoring program, and invite them to be a patient advocate, emphasizing that the role is voluntary. If an individual agrees to be a patient advocate, UMSI study staff will ask clinic staff to provide the patient with the Patient Advocate Agreement (See "Patient Advocate Agreement" document) for signature, provide a copy of the signed agreement to the patient advocate, and upload the signed document to a secure Sharepoint. UMSI study staff will conduct a 15 minute phone call with advocates to describe their role and answer any questions or concerns. (See "Patient Advocate Discussions" document for advocate training plan.) Patient advocates may discuss their experience in the peer mentoring program with other patients in their clinic, participate in "lobby days" as approved and facilitated by their local clinic staff, and direct any interested patients to contact the UMSI study staff to learn more about joining the peer mentoring program. Patient advocates will not consent any patients for the peer mentoring program (see "Patient Advocate Discussions" document for the scope of the patient advocate role; see "Peer Mentor Program Flyer" for handout in clinic). Up to three Patient Advocates may be recruited for each shift in the clinic. Data for patients who agree to participate in the patient activation intervention will be entered into the HIPAA-compliant, web-based peer mentoring management system for intake by the National Kidney Foundation. Those who refuse will be recorded on the patient list located in the FMCNA SharePoint environment (see attached document, *HIPAA Compliance of Dialysafe Tools*).

Retention of participants in patient activation intervention. While participant retention is an issue in virtually any trial, dialysis patients are likely to experience fatigue, pain and other symptoms; thus there is a greater than average risk of patients not completing the intervention. In the two aforementioned published studies regarding peer mentoring and coaching for hemodialysis patients, participant retention rates were 85.7% for the 2-4 month study and 100% for the 10-week study, respectively. [18, 153] Another study involving one-to-one peer support to people with diabetes had a 75.7% retention rate for a study that was 8-12 months long. [154] Notably, all of the aforementioned studies were more demanding than ours in terms of numbers of sessions with patients (8-30 sessions). Therefore, based on these prior studies, but recognizing the uncertainties of the COVID-19 pandemic, we estimate a retention rate of at least 73% for the peer mentoring intervention. In summary: if 60 patients in a facility are offered peer mentoring, we predict that approximately 30 of them will agree to receive peer mentoring; of these patients, at least 22 will complete the entire intervention. Under this circumstance, an additional 8 will thus complete part of the intervention.

In order to achieve our estimated retention rate of 65-75% for the complete intervention, and in keeping with published research,[155] our study team will use a combination of retention strategies. The following general evidence-based retention strategies will be used in

combination: patient/community involvement;[156] offering participant incentives;[156] using a participant-tracking database[157]; using systematic methods for participant contact and scheduling of peer mentoring appointments;[156] issuing reminders prior to appointments;[156]; interpersonal skill training for project staff;[157] monitoring retention;[156] and monitoring satisfaction with the study[158] via the planned peer mentoring survey.

Furthermore, we will follow best practices for retaining older and seriously ill study participants including: demonstrating care for participants by sending birthday or holiday cards;[158] flexibility in scheduling and dividing up peer mentoring sessions over time[158]; facilitating home-based participation in the study;[158] developing a protocol for managing missed follow-ups;[158] and keeping response burden for patient data collection very low.[159]

5.4 TREATMENT ASSIGNMENT PROCEDURES

5.4.1 Randomization Procedures

The 20 hemodialysis facilities will be randomized to the four intervention combinations of the 2x2 factorial design, assigning 5 facilities to each of the 4 combinations (both provider education and patient activation using peer mentoring; provider education alone; patient activation alone; and neither intervention). Facilities will be stratified by geographic region and socio-economic status to ensure treatment balance on those factors.

With regard to peer mentoring only, we will randomly select patients who are not vulnerable and have not opted out of the study in succession, until approximately 30 English-speaking patients in a facility accept peer mentoring. Patient randomization will be stratified by treatment shift. Every time a patient declines to participate, we will choose another patient randomly until the enrollment target is reached. Patients entering a facility randomized to the patient activation intervention during weeks 1-18 of the 24-week intervention period will be added to the list of patients eligible for peer mentoring from which patients are randomly selected for peer mentoring. We anticipate that 15-20% of patients in the study facilities will be replaced by new patients during the 11-month study period due to mortality, change in ESRD treatment modality (e.g., a kidney transplant), or changing facilities.

5.4.2 Blinding Procedures

Study participants and facilities will not be blinded to treatment status. However, during the initial analyses, study analysts will be blinded to treatment status in that they will not know which facilities are in which intervention group. Each intervention group will be given a non-identifying code, and each facility assigned to one of those codes (e.g., group A, group B, group C) while a list of facilities by treatment status is kept separate during the analyses. Analyses will then be conducted using intervention group codes that do not reveal which intervention in which a facility is participating. Supplementary as-treated analyses cannot practicably be completed in a blinded fashion due to heterogeneity of measures (e.g., number of peer mentoring sessions completed by a patient).

5.4.3 Reasons for Withdrawal

Because ours is an educational intervention with support from the dialysis facility's parent organization, we expect facility attrition to be very low. Nevertheless, if facilities do drop out

during the intervention phase, they will be replaced and the intervention will take place at a new facility. A facility would need to be replaced if: 1) they request to leave the study; or 2) 75% of the staff do not complete at least 90 minutes of the training within the first 14-16 weeks of the intervention period.

As for missing outcome data for facilities in the study, data for our primary outcome as well as two secondary outcomes (fluid adherence/Interdialytic weight gain and dialysis session adherence) are gathered at the dialysis session level, using data that are automatically gathered when treatment is delivered.

With IRB waiver of consent and waiver of HIPAA authorization with an opt out process, we expect that we will not have significant attrition due to patient withdrawal since interventions will be provided at the facility-wide level. Attrition may be seen in the patient activation (peer mentoring) intervention if patients choose not to participate in the peer mentoring program or if patients drop-out after starting the program.

A final type of attrition may be the possibility of missing data due to patients not completing the self-reported quality of life (KDQOL) survey or the patient symptom question regarding recovery time. For example, some participants may refuse to answer certain questions or may miss follow-up surveys. Where possible, we will note reasons for missing data by triangulating data sources to determine whether a patient has moved to another facility, or in accordance with two of our outcomes, been hospitalized or die. Although every effort will be made to collect these data, some missing surveys are still likely, particularly among those in ill health. We do not expect missing surveys to be associated with study arm, but missingness itself can be analyzed for treatment differences as a tertiary outcome measure. The sample in each cross-section will include living patients only, so death will not be a problem as it would be in a longitudinal QOL study. We believe that this approach, along with our conservative assumptions regarding sessions needed as described previously, will largely prevent missing data for our primary outcome, as well as two secondary ones. Death will be tracked as an outcome, although the trial is not powered to assess this as a primary outcome. Data on subjects who leave the study site, will be used until their time of departure from the study. In other words, we will not track data for patients after they transfer to a non-study facility.

We will compare the characteristics of those with missing data to those without missing data, to test whether characteristics are similar between the groups. In addition to complete case analyses, we will use state-of-the-art statistical methods such as likelihood approaches and multiple imputation to deal with missing data.[160] These sensitivity analyses will assess the robustness of the results to missing data.

5.4.4 Handling of Withdrawals

If facilities do drop out during the intervention phase, they will be replaced and the intervention will take place at a new facility. A facility would need to be replaced if: 1) they request to leave the study; or 2) 75% of the staff do not complete at least 90 minutes of training within the first 14-16 weeks of the intervention period. Data will be retained for facilities that withdraw from the study, unless they explicitly request that the data not be used. It is important to note that patients who drop out of the patient activation intervention will not be dropped from the overall study unless requested, and collection of outcome measures will continue. Data will be retained for patients who opt out of the study after the initial opt out period up until the decision to opt

out, unless otherwise requested by the patient. Any attrition (lack of participation in the patient activation intervention) could contribute to a reduced estimate of treatment effect in analyses using the intent-to-treat principle; this reduction in estimated treatment effect would appropriately reflect the expected effect of this intervention in the general dialysis population.

5.4.5 Termination of Study

There are no stopping rules for the study.

6 STUDY INTERVENTION/INVESTIGATIONAL PRODUCT

6.1 STUDY PRODUCT DESCRIPTIONS

6.1.1 Multimodal Provider Education Intervention

The staff training will be implemented on a team basis within the facilities and will include instruction on how to use a tablet-based IDH prevention checklist during the assessment of every patient. The online training itself will involve a mixture of material for presentation, discussion and online modules to complete independently. The training will be implemented by the University of Michigan Project Coordinator(s). A “Study Champion,” ideally a Clinic Manager or Staff Nurse, will attend a train-the-trainer session with other Study Champions prior to intervention start at their sites. At the training sessions, there will be facilitated discussions regarding checklist implementation so that the facility staff can evaluate how to make checklist implementation fit into their workflows. The checklist is designed to enhance: (1) critical thinking regarding factors which place patients at risk for IDH; and (2) increased focus on IDH prevention in routine hemodialysis care. The checklist has two main parts: (1) four questions to be answered with “yes,” “no,” or “data not available;” and (2) A list of potential treatment considerations for interventions, which are presented as reminders/prompts if any of the answers to the questions are “yes”. In line with the value of team training for patient safety,[152] training will be provided to the care team, and to individuals through a self-study online curriculum. This holds promise for stimulating both collective ownership and for influencing providers’ subjective norms.

The checklist will be made available as an application on an Android tablet computer; the tablet computer, with the checklist application preloaded, will be provided to clinics as part of the study. The checklist will not identify the patient or the staff member, but it will automatically log the facility, date, time, items displayed, and items clicked on a HIPAA-compliant server.

6.1.2 Patient Activation Intervention

We will extend the peer mentoring program offered by the National Kidney Foundation (NKF). Peer Mentors are trained ESRD patients who volunteer to support other patients. Mentors can speak from experience about the challenges of life on hemodialysis; thus patients often view mentors as credible and accessible information sources.[100, 109-111] Mentors can role model health behavior change as they share their experiences.[110]

Peer mentoring model. NKFs telephone-based peer mentoring model for ESRD patients is flexible and compatible with rigorous hemodialysis schedules. The mentor's current role is to provide social support to other patients; this will be expanded in the intervention to include teaching and motivation with appropriate training and multimedia support. Peer mentoring sessions will incorporate behavior change techniques drawn from SCT,[150] including providing information about cardiovascular complications related to hemodialysis, teaching skills, encouragement, and role modeling (Figure 1). To enhance motivation, mentors will use MI techniques, including exploration of feelings and personalized goal setting. *Peer Mentor Selection.* Peer Mentors must: (1) have dialysis experience, and (2) not have an active substance use disorder, disorders with psychotic features, or suicidal ideation.[151]

Peer mentor-mentee matching. Mentees will undergo an intake procedure with NKF staff to understand the patient's characteristics, interests, illness experiences/challenges; these data will be used to match compatible mentors with them.

Peer mentor training. The training manual has been adapted from NKF's existing curriculum in consultation with peer mentors and the Advisory Committee. There will be multiple training cycles over the course of the project. Training will be seven hours long, divided into 10 self-paced training modules, with one live, virtual training session for role plays and mentor skill assessment. Training will include information on (1) the role of the peer mentor, (2) cardiovascular stability, (3) listening and communication skills, including MI techniques, (4) sharing experiences and strategies; (5) confidentiality and boundaries, and (5) program protocol/logistics such as using multimedia tools, intervention fidelity and record-keeping (see Figure 1). Peer mentors will be trained to refer patients with obvious symptoms of depression or other mental health issues to NKF staff. Trainers for the peer mentor program training will consist of NKF staff and peer mentors; they will receive training on motivational interviewing. To ensure mentors have gained needed skills, each mentor will be assessed during role plays. The fidelity of training sessions will be tracked with the use of checklists.

Peer mentors will receive human subjects training using Harvard Catalyst's Community Partner Human Subjects Training, as suggested by UM IRBMED. We have been granted permission to modify the training in the following ways:

1) All materials will be delivered through Canvas, the online learning tool used for coursework at the University of Michigan
2) Prior to the first live seminar training, all peer mentors will be enrolled in a "class" using their personal email addresses
3) The educational slide deck will be divided into thematic sections and made into short videos with voice over
4) Each video will be accompanied by the quiz. This quiz will contain the part of Harvard Catalyst's suggested assessment that relates its respective training section. Some questions may be modified to make them more relevant to the Dialysafe project. The quiz may be re-taken in the case of wrong answers.
5) Study staff will monitor activity on the Canvas page to ensure that each mentor watches each video and completes every quiz. Those who complete every section of the video/quiz course will receive a certificate of completion.
6) The first live seminar will include a discussion section regarding the training, including examples tailored to study-specific scenarios, edited from the last portion of the catalyst training.

Harvard Catalyst will receive attribution credit on all materials.

6.2 DOSAGE, PREPARATION AND ADMINISTRATION OF STUDY INTERVENTION/INVESTIGATIONAL PRODUCT

6.2.1 Dosage, Preparation and Administration of Study Intervention/Investigational Product – Multimodal Provider Education Intervention

The University of Michigan study coordinator(s) will present online training for each hemodialysis clinic randomized to receive the multimodal provider intervention . This will be two separate 60-minute online training sessions with all available patient care staff. Any dialysis staff members who are unavailable for training will be provided with the slides to review. All dialysis staff members will complete a computerized introductory training before the online sessions and a computerized quiz to assess learning after the online sessions are complete; these will be delivered via the FMCNA or University of Michigan Learning Management System (for facilities affiliated with UM). Staff participation is expected to be 75% for the first and fourth parts of training, and 75% attendance at the online training in parts 2 and 3. Up to 25% of staff may complete independent review of the slides for the third and fourth parts of the training. Therefore, 100% of facility staff will ultimately complete parts 2 and 3 of the training. Staff are also expected to pass the multiple choice quiz with 80% or greater. Use of the tablet-based checklist is intended to be used during the initial assessment for every dialysis session during the 24-week intervention period.

6.2.2 Dosage, Preparation and Administration of Study Intervention/Investigational Product – Patient Activation Intervention

Hemodialysis patients enrolled in the patient activation intervention will complete five computerized learning modules followed by a video conference call with their peer mentor to discuss content and goal setting. All learning modules and video conference calls will take place on a tablet computer in the patient's home or skilled nursing facility. The schedule for learning modules and peer mentor sessions will be created and maintained by the National Kidney Foundation.

6.3 MODIFICATION OF STUDY INTERVENTION/INVESTIGATIONAL PRODUCT FOR A SUBJECT

N/A

6.4 ACCOUNTABILITY PROCEDURES FOR THE STUDY INTERVENTION/INVESTIGATIONAL PRODUCT(S)

Tablet computers for both multimodal provider intervention and the patient activation intervention will be configured by the study team. Tablet computers for the provider intervention will be shipped to each dialysis center; tablet computers for the patient activation will be shipped directly to the patient's home or skilled nursing facility by the study team. Facilities will be able to keep the tablet computers and charging stations at the end of the study period.

In the event that a patient is interested in joining the peer mentoring program but does not have regular access to a phone to contact UMSI study staff and/or NKF, a pre-paid cell phone will be provided for the patient to use. The phone will be shipped to the patient's home address with a limited number of minutes pre-loaded for their use. At the end of the study, the phone may be discarded, or the patient may choose to purchase more minutes and retain the phone as a personal device. The pre-paid phone is not considered an incentive because it will not be preloaded with enough minutes to be used for personal use. The estimated value of the phone without minutes is $25. Neither study nor clinic staff will have the ability to track the phone's use after it has been activated by the patient.

In the event that a patient has joined the peer mentoring program but is unable to connect their tablet to a secure and reliable internet connection, we will send a mobile hotspot. The mobile hotspot will be returned at the completion of the peer mentoring program along with the tablet.

6.5 ASSESSMENT OF SUBJECT COMPLIANCE WITH STUDY INTERVENTION/INVESTIGATIONAL PRODUCT

Intervention fidelity tracking methods will include data automatically collected as part of digital interventions, as well as checklists manually completed by UM and National Kidney Foundation Study Coordinators and peer mentors. These data collection methods include:

- *Checklist completion*, which includes date/time-stamped records of each checklist completion session, logins to identify the facility at which it was completed, and records of buttons clicked and screens displayed.
- *Patient Intervention completion,* which includes records of completed peer mentoring sessions by patient login, with date, time, session length, and the number of people present at the session. Additionally, it will record patient views of specific content on the tablet-based peer mentoring education, as well as length of time spent viewing each part of the content.
- *Peer Mentoring Fidelity*. Peer mentors will use a checklist to record their coverage of all required content as part of each mentoring session. The checklist will include items such as whether the patient understands the benefits of getting enough dialysis, and whether the peer mentor has encouraged the patient towards reaching a behavioral goal.
- *Staff Training Fidelity*. UM Study Coordinators will use a checklist to record their coverage of all required content as part of each online, staff-delivered training session, and record attendance by role at the sessions. FMCNA's learning management system (LMS) will also produce reports for each facility regarding the number of staff in each role who have completed two LMS training sessions. Similarly, FMCNA staff will provide this information to UM Study Coordinators for the online sessions via UM Study Coordinators' FMCNA email accounts.
- *Patient Technology Training Fidelity*. Patient who join the peer mentoring program will be offered a "tech training call" to ensure that they are comfortable with the study-provided tablet. UM study staff will use a checklist (see "Dialysafe_pt_tablet_training_plan") to record items discussed during the training call, including: how to navigate the tablet and website, any major issues or questions, the start and stop time of the call, the date of the call, and the name of the UMSI staff member providing training. No identifying patient information will be recorded.
- *Patient Technology Training Recruitment Records*. UM study staff will track the number of patients receiving peer mentoring who accept or decline a tech training call. Whether training was accepted or refused, the reason for refusal (as applicable), and whether

training was completed and/or rescheduled will be recorded. (See “tech calls” log.) No identifying patient information will be recorded.

- *Tracking Technical Support*. UM study staff will log questions received from calls to the study 1-800 number, and/or emails from clinic staff. The question, whether it was solved, and the type of participant making the inquiry (clinic staff/patient/peer mentor) will be recorded along with the time, date and name of the UMSI study staff addressing the question. (See “tech calls” log.) No identifying patient information will be recorded.

We will use the captured fidelity data to create and track the following metrics:

- Staff Checklist
  - Checklist completion rate by facility over specific time points (number of completed checklists / number of patient sessions (for patients included in the study) calculated over a given time period (e.g., a month)
  - Proportion of checklist sessions in which patients are identified as being at risk of IDH
  - Prevalence of reasons why patients were identified as being at risk of IDH
- Staff Training
  - Proportion of staff by role who completed each training session, tracked by facility
  - Average proportion of training elements completed
  - Proportion of training sessions in which all training elements completed
- Patient Intervention
  - Average number of mentoring sessions completed per patient
  - Patient retention rates across all five peer mentoring sessions
  - Average peer mentoring session length
  - Education module completion rates by topic and section
  - Quiz completion rates
  - Average time spent on each educational module section
  - Average proportion of peer mentoring session components completed by session
  - Proportion of peer mentoring sessions in which all session components completed
  - Mentor-specific peer mentoring completion rates – for use by NKF in training and supporting mentors

6.6 CONCOMITANT MEDICATIONS/TREATMENTS

N/A

7 STUDY SCHEDULE

The active intervention will begin in sets of four clinics at a time, each randomized to one of four treatments. See Schedule of Events in Appendix A for staggered roll out dates. The study coordinator will contact each clinic manager by phone -7 to -4 months from data collection start. The Study Coordinator helpline will be available during the preparation and enrollment periods, one month prior to data collection, in order to assist with patient or clinic questions. The study coordinator will schedule digital meetings for each provider education clinic in intervention weeks 1-3 to conduct the first online training and in weeks 4-6 to conduct the second online

training. Study coordinator(s) will be available by phone for questions or concerns throughout the study. See the Schedule of Events for an overview of the study schedule.

The patient activation intervention should take 5-6 weeks on average to complete. We anticipate staggered participation of patients in the patient activation intervention due to limits on the number of tablet computers and the number of peer mentors.

7.1 SCREENING

To ensure national representation, a list of 60 candidate regions covering the Midwest, Northeast, Southeast and Southwest were generated. From these areas, all eligible facilities are returned from the FMCNA corporate data warehouse with a query applying the following eligibility criteria: (1) outpatient HD facilities, (2) at least 70 adult patients (≥>=21 years of age), (3) not involved in other Frenova research, (4) facilities with two to five stars in CMS's Dialysis Facility Compare; (5) not in immediate jeopardy in previous two years, (6) not a facility in which the entire facility has been designated for isolation of patients with suspected or confirmed COVID-19, and (7) not a Kaiser facility. A list of facilities within candidate regions meeting criteria 1-7 will be generated. Facility randomization procedures will then performed on this list.

Patients within clinics will be screened for vulnerable status. Patients will be screened in two ways per Table 3 below: 1) By the FMCNA Custom Reporting and Data Analytics group team for electronically available criteria, and 2) by the local clinic team (Clinical Manager, Medical Director, Social Worker) for criteria not electronically available.

Table 3 – Screening for Patient Vulnerable Status

Criteria	Determined Electronically	Determined by Local Clinic Team
Exclusion Criteria		
Age <21 years old	√	
Transient Patients	√	
Acute Renal Failure	√	
Prisoner		√
Cognitive Barrier (poor cognition or cognitive impairment)		
Patients who were excluded from the most recent KDQOL on basis of poor cognition (determined by social worker)	√	
Per the judgement of the Clinical Manager, Medical Director, and Social Worker, with consultation with the Medical Attending as needed, regarding: Cognitive impairment. As needed, the Social Worker may utilize existing policy for Cognitive Functioning Assessment that utilizes the Montreal Cognitive Assessment-Basic tool.		√
Patient is unable to comprehend the patient information sheet due to lack of facility in English or Spanish (patients whose primary spoken language is not English or Spanish)		√

Those deemed vulnerable per above will not be included in the study. All other patients will be given the opportunity to opt out of the study if desired.

7.2 ENROLLMENT/BASELINE

Details for the opt-out process can be found in the attached *Opt out process* document. The initial patient opt out process is planned to last up to 4 weeks, with patients being given 1 week to opt out after receiving the Patient Information Sheet (PIS). All clinics will have the 12-week baseline data collected retrospectively. The estimated timeline for the staggered rollout of the study for the 20 clinics will begin with the first clinic opt out process in January 2023, and the last clinic post intervention data collection period ending in October 2024. We do not anticipate monitoring for changes in facility or participant eligibility during the course of the study.

The Patient Information Sheet (PIS) will be distributed to all patients during a hemodialysis session by an FMCNA study facility staff member. The Staff member will use wording similar to this script when giving the information sheet to the patients.

> "This sheet tells you about a study from the University of Michigan that Fresenius Medical Care and our Medical Director have approved for our clinic. The goal of the study is to help patients feel better by taking steps to prevent low blood pressures during dialysis. All patients in the clinic will be in the study. However, after you review the details on this sheet you can choose to opt out of the use of your data by letting me know or by calling the toll-free number on the last page. You can also get more information about the study by calling the toll-free number."

The Dialysafe PIS will inform the patient about the Dialysafe Study data collection, provider intervention, follow-up period, and that the patient may be called about optional peer mentoring if the clinic is randomized to receive peer mentoring. The PIS will indicate that opting out means that the patient's data will not be shared, the Chairside questions will not be asked of him/her, and the patient will not be called to be offered peer mentoring. However, all patients in the 10 clinics randomized to the Provider Intervention will still receive the Provider Intervention because it is a facility-level intervention that will be applied to all ESRD patients. Refer to Table 4 for how opting out applies to the four types of study groups. If a patient opts out after data collection has started, the patient will be removed from data transfers from the date of opt out forward; 5 working days are allowed to process the opt out and discontinue the Chairside study questions.

Table 4 - Effect of Opting Out of Dialysafe According to Study Group

Study Group	# of Clinics	Effect of Opting Out[1]
Control Group	5	● No data collection about that patient ● No Chairside study questions asked of that patient
Provider Intervention Only (staff education and IDH checklist)	5	● No data collection about that patient ● No Chairside study questions asked of that patient ● Provider Intervention still applies, regardless of opt out
Peer Mentoring Only	5	● No data collection about that patient ● No Chairside study questions asked of that patient ● Patient will not be called and offered Peer Mentoring

Peer Mentoring + Provider Education (staff education and IDH checklist)	5	● No data collection about that patient ● No Chairside study questions asked of that patient ● Patient will not be called and offered Peer Mentoring ● Provider Intervention still applies, regardless of opt out

[1]If a patient opts out after data collection has started, the patient will be removed from data transfers from the date of opt out forward; 5 working days are allowed to process the opt out and discontinue the Chairside study questions.

After the initial opt out process, new patients (new to dialysis and new to the clinic) who enter the clinic will be offered opt out whose date of entering the clinic is >=8 weeks prior to the end of the intervention period. However, to minimize staff time used to distribute the PIS, the PIS distribution will occur every 2 months to capture new patients who have been in the clinic for >=30 days.

Patient participation in the study will be recorded in the form of an "ancillary order" in the patient's electronic health record at FMCNA (called "eCC"). The Dialysafe Ancillary Order in eCC will be entered on all Dialysafe study patients who are eligible and do not opt out. The data entered in this Order will be retrieved by the FMCNA Custom Reporting and Data Analytics group team to identify study patient start and stop dates for the purpose of study data extraction. The Order will trigger two new Chairside questions programmed for the study to appear weekly as specified in the Order between the start and stop dates. The date on which the patient was given the patient information sheet will also be recorded in the Ancillary Order.

For recruitment into the Dialysafe Peer Mentoring Program, FMCNA staff will provide a card to patients in their clinic advising if they have been randomly selected to be offered peer mentoring, and letting them know to expect a call from UM staff to offer them peer mentoring. The card encourages them to pick up the phone when UM staff call (see "Peer Mentor Reminder Cards"). In the event that clinic staff identifies a patient as interested in learning about the peer mentoring program, but without regular access to a personal phone, UMSI study staff will mail a pre-paid phone to that patient. The phone may be used to reach UMSI study staff and NKF for the purpose of joining the peer mentoring program. UM staff will call patients up to 10 times to offer them peer mentoring, after which the patient will be listed as "could not be reached." Each patient who cannot be reached or refuses will be replaced by the next randomly-selected patient (see "Recruitment and Retention Procedure Final"). Patient advocates within the clinics may discuss the peer mentoring program with patients who are willing to talk with them while waiting for treatment in the lobby or during a clinic-wide "lobby day" (if applicable).

University of Michigan Study Coordinator will use words similar to this script when calling patients to offer them peer mentoring.

"I'm calling to talk about a research study being done at your dialysis clinic. You should have received an information sheet about this study at your clinic. The study is being done by the University of Michigan, working with Fresenius Medical Care and the National Kidney Foundation. The goal of this study is to reduce the risk of low blood pressures during your treatments. As part of the study, we are now calling patients to offer a peer mentor program. I'd like to tell you more about this program- is that okay?" ... (If yes, continue…If no, thank the patient and end the call).

The goal of the peer mentoring program is to help patients feel better by coaching them on ways

to prevent low pressure during treatment. A peer mentor is someone who has been on dialysis and is trained and supervised by the National Kidney Foundation. If you choose to be in the program, you will be scheduled for five sessions with a peer mentor. The sessions will take place over 5-12 weeks. These will be done by using a computer tablet, which is like an iPad, that will be shipped to your house. You will be taught how to use the tablet so that you can watch a learning module before each peer mentor session. A learning module is like a set of slides with information viewed on the tablet's screen, and includes videos that shows you information while a voice reads the screen. The content of the modules is designed to provide you with ways to help you prevent and manage low blood pressures during your treatments. Each module will last about 1 hour and after each module, you will be asked to set a goal for your health. After the second time you meet with your peer mentor, we will send you a blanket from the University of Michigan. Additionally, you will receive an increasing stipend for every module that you complete. You will receive $10 for completing the first module, $15 for completing the second, $20 for completing the third, $25 for completing the forth, and $50 for completing the fifth module and Peer Mentee Satisfaction Survey. These incentives total $120 for the completion of the entire program. It is possible that some of the topics discussed with your peer mentor or in the goal setting part of the educational modules could make you feel uncomfortable. It is your choice whether to answer any question or discuss any topic. You can skip questions or discussion topics if you wish. You will be connected with your peer mentor for a live video-chat to go over what you watched and how you are doing with your goals based on what days and times work for you and your matched Peer Mentor. The topics you will discuss will include getting enough dialysis, using less salt, fluid limits, feeling better during treatments, and getting more involved in your care. All of your learning modules and talking to your peer mentor will take place in the comfort of your own home. The program and use of the tablet will be provided for you at no cost. At the end of the program, we do ask that you ship the provided tablet back to the University of Michigan. We will provide the required shipping materials and postage by mail so that participating in this program involves no cost to you. You need to know that if you join the peer mentor program, information about you and your peer mentor sessions will be entered into a database by the University of Michigan study staff and will be shared with your peer mentor and the National Kidney Foundation. This information will include your first and last name, gender, clinic name and ID, treatment day and shift, phone numbers, the dates when you start and stop the program, and how many sessions you completed. It may also include other information you share with your peer mentor such as the goals and personal values you identify as part of the program. The peer mentor sessions will not be recorded. After the program is over, the data will be sent to the University of Michigan Kidney Epidemiology & Cost Center to be analyzed, but only a code number will be used to identify your data. Your name and identity will be kept confidential. At the end of the peer mentoring program, you will also be asked to complete a survey that will ask your experiences and opinions about the peer mentoring program. As previously mentioned, by completing this survey, you will receive the full stipend amount of $120 for finishing the entire program.

Joining the peer mentor program is voluntary and you can withdraw at any time. If you withdraw, your data will be used for the study only up to the time you withdraw. Do you have any questions I can answer? Would you like to sign up for the peer mentor program?"

Once a patient asks to be signed up for peer mentoring, their name and contact information will be shared with National Kidney Foundation who will match them with a mentor. They will also be offered the option of setting up a phone or web conference call with a UM study coordinator to learn how to use the Android tablet.

7.3 FOLLOW-UP

If patients miss two peer mentoring sessions in a row and have not responded to other program communications, UM staff will contact their clinic in an attempt to reach them to determine if they want to continue in the program (see "Recruitment and Retention Procedure Final").

Study outcomes will be monitored in all facilities for 12 weeks after the 24-week intervention period. The same routinely-collected data from FMCNA will be collected during this period. This is a pragmatic clinical trial and therefore no special follow-up will occur as a result of the study.

7.4 FINAL STUDY VISIT

N/A

7.5 EARLY TERMINATION VISIT

N/A

7.6 UNSCHEDULED VISIT

N/A

8 STUDY PROCEDURES/EVALUATIONS

8.1 CLINICAL EVALUATIONS

Routine dialysis care will continue throughout the study but may be influenced by the provider intervention training and IDH checklist, and by the peer mentoring if patients begin to engage more in fluid management. Please refer to previous section on interventions regarding the provider training, IDH Checklist and peer mentoring. Data from FMCNA are routinely gathered as part of this routine care. The only change to the usual clinical evaluation is that two aforementioned extra questions will appear in the Chairside documentation system once per week during the study period: (1) the question about patients' post-dialysis recovery time; and (2) the question in which the FMCNA staff member records whether the patient made a request that day about their fluid removal goal.

8.2 LABORATORY EVALUATIONS

8.2.1 Clinical Laboratory Evaluations

Routine dialysis care will continue throughout the study. No changes to usual laboratory evaluations are expected.

8.2.2 Special Assays or Procedures

N/A

8.2.3 Specimen Preparation, Handling, and Shipping

8.2.3.1 Instructions for Specimen Preparation, Handling, and Storage

N/A

8.2.3.2 Specimen Shipment

N/A

9. ASSESSMENT OF SAFETY

9.1 SPECIFICATION OF SAFETY PARAMETERS

Intradialytic hypotension is the primary study outcome.

9.2 METHODS AND TIMING FOR ASSESSING, RECORDING, AND ANALYZING SAFETY PARAMETERS

9.2.1 Adverse Events

This study has low risk to patients. The study uses current, accepted ways to reduce low blood pressure during dialysis.

9.2.2 Expected Adverse Reactions

There are no expected adverse reactions to the interventions.

9.2.3 Serious Adverse Events

This study has low risk to patients. The study uses current, accepted ways to reduce low blood pressure during dialysis.

9.2.4 Unanticipated Problems

This study has low risk to patients. The study uses current, accepted ways to reduce low blood pressure during dialysis.

9.2.5 Procedures to be Followed in the Event of Abnormal Laboratory Test Values or Abnormal Clinical Findings

This study has low risk to patients. The study uses current, accepted ways to reduce low blood pressure during dialysis.

9.3 REPORTING PROCEDURES

Adverse events (AEs) other than potential breach of confidentiality will not be systematically collected since this is an educational intervention that provides content on current, accepted

ways to reduce low blood pressure during dialysis. Thus the risk profile for such approaches is well known, and the risk to patients is very low.

Non-confidentiality-related AEs will also not be systematically tracked since the hemodialysis patient is very ill at baseline. Most patients have multiple chronic diseases, including cardiovascular disease. Approximately 15-20% of hemodialysis patients die per year and the patient population has an average of two hospitalizations per patient year. The primary outcome, intradialytic hypotension (IDH), occurs in 20% of hemodialysis sessions in the United States. More than 50% of patients experience symptoms during or shortly after hemodialysis. These data (mortality, hospitalizations, IDH, and symptoms) are tracked as outcomes in our study; these events occur routinely in the hemodialysis population and thus these events would be expected without our study, thus making “relatedness” of these events to the study exceedingly difficult to determine. These outcomes will be collected between two months and two years from the occurrence based on the data source available.

- ***The only expected risk for this study is of breach of confidentiality. The likelihood of this risk is very low and unexpected because of the confidentiality measures outlined in section 14.5 ll. However, in the unlikely event that there were an adverse event related to breach of confidentiality, this would be reported to the IRB using the following generalized rating scale:***0 - No adverse event

- 1 - Mild AE – No treatment needed

- 2 - Moderate AE – Resolved with treatment

- 3 - Severe AE – Inability to carry on normal activities, required professional medical attention

- 4 - Life-threatening or disabling AE

- 5 - Fatal AE

While breach of confidentiality is extremely unlikely and if it were occur it would be unlikely to be severe, if needed, we would nonetheless report any serious AEs according to the following typology:

- Death

- A life-threatening adverse drug experience

- Inpatient hospitalization or prolongation of existing hospitalization

- A persistent or significant disability/incapacity

- A congenital anomaly/birth defect

- Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered a serious adverse drug experience when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such medical events include allergic bronchospasm requiring

intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse.

Potential confidentiality breaches will be tracked as follows by UMSI and UM-KECC:

- A log of data transfers, which will record the transfer's date, time, sender, receiver, data contents, transmission vehicle, a yes/no checkbox identifying whether or not there was a potential confidentiality breach in that transfer, and a free-text box in which to describe the issue. Another free-text box will capture any remedies taken to address the issue (e.g., notifications, data deletion).

- A log of security events, in which any attempted or successful security breaches, their dates/times, involved parties, data accesses, and remedies taken will be recorded. This will include any the details of any hacking attempts or inadvertent disclosures not involving data transfers, which would be captured as per above.

Finally, the PI or a co-investigator will assess the relatedness of any breach of confidentiality to the study according to the following typology:

- Definitely related
- Probably related
- Possibly related
- Unlikely to be related
- Definitely not related.

We will also assess the expectedness of the event, although any breach of confidentiality would be inherently unexpected.

9.3.1 Serious Adverse Events

N/A

9.3.2 Regulatory Reporting for Studies Conducted Under IND

N/A

9.3.3 Regulatory Reporting for Studies Not Conducted Under IND

N/A

9.3.4 Other Adverse Events (if applicable)

N/A

9.3.5 Other Unanticipated Problems

N/A

9.3.6 Reporting of Pregnancy

N/A

9.4 Type and Duration of Follow-up of Subjects after Adverse Events

N/A

9.5 Halting Rules

N/A

9.6 Safety Oversight

An external data safety monitoring board (DSMB) consisting of 5 members (outside of the University of Michigan) has been identified. The DSMB includes a biostatistician unrelated to the trial, a patient, a nephrologist, and a layperson unrelated to the field (e.g., bioethicist).

The DSMB met in 2021 for orientation to the protocol, and to advise on desired data for reporting. The DSMB will then meet annually during the trial implementation and analysis periods, or more frequently as requested by DSMB members.

The study team will produce interim analyses every year of the trial implementation period, or as requested by the DSMB. We currently anticipate reporting annually to the DSMB blinded data on IDH and mortality rates in each treatment arm. The study has no stopping rules.

10 Clinical Monitoring

10.1 Site Monitoring Plan

I. Study Governance

FMCNA and NKF will participate in the study in accordance with executed subcontracts. Prior to participation in the study, each facility's Governing Body will review study materials and approve participation.

II. Study Champion

The Medical Director and Clinical Manager at each site with an intervention (n=15; the 5 clinics doing data collection only will not have a Study Champion) will then identify a "Study Champion," who will ideally be a Clinic Manager or Staff Nurse. Each Study Champion will attend a train-the-trainer session with other Study Champions prior to intervention start at their sites. The Study Champion will speak with a University of Michigan Project Manager at least monthly during the trial in study facilities. The Study Champion's role will involve:

- Participating in quarterly Operations Committee meetings (to take place during the baseline and intervention periods)
- Serving as a liaison to provide staff feedback to the University of Michigan Project Coordinator(s).
    - Examples: Post a study comments notebook in the break room, accept verbal comments from staff, and convey comments during Operations Committee calls.
- Co-leading with Clinical Manager, discussion about checklist implementation at two staff meetings
- Updating the Research Binder with current patient lists and any other updated documents throughout the study
- Conveying positive messaging about the study

III. Operations Committee

An Operations Committees will be formed in each study facility with an intervention (no Operations Committee will be formed for clinics randomized to data collection only); this Committee will include staff members in authority positions such as the local Clinical Manager and Directors of Operations. The Clinical Manager is accountable for the operation of the facility, has authority over the staff in his or her assigned clinic, and has physical presence in the clinic on a regular basis. The Director of Operations is accountable for a group of clinics in the geographic area, and has authority over the Clinical Manager. The Operations Committee will meet three times over the course of the study, and include the Study Champion as per above, and others selected to represent different organizational levels and perspectives. Patient representatives (n=1-2) will also participate in the Operations Committee and will be selected based on the following criteria:

1) Not excluded from the study on the basis of vulnerable status or opting out
2) Access to email for receipt of meeting materials
3) Sufficient English ability to participate in meetings (English as primary language)
4) Sufficient hearing ability to participate in meetings by phone (per patient's judgement)
5) Nomination by Clinic Manager, or self-nomination.

The Operations Committee will oversee intervention implementation in each of the study facilities. At the meetings, the UM Study Coordinator will provide feedback to the facility regarding intervention fidelity (e.g., checklist completion rates, staff training completion rates, patient retention rates across all five peer mentoring sessions). Feedback will be sought from facility staff regarding the intervention, and its impact upon facility operations. The Committee will also engage in collective problem-solving as needed as led by the UM study coordinator, who will schedule, plan, organize and lead Operations Committee meetings.

IV. Role of Medical Director at Study Facilities

In addition, the Medical Director at each site will communicate initial study information to medical colleagues (attending nephrologists and other providers) in the facility, and then communicate as needed to these colleagues throughout the study. In order to increase the appeal of participation, UM has also incorporated a total of $500 divided into two payments ($250 each payment) for each of the Medical Directors of study facilities in the project budget for carrying out their responsibilities related to the study as described below. UM will be responsible for managing the payment process. Each payment will be triggered by completion of the Practice Patterns Survey associated with that payment (see attached Practice Patterns Survey - Medical Directors and Practice Patterns Survey - Nurse Managers).

Payment #1 of $250 shall be compensation for the following activities:

- Participate in the process of Governing Body approval for the study.
- Communication of initial study information to medical colleagues (attending nephrologists and other providers) in the clinic.
- Work with Clinical Manager to identify a Study Champion, if applicable.
- Work with Clinical Manager to identify patients deemed vulnerable that should be excluded from the study, per the study's exclusion criteria.
- Complete the pre-intervention phase Practice Patterns Survey, to be completed during the 12- week baseline data collection period before the intervention phases begins.

Payment #2 of $250 shall be compensation for the following activities:

- General support of the study and communication as needed to medical colleagues (attending nephrologists and other providers) in the clinic.
- Completion of the post-intervention phase Practice Patterns Survey, to be completed during the 12-week follow-up period following the intervention phase.

V. UM staff monitoring of opt out process

The University of Michigan is responsible for the opt out processes for patients. Under the direction of a UM study coordinator available online via initial enrollment, each patient will be given an information sheet by FMCNA staff. FMCNA staff will distribute the information sheet to patients, and record the date that a patient received the information sheet and the date of any opt outs (as applicable) on an Opt Out Worksheet, adding any new patients missing on the worksheet as needed. The UM study coordinator will be granted an FMCNA secure email address for communications concerning the opt out process and other study matters.

VI. Assessment of Intervention Implementation (Aim 3)

Feasibility Evaluation. The study will involve an initial pilot feasibility assessment for current study procedures. This will involve assessment of metrics concerning:
(1) availability of a sufficient amount patient dialysis session data to measure the impact of the interventions on the primary outcome (data for 3,600 dialysis sessions for each of the 8 pilot clinics during the pilot intervention period);
(2) sufficient patient participation in the peer mentoring program (up to 30 patients start peer mentoring in each of the trial period clinics with peer mentoring, and up to 22 patients finish peer mentoring in each of the pilot clinics with peer mentoring); and

(3) sufficient staff participation in the online training sessions (at least 75% of the staff complete at least 90 minutes of training during the first 14-16 weeks of the intervention period in the pilot clinics with the provider intervention).

To assess intervention implementation (Aim 3), monitoring activities will also seek to identify variation in implementation approaches adopted within different study facilities, and to characterize differences in intervention acceptance and workflow integration. These analyses will help with understanding any potential differences in intervention effects between sites, and with identifying and responding to any emergent implementation challenges throughout the trial.

Meeting-based data collection will support study monitoring, and related Aim 3 analyses. Meeting data will be unobtrusively collected in all facilities in which there is an intervention. Specifically, these data collection activities will leverage already-planned project activities; no additional meetings will be planned specifically for this form of data collection. UM researchers will attend the following events which are already planned as part of the trial; no audio or video-recordings will be made of any meetings or sessions:

- Online Staff Training Sessions
    - Staff Training regarding IDH prevention Parts 2 and 3 (14 facilities)
    - Staff Training regarding peer mentoring intervention and tablet management (14 facilities)
- Operations Committee (OC) meetings (15 facilities; the 5 clinics doing data collection only, will not have an Operations Committee)

Online Training Sessions. At the Online Training Sessions, UM researchers will take descriptive field notes.[161] Attendees will be informed that notes will be taken, the purpose of the notes, and that comments made during meetings may be tied to a staff member's role but staff names will not be recorded. The attendees will be informed that they can decline to have their comments recorded. The field notes will document:

- staff questions during the sessions;
- staff members' stated reactions to the interventions; and
- discussions in which the staff talk about their plans for, and experience with, integrating the provider intervention into their workflows.

OC meetings. At the OC meetings for each site, the meeting agendas will include a small number of questions directly related to study intervention implementation as provided in this document which UM investigators and/or staff will pose, then recording the answers in descriptive field notes. These questions are directed to FMCNA staff and will be asked after any patient representatives have left the meeting. The questions are as follows:

- At Pre-intervention OC meeting:
    - Staff Intervention Facilities
        - We are planning to train you to use a checklist to identify patients at risk of intradialytic hypotension. The checklist will rely on information from the fluid management tab. Is there anything that we should consider about how you use the fluid management tab now that we should take into account in planning your training?
- At the two OC meetings during intervention period:
    - Staff Intervention Facilities:
        - Your facility has been given a checklist to use to identify patients at

increased risk of IDH. Please tell us about how you are using the checklist.
    - *Follow-up questions as needed:*
        - Who is completing the checklist?
        - When are they completing the checklist?
        - What do they do before completing the checklist?
        - What do they do after completing the checklist?
- What is working well about using the checklist?
- Are there things that are not working well with using the checklist? If so, what are they?

- Patient Intervention Facilities:
    - Some patients at your facility have been given tablet computers for patients to use at home to obtain peer mentoring and education about IDH prevention.
        - *Follow-up questions as needed:*
            - Have patients brought their tablet computers into the clinic? If so, please tell us what happened.
            - Have patients talked to any of you about anything regarding tablet use?
            - Have you noticed any changes in topics that patients are bringing up in their appointments with you?
            - Has anyone started to record things at home and bring in data and do you have reason to believe it's because of the intervention?
            - Have you noticed patients talking to each other about the intervention?

VII. Surveys

A Practice Patterns survey will be completed by the Medical Director and Clinical Manager prior to, and after the intervention period. The survey will document fluid management practices used in each facility, including the no-intervention (usual care) sites.

A patient satisfaction survey will be given by the NKF to patients after they complete the patient activation intervention. Results will be monitored in order to identify patient experiences with the multimedia educational modules and peer mentoring intervention. Aggregate results will be shared with NKF so that any necessary program adjustments can be made.

A peer mentor satisfaction survey will be given by the NKF to peer mentors to assess their experiences with the study's digital tools, training, and support. Aggregate results will be shared with NKF so that any necessary program adjustments can be made.

VIII. Monitoring by Study Team

The study team will conduct scheduled assessments of study recruitment, data integrity and quality, withdrawals, and compliance with protocol plan on a monthly basis. This information will be reported at the monthly project Steering Committee meetings.

11 STATISTICAL CONSIDERATIONS

11.1 STUDY HYPOTHESES

We will compare two interventions to improve the cardiovascular/hemodynamic stability of hemodialysis care by pursuing the following specific aims:

- **Aim 1** Conduct a cluster-randomized controlled trial (CRCT) to test and compare the effects of the above HD facility-level interventions on the primary outcome of dialysis session stability over an intervention period of 24 weeks and a post-intervention follow-up period of 12 weeks.
- **Aim 2** Test and compare the effects of the two HD facility-level interventions on secondary patient-centered clinical outcomes, including: patient symptoms, fluid adherence, dialysis adherence, quality of life, hospitalizations and mortality over the same timeframe.
- **Aim 3** Identify factors associated with successful implementation of the interventions, and ways in which implementation may influence intervention effectiveness.

Our main study hypothesis is that hemodialysis session stability will significantly improve with either multimodal provider education or patient activation interventions, and that multimodal provider education will show a larger improvement. This hypothesis is based on our expectation that some hemodialysis patients might refuse or be unable to participate in peer mentoring, potentially leading to greater penetration of the provider intervention. We will test this main hypothesis and explore this potential explanation of any differential improvement as part of our planned sensitivity, mediation and moderation analyses.

11.2 SAMPLE SIZE CONSIDERATIONS

I. Primary Outcome

For Aim 1, the outcome is a dichotomous measure of HD stability, where an unstable session is defined as the dialysis session stability, where an unstable session is defined as SBP falling below 100 when the starting SBP was >=100. This outcome will be collected through digital records for all HD sessions of all patients at each facility during the study period. The analysis will be done in two ways. First, as a continuous variable, as described in the power analysis. Using individuals with a minimum of 60 dialysis sessions, the proportion of unstable sessions will be computed. Linear mixed models will be employed to compare individuals in facilities in the two treatment arms to individuals in the non-intervention facilities. Random effects for facility clustering will be accounted for using the MIXED procedure in SAS. As a sensitivity analysis, dialysis session stability will also be examined as a yes/no variable and analysis will be carried out on the longitudinal dataset using logistic regression with a random effect for both patients and facilities, using the GLIMMIX procedure in SAS. The random effects will model the correlations among the measurements at each level. This analysis will use data from all patients, not just those with at least 60 dialysis sessions.

Dialysis facilities will be randomized in a 2x2 factorial design to two study intervention or control groups. Sample size is based on separate tests for each of the two treatment comparisons, and assumes no interaction between treatment types. The primary outcome measure is session instability, particularly IDH, which occurs in approximately 20% of hemodialysis sessions in the usual practice setting in the US. The study is powered to detect a decrease from 20% to 15-

16% in the intervention group. It is assumed that a minimum of 60 hemodialysis patients will be observed for at least 60 dialysis sessions and the outcome will be the proportion of unstable sessions, which we treat as a continuous variable. These proportions among patients in a facility are assumed to be normally distributed with mean 0.20 in the control group and mean between 0.16 and 0.17 in the intervention group (a difference, d, of 0.034 to 0.043), with standard deviation (SD, or 'sigma') assumed to be in the range 0.08 to 0.10. We conservatively assume n=60 patients per facility, i.e., a total of 60x20=1,200 patients. The power calculation is robust to changes in number of patients (**m**), as the calculation of **K** (number of clusters) only increases by ~1 if m is increased to 90. The intraclass correlation coefficient for hemodialysis facilities is assumed to be 0.10. A significance level of 0.05 was assumed in all calculations. Table 5 gives the statistical power to detect a given difference (D, 0.034-0.043), with sigma values of 0.08 and 0.10, and number of clusters (dialysis units, k) per treatment group of 10 (20 facilities total).

Table 5 shows that detecting a difference of ~0.03 (i.e., 20% versus 17% of sessions unstable) with 80% power is only feasible with a SD (sigma) of 0.08 or less. If the standard deviation is as large as 0.10, we can detect a difference of 0.043 (i.e., 20% vs. 16%) with 81% power. Put another way, if the smallest variance estimate is correct (sigma=0.08), we have 91% power to detect a 4% difference, and 80% power to detect a 3% difference.

Table 5 - The power is shown to detect a difference in IDH rates (D) between groups assuming 3 possible standard deviations (sigma). The minimum number of facilities (k) is also shown, illustrating some flexibility to accommodate drop-out. Bolded cells show power >=80%.

D	**0.034**	0.034		**0.040**	**0.043**	
Sigma	**0.08**	0.10		**0.08**	**0.10**	
K	**10**	10		**10**	**10**	
Power	**80%**	61%		**91%**	**81%**	

II. Secondary Outcomes

Aim 2 incorporates six outcome measures: (1) patient symptoms (including a patient burden measure, dialysis recovery time, and proportion of sessions with each symptom), (2), fluid adherence (inter-dialytic weight gain), (3) dialysis adherence, (4) quality of life, (5) hospitalization (all-cause and by specific cause), and (6) mortality (all-cause and by specific cause), with will be analyzed at the individual level and summarized at the facility level. Each will use a model format appropriate to the outcome type, but will otherwise follow the model strategy, including the secondary analyses, described for Aim 2 above. The fluid adherence (Interdialytic weight gain), symptom and quality of life analyses, based on continuous outcome measures, will be carried out using mixed models (the MIXED procedure of SAS). Note that the quality of life analyses will be based on data from two time points, one before intervention (the latest KDQOL survey that is within 12 months prior to the start of the intervention) and one during or after intervention (the earliest KDQOL survey that is within 12 months after the start of the intervention), rather than session-specific data as analyzed for the other outcomes. Analyses of missed or shortened HD sessions will employ logistic regression for longitudinal data, as in Aim 1. Analyses of hospitalization and mortality will use logistic regression for individual level data. As part of these models, we will test IDH-related variables (e.g., recent

IDH, frequency of IDH in the past month) as potential predictors. In each case, the appropriate regression diagnostics will be used to assess model fit.

Although the study was not powered specifically for these outcomes, many of the secondary outcomes are continuous variables for which power can be calculated based on effect sizes (multiples of the standard deviation) for any specific outcome, given the sample size of 20 facilities required for Aim 1 analyses. In the power analyses below, we present calculations based on four outcomes, percentage point change in facility proportion of individuals within optimum weight gain ranges between dialysis sessions (interdialytic weight gain between 2-5% of body weight, a measure of fluid adherence), patient recovery time, patient symptoms, and health-related quality of life scores.

(a) Interdialytic Weight Gain (IDWG)

The IDWG outcome for each patient will be the percentage of sessions in the optimum weight gain range between dialysis sessions (IDWG between 2-5% of body weight, a measure of fluid adherence). We consider this patient-specific percentage over the 24-week intervention period as a continuous variable for the comparison of intervention versus control groups. As above, we assume 20 facilities, and anticipate an average of 60 study patients per facility. The patient-specific percentages will then be used in the analysis testing intervention effects. We will consider the average of the patient-level percentages to test intervention vs control groups.

We assess the power to detect various differences between the intervention and control groups in percentage of IDWG values in the optimum weight gain range. For example, a mean of 27% in the control group and 32% in the intervention group would be a difference of 5% more patients in the optimum range. We assume an intra-class correlation coefficient (ICC, which measures how strongly patients are similar within center and differ between facilities) of either 0.1 or 0.2 (lower ICC results in higher power). We assume a standard deviation (SD) among patients of between 0.08 and 0.16 (expressed as a proportion rather than a percent to avoid confusion with other percentages), and a 2-sided significance level of 0.05.

Table 6 - Entries are the statistical power for the given standard deviation (SD), intra-class correlation coefficient (ICC), and control vs. intervention difference. Power values ≥ 0.80 are boldface.

Control vs. Intervention Difference in % IDWG within optimum range	SD=0.10		SD=0.15	
	ICC=0.1	ICC=0.2	ICC=0.1	ICC=0.2
5% (e.g., 25% vs 30%)	**0.91**	0.68	0.59	0.36
6%	**0.98**	**0.83**	0.75	0.49
7%	**0.99**	**0.92**	**0.87**	0.62
8%	**0.99**	**0.97**	**0.94**	0.73

Table 6 above shows the statistical power for a range of SD, ICC, and Control vs. Intervention differences (D). Power is around 90% or higher to detect differences of 7% or higher for all cases except SD=0.10, ICC=0.1 or 0.2. In this worst case, we still have 73% power to detect a difference of 8% between intervention and control groups. A difference of 6% to 8% would be clinically meaningful, as any difference in this range would likely be associated with less risk of

IDH. Effect sizes calculated from Table 5 values range from 0.04 to 0.12, reflecting a range from low/moderate to high/moderate effects. In summary, the IDWG outcome measure is adequately powered to detect clinically meaningful effects, and is well powered for many of the scenarios in Table 5.

(b) Patient Symptoms – Recovery Time

At one dialysis session per week for the duration of the 24-week intervention, each study patient will report their recovery time from the previous dialysis session. We conservatively assume that measures are recorded for 20 sessions per person. We assume 20 facilities, and anticipate an average of 60 study patients per facility, including all shifts. The recovery-time question shown on page four has eight ordinal answer choices plus "unable/declined" (which will be excluded from analyses).

For the data analysis, we will consider the ordinal scale (1-8) as a continuous variable. We will separately test recovery time for each intervention (provider education or patient activation) versus the control group. Each patient's data over the 24-week intervention period will be averaged and used as their individual Mean Recovery Time (MRT). The patient-specific MRTs will then be used in the analyses of intervention effects. We will then consider the group-level MRTs (the average of the patient-level MRTs) for comparing the intervention and control groups.

In Table 7, we assess the power to detect various differences between the intervention mean and the control mean. For example, an MRT of 4 (“after a long nap”) in the control group and 3 (“after a short nap”) in the intervention group would be a difference of 1. We assume an intra-class correlation coefficient (ICC, which measures how strongly patients are similar within center and differ between facilities) of either 0.1 or 0.2 (lower ICC results in higher power). We assume a MRT standard deviation (SD) among patients of between 1.5 (if the full range is not expressed) and 2.0 (estimated by full range/4), and a 2-sided significance level of 0.05.

Table 7 - Entries are the statistical power for the given standard deviation (SD), intraclass correlation coefficient (ICC), and control vs. intervention difference. Power values ≥ 0.80 are boldface.

Control vs. Intervention Difference	SD=1.5		SD=2	
	ICC=0.1	ICC=0.2	ICC=0.1	ICC=0.2
0.7	**0.87**	0.62	0.64	0.40
0.8	**0.94**	0.73	0.75	0.49
0.9	**0.98**	**0.83**	**0.84**	0.59
1.0	**0.99**	**0.90**	**0.91**	0.68

Table 7 above shows the statistical power for a range of SD, ICC, and Control vs. Intervention differences (D). Power is around 80% or higher to detect differences of 0.9 or higher for all cases except SD=2, ICC=0.2. In this worst case, we still have 68% power to detect a difference of 1.0 between intervention and control groups. A difference of 0.8 to 1.0 would be clinically meaningful, and is much smaller than a SD by either assumption (effect size range from 0.40 to 0.67, all considered a moderate effect size). In summary, the recovery time outcome measure is well powered to detect meaningful effects.

(c) Patient Symptoms – Symptom Burden Measure

The Patient Symptom Burden measure will combine symptom frequency and severity for each of the following symptoms that are often indicative of IDH, if they occur during or after the dialysis session (not pre-dialysis): nausea, vomiting, abdominal pain, dizziness, muscle cramps, headache, chest pain, shortness of breath, palpitations, diaphoresis, and blurred vision (as listed in the Chair-side symptom module). Although not yet fully developed, we assume that the range of the scale will be 0-100. As above, we assume 20 facilities, and anticipate an average of 60 study patients per facility.

Each patient's data over the 24-week intervention period will be averaged and used as their individual Symptom Burden (SB) mean. We will use the group-level means (the average of the patient-level means) for comparing the intervention and control groups.

In Table 7, we assess the power to detect various differences between the intervention mean and the control mean. For example, a SB of 15 in the control group and 10 in the intervention group would be a difference of 5. We assume an intra-class correlation coefficient (ICC, which measures how strongly patients are similar within center and differ between facilities) of either 0.1 or 0.2 (lower ICC results in higher power). We assume a SB standard deviation (SD) among patients of 10, and a 2-sided significance level of 0.05.

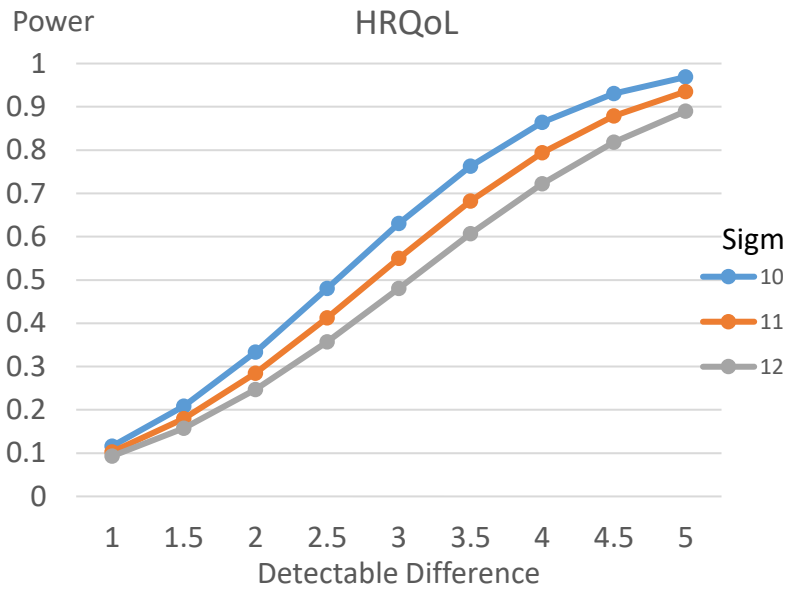
Table 8 - Entries are the statistical power for a standard deviation (SD) of 10, intraclass correlation coefficient (ICC) of 0.1 and 0.2, and control vs. intervention difference of 4, 5, and 6 (on a 0-100 scale). Power values ≥ 0.80 are in boldface.

Control vs. Intervention Difference	ICC=0.1	ICC=0.2
4	0.75	0.49
5 (Effect Size=0.5)	**0.91**	0.68
6	**0.98**	**0.83**

Table 8 above shows the statistical power for a range of ICC, and Control vs. Intervention differences. Power is around 90% or higher to detect differences of 5 or higher for ICC=0.1, and over 80% to detect differences of 6 or higher for ICC=0.2. A difference of 5 would be an effect size of 0.5 (half of the SD), which is considered moderate, and clinically meaningful. In summary, while we do not have data to provide more precise power estimates, the patient symptom burden outcome measure appears to be well powered to detect meaningful effects.

(d) Health-Related Quality of Life (HRQoL). The Kidney Disease Quality of Life instrument (KDQOL) is defined to have a mean of 50 and a standard deviation of 10. A 5-unit change is considered to be clinically meaningful.[162] Based on data to which our team has access from the Dialysis Outcomes and Practice Patterns Study (DOPPS), we determined appropriate facility-level intra-class correlation coefficient (ICC) for HRQoL scores to be 0.07. As shown in Figure 1, we explored power for detectable differences between 1-5 points and a range of sigma between 10 and 12. We determined that with our planned 20 facilities containing 60 patients each, that we are adequately powered (>0.80) to detect differences as small as 4.5 points for all three assumed sigma values. This provides excellent power for detecting a difference between study arms in HRQoL.

Figure 1 - Detectable differences in Health-Related Quality of Life (HRQoL)



11.3 PLANNED INTERIM ANALYSES (IF APPLICABLE)

The study team will produce interim analyses of selected study outcomes (IDH, mortality) every year of the trial implementation period, or as requested by the DSMB. We currently anticipate reporting annually to the DSMB blinded data on IDH and mortality rates in each treatment arm. The study has no stopping rules.

11.3.1 Safety Review

The DSMB will meet early in the trial to advise on desired data for reporting. We will then meet annually in the trial implementation and analysis periods of the study, or more frequently as requested by DSMB members. We currently anticipate reporting annually to the DSMB blinded data on mortality rates in each treatment arm. The study has no stopping rules.

11.3.2 Efficacy Review

The DSMB will meet early in the trial to advise on desired data for reporting. We will then meet annually in the trial implementation and analysis periods of the study, or more frequently as requested by DSMB members. We currently anticipate reporting annually to the DSMB blinded data on IDH rates in each treatment arm. The study has no stopping rules.

11.4 FINAL ANALYSIS PLAN

Aim 1. Test and conduct a cluster-randomized controlled trial (CRCT) to compare the effects of the above HD facility-level interventions on the primary outcome of dialysis

session stability over an intervention period of 24 weeks and a post-intervention follow-up period of 12 weeks.

Preliminary data analysis. We will compare the four randomized groups to assess covariate balance on participant characteristics, such as demographics. This analysis will test for potential selection bias that might lead to confounding of study results. If study arms are found to be imbalanced on baseline characteristics, in addition to those specified in the analyses below, these characteristics will be included in the regression models as a sensitivity analysis.

Analysis of Primary Outcome. For Aim 1, the outcome is a dichotomous measure of HD stability, where an unstable session is defined as the dialysis session stability, where an unstable session is defined as SBP falling below 100 when the starting SBP was >=100. This outcome will be collected through digital records for all HD sessions of all patients at each facility during the study period. The analysis will be done in two ways. First, as a continuous variable, as described in the power analysis. Using individuals with a minimum of 60 dialysis sessions, the proportion of unstable sessions will be computed. Linear mixed models will be employed to compare individuals in facilities in the two treatment arms to individuals in the non-intervention facilities. Random effects for facility clustering will be accounted for using the MIXED procedure in SAS. As a sensitivity analysis, dialysis session stability will also be examined as a yes/no variable and analysis will be carried out on the longitudinal dataset using logistic regression with a random effect for both patients and facilities, using the GLIMMIX procedure in SAS. The random effects will model the correlations among the measurements at each level. This analysis will use data from all patients, not just those with at least 60 dialysis sessions.

For the above analyses, the variables of primary interest are the main effects of the interventions. *Session-level* covariate adjustment will include: (1) weekday of session, (2) dialysis session shift, (3) average session blood flow rate; (4) average session dialysate flow rate, and (5) dialysate composition (sodium, potassium, magnesium). *Patient-level* covariate adjustment will comprise: (1) patient demographics (age, race, ethnicity, sex, employment, literacy, education level, language spoken); (2) time since first dialysis; (3) cause of ESRD, (4) treatment history; (5) total transplants; (6) vascular access type; (7) patient laboratory data (serum phosphorous, dialysis adequacy, anemia management (hemoglobin), iron indices (serum ferritin, serum iron), mineral metabolism indices (calcium, phosphate, PTH)); (8) comorbidity index; (9) individual comorbidities and comorbidities in combination, including COVID-19; (10) patient's heart rate variability (based on variability in heart rate (HR) during dialysis session (difference between the highest and lowest heart rates, standard deviation of the heart rate measures, the square root of the mean squared differences of successive heart rate measures); (11) patient medications (prescriptions medications administered outside of center or in-center (including ESA prescription, iron, antibiotics and vitamin D analog), and non-in-center prescriptions). Patient data will be censored while they are at COVID-19 isolation facilities. Regression diagnostics will be used to assess model fit. Checks for functional form of continuous adjustment covariates will be carried out and any transformations will be implemented prior to adding the intervention variables to the model.

Three secondary analyses are planned for this Aim. The first will test the treatment effects in a similar model but adding adjustment for any covariates found to be unbalanced between treatment groups in preliminary analyses. This has the ability to further adjust for important confounders of treatment effects, but because it will use data-driven covariate decisions that are subject to analysis bias, it will be interpreted with caution. The next secondary analysis will test the interaction between the two interventions to detect a possible synergistic or antagonistic

effect. (Further discussed in the heterogeneity of effects section). Although the study is not powered to detect even moderate interaction effects, it is possible that a strong interaction could be detected, and such an effect would be of interest.

The primary results will be based on the treatment effects tested in the initial models described for cluster-randomized trials with pre-planned covariates. Intent-to-treat analyses will be carried out, so that any deviations from the randomized interventions will not be taken into account in the primary test of treatment effects. Additionally, we will conduct as-treated analyses for the peer mentoring intervention whereby only patients who received peer mentoring are compared to patients in the other treatment arms, with adjustment for the same factors as in the intent-to-treat analyses. The small number of facilities (20) will preclude post-hoc adjustment for facility non-compliance with the interventions.

The third will be a secondary analysis of patient proportion with IDH before versus after the intervention phase to test whether the intervention effects are maintained. The basic analysis is a paired comparison of % IDH pre- versus post-intervention, with a few necessary adjustments. First, because the intervention phase will span 24 weeks and the maintenance phase will span only 12 weeks, the variance of the percent IDH will differ between periods. We will address that by using a mixed model with heterogeneous variance. This strategy will work for the situation of full duration of each patient's participation (24 weeks plus 12 weeks). If there are enough patients who enter or exit during either period, we will do a similar analysis, but use patient-and phase-specific weights to adjust for differing variances. Second, there may be carry-over effects after the intervention phase that only last for a few weeks. We will test that possibility by classifying the 12 weeks of the post-intervention phase as separate one-month periods, and testing whether the monthly post-intervention IDH percentages are individually different from the intervention phase IDH percentages. Testing for a decreasing trend during the maintenance period will also be performed. Third, these analyses will be carried out separately among the four groups (provider training/checklist alone; peer mentoring alone; both interventions together, and neither intervention). A joint analysis may also be performed to test for additive or interactive effects.

Missing Data Issues (MD-1). Because ours is an educational intervention with support from the dialysis facility's parent organization, we expect facility attrition to be very low. Nevertheless, if facilities do drop out during the intervention phase, they will be replaced and the intervention will take place at a new facility. A facility would need to be replaced if: 1) they request to leave the study; or 2) 75% of the staff do not complete the training within the first 14-16 weeks of the intervention period.

As for missing outcome data for facilities in the study, data for our primary outcome as well as two secondary outcomes (fluid adherence/Interdialytic weight gain and dialysis session adherence) are gathered at the dialysis session level, using data that are automatically gathered when treatment is delivered.

With IRB waiver of consent and waiver HIPAA authorization with an opt out process, we expect that we will not have significant attrition due to patient withdrawal since interventions will be provided at the facility-wide level. Attrition may be seen in the patient activation (peer mentoring) intervention if patients choose not to participate in the peer mentoring program or if patients drop-out after starting the program. It is important to note that patients who drop out of the patient activation intervention will not be dropped from the overall study unless requested, and collection of outcome measures will continue. Any attrition (lack of participation in the

patient activation intervention) could contribute to a reduced estimate of treatment effect in analyses using the intent-to-treat principle; this reduction in estimated treatment effect would appropriately reflect the expected effect of this intervention in the general dialysis population.

A final type of attrition may be the possibility of missing data due to patients not completing the self-reported quality of life (KDQOL) survey or the patient symptom question regarding recovery time. For example, some participants may refuse to answer certain questions or may miss follow-up surveys. Where possible, we will note reasons for missing data by triangulating data sources to determine whether a patient has moved to another facility, or in accordance with two of our outcomes, been hospitalized or died (MD-4).Although every effort will be made to collect these data, some missing surveys are still likely, particularly among those in ill health. We do not expect missing surveys to be associated with study arm, but missingness itself can be analyzed for treatment differences as a tertiary outcome measure. The sample in each cross-section will include living patients only, so death will not be a problem as it would be in a longitudinal QOL study. We believe that this approach, along with our conservative assumptions regarding sessions needed as described previously, will largely prevent missing data for our primary outcome, as well as two secondary ones. Death will be tracked as an outcome, although the trial is not powered to assess this as a primary outcome. Data on subjects who leave the study site, will be used until their time departure from the study.

We will compare the characteristics of those with missing data to those without missing data, to test whether characteristics are similar between the groups (see Preliminary Data Analysis) (MD-2). In addition to complete case analyses, we will use state-of-the-art statistical methods such as likelihood approaches and multiple imputation to deal with missing data (MD-3).[160] These sensitivity analyses will assess the robustness of the results to missing data (MD-5).

Heterogeneity of Treatment Effect Analyses (HT-2; Moderation). The primary analysis will examine average treatment effects (ATE), but we will also examine heterogeneity of treatment effects (HTE) on HD session instability (IDH) rate for a variety of covariates, particularly those that are characterized by differential outcomes among HD patients (HT-1). Covariates of interest for HTE analyses include: age, race,[163], ethnicity, level of education[164], literacy, presence of comorbidities, and heart rate variability (HT-4). Supporting these HTE analyses, greater benefits from peer mentoring for African Americans were found in a trial conducted by our advisory partner, NKFM.[18] Depending on sample sizes obtained for each of the covariates of interest, either a subgroup analysis or an analysis including interaction terms will be employed to examine HTE (HT-3). Only two-way interactions between the treatment indicator and each of the covariates will be analyzed. There may be different moderators for the two interventions.

Mediation Analyses. The second part of these analyses aim to identify mechanisms of action for the interventions, such as changes in patient or practitioner behavior and session characteristics; these changes in behavior will identify important pathways for improvement in reducing IDH. However, these analyses are not intended to be used for causal inferences. The basic mediation analysis involves 3 steps: (1) confirm that the intervention predicts the outcome (and if not, then mediation analysis is not relevant), (2) confirm that the intervention predicts the mediator (i.e., that the intervention has resulted in specific changes in patient or practitioner behavior; if not, then the potential mediator cannot mediate an intervention effect), and (3) in a model predicting the outcome with covariates including both the intervention and the mediator, confirm that the intervention effect has been reduced after adding the mediator to the model, and confirm that the mediator is a statistically significant predictor of the outcome. The role of moderation in a mediation analysis can also be tested. Each potential mediator is tested

separately, without adjusting for other mediators, although associations between mediators can separately be assessed for improved interpretation.

Mediators of the Primary Outcome: The following variables will be examined as potential mediators of the treatment effect on the primary outcome of dialysis session stability:

Patient-level variables: (1) patient session instability prevention behavior;(2) fluid management practice patterns; (3) number and categories of BP medications patient is taking; (4) fluid adherence (inter-dialytic weight gain); (5) dialysis adherence; (6) patient symptoms (symptom burden measure and recovery time); (7) hospitalizations for cardiovascular or fluid-related causes; and (8) quality of life.

Session-level variables to be assessed for potential mediation effects include: (1) treatment time delivered; (2) average session UFR; (3) cooled dialysate used; (4) sodium modeling used; (5) ultrafiltration modeling used; (6) ultrafiltration variability for whole session, or up until incident of IDH (if IDH occurs) (difference between the highest and lowest UFR, standard deviation of the UFR measures, the square root of the mean squared differences of successive UFR measures); (7) sitting-to-standing difference in SBP (orthostasis at beginning of session); (8) starting SBP; (9) slope of changes in SBP over 30 minute intervals for whole session, or up until incident of IDH (if IDH occurs); (10) values and times of lowest and highest SBP readings as a measure of range of SBP during the dialysis session; (11) patient request re: fluid removal at this session; (12) fluid adherence (inter-dialytic weight gain) at this session; (13) previous achievement of post-dialysis target weight; and (14) previous session instability.

Sensitivity Analyses. In addition to the sensitivity analyses described above, we will examine the effect that patient compliance/non-compliance rates, i.e., percent of patients who accept peer mentoring and checklist adherence for provider intervention, have on the results. The sensitivity analyses aim to assess the robustness of the conclusions based on the analyses of the primary outcome – specifically to determine whether the findings hold under different methods of defining the primary outcome. Thus we will conduct sensitivity analyses for the secondary measures of session instability described above. As part of this, because we will know the dates and causes of hospitalization and death by cardiovascular- or fluid-related causes, we will identify those events that took place on days in which dialysis was administered. Accordingly, we will conduct a sensitivity analysis of the primary outcome of dialysis session stability both with, and without, those events on dialysis days included. For the primary outcome analyses, we will also conduct a sensitivity analysis without the sessions of patients who begin that session with a sitting pre-dialysis SBP of 100-110 MmHg and whether the sitting SBP falls below 90 mmHg (using lowest SBP during session) if starting SBP ≥100.

Aim 2. Test and compare the effects of the two HD facility-level interventions on secondary patient-centered clinical outcomes, including: patient symptoms, fluid adherence, dialysis adherence, quality of life, hospitalizations and mortality over the same timeframe.

Aim 2 incorporates six outcome measures: (1) patient symptoms (including a patient burden measure, dialysis recovery time, and proportion of sessions with each symptom), (2), fluid adherence (inter-dialytic weight gain), (3) dialysis adherence, (4) quality of life, (5) hospitalization (all-cause and by specific cause), and (6) mortality (all-cause and by specific cause) , with will be analyzed at the individual level and summarized at the facility level. Each

will use a model format appropriate to the outcome type, but will otherwise follow the model strategy, including the secondary analyses, described for Aim 2 above. This includes censoring of patient data while they are at another facility. The fluid adherence (Interdialytic weight gain), symptom and quality of life analyses, based on continuous outcome measures, will be carried out using mixed models (the MIXED procedure of SAS). Note that the quality of life analyses will be based on data from two time points, one before intervention and one during intervention, rather than session-specific data as analyzed for the other outcomes. Analyses of missed or shortened HD sessions will employ logistic regression for longitudinal data, as in Aim 2. Analyses of hospitalization and mortality will use logistic regression for individual level data. As part of these models, we will test IDH-related variables (e.g., recent IDH, frequency of IDH in the past month) as potential predictors. In each case, the appropriate regression diagnostics will be used to assess model fit.

In both Aims 1 and 2, the primary results will be based on the treatment effects tested in the initial models described for CRCTs with pre-planned covariates. Depending on the specific outcome, covariate adjustment for these analyses will include: (1) patient demographics (age, race, ethnicity, sex, employment, literacy, education level, language spoken), (2) time since first dialysis, (3) cause of ESRD, (4) treatment history, (5) total transplants, (6) vascular access type, (7) patient laboratory data (serum phosphorous, dialysis adequacy, anemia management (hemoglobin), iron indices (ferritin, serum Iron), mineral metabolism indices (calcium, phosphate, PTH)); (8) comorbidity index; (9) individual comorbidities and comorbidities in combination, including COVID-19; (10) patient's heart rate variability for the whole session or up until IDH occurs (if IDH occurs) (based on variability in heart rate (HR) during dialysis session (Difference between the highest and lowest heart rates, standard deviation of the heart rate measures, the square root of the mean squared differences of successive heart rate measures)); and (11) patient medications (prescriptions medications administered outside of center or in-center (including ESA prescription, iron, antibiotics and vitamin D analog)). Intent-to-treat analyses will be carried out, which means that any deviations from the randomized interventions will not be taken into account in the primary test of treatment effects. Additionally, we will conduct as-treated analyses for the peer mentoring intervention whereby only patients who received peer mentoring are compared to patients in the other treatment arms, with adjustment for the same factors as in the intent-to-treat analyses. The small number of facilities (20) will preclude post-hoc adjustment for facility non-compliance with the interventions.

Heterogeneity of Treatment Effect Analyses (Moderation). As with the primary outcome analyses, the following potential moderators will be assessed: 1) patient demographics, including age, race, ethnicity, literacy, and education level; (2) comorbidities; and (3) heart rate variability.

Mediation Analyses. Mediation analyses will be conducted for each of the six patient-level secondary outcomes: (1) patient symptoms; (2) fluid adherence (inter-dialytic weight gain); (3) dialysis adherence; (4) quality of life; (5) hospitalization; and (6) mortality. Depending on the secondary outcome in question, the following variables will be examined as potential mediators.

Mediators of the Secondary Outcomes: Patient-level variables to be examined include: (1) patient session instability prevention behavior; (2) fluid management practice patterns; (3) number and categories of blood pressure medications patient is taking; (4) fluid adherence (inter-dialytic weight gain); (5) dialysis adherence; (6) patient symptoms (symptom burden and recovery time); (7) hospitalizations for cardiovascular or fluid-related causes in the past 4 weeks; and (8) quality of life.

The following *session-level* variables will be variables will be transformed into patient-level variables for the appropriate time period depending on the secondary outcome under examination, and assessed for mediation effects: (1) treatment time delivered; (2) average session UFR; (3) cooled dialysate used; (4) sodium modeling used; (5) ultrafiltration modeling used; (6) ultrafiltration variability for whole session, or up until incident of IDH (if IDH occurs) (ex: difference between the highest and lowest UFR, standard deviation of the UFR measures, the square root of the mean squared differences of successive UFR measures); (7) sitting-to-standing difference in SBP (Orthostasis at beginning of session); (8) starting SBP; (9) slope of changes in SBP over 30 minute intervals for whole session, or up until incident of IDH (if IDH occurs); (10) values of lowest and highest SBP readings as a measure of range of SBP during the dialysis session; (11) patient requests regarding fluid removal; (12) fluid adherence (inter-dialytic weight gain) prior to this session; (13) achievement of post-dialysis target weight; and (14) session instability (IDH).

Aim 3. Identify factors associated with successful implementation of the Dialysafe interventions, and ways in which implementation may influence intervention effectiveness.

Analysis of meeting data. Field notes compiled through training session and Operations Committee participation will serve as the basis for a rapid assessment process; information collected will be used to identify and understand barriers and facilitators and make any necessary modifications while the trial is ongoing.

Using NVivo qualitative data analysis software, we will also analyze data thematically (Saldana, 2016) to identify and explain types of implementation barriers and facilitators, and use qualitative analyses as supplementary explanations as we seek to explain the results of the trials, especially if there are differences in effectiveness between facilities implementing the same interventions.

Usability data analysis. To assess usability of the checklist and patient intervention technologies, we will analyze usage data, with attention to compiling the following metrics: (1) time spent on each page; (2) number of abandoned checklist sessions, videoconferencing or patient education module sessions; (3) pages and click-through patterns preceding abandonment. Patient Intervention technology data may be included in publications and/or form the basis of future research.

Implementation fidelity analyses. As mentioned above, we will use the captured fidelity data to create and track the following metrics:

- Staff Checklist
    - Checklist completion rate by facility over specific time points (number of completed checklists / number of patient sessions (for patients included in the study) calculated over a given time period (e.g., a month)
    - Proportion of checklist sessions in which patients are identified as being at risk of IDH
    - Prevalence of reasons why patients were identified as being at risk of IDH
- Staff Training
    - Proportion of staff by role who completed each training session, tracked by facility

    - Average proportion of training elements completed
    - Proportion of training sessions in which all training elements completed
- Patient Intervention
    - Average number of mentoring sessions completed per patient
    - Patient retention rates across all five peer mentoring sessions
    - Average peer mentoring session length
    - Education module completion rates by topic and section
    - Quiz completion rates
    - Average time spent on each educational module section
    - Average proportion of peer mentoring session components completed by session
    - Proportion of peer mentoring sessions in which all session components completed
    - Mentor-specific peer mentoring completion rates – for use by NKF in training and supporting mentors
    - Number of mentees who continue as mentees or mentors in the existing NKF peer mentoring program after intervention
    - Number of patients who accept the optional “tablet training call,” the length of the call, and the topics covered during the session (see section 44, “dialysafe pt tablet training plan”)
    - Whether patients have prior experience in using Apple or Android products
- Technology Training Fidelity
    - Training completion rates
    - Average length of call
    - Percentage of calls completed as-scheduled vs. after rescheduling
    - Compilation of frequently asked questions
    - Compilation of common reasons for refusal to schedule call
- Technology Support Calls
    - Number of tech support calls
    - Number of calls from each category of caller (mentee, mentor, clinic staff)
    - Average length of calls
    - Compilation of frequently asked questions
    - Compilation of common solutions to questions
    - Number of caller questions resolved after one call vs. after additional followup
- Patient Activation Intervention Uptake
    - Stated interest in intervention, but lost to follow up by intervention stage (e.g. tablet received, tech training, starting peer mentoring, completion of peer mentoring, tablet returned)
    - Tech training completion
    - No shows for tech training
    - Number of peer mentoring sessions completed
    - No shows for peer mentoring sessions
    - List of educational sessions completed
    - List of quizzes completed
    - Frequency of fluid management goal setting module responses by patient in educational sessions, by session
    - Frequencies of values endorsed in values module in educational sessions
    -

12 SOURCE DOCUMENTS AND ACCESS TO SOURCE DATA/DOCUMENTS

Table 9 – Sources of Materials and Access to Materials			
Patient activation intervention using peer mentoring			
Source	**Data Collection Mode**	**Variables (examples)**	**Who will have access**
FMCNA	Electronic health record (EHR) and session data for each dialysis session	Personal health information (PHI) (includes demographic information, comorbidities, medications, lab tests, dialysis session data, Quality of life survey)	FMCNA will transfer a limited data set using unique FKC identifier for each patient UM-KECC Programmer/Analysts Co-PI Rajiv Saran, Biostatisticians
National Kidney Foundation	Peer Mentoring Management System (PMMS) stored on secure, HIPAA-compliant server at the University of Michigan Medical School	Peer Mentor demographics (age, gender, race ethnicity, education) Mentor-mentee matches Scheduled peer mentoring sessions Average number of mentoring sessions completed per patient Patient retention rates across all five peer mentoring sessions	National Kidney Foundation Principal Investigator, Study Coordinators and Postdoctoral Research Fellow at University of Michigan School of Information University of California at Irvine staff (system developers)
National Kidney Foundation	Patient Intervention Completion Data – Peer Mentoring live sessions Peer mentoring videoconference completion data via VSee stored in Peer Mentoring Management System (PMMS) with non-identifying patient login	Whether session was completed Number of people in session Session length Average peer mentoring session length	National Kidney Foundation Principal Investigator, Study Coordinators and Postdoctoral Research Fellow at University of Michigan School of Information University of California at Irvine staff (system developers)
Study team	Patient Intervention Completion Data – Tablet-based Educational Modules - each patient will be given a	Education module completion rates by topic and section	Principal Investigator, Study Coordinators and Postdoctoral Research Fellow at University of

	unique login ID at the beginning of the study, and this will be used to track usage of the educational modules; this log in ID will be identifiable only to study coordinators through the Peer Mentoring Management System (PMMS) No PHI will be stored on the tablets at any time	Quiz completion rates Average time spent on each educational module section Usability: (1) time spent on each page; (2) number of abandoned checklist sessions, videoconferencing or patient education module sessions; (3) pages and click-through patterns preceding abandonment.	Michigan School of Information University of California at Irvine staff (system developers)
National Kidney Foundation	Checklist of peer mentoring training topic coverage Data transferred to Excel or Word format	Fidelity of the peer mentoring training Proportion of training session in which all elements completed	National Kidney Foundation Principal Investigator, Study Coordinators and Postdoctoral Research Fellow at University of Michigan School of Information
National Kidney Foundation	Checklists of topic coverage and behavior change technique implementation Data transferred to Excel or Word format	Fidelity of the peer mentoring intervention Proportion of peer mentoring sessions in which all session components completed Mentor-specific peer mentoring completion rates	National Kidney Foundation Principal Investigator, Study Coordinators and Postdoctoral Research Fellow at University of Michigan School of Information
National Kidney Foundation	Survey on Qualtrics Platform	Peer Mentor satisfaction with peer mentoring	National Kidney Foundation Principal Investigator, Study Coordinators and Postdoctoral Research Fellow at University of Michigan School of Information
National Kidney Foundation	Survey on Qualtrics Platform	Patient mentee satisfaction with peer mentoring (see attached documents: Peer Mentee Satisfaction Survey and Peer Mentor Satisfaction Survey)	National Kidney Foundation Principal Investigator, Study Coordinators and Postdoctoral Research Fellow at University of

			Michigan School of Information
FMCNA	Report on patient peer mentoring program completion, transferred from Peer Mentoring Management System by UMSI Principal Investigator and/or Study Coordinators with FKC ID2, which FMCNA will match to FKC ID1 Report on patient peer mentoring completion send to UM-KECC using FKC ID1	Number of Peer Mentoring Sessions Completed Peer Mentoring Start Date Peer Mentoring Stop Date	FMCNA Data Analysts UM-KECC Programmer/Analysts Co-PI Rajiv Saran, Biostatisticians
Study team	Patient Training Fidelity Checklist Completed by UMSI study staff following technology training calls to patients who have joined peer mentoring Data transferred from paper form to Excel or Word format	Items discussed during tech training call Major questions or issues outside of fidelity checklist “25.1_PM_Recruitment_and_Retention_Procedure”	Tiffany Veinot UMSI Project Coordinators
Study team	Patient Technology Training Records Completed by UMSI study staff to track number of technology training calls without identifying patient names Stored on UMSI secure server and PMMS	Whether patients in the peer mentoring program accept or decline a tech training call “Training Records” tab of “Tech Calls” document	Tiffany Veinot UMSI Project Coordinators National Kidney Foundation Project Coordinators Kai Zheng, University of California at Irvine (Co-Investigator) Paid Developer at University of California at Irvine, supervised by Kai Zheng
Study team	Technology Support Records Completed by UMSI study coordinators to track the technical support provided to clinics and members of the	Major questions or items discussed from calls to the study helpline Who contacted UMSI (mentee, mentor, clinic staff)	Tiffany Veinot UMSI Project Coordinators

	peer mentoring program, without identifying patient or provider names Stored on UMSI secure server and PMMS	Date and time of call "Tech support log" tab of "Tech Calls" document	National Kidney Foundation Project Coordinators Kai Zheng, University of California at Irvine (Co-Investigator) Paid Developer at University of California at Irvine, supervised by Kai Zheng
Provider education intervention			
FMCNA	Electronic health record (EHR) and session data for each dialysis session	Personal health information (PHI) (includes demographic information, comorbidities, medications, lab tests, dialysis session data, Quality of life survey)	FMCNA will transfer a limited data set using unique FKC identifier for each patient UM-KECC Programmer/Analysts Co-PI Rajiv Saran, Biostatisticians
Study team	Practice Patterns Survey for (1) Medical Directors and (2) Nurse Managers delivered before and after intervention via Qualtrics Platform	Practices for assessing patient estimated dry weight at facility Practices for managing intradialytic weight gain at facility Facility policies regarding fluid removal and ultrafiltration rates	Principal Investigator, Study Coordinators and Postdoctoral Research Fellow at University of Michigan School of Information UM-KECC Programmer/Analysts Co-PI Rajiv Saran, Biostatisticians
Study team	Provider team training fidelity checklists – completed on paper and transferred to Excel	Average proportion of training elements completed Proportion of training sessions in which all training elements completed	Principal Investigator, Study Coordinators and Postdoctoral Research Fellow at University of Michigan School of Information Co-Investigator Sarah Krein
Dialysis facilities	Checklist Completion Data from Checklist application on tablet computer used at facility with facility-level login	Checklist completion rate by facility over specific time points	Principal Investigator, Study Coordinators and Postdoctoral Research Fellow at University of

	only; no tracking of individual staff Checklist completion data stored in database on secure, HIPAA-compliant server at the University of Michigan Medical School	Proportion of checklist sessions in which patients are identified as being at risk of IDH Prevalence of reasons why patients were identified as being at risk of IDH	Michigan School of Information University of California at Irvine staff (system developers)
Study team	Online training attendance records - Paper form lists number in attendance by role only FMCNA clinics to share attendance by role in digital form via secure FMCNA email Data from paper form transferred to Excel or Word format and stored on secure research server at the University of Michigan School of Information (UMSI)	Proportion of staff by role who completed each training session, tracked by facility	Principal Investigator, Study Coordinators and Postdoctoral Research Fellow at University of Michigan School of Information Co-Investigator Sarah Krein
FMCNA	Completion of training in learning management system FMCNA shares training completion reports via SharePoint Data transferred to Excel or Word format and stored on secure research server at the University of Michigan School of Information (UMSI)	Proportion of staff by role who completed each training session, tracked by facility	Principal Investigator, Study Coordinators and Postdoctoral Research Fellow at University of Michigan School of Information Co-Investigator Sarah Krein
Study team	Field Notes from Meetings tracked by facility ID; will include participant IDs which refer to facility and professional role (e.g., dietitian, NP) Data will be stored in a Word Processing Program – Word and a Qualitative Data	Identify and explain types of implementation barriers and facilitators Use qualitative analyses as supplementary explanations as we seek to explain the results of the trials, especially if there are differences in effectiveness	Principal Investigator, Study Coordinators and Postdoctoral Research Fellow at University of Michigan School of Information Co-Investigator Sarah Krein

	Analysis Software package (e.g., NVivo) Files will be stored on a secure research server at the University of Michigan School of Information (UMSI)	between facilities implementing the same interventions	

Note: data in the above table have been compiled based on the attached data flow diagram and the following attached documents: (1) implementation assessment plan; (2) peer mentor data relinking plan, (3) provider training fidelity checklists; (4) peer mentoring fidelity checklists; (5) peer mentee satisfaction survey; (6) peer mentor satisfaction survey; (7) practice patterns survey for Medical Directors; (8) practice patterns survey for Nurse Managers; and (8) HIPAA compliance of Dialysafe Tools; and (9) Data elements list.

See attached data use agreement for use of data from FMCNA and Study Facilities.

13 QUALITY CONTROL AND QUALITY ASSURANCE

All UM study personnel who have access to patient data will be educated regarding the need to protect confidentiality and the procedures to be followed to ensure such protection; all relevant staff will be required to sign a confidentiality agreement. All study personnel are required to complete and be certified by the Program for Education and Evaluation in Responsible Research and Scholarship (PEERRS) at the University of Michigan every 3 years. External key personnel will also be required to have human subjects certification via the UM PEERRS modules or equivalent training as approved by UM. NKF's peer mentoring program coordinator and program assistant will have access to patient names, gender, clinic, treatment schedule, and telephone number, after patients have agreed to the peer mentoring program and have given permission for a UM Study Coordinator to share this information with NKF. While NKF is not a HIPAA-covered entity, it has offered a patient peer mentoring program for over seven years, and has handled this type of patient information on an ongoing basis in order to deliver this program. Study personnel will also be required to complete annual HIPAA training.

14 ETHICS/PROTECTION OF HUMAN SUBJECTS

This section should include a description of the ethical considerations and context for the conduct of the trial.

14.1 ETHICAL STANDARD

The investigator will ensure that this study is conducted in full conformity with the principles set forth in The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research, as drafted by the US National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (April 18, 1979) and codified in 45 CFR Part 46; 62 Federal Regulations 25691 (1997) and the Declaration of Helsinki and Good Clinical Practice (GCP).

14.2 INSTITUTIONAL REVIEW BOARD

We are applying to have the University of Michigan IRB-MED serve as the central IRB for all study sites. FMCNA will have completed an Agreement to cede IRB review to the University of Michigan IRBMED. All 20 hemodialysis facilities are operated by FMCNA, and FMCNA will provide all data centrally through its corporate data warehouse to University of Michigan.

14.3 INFORMED CONSENT PROCESS

I. Requested alterations to the informed consent process

PATIENTS

The patient information sheet contains content on the key elements of informed consent, but they will not be accompanied by a verbal dialogue to ensure informed consent nor records of having obtained consent. Staff at hemodialysis facilities will not obtain informed consent from patients.

For the overall study, at each participating facility, the following actions will take place:

1) A staff member (likely a patient care technician or nurse) will give each patient in the facility the patient information sheet, using the enclosed script.
2) On a list, the facility staff member or UM Study Coordinator will record the fact that each individual patient received the information sheet, and record any opt-outs from patients.
3) Patients may also call the UM School of Information research team via a 1-800 number (1-844-864-3228) to ask questions and/or opt out of the study and/or discontinue peer mentoring.
4) The list of informed patients, including opt-outs, will be shared with an FMCNA nurse, who will create an "ancillary order" in the electronic health record for each patient who does not opt out of the study.
5) A list of patients participating in the study will be produced (and regularly updated); this will be kept in a research binder at each study facility.

To offer patients peer mentoring:

1) The patient information sheet indicates that patients may be contacted to offer them peer mentoring.
2) Using SharePoint, a secure computing environment hosted by FMCNA, the list of patients in the study, their sex, clinic, phone number and treatment schedule (to find the best time to call the patient) will be shared with the UM School of Information Study Coordinator.
3) The UM Study Coordinator will call the patient to offer them peer mentoring, using the script provided.
    Patients without regular access to a personal phone will be sent a pre-paid cell phone if they indicate interest in the peer mentoring program to their clinic manager.
4) A volunteer Patient Advocate, as described in Section 5.3, may discuss the peer mentoring program with other patients or hand out a flyer (“Peer Mentor Program Flyer”). Discussion will be limited to that which is described in the “Patient Discussions” document; namely, the Patient Advocate’s experience as part of the peer mentor program and the contact information for the UMSI study staff.

Again, this will not be a formal informed consent process, as we are concerned about creating bias since informed consent will introduce preferential uptake of peer mentoring. Additionally, obtaining consent may create an imbalance in study arms (i.e., consent of patients in only one arm of the study).

FACILITY STAFF
In addition to approval by the Regional Vice President and Medical Director, each facility will approve their participation in the trial through their governing body. Facility staff do not constitute human subjects in the research as we will not gather private identifiable information directly about any individual, and the educational intervention will take place at the facility as a whole; it would be impossible to offer the intervention to some staff but not others. Furthermore, with regard to fidelity measurement, only aggregate reports concerning completion of training and the use of the checklist will be produced. Field notes will also not contain any individual identifiers for staff.

II. Rationale for waiver of informed consent requirement

We are seeking to obtain IRB agreement to waive the usual requirement for individual patient consent for this pragmatic cluster randomized trial of educational interventions at the dialysis facility level; this request applied to the complete study. The following points are to serve as underlying rationale for requesting a waiver of informed consent in this context:

1) The research involves no more than minimal risk to the subjects

The project uses a facility-level educational intervention that utilizes proven educational/quality improvement approaches, with a goal of improving the cardiovascular/hemodynamic stability of hemodialysis care. There will be 20 hemodialysis facilities in the study, of which 10 will receive a healthcare provider-focused intervention (training and a checklist) and 10 will receive a patient activation intervention (peer mentoring and multimedia education materials). There will be no interruption in usual care, and care will be provided to the usual standard at minimum — and perhaps improved. Patients who participate in peer mentoring may benefit by learning new and better ways to care for themselves so as to prevent hypotensive episodes during hemodialysis.

2) The research could not practicably (i.e., feasibly) be carried out without the waiver or alteration.

This is a pragmatic cluster-randomized trial of educational interventions at the dialysis facility level. When an educational effort is initiated at any facility, all patients, without bias, should be afforded the opportunity to experience its potential benefits. Additionally, it would be impossible to make provider education apply to some patients but not others. The study could not practicably be carried out without the waiver of consent for the following reasons that relate to the validity of study findings:

(a) The primary outcome is measured at the facility level, and missing data will undermine internal validity. The study's primary outcome, intradialytic hypotension rate, is a facility-level outcome determined at the level of the entire facility. There is a need for as close to 100% participation as possible in order to accurately determine rates of intradialytic hypotension. Administration of informed consent would lead to a loss of subjects, leading to an inaccurate estimation of a facility's intradialytic hypotension rate.

(b) Potential introduction of bias will threaten internal validity. Those who consent to participate in the study are more likely to be people who have a better outcome – that is, they may be less likely to have intradialytic hypotension, or to have it regularly. This is because intradialytic hypotension is intimately linked to patient behaviors, including adherence to fluid and dietary restrictions, as well as adhering to regular dialysis sessions. People who do not follow these guidelines, and are not motivated to change this, are less likely to choose to be involved in a study in which these behaviors will be scrutinized. This would lead to systematic exclusion of patients who experience intradialytic hypotension most frequently, and undermine the generalizability of the findings to the full patient population, particularly those most in need of the intervention.

(c) Interference with the pragmatic nature of the trial will affect external validity. The interventions are meant to be delivered in the context of routine care, so that hemodialysis care providers can estimate the likely effect of intervention implementation on everyday practice. Seeking informed consent from all patients will alter usual care, and potentially undermine the pragmatic nature of the trial, and the related conclusions that can be drawn from study findings.

In addition, the following pragmatic reasons makes individual-level consent impracticable:

(d) This is designed as a large, population-based, pragmatic, facility-level study of previously validated educational interventions. There are approximately 1,400 prevalent patients at the 20 facilities to be included in the study (of whom we estimate 1,200 will not be excluded due to vulnerable status or opting out). It is not possible to obtain informed consent from this many patients within available funding levels.

(e) This is a multi-state study that will take place in hemodialysis facilities in Michigan, Ohio, Massachusetts, Connecticut, California, Alabama, and other states to be determined.

d) We remain committed to providing detailed feedback about the results of the trial to the participating facilities, so that any potential benefits can continue to be experienced.

There is precedence for the above approach in the context of pragmatic clinical trials[86], the most recent examples in hemodialysis care being the time trial (https://clinicaltrials.gov/ct2/show/nct02019225), and the national opportunity to improve infection control in ESRD (NOTICE) project,[81, 82] in which Co-PI Saran participated.

3) The waiver or alteration will not adversely affect the rights and welfare of the subjects

Intradialytic hypotension is an important concern among patients, and the research has received significant support from patients consulted via three focus groups in two parts of the country, a Steering Committee with two patient advocates, and a national Advisory Committee that involves seven patient advocates. This research will exclude vulnerable patients. Although a consent process is not practicable (see below), all patients in the study facilities will be given an information sheet about the study, and will be given an opportunity to opt-out of the research. All clinical data regarding patients will be received from FMCNA as a limited data set with a unique random FKC identifier. All data shall be destroyed seven years after completion of study.

4) Whenever appropriate, the subjects or their Legally Authorized Representative will be provided with additional pertinent information after participation.

At the end of the intervention in their facility, patient participants will be given access to a study Web site that will provide updates about the trial's progress. Through this Web site and other communication vehicles, the study team will be available to answer questions from patients or staff at study facilities. We will work with the National Kidney Foundation (NKF) to present study results to peer mentors as part of a teleconference at the end of the study. We will also work with NKF to create user-friendly, written results summaries to be shared with focus group participants and mentors. Furthermore, upon completion of data analyses, a results "fact sheet" – an abridged final report detailing the study's findings – will be made available at all study facilities (e.g., in the waiting room or on bulletin boards). These documents will be developed by the Steering Committee in consultation with the National Kidney Foundation and the Advisory Committee.

14.4 EXCLUSION OF WOMEN, MINORITIES, AND CHILDREN (SPECIAL POPULATIONS)

We aim to include all non-vulnerable in-center patients at participating dialysis facilities. The trial is designed so as not to exclude anyone, including women and minorities to the extent they are represented at the dialysis facilities from the ages of 21 and older. We will only exclude vulnerable patients: those under 21 years of age, prisoners, those with a cognitive barrier, and those deemed vulnerable based on a cognitive barrier by the Clinical Manager, Medical Director, and/or Social Worker, and those with a lack of facility in English or Spanish (patients whose primary language is not English or Spanish).

14.5 SUBJECT CONFIDENTIALITY

Subject confidentiality is strictly held in trust by the participating investigators, their staff, and the sponsor(s) and their agents. The study documentation, data, and all other information generated will be held in strict confidence.

We understand the sensitive nature of patients' medical records and of patient and provider input, and we have utmost concern for the human subjects who will be part of this study. We will seek a waiver of authorization from the Privacy Board and will take steps to ensure protection of confidentiality. Data obtained will be held strictly confidential in locked facilities and password-protected computers. All information will be kept in password-protected databases, with secure servers. Computers will be locked or kept with only key study personnel at all times. Key study personnel will be restricted to only data they need to access. Electronic patient data described above will be transmitted to UM-KECC for archiving on their password-protected secure servers. Only FMCNA personnel, Co-PIs, study statisticians, and the programmer analysts at UM-KECC will have access to PHI for the purposes of Aim 1 and Aim 2 analyses, and Study Coordinators and the PI will have access to PHI for the purposes of managing the opt out process and offering patients peer mentoring. The National Kidney Foundation will have patient contact information and records of peer mentoring, but NKF is not a HIPAA-covered entity. Data sets created for analysis will not have personal identifiers. See the attached data flow diagram for further information. These safeguards have proven effective in securely keeping existing national data on all ESRD patients in the United States. Additional special provisions are outlined below.

I. Limited Data Set

All data held by the University of Michigan Kidney Epidemiology and Cost Center (UM-KECC) will be in the form of a limited data set, with patient data linked across sources using random identifiers created by FMCNA for each individual. For the session-level outcomes of intradialytic hypotension, adherence and symptoms, it will be important to conduct analyses that cluster according to the patient, and adjust for patient-level factors such as medications and comorbidities. As-treated analyses for peer mentoring also require identification of patients who received peer mentoring, the amount of peer mentoring received, and when it was received. Such analyses cannot be completed without patient-level identifiers.

II. Handling of Protected Health Information (PHI)

We are applying for a HIPAA Authorization Waiver Request as part of this study. The study involves examination of the impact of two educational interventions on clinical outcomes including intradialytic hypotension rates (primary outcome), dialysis adherence, fluid adherence (interdialytic weight gain), patient symptoms, quality of life, mortality and hospitalization. For these analyses, it is necessary to be able to link clinical information to a specific patient, and to be able to identify their facility and the amount of peer mentoring they have received (if applicable). It is also necessary to use medical records to identify whether a patient is vulnerable and should be included from the study (e.g., under age 21, prisoner). Thus, without the PHI to be used in the study, it will be impossible to assess who received the intervention, in what amount (e.g., peer mentoring receipt), and the effects of the interventions on the outcomes of intradialytic hypotension, dialysis adherence, interdialytic weight gain, patient symptoms, quality of life, hospitalizations, and mortality. Our plan to protect patient-subject identifiers from improper use or disclosure is as follows:

1) Each patient already will be given a unique ID (FKC ID1) that will be linked to patient data and stored at UM-KECC. UM-KECC is compliant with the Federal Information Security Management Act (FISMA). Furthermore, the organization undergoes an annual, comprehensive IT Risk Assessment, and monthly vulnerability scans to test the system. UM-KECC staff undergo background checks and training specifically for handling PHI.

2) Patient Study data from FMCNA to UM-KECC will be transferred using a secure file transfer service, as a limited data set using the FKC random patient identifier (FKC ID1).

3) Patients who are to be offered peer mentoring will be identified by FMCNA, and their names, clinics, genders, treatment schedules, telephone numbers and a random FKC ID2 given to the UM Study Coordinator (Note: this ID is different from that identified in 1) and 2) above). Participants will also be given a non-identifying ID automatically generated by PMMS based on the order they are added to the secure PMMS site. This will be used for for communication between UMSI study staff and NKF, as well as record keeping for technology training fidelity, technology training recruitment, and tech support calls. To obtain this information, the Study Coordinators will log into SharePoint, hosted on FMCNA's secure servers, from which no information can be printed, transferred, or removed. The Study Coordinators will phone the patient, explain peer mentoring, and offer it to them. If the person agrees to receive peer mentoring, their contact information will be entered into the secure Peer Mentoring Management System (PMMS), which will be posted on a HIPAA-compliant server at the University of Michigan Medical School. The PMMS will then be accessed by the National Kidney Foundation (NKF) staff member, who will then conduct intake with that person. The patient will agree to UM sharing their information with NKF prior to doing so, and their date of birth (to facilitate matching

to the FKC ID1 identifier) will be obtained from the patient, either by a University of Michigan School of Information Study Coordinator or the National Kidney Foundation.

4) The NKF is not a HIPAA-covered entity. It will maintain records of peer mentoring provision, and schedules of peer mentoring sessions. For data analysis, peer mentoring records linked to a FKC ID2 identifier will permit linkage to clinical data that will be stored and analyzed by UM-KECC for the study.

5) Patients will use a study-provided tablet computer to be shipped to each patient. Using the tablet, they will connect with their peer mentor and to review multimedia educational modules (with quizzes). Each patient will be given a unique login ID at the beginning of the study, and this will be used to track usage of the educational modules (e.g., page views, modules completed, quiz completion). This log in ID will be identifiable only to study coordinators through the PMMS. An easily-remembered but non-identifying password will be supplied upon setting up each patients' ID. Patients will be prompted to change the password to something private to them when signing into a tablet for the first time.

When setting up this ID, a study coordinator will help each patient set up a series of easily remembered security questions. In the case that a patient forgets their password, they may answer these questions to gain access to their account and reset their password. If a patient needs additional assistance in accessing their account or resetting their password, they may contact the Dialysafe helpline, where a study coordinator may manually reset a patient's password after confirming security questions.

After completion of the patient activation intervention, UM Study Coordinators will mail return shipping materials to each patient. The patient will then be asked to use these materials to ship the tablets back to UM for cleaning and re-use with other patients. Prior to shipping, UM Study Coordinators will wipe all data off of the patient's tablet using the remote tablet management program recommended by HITS (Health Information Technology & Services at Michigan Medicine).

6) Patient peer mentoring sessions will be conducted through VSee videoconferencing software, a HIPAA-compliant tool (see Section 15 for details).

7) FMCNA will share information with UM using its secure SharePoint computing environment (see Section 15 for details).

8) Surveys will be administered using the HIPAA-compliant Qualtrics.com survey tool (see Section 15 for details).

9) FMCNA will share the name of patient advocates as described in Section 5.3 with patients and visitors and other individuals associated with the Study such as UM Study Coordinators. UM Study Coordinators will call the patient advocates using the contact information they already have as part of the peer mentoring program to provide patient advocate training.

UM-KECC and UMSI will never possess a crosswalk file with which to re-identify patients. Peer mentoring data (which includes patient name and date of birth) held in the peer mentoring management system will be retained according to terms of PCORI contract: for a period of three (3) years from the a) Contract Term Date, b) date of the final payment under the UM-PCORI Contract, or c) conclusion of any audit or litigation related to the UM-PCORI Contract, whichever

is later. The crosswalk file with the FKC Random ID1 and FKC Random ID2 will be destroyed by FMCNA upon completion of data analyses.

Information will not be reused or disclosed to anyone outside of the research team, unless required by law or oversight of the research study.

III. Facilitating Patient Activation Intervention by National Kidney Foundation, and relinking of data for analyses by UM-KECC

The University of Michigan School of Information (UMSI) will also have access to the patient's name, sex, dialysis shift, telephone number and FKC ID1 so that they can be offered peer mentoring. If the patient agrees to receive peer mentoring, their name, gender, facility, treatment schedule, phone number and date of birth (obtained by a UMSI Study Coordinator, Postdoctoral Research Fellow or PI) will be entered into the Peer Mentoring Management System for use by the National Kidney Foundation. It will be impossible to provide them with peer mentoring if we do not know who they are; this information will be retained by the National Kidney Foundation as they provide the peer mentoring service. This information will be kept separate from the data held by UM-KECC. FMCNA will re-link peer mentoring data to patient data held by UM-KECC through the use of FKC ID1 and FKC ID2; which FMCNA will use to link data prior to sending the peer mentoring data to UM-KECC using FKC ID1 as a unique identifier. UMSI and UM-KECC will not have a crosswalk file to permit re-identification of any patients in peer mentoring (identified by FKC ID2) with the FKC ID1 identifier. Neither FMC nor UM-KECC will have access to the PMMS containing the automatically generated patient DS ID alongside other patient information contained in the system.

At the conclusion of the peer mentoring intervention, using the Peer Mentoring Management System (PMMS), UMSI will generate a report of peer mentoring records with the data elements shown in the column headers of Table 10. This report will then be sent to FMCNA for linking of the FKC ID2 to the FKC ID1.

Table 10 - Peer Mentoring Management System Sample Report

FKC ID2	Number of Peer Mentoring Sessions Completed	Peer Mentoring Start Date	Peer Mentoring Stop Date	Number of Missed Peer Mentoring Sessions	Completed Tech Training (Yes/No/ Not needed)	Number of Missed Tech Training Sessions	List of Educational Sessions Completed	List of Educational Session Quizzes Completed	Tablet Returned (Y/N)
1489	5	6/1/2021	8/24/2021	2	Yes	1	1, 3, 5	1, 3, 5	Y
4572	4	6/5/2021	8/15/2021	1	Not needed	0	1, 2, 3, 4	1, 2, 3, 4	N

FMCNA will link the data in Table 10 with the FKC ID1 previously generated for purposes of the study, replacing FKC ID2 with FKC ID1. The FKC ID1 will be used to identify study participants and will be included in the data transferred from FMCNA to UM-KECC. FMCNA will generate a Peer Mentoring Report for UM-KECC that includes the FKC ID1 and it will contain the peer mentoring data required for data analysis (see Table 11). FMCNA will then provide this report to UM-KECC using the same procedure established for sharing other study data from FMCNA.

This “Plan for Linking Peer Mentoring Records to UM-KECC Patient Data” (see attached document) preserves UM-KECC’s receipt of a limited data set by ensuring that identifiable patient data used by UMSI and NKF for the purposes of peer mentoring is kept separate from the limited data set used for analyses at UM-KECC. In this plan, FMCNA acts as an intermediary between UMSI and UM-KECC by linking patient peer mentoring data to the FKC ID1, which UM-KECC will then use to link peer mentoring records to other patient data. Therefore, UM-KECC will only receive the information outlined in Table 11 below. At the same time, project staff at UMSI will not have access to the limited data set which UM-KECC will use to analyze the data.

Table 11 - Sample Peer Mentoring Report for UM-KECC

FKC ID1	Number of Peer Mentoring Sessions Completed	Peer Mentoring Start Date	Peer Mentoring Stop Date	Number of Missed Peer Mentoring Sessions	Completed Tech Training (Yes/No/Not needed)	Number of Missed Tech Training Sessions	List of Educational Sessions Completed	List of Educational Session Quizzes Completed	Tablet Returned (Y/N)
90000	5	6/1/2023	8/24/2023	2	Yes	1	1, 3, 5	1, 3, 5	Y
90001	4	6/5/2023	8/15/2023	1	Not needed	0	1, 2, 3, 4	1, 2, 3, 4	N

14.6 STUDY DISCONTINUATION

If the study were discontinued, all patients would continue to receive routine hemodialysis care.

14.7 FUTURE USE OF STORED SPECIMENS

N/A

15 DATA HANDLING AND RECORD KEEPING

The Principal Investigators are responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported. Security measures to protect the privacy of research subjects are secure servers and file transfers, as well as password access will be used to protect the privacy of the research subjects. Qualtrics, a videoconferencing platform, checklist application and the peer mentoring management system are all HIPAA-compliant tools.

UM-KECC. UM-KECC is the Data Coordinating Center for the Dialysafe study. Established in 1993, UM-KECC is an interdisciplinary research group primarily drawing from the SPH Departments of Biostatistics, Epidemiology and Health Management and Policy, and the UM Medical School Departments of Internal Medicine (Nephrology, Transplantation, and Cardiology), Surgery, and Pediatrics, as well as other UM departments. With 50 staff and 40 associated faculty members, it conducts major projects in end-stage renal disease, chronic kidney disease, and organ transplantation. UM-KECC has substantial experience working with

large databases in ESRD, CKD and transplantation. Its mission is to promote health, improve clinical practice and patient outcomes, optimize resource utilization, and inform public policy. UM-KECC facilities will serve as the home location for the work outlined in this proposal.

The offices of the UM-KECC are located in a suite at the University of Michigan School of Public Health (SPH) on the central campus in Ann Arbor, Michigan. Exterior building doors are locked outside of usual business hours. UM-KECC and suite doors are locked at all times. Only authorized personnel have access via an electronic access system. Intra-building wiring connections between floors are made through locked basement phone closet.

The UM-KECC system is connected to the Internet through the University of Michigan network. This connection is routed through a dedicated single-purpose firewall. Authentication of users and control of access to files is through Windows Server 2008 R2 security.

UM-KECC is compliant with the Federal Information Security Management Act (FISMA), and has in place an Authority to Operate (ATO) from the Department of Health and Human Services (DHHS). Furthermore, the organization undergoes an annual, comprehensive IT Risk Assessment, and monthly vulnerability scans to test the system.

Fresenius Medical Care North America. FMCNA's SharePoint is hosted on a secure shared drive on a windows file server and a secure Citrix server which contains computer applications needed for the research studies. Only approved research personnel will be granted access. The University of Michigan will log in remotely to access the secure environment.

Virtual Environment for Peer Mentoring Management System (PMMS) and Checklist Usage tracking at University of Michigan Medical School. The storage of Information relating to Dialysafe interventions, such as that which is needed to facilitate peer mentoring and collect checklist completion data, is imperative for study progress and completion. Data to be tracked on the PMMS includes basic patient demographics needed for peer mentor matching, patient dialysis schedules, and goals that the patient has selected as part of the program's educational sessions. This information will be stored on a custom-configured Michigan Medicine virtual environment, which is also the system utilized by the University of Michigan hospital system. The checklist tracking system will record the date, time, and IP address of each checklist usage session on the tablet computer to be provided to each facility, as well as all clicks on the system and time spent on each screen.

The Michigan Medicine virtual environment is aligned with HIPAA requirement by adapting the process of Risk Assessment. Michigan Medicine conducts Risk Assessment and Risk Management on the virtual environment and they follow the Risk Analysis and Risk Management documented as stated below. The last risk assessment was completed in 2018 and Michigan Medicine worked with IA on another risk assessment that was completed in 2022.

- *164.308(a)(1)(ii)(A) – **Risk Analysis** – "Conduct an accurate and thorough assessment of the potential risks and vulnerabilities to the confidentiality, integrity, and availability of electronic protected health information held by the covered entity."*
- *164.308(a)(1)(ii)(B) - **Risk Management** - "Implement security measures sufficient to reduce risks and vulnerabilities to a reasonable and appropriate level to comply with the above"*

Michigan Medicine virtual machines (VMs) are routed through a Distributed Switch through the CISCO Fiber Interconnect on a CISCO switch that is managed by the Michigan Medicine Health Information Technology & Services network team. VMs are connected to the Internet through the University of Michigan network.

Only privileged account access is allowed with required two factor authentication and the passwords are recycled every 12 hours. All VMs are on private VLAN subnets that use Network address translation (NAT) behind our Information Assurance Firewall router. All Public network IP addresses ports are blocked by default and opened as needed by the applications. Authentication of users and control of access to files is through Active Directory.

In addition, Michigan Medicine adheres to the following safeguards for all Michigan Medicine systems:

- **Administrative Safeguards.** These focus on policies, procedures, and documentation to train workforce members and appropriately permit or restrict their access to protected health information regulated by HIPAA.

Examples include:

  - Security awareness training program for all staff

- **Physical Safeguards.** These focus on limiting access to facilities and information systems in which electronic information systems are housed, as well as any physical media that contains or is used to access PHI.

Examples include:

  - Applying Security updates regularly to Operating Systems
  - Annual audit of administrative access on servers

- **Technical Safeguards.** These focus on limiting access to PHI to specific persons.

Examples include:

  - Automatic password lockout
  - Assigning unique name or number to track user identity

Sources: Correspondence with John Herlocher with technical writing from Emily Fuentes, Michigan Medicine Health Information Technology Services. (Note: this information can also be found in the attached document, *HIPAA compliance of Dialysafe Tools.*)

VSee for Peer Mentoring Sessions. VSee is a cloud-based audio/video/content sharing conferencing service approved for use at Michigan Medicine. As part of the Dialysafe project, we will use VSee to conduct peer mentoring sessions in which a patient dialyzing at an FMC facility will communicate with a peer mentor for five discussion sessions over approximately a 12 week period. The patient will connect to VSee using a study-provided tablet computer. Using the VSee Application Program Interface (API), the VSee-based peer mentoring sessions will be launched directly from the secure peer mentoring website for the educational modules. Any utilization of VSee by any Dialysafe team member, including associates at National Kidney Foundation, will occur through UM-hosted and protected accounts. Using a secure account provided to the NKF peer mentoring coordinator, the encrypted sessions will be scheduled in advance, and emails sent to the peer mentor and mentee will serve as confirmations and reminders. Additionally, for those patients who consent to receiving text messages, an automated SMS reminder will be sent prior to their session (See “Peer Mentor SMS Scripts”). VSee will store a record of all completed sessions and the number of attendees. This data will be collected to enable both verification that the session took place and the production of program statistics. VSee has a Business Associate Agreement with the University of Michigan, making it acceptable for use with PHI.

Educational Modules and Staff Checklist on Tablet Computers. In addition to using the tablet computer to connect with their peer mentor, patients will also be asked to review multimedia educational modules (with quizzes) to be located on the study-provided tablet computer. In addition to using the tablet computer to connect with their peer mentor, patients will also be asked to review multimedia educational modules (with quizzes) to be located on the study-provided tablet computer.

Tablet computers also will be supplied to clinics randomized to the provider training intervention. Staff who fill out the checklist will do so using a tablet computer, using a single secure login that the clinic will share. A shared facility password will be used for simplicity. The data entry into this tablet by clinic staff will be to place check marks on a checklist that is used for each patient treatment; there will be no patient identifiers associated with the data. Usage data, such as number and composition of completed checklists, will be collected at the clinic level and stored in the virtual environment described below.
No PHI will be stored on tablets at any time. Tablets will solely be used to access applications, which will store only the aforementioned usage data on the device. (Note: this information can also be found in the attached document, *HIPAA compliance of Dialysafe Tools.*)

As part of the patient activation intervention, email and text messages will be used to communicate with patients as follows:

1) Reminders of upcoming peer mentoring sessions: with first name and last initial (not last name) - will include date and time of session
2) Action plans: with first name and last initial (not last name), selected goal, and plan for addressing barriers (see the patient intervention materials for the action plan format) (optional if patient wants to receive this after their session)
3) Patients can choose to email pdf resources to themselves (optional; triggered by the patient)
4) If the patient decides to do change their login ID, email addresses may be used as a login ID for the patient tablets
5) Administration of intervention, including scheduling and rescheduling peer mentoring sessions and technology training sessions, and follow up regarding missed peer mentoring sessions or technology training sessions

Emails and texts may be sent through: Michigan Medicine (level 2) email, the Peer Mentoring Management System, VSee, and/or a project phone. The project phone will be kept in a locked drawer when not in use. Email and text message scripts may be found in the following documents: 21. Peer Mentor Email Scripts; 26. Peer Mentor SMS Scripts.

UM School of Information (UMSI) Servers. Data for Aim 3 will be stored and analyzed on a secure S-core Linux server at UMSI. These data do not include any PHI. These servers have regular automated backups scheduled by the UM School of Information computing support. The storage media will conform to industry-standards for stability and accessibility. The investigators will ensure that the research data is migrated to new formats, platforms, and storage media as required by good practice in a secure environment (e.g., lockable computer systems with passwords, firewall system in place, power surge protection, virus/malicious intruder protection).

Qualtrics.com survey platform. The Provider Practice Patterns Survey and the Peer Mentor and Mentee satisfaction surveys will be delivered via the secure Qualtrics.com software

platform. Qualtrics, the web-based software to be used for surveys and referral of patients to peer mentoring is HIPAA-compliant, and UM has a contract with the company. These data will be downloaded onto UMSI servers for statistical analyses.

15.1 DATA MANAGEMENT RESPONSIBILITIES

The limited patient data set will be transferred centrally from FMCNA to the Data Coordinating Center, UM-KECC. At UM-KECC, study data will be cleaned and transformed as needed. Codebooks will be created for study variables. Data cleaning and analysis will be performed by Data Analysts at UM-KECC under the supervision of the senior and junior biostatisticians for the study (Gillespie and Bragg-Gresham, respectively).

The opt out process, as outlined in the attached document, will involve remote, virtual support by a UM staff member (see attached opt out process document for more detail). A scanned version of the Opt Out Worksheet document will be uploaded into FMCNA's SharePoint environment; it is not possible to download or print from this environment.

As shown in the attached data flow diagram, the patient data to be used to contact patients who have not opted out of the study will be shared with the team at the UM School of Information via FMCNA's SharePoint environment. It will not be possible to print or download from this system. If a patient agrees to participate in peer mentoring, their name, date of birth, email address, clinic name, clinic ID and treatment shift will be entered into the peer mentoring management system (PMMS). The National Kidney Foundation will then use these data, and the PMMS scheduling and matching functions, to administer the peer mentoring component of the patient activation intervention. UM School of Information staff will generate reports of peer mentoring participation and share these with FMCNA for linking to the FKC ID1. The FKC ID1 and patient records will then be sent to UM-KECC (see attached data relinking process document).

For Aim 3 analyses, checklist completion data will be located on a HIPAA compliant server at the University of Michigan School of Medicine (see attached document entitled, *HIPAA compliance of Dialysafe tools*). These data will be tracked by facility, but not by individual staff member. The PI, co-Investigator Zheng at the University of California at Irvine, a paid developer at University of California at Irvine (supervised by Dr. Zheng), a Postdoctoral Research Fellow, and UMSI Study Coordinators will have access to these data. Implementation data from the patient activation intervention for Aim 3 will be stored on the University of Michigan School of Information's Peer Mentoring Management System, which will be stored on a HIPAA compliant server at the University of Michigan School of Medicine (see attached document entitled, *HIPAA compliance of Dialysafe tools*). The PI, co-Investigator Zheng at the University of California at Irvine, a paid developer at University of California at Irvine (supervised by Dr. Zheng), a Postdoctoral Research Fellow, UMSI Study Coordinators and staff at the National Kidney Foundation will have access to these data.

Also for Aim 3 analyses, as shown in the attached Implementation Assessment document, a secure research server at the University of Michigan School of Information (UMSI) will be used to store: Field Notes from Meetings, training attendance records, LMS Training Completion Records, Online Training Fidelity Checklist (see attached). Only the Principal Investigator, co-Investigator Krein, a Postdoctoral Research Fellow and UMSI Study Coordinators will have access to these data. This information will be linked to a Study Facility ID, but there will be no identifying information about individuals on this server.

15.2 DATA CAPTURE METHODS

Data are collected routinely by FMCNA study. Data will be securely transferred for all study sites by FMCNA as part of limited data set transfers during the course of the study.

15.3 TYPES OF DATA

Data for this study will include outcome measures, covariates, and potential mediators obtained from the electronic health record system at FMCNA. Additionally, intervention fidelity data will be gathered using digital platforms (e.g., checklist application, peer mentoring management system, learning management system), attendance sheets and checklists. A provider survey for medical directors and nurse managers at each facility will document fluid management practice patterns before and after the study. Satisfaction surveys will be completed by peer mentors and mentees. Field notes will be completed by Study Investigators at meetings associated with the interventions at study facilities: online staff training sessions and Operations Committee (OC) meetings.

15.4 TIMING/REPORTS

An external data safety monitoring board (DSMB) consisting of 5 members (outside of the University of Michigan) has been identified after IRB review of the project. The DSMB includes a biostatistician unrelated to the trial, a patient, a nephrologist, and a layperson unrelated to the field (e.g., bioethicist).

The DSMB has met for an orientation to the protocol, and to advise on desired data for reporting. The DSMC will then meet annually in the trial implementation and data analysis periods of the study, or more frequently as requested by DSMB members.

The study team will produce interim analyses every year of the trial implementation period, or as requested by the DSMB. We currently anticipate reporting annually to the DSMB blinded data on IDH and mortality rates in each treatment arm. The study has no stopping rules.

15.5 STUDY RECORDS RETENTION

Data contained in the peer mentoring management system will be retained according to terms of PCORI contract: for a period of three (3) years from the a) Contract Term Date, b) date of the final payment under the UM-PCORI Contract, or c) conclusion of any audit or litigation related to the UM-PCORI Contract, whichever is later. All other data will be retained for seven years from the end of the study.

15.6 PROTOCOL DEVIATIONS

Because this is a pragmatic trial, interventions will be delivered as part of routine care, and the majority of data are collected routinely by hemodialysis facilities. Any deviations from or modifications to the protocol will be reported to the project manager who will then in return report it to IRB. Study coordinators will meet with the Operations Committee and Study Champion at each trial facility at regular intervals, and assess (as applicable, depending on site randomization) checklist completion rates, training implementation, and implementation of the patient activation intervention via tablet computer as patients dialyze (see Protocol). The Study

Coordinator at the National Kidney Foundation will communicate at regular intervals with peer mentors and participants as specified in the study protocol. During this time, they will discuss the progress of the study, and questions related to peer mentor training and support, and study reporting, frequency, duration and quality of peer mentor–mentee interaction using the peer mentoring management system where applicable will be discussed and assessed. The Study Coordinators, in each meeting with facility staff and peer mentors, will recapitulate and reinforce study procedures.

Protocol deviations that could occur would be the data of a patient who had opted out of the study mistakenly being sent to UM-KECC. This will be identified through spot audits conducted by the FMCNA Corporate Study Manager using the following process:

- A UM research study coordinator will develop a schedule to audit a random selection of 25% of clinics once during their 11-month study period. This is a total of 5 audits over the prospective study period.

- For each audit, a UMSI research study coordinator will select 25% of patient names and compare the records of patient opt outs contained on a worksheet in FMCNA's SharePoint computing environment. The Study Coordinator will compare the opt out Worksheet data with that clinic's Ancillary Order Report in the Electronic Health Record System from which study data transfers are generated. If discrepancies are found, the Corporate Study Manager will inform a UM Study Coordinator. If any patient who opted out is found to have an order, a 100% audit is triggered and the FMCNA Custom Reporting and Data Analytics group will be contacted to see if any data was sent to UM. If data were sent, the FMCNA Custom Reporting and Data Analytics group will notify UM-KECC to delete the data as of the date of opt out, using the FKC ID1 to identify the patient. If other errors are identified, further audits depending on type and frequency of errors will be done. Possible discrepancies:
  a) Patient who opted out has an Order,
  b) Patient who did not opt out does not have an Order,
  c) Order has a start date, stop date, or Patient Information Sheet date different from the Opt Out Worksheet

Note: this information is also found in the attached document entitled *Opt Out Process.*

16 PUBLICATION POLICY

Following completion of the study, the investigator is expected to publish the results of this research in a scientific journal. The International Committee of Medical Journal Editors (ICMJE) member journals have adopted a trials-registration policy as a condition for publication. This policy requires that all clinical trials be registered in a public trials registry such as *ClinicalTrials.gov**, which is sponsored by the National Library of Medicine. Other biomedical journals are considering adopting similar policies. The study's sponsor, the Patient-Centered Outcomes Research Institute (PCORI) requires that the Dialysafe be registered with ClinicalTrials.gov, and its results released on this site. The UM Principal Investigator is responsible for ensuring registration with ClinicalTrials.gov.

The ICMJE defines a clinical trial as any research project that prospectively assigns human subjects to intervention or comparison groups to study the cause-and-effect relationship between a medical intervention and a health outcome.

17 LITERATURE REFERENCES

1. Shekelle PG, Pronovost PJ, Wachter RM, Taylor SL, Dy SM, Foy R, et al. Advancing the science of patient safety. Ann Intern Med. 2011;154(10):693-6.
2. Medical Research Council. A Framework for Development and Evaluation of RCTs for Complex Interventions to Promote Health. London, UK: Medical Research Council; 2000. Available from: *http://www.mrc.ac.uk/Utilities/Documentrecord/index.htm?d=MRC003372*.
3. Shekelle PG, Pronovost PJ, Wachter RM, McDonald KM, Schoelles K, Dy SM, et al. The top patient safety strategies that can be encouraged for adoption now. Ann Intern Med. 2013;158(5 Pt 2):365-8.
4. Bergs J, Hellings J, Cleemput I, Zurel Ö, De Troyer V, Van Hiel M, et al. Systematic review and meta-analysis of the effect of the World Health Organization surgical safety checklist on postoperative complications. Br J Surg. 2014;101(3):150-8.
5. Hales BM, Pronovost PJ. The checklist—a tool for error management and performance improvement. Journal of critical care.21(3):231-5.
6. Pentland BT, Feldman MS. Organizational routines as a unit of analysis. Industrial and Corporate Change. 2005;14(5):793-815.
7. Lazaric N. Routines and routinization: an exploration of some micro-cognitive foundations. In: Becker MC, editor. Handbook of organizational routines. Northampton, MA: Edward Elgar; 2008. p. 205-27.
8. Roys E, Scholz N, Kalbfleisch J, Saran R, Chenoweth C, Hines SC, et al. Infection Rates for U.S. Dialysis Facilities: Comparing Sources. American Society of Nephrology Kidney Week; October 30-November 4, 2012; San Diego, CA2012.
9. Messana JM, Hines SC, Saran R, Kalbfleisch J, Spencer T, Frank KM, et al. Variation in Observed Infection Control Practices in the NOTICE Project. American Society of Nephrology Kidney Week; October 30-November 4, 2012; San Diego, CA2012.
10. Silver SA, Thomas A, Rathe A, Robinson P, Wald R, Harel Z, et al. Development of a hemodialysis safety checklist using a structured panel process. Canadian journal of kidney health and disease. 2015;2:5.
11. Borchard A, Schwappach DLB, Barbir A, Bezzola P. A systematic review of the effectiveness, compliance, and critical factors for implementation of safety checklists in surgery. Annals of Surgery. 2012;256(6):925-33.
12. Salas E, DiazGranados D, Klein C, Burke CS, Stagl KC, Goodwin GF, et al. Does team training improve team performance? A meta-analysis. Human factors. 2008;50(6):903-33.
13. Weaver SJ, Dy SM, Rosen MA. Team-training in healthcare: a narrative synthesis of the literature. BMJ Qual Saf. 2014;23(5):359-72.
14. Neily J, Mills PD, Young-Xu Y, Carney BT, West P, Berger DH, et al. Association between implementation of a medical team training program and surgical mortality. Jama. 2010;304(15):1693-700.
15. Allen LB, Tsao JCI, Hayes LP, Zeltzer LK. Peer mentorship to promote effective pain management in adolescents: study protocol for a randomised controlled trial. Trials [Electronic Resource]. 2011;12:132.
16. Dale JR, Williams SM, Bowyer V. What is the effect of peer support on diabetes outcomes in adults? A systematic review. Diabetic Medicine. 2012;29(11):1361-77.
17. Davey-Rothwell MA, Tobin K, Yang C, Sun CJ, Latkin CA. Results of a randomized controlled trial of a peer mentor HIV/STI prevention intervention for women over an 18 month follow-up. AIDS & Behavior. 2011;15(8):1654-63.
18. Erica P, June S, Stephanie B, Dylan S, George K, Richard S. Peer Mentoring: A Culturally Sensitive Approach to End-of-Life Planning for Long-Term Dialysis Patients. Am J Kidney Dis. 2005;46(1):111-9.

19. Haney A, Andrews A, Jenkins-Riley H, Chapman R, Yee J, Resnicow K. Poster presentation: Peer mentoring to increase deceased organ donation in end-stage renal disease patients through community partnerships. MICHR Community Engagement Symposium; April 25, 2012; Ann Arbor, MI2012.
20. Andrews A, Jenkins-Riley H, Haney A, Resnicow K, Yee J. Poster presentation: Peer mentoring to increase deceased organ donation in end-stage renal disease patients. National Kidney Foundation Spring Clinical Meeting; May 9-13, 2012; Washington, D.C.2012.
21. Coull AJ, Taylor VH, Elton R, Murdoch PS, Hargreaves AD. A randomised controlled trial of senior Lay Health Mentoring in older people with ischaemic heart disease: The Braveheart Project. Age and ageing. 2004;33(4):348-54.
22. Webel AR, Okonsky J, Trompeta J, Holzemer WL. A systematic review of the effectiveness of peer-based interventions on health-related behaviors in adults. American journal of public health. 2010;100(2):247-53.
23. Long JA, Jahnle EC, Richardson DM, Loewenstein G, Volpp KG. Peer mentoring and financial incentives to improve glucose control in African American veterans: a randomized trial. Ann Intern Med. 2012;156(6):416-24.
24. Dale J, Caramlau IO, Lindenmeyer A, Williams SM. Peer support telephone calls for improving health. Cochrane Database Syst Rev. 2008(4):CD006903.
25. Parry M, Watt-Watson J. Peer support intervention trials for individuals with heart disease: a systematic review. Eur J Cardiovasc Nurs. 2010;9(1):57-67.
26. Ricci-Cabello I, Ruiz-Pérez I, Rojas-García A, Pastor G, Rodríguez-Barranco M, Gonçalves DC. Characteristics and effectiveness of diabetes self-management educational programs targeted to racial/ethnic minority groups: A systematic review, meta-analysis and meta-regression. BMC Endocr Disord. 2014;14.
27. U.S. Renal Data System. USRDS 2012 Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States. Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 2012 February 15, 2013]. Available from: *http://www.usrds.org/atlas.aspx*.
28. Veterans' Health Administration. Consumer demand for clinical quality: The giant awakens. Irving, TX: Veterans' Health Administration; 2001.
29. Entwistle V. Nursing shortages and patient safety problems in hospital care: is clinical monitoring by families part of the solution? Health Expect. 2004;7(1):1-5.
30. Lyons M. Should patients have a role in patient safety? A safety engineering view. Qual Saf Health Care. 2007;16(2):140-2.
31. Small N, Blickem C, Blakeman T, Panagioti M, Chew-Graham CA, Bower P. Telephone based self-management support by 'lay health workers' and 'peer support workers' to prevent and manage vascular diseases: a systematic review and meta-analysis. BMC Health Serv Res. 2013;13:533.
32. Kochanek KD, Xu J, Murphy SL, Minino AM, Kung HC. Deaths: final data for 2009. National vital statistics reports : from the Centers for Disease Control and Prevention, National Center for Health Statistics, National Vital Statistics System. 2011;60(3):1-116.
33. Heron. Preliminary data for 2011. National Vital Statistics Reports. 2013;61(6):1-65.
34. U.S. Renal Data System. 2014 Annual Data Report, Volume Two: End-Stage Renal Disease in the United States. Ann Arbor, MI: USRDS; 2015.
35. United States Renal Data System (USRDS). The 2018 USRDS Annual Data Report (ADR) Ann Arbor, MI: United States Renal Data System; 2018 [December 20, 2018]. Available from: *https://www.usrds.org/adr.aspx*.
36. Gilbertson DT, Solid C, Collins AJ, editors. A Comparison of Projected ESRD Incidence and Prevalence with Recent Data. American Society of Nephrology Kidney Week 2011.

37. Foley RN, Parfrey PS, Sarnak MJ. Epidemiology of cardiovascular disease in chronic renal disease. Journal of the American Society of Nephrology. 1998;9(12 Suppl):S16-23.
38. Green D, Roberts PR, New DI, Kalra PA. Sudden cardiac death in hemodialysis patients: an in-depth review. Am J Kidney Dis. 2011;57(6):921-9.
39. Unruh ML, Weisbord SD, Kimmel PL. Psychosocial factors in patients with chronic kidney disease: Health-related quality of life in nephrology research and clinical practice. Seminars in Dialysis. 2005;18(2):82-90.
40. Caplin B, Kumar S, Davenport A. Patients' perspective of haemodialysis-associated symptoms. Nephrology Dialysis Transplantation. 2011;26(8):2656-63.
41. Kimmel PL, Cohen SD, Weisbord SD. Quality of life in patients with end-stage renal disease treated with hemodialysis: survival is not enough! J Nephrol. 2008;21 Suppl 13:S54-8.
42. Kimmel PL, Cukor D, Cohen SD, Peterson RA. Depression in end-stage renal disease patients: a critical review. Adv Chronic Kidney Dis. 2007;14(4):328-34.
43. Kimmel PL. Psychosocial factors in dialysis patients. Kidney Int. 2001;59(4):1599-613.
44. U.S. Renal Data System. 2013 Annual Data Report, Volume Two: Atlas of End-Stage Renal Disease in the United States. Ann Arbor, MI: USRDS; 2013.
45. Santoro A, Mancini E, Basile C, Amoroso L, Di Giulio S, Usberti M, et al. Blood volume controlled hemodialysis in hypotension-prone patients: a randomized, multicenter controlled trial. Kidney Int. 2002;62(3):1034-45.
46. Kooman JP, Moret K, van der Sande FM, Gerlag PG, van den Wall Bake AW, Leunissen KM. Preventing dialysis hypotension: a comparison of usual protective maneuvers. Kidney Int. 2001;60(2):802-3.
47. Shoji T, Tsubakihara Y, Fujii M, Imai E. Hemodialysis-associated hypotension as an independent risk factor for two-year mortality in hemodialysis patients. Kidney International. 2004;66(3):1212-20.
48. Sands JJ, Usvyat LA, Sullivan T, Segal JH, Zabetakis P, Kotanko P, et al. Intradialytic hypotension: frequency, sources of variation and correlation with clinical outcome. Hemodial Int. 2014;18(2):415-22.
49. Hayes W, Hothi DK. Intradialytic hypotension. Pediatr Nephrol. 2011;26(6):867-79.
50. Twardowski ZJ. Treatment time and ultrafiltration rate are more important in dialysis prescription than small molecule clearance. Blood Purif. 2007;25(1):90-8.
51. Karnik JA, Young BS, Lew NL, Herget M, Dubinsky C, Lazarus JM, et al. Cardiac arrest and sudden death in dialysis units. Kidney International. 2001;60(1):350-7.
52. Pun PH, Lehrich RW, Honeycutt EF, Herzog CA, Middleton JP. Modifiable risk factors associated with sudden cardiac arrest within hemodialysis clinics. Kidney International. 2011;79(2):218-27.
53. Pun PH, Lehrich RW, Smith SR, Middleton JP. Predictors of Survival after Cardiac Arrest in Outpatient Hemodialysis Clinics. Clinical Journal of the American Society of Nephrology. 2007;2(3):491-500.
54. Usyvat DPKaDL. In: Saran DR, editor. July 2013.
55. McIntyre CW. Haemodialysis-induced myocardial stunning in chronic kidney disease - a new aspect of cardiovascular disease. Blood Purification. 2010;29(2):105-10.
56. Burton JO, Jefferies HJ, Selby NM, McIntyre CW. Hemodialysis-induced repetitive myocardial injury results in global and segmental reduction in systolic cardiac function. Clinical Journal of The American Society of Nephrology: CJASN. 2009;4(12):1925-31.
57. Burton JO, Jefferies HJ, Selby NM, McIntyre CW. Hemodialysis-induced cardiac injury: determinants and associated outcomes. Clinical Journal of The American Society of Nephrology: CJASN. 2009;4(5):914-20.
58. Eldehni MT, McIntyre CW. Are there neurological consequences of recurrent intradialytic hypotension? Semin Dial. 2012;25(3):253-6.

59. Sands J, Usyvat L, Sullivan T, Zabetakis P, Kotanko P, Maddux FW. Intradialytic Hypotension (IH): An important predictor of patient mortality and hospitalizations. 33rd Annual Dialysis Conference; March 10-12, 2013; Seattle, WA2013.
60. Saran R, Bragg-Gresham JL, Levin NW, Twardowski ZJ, Wizemann V, Saito A, et al. Longer treatment time and slower ultrafiltration in hemodialysis: associations with reduced mortality in the DOPPS. Kidney Int. 2006;69(7):1222-8.
61. Zhang H, Schaubel DE, Kalbfleisch JD, Bragg-Gresham JL, Robinson BM, Pisoni RL, et al. Dialysis outcomes and analysis of practice patterns suggests the dialysis schedule affects day-of-week mortality. Kidney Int. 2012;81(11):1108-15.
62. Gordon EJ, Leon JB, Sehgal AR. Why are hemodialysis treatments shortened and skipped? Development of a taxonomy and relationship to patient subgroups... including commentary by Hoffart N with author response. Nephrology Nursing Journal. 2003;30(2):209-18.
63. Renal Physicians Association. Health and safety survey to improve patient safety in end stage renal disease: Report of findings from the ESRD patient survey Rockville, MD: Renal Physicians Association; 2007 [February 25, 2013]. Available from: *http://www.kidneypatientsafety.org/uploadedFiles/HSS%20Patient%20Survey%20Report_FNL_3-21-07.pdf?n=448*.
64. Lin N. Social capital: A theory of structure and action. Cambridge, MA: Cambridge University Press; 2001.
65. Jepson R. Protect your patient from dialysis hypotension. Nursing. 2009;39(11):55-6.
66. Lindberg M, Ludvigsen MS. Ultrafiltration rate as a nursing-sensitive quality indicator in haemodialysis. International Journal of Nursing Studies. 2012;49(10):1320-4.
67. Weiner DE, Brunelli SM, Hunt A, Schiller B, Glassock R, Maddux FW, et al. Improving clinical outcomes among hemodialysis patients: a proposal for a "volume first" approach from the chief medical officers of US dialysis providers. Am J Kidney Dis. 2014;64(5):685-95.
68. Kohn LT, Corrigan J, Donaldson MS, Institute of M. To err is human building a safer health system. Washington, DC: National Academy Press; 2000.
69. Pronovost P, Needham D, Berenholtz S, Sinopoli D, Chu H, Cosgrove S, et al. An intervention to decrease catheter-related bloodstream infections in the ICU. N Engl J Med. 2006;355(26):2725-32.
70. Pronovost PJ, Goeschel CA, Colantuoni E, Watson S, Lubomski LH, Berenholtz SM, et al. Sustaining reductions in catheter related bloodstream infections in Michigan intensive care units: observational study. BMJ. 2010;340:c309.
71. Malpiedi P, Peterson K, Soe M, al. e. National and State Healthcare-Associated Infection Standardized Infection Ratio Report. Atlanta, GA: Centers for Disease Control and Prevention; 2011. Available from: *http://www.cdc.gov/hai/national-annual-sir/index.html*.
72. Borchard A, Schwappach DL, Barbir A, Bezzola P. A systematic review of the effectiveness, compliance, and critical factors for implementation of safety checklists in surgery. Ann Surg. 2012;256(6):925-33.
73. Jain R, Kralovic SM, Evans ME, Ambrose M, Simbartl LA, Obrosky DS, et al. Veterans Affairs initiative to prevent methicillin-resistant Staphylococcus aureus infections. N Engl J Med. 2011;364(15):1419-30.
74. Lorincz C, E D, PE S, al. e. Research in Ambulatory Patient Safety 2000-2010: A Ten Year Review Chicago, IL: American Medical Association Center for Patient Safety, 2011.
75. United Kingdom. Department of Health. Creating a Patient-Led NHS: Delivering the NHS Improvement Plan. London, UK: Department of Health; 2005.
76. Spath P. Partnering with patients to reduce medical errors. Chicago: Health Forum; 2004. xxiv, 198 p. p.

77. Joint Commission on Accreditation of Health Care Organizations. Speak Up: Help Prevent Errors in Your Care (Hospital Brochure) Chicago, IL: JCAHO; 2003 [August 10, 2013]. Available from: *http://www.jointcommission.org/assets/1/6/speakup.pdf*.
78. Berger Z, Flickinger T, Dy S. Promoting Engagement by Patients and Families To Reduce Adverse Events. Making Health Care Safer II: An Updated Critical Analysis of the Evidence for Patient Safety Practices. Evidence Report/Technology Assessment. Number 211 ed. Rockville, MD: Agency for Healthcare Research and Quality; 2013. p. 351-61, C-69-C-75, D-193-D-214.
79. Kuo P-Y, Saran R, Argentina M, Heung M, Gillespie B, Bragg-Gresham J, et al. Cramping, Crashing, Cannulating, and Clotting: A Qualitative Study of Patients' Definitions of a "Bad Run" on Hemodialysis. Clinician Journal of the American Society of Nephrology. under review.
80. Stefansson BV, Brunelli SM, Cabrera C, Rosenbaum D, Anum E, Ramakrishnan K, et al. Intradialytic hypotension and risk of cardiovascular disease. Clin J Am Soc Nephrol. 2014;9(12):2124-32.
81. Flythe JE, Katsanos SL, Hu Y, Kshirsagar AV, Falk RJ, Moore CR. Predictors of 30-Day Hospital Readmission among Maintenance Hemodialysis Patients: A Hospital's Perspective. Clin J Am Soc Nephrol. 2016;11(6):1005-14.
82. Flythe JE, Xue H, Lynch KE, Curhan GC, Brunelli SM. Association of mortality risk with various definitions of intradialytic hypotension. J Am Soc Nephrol. 2015;26(3):724-34.
83. Yu J, Liu Z, Shen B, Teng J, Zou J, Ding X. Intradialytic Hypotension as an Independent Risk Factor for Long-Term Mortality in Maintaining Hemodialysis Patients: A 5-Year Follow-Up Cohort Study. Blood Purif. 2018;45(4):320-6.
84. Chou JA, Streja E, Nguyen DV, Rhee CM, Obi Y, Inrig JK, et al. Intradialytic hypotension, blood pressure changes and mortality risk in incident hemodialysis patients. Nephrol Dial Transplant. 2018;33(1):149-59.
85. Urquhart-Secord R, Craig JC, Hemmelgarn B, Tam-Tham H, Manns B, Howell M, et al. Patient and Caregiver Priorities for Outcomes in Hemodialysis: An International Nominal Group Technique Study. Am J Kidney Dis. 2016;68(3):444-54.
86. Santos SFF, Peixoto AJ, Perazella MA. How should we manage adverse intradialytic blood pressure changes? Advances in Chronic Kidney Disease. 2012;19(3):158-65.
87. Parker TF, Straube BM, Nissenson A, Hakim RM, Steinman TI, Glassock RJ. Dialysis at a Crossroads—Part II: A Call for Action. Clinical Journal of the American Society of Nephrology. 2012;7(6):1026-32.
88. Parker T, Hakim R, Nissenson AR, Steinman T, Glassock RJ. Dialysis at a Crossroads: 50 Years Later. Clinical Journal of the American Society of Nephrology. 2011;6(2):457-61.
89. Agarwal R, Weir MR. Dry-weight: a concept revisited in an effort to avoid medication-directed approaches for blood pressure control in hemodialysis patients. Clin J Am Soc Nephrol. 2010;5(7):1255-60.
90. Hecking M, Karaboyas A, Antlanger M, Saran R, Wizemann V, Chazot C, et al. Significance of Interdialytic Weight Gain versus Chronic Volume Overload: Consensus Opinion. Am J Nephrol. 2013;38(1):78-90.
91. Usyvat L, Sullivan T, Zabetakis P, Kotanko P, Maddux FW, Diaz-Buxo J. Intradialytic Hypotension (IH): Variation in Dialysis Facilities. 33rd Annual Dialysis Conference; March 10-12, 2013; Seattle, WA2013.
92. Saran R, Bragg-Gresham JL, Rayner HC, Goodkin DA, Keen ML, Van Dijk PC, et al. Nonadherence in hemodialysis: associations with mortality, hospitalization, and practice patterns in the DOPPS. Kidney Int. 2003;64(1):254-62.
93. Movilli E, Gaggia P, Zubani R, Camerini C, Vizzardi V, Parrinello G, et al. Association between high ultrafiltration rates and mortality in uraemic patients on regular haemodialysis. A 5-year prospective observational multicentre study. Nephrology, Dialysis, Transplantation. 2007;22(12):3547-52.

94. Flythe JE, Brunelli SM. The risks of high ultrafiltration rate in chronic hemodialysis: implications for patient care. Seminars in Dialysis. 2011;24(3):259-65.
95. Flythe JE, Curhan GC, Brunelli SM. Shorter length dialysis sessions are associated with increased mortality, independent of body weight. Kidney Int. 2013;83(1):104-13.
96. Kalantar-Zadeh K, Amin AN. Toward more accurate detection and risk stratification of chronic kidney disease. JAMA. 2012;307(18):1976-7.
97. Bandura A. Self-efficacy: the exercise of control. New York: W.H. Freeman; 1997. ix, 604 p. p.
98. Bandura A. Social foundations of thought and action: a social cognitive theory. Englewood Cliffs, N.J.: Prentice-Hall; 1986. xiii, 617 p. p.
99. Bandura A. Social cognitive theory of self-regulation. Organizational Behavior and Human Decision Processes. 1991;50(2):248-87.
100. Turner G, Shepherd J. A method in search of a theory: peer education and health promotion. Health Education Research. 1999;14(2):235-47.
101. Simoni JM, Franks JC, Lehavot K, Yard SS. Peer Interventions to Promote Health: Conceptual Considerations. American Journal of Orthopsychiatry. 2011;81(3):351-9.
102. Miller WR, Rollnick S. Motivational interviewing: helping people change. New York, NY: Guilford Press; 2013. xii, 482 p. p.
103. Gao X, Man Lo EC, Ching Ching Kot S, Wai Chan KC. Motivational Interviewing in Improving Oral Health: A Systematic Review of Randomized Controlled Trials. J Periodontol. 2013.
104. Mathes T, Pieper D, Antoine SL, Eikermann M. Adherence-enhancing interventions for highly active antiretroviral therapy in HIV-infected patients - a systematic review. HIV Med. 2013.
105. Vanbuskirk KA, Wetherell JL. Motivational interviewing with primary care populations: a systematic review and meta-analysis. J Behav Med. 2013.
106. Witt DR, Lindquist R, Treat-Jacobson D, Boucher JL, Konety SH, Savik K. Motivational Interviewing to Reduce Cardiovascular Risk in African American and Latina Women. West J Nurs Res. 2013.
107. Dale J, Caramlau I, Docherty A, Sturt J, Hearnshaw H. Telecare motivational interviewing for diabetes patient education and support: a randomised controlled trial based in primary care comparing nurse and peer supporter delivery. Trials. 2007;8:18.
108. Noordman J, van der Weijden T, van Dulmen S. Communication-related behavior change techniques used in face-to-face lifestyle interventions in primary care: a systematic review of the literature. Patient Educ Couns. 2012;89(2):227-44.
109. Embuldeniya G, Veinot P, Bell E, Bell M, Nyhof-Young J, Sale JEM, et al. The experience and impact of chronic disease peer support interventions: A qualitative synthesis. Patient Education and Counseling. 2013;92(1):3-12.
110. Durantini MR, Albarracín D, Mitchell AL, Earl AN, Gillette JC. Conceptualizing the influence of social agents of behavior change: A meta-analysis of the effectiveness of HIV-prevention interventionists for different groups. Psychological Bulletin. 2006;132(2):212-48.
111. Dennis CL, Hodnett E, Kenton L, Weston J, Zupancic J, Stewart DE, et al. Effect of peer support on prevention of postnatal depression among high risk women: multisite randomised controlled trial. BMJ. 2009;338:a3064.
112. Perkins MB, Jensen PS, Jaccard J, Gollwitzer P, Oettingen G, Pappadopulos E, et al. Applying theory-driven approaches to understanding and modifying clinicians' behavior: what do we know? Psychiatr Serv. 2007;58(3):342-8.
113. Godin G, Belanger-Gravel A, Eccles M, Grimshaw J. Healthcare professionals' intentions and behaviours: a systematic review of studies based on social cognitive theories. Implement Sci. 2008;3:36.

114. Mascherek AC, Schwappach DLB, Bezzola P. Frequency of use and knowledge of the WHO-surgical checklist in Swiss hospitals: A cross-sectional online survey. Patient Saf Surg. 2013;7(1).
115. Ajzen I. Attitudes, personality, and behavior: McGraw-Hill International; 2005.
116. Ajzen I. The theory of planned behavior. Organizational Behavior and Human Decision Processes. 1991;50(2):179-211.
117. Thorpe KE, Zwarenstein M, Oxman AD, Treweek S, Furberg CD, Altman DG, et al. A pragmatic–explanatory continuum indicator summary (PRECIS): a tool to help trial designers. Journal of Clinical Epidemiology.62(5):464-75.
118. Patient-Centered Outcomes Research Institute. The PCORI Methodology Report Appendix A: Methodology Standards. Washington, DC: Patient-Centered Outcomes Research Institute, 2013.
119. Long JA. "Buddy system" of peer mentors may help control diabetes. LDI Issue Brief. 2012;17(6):1-4.
120. Ljungberg I, Kroll T, Libin A, Gordon S. Using peer mentoring for people with spinal cord injury to enhance self-efficacy beliefs and prevent medical complications. Journal of Clinical Nursing. 2011;20(3-4):351-8.
121. Sledge WH, Lawless M, Sells D, Wieland M, O'Connell MJ, Davidson L. Effectiveness of peer support in reducing readmissions of persons with multiple psychiatric hospitalizations. Psychiatric Services. 2011;62(5):541-4.
122. Veinot TC, Meadowbrooke CC, Newman MW, Zheng K, Perry EE, editors. Routines That Ease the Pain: The Information World of a Dialysis Clinic. American Society for Information Science & Technology Annual Conference; 2010 Nov 8-11, 2009; Pittsburgh, PA: American Society for Information Science & Technology.
123. Meredith DJ, Pugh CW, Sutherland S, Tarassenko L, Birks J. The relationship between symptoms and blood pressure during maintenance hemodialysis. Hemodialysis International International Symposium on Home Hemodialysis. 2015;19(4):543-52.
124. MacEwen C, Sutherland S, Daly J, Pugh C, Tarassenko L. Relationship between Hypotension and Cerebral Ischemia during Hemodialysis. J Am Soc Nephrol. 2017;28(8):2511-20.
125. Saran R, Bragg-Gresham JL, Rayner HC, Goodkin DA, Keen ML, Van Dijk PC, et al. Nonadherence in hemodialysis: Associations with mortality, hospitalization, and practice patterns in the DOPPS. Kidney Int. 2003;64(1):254-62.
126. Rayner HC, Zepel L, Fuller DS, Morgenstern H, Karaboyas A, Culleton BF, et al. Recovery time, quality of life, and mortality in hemodialysis patients: the Dialysis Outcomes and Practice Patterns Study (DOPPS). Am J Kidney Dis. 2014;64(1):86-94.
127. United States. Department of Health and Human Services. Food and Drug Administration. Guidance for industry: patient-reported outcome measures: use in medical product development to support labeling claims: draft guidance. Health and quality of life outcomes. 2006;4:79.
128. Hays RD, Kallich JD, Mapes DL, Coons SJ, Carter WB. Development of the Kidney Disease Quality of Life (KDQOLTM) Instrument. Quality of Life Research. 1994;3(5):329-38.
129. Hays RD, Kallich JD, Mapes DL, Coons SJ, Amin N, Carter WB, et al. Kidney Disease Quality of Life Short Form (KDQOL-SF), Version 1.3: A Manual for Use and Scoring. Washington, DC: RAND, 1997.
130. Naik N, Hess R, Unruh M. Measurement of Health-Related Quality of Life in the Care of Patients with ESRD: Isn't This the Metric That Matters? Semin Dial. 2012;25(4):439-44.
131. Smith K, Coston M, Glock K, Elasy TA, Wallston KA, Ikizler TA, et al. Patient Perspectives on Fluid Management in Chronic Hemodialysis. Journal of renal nutrition : the official journal of the Council on Renal Nutrition of the National Kidney Foundation. 2010;20(5):334-41.

132. Arneson TJ, Liu J, Qiu Y, Gilbertson DT, Foley RN, Collins AJ. Hospital Treatment for Fluid Overload in the Medicare Hemodialysis Population. Clinical Journal of the American Society of Nephrology : CJASN. 2010;5(6):1054-63.
133. Magnus L, Björn W, Per L. A behavioural nursing intervention for reduced fluid overload in haemodialysis patients. Initial results of acceptability, feasibility and efficacy. Journal of Nursing and Healthcare of Chronic Illness. 2011;3(2):87-98.
134. Kimmel PL, Varela MP, Peterson RA, Weihs KL, Simmens SJ, Alleyne S, et al. Interdialytic weight gain and survival in hemodialysis patients: effects of duration of ESRD and diabetes mellitus. Kidney Int. 2000;57(3):1141-51.
135. Kalantar-Zadeh K, Regidor DL, Kovesdy CP, Van Wyck D, Bunnapradist S, Horwich TB, et al. Fluid retention is associated with cardiovascular mortality in patients undergoing long-term hemodialysis. Circulation. 2009;119(5):671-9.
136. Tong A, Sainsbury P, Carter SM, Hall B, Harris DC, Walker RG, et al. Patients' priorities for health research: Focus group study of patients with chronic kidney disease. Nephrology Dialysis Transplantation. 2008;23(10):3206-14.
137. Evangelidis N, Tong A, Manns B, Hemmelgarn B, Wheeler DC, Tugwell P, et al. Developing a Set of Core Outcomes for Trials in Hemodialysis: An International Delphi Survey. Am J Kidney Dis. 2017;70(4):464-75.
138. Patient-Centered Outcomes Research Institute. Patient-Centered Outcomes Research Washington, DC: PCORI; 2013 [June 29, 2018]. Available from: *https://www.pcori.org/research-results/patient-centered-outcomes-research*.
139. Danquah FV, Wasserman J, Meininger J, Bergstrom N. Quality of life measures for patients on hemodialysis: a review of psychometric properties. Nephrol Nurs J. 2010;37(3):255-69; quiz 70.
140. Mapes DL, Lopes AA, Satayathum S, McCullough KP, Goodkin DA, Locatelli F, et al. Health-related quality of life as a predictor of mortality and hospitalization: The Dialysis Outcomes and Practice Patterns Study (DOPPS). Kidney Int. 2003;64(1):339-49.
141. Kimmel PL, Peterson RA, Weihs KL, Simmens SJ, Alleyne S, Cruz I, et al. Psychosocial factors, behavioral compliance and survival in urban hemodialysis patients. Kidney Int. 1998;54(1):245-54.
142. Hayes RJ, Moulton LH. Cluster randomised trials. Boca Raton, FL: CRC Press; 2009.
143. Cals JWL, Butler CC, Hopstaken RM, Hood K, Dinant G-J. Effect of point of care testing for C reactive protein and training in communication skills on antibiotic use in lower respiratory tract infections: cluster randomised trial2009 2009-05-05 11:12:15.
144. Torgerson DJ. Contamination in trials: is cluster randomisation the answer? Bmj. 2001;322(7282):355-7.
145. Piantadosi S. Chapter 19: Factorial Designs Clinical trials: a methodologic perspective. Hoboken, N.J.: Wiley-Interscience; 2005. p. 501-14.
146. Montgomery AA, Astin MP, Peters TJ. Reporting of factorial trials of complex interventions in community settings: a systematic review. Trials. 2011;12:179.
147. Thomassen O, Storesund A, Softeland E, Brattebo G. The effects of safety checklists in medicine: a systematic review. Acta Anaesthesiol Scand. 2014;58(1):5-18.
148. Ford I, Norrie J. Pragmatic Trials. New England Journal of Medicine. 2016;375(5):454-63.
149. Brown CA, Lilford RJ. The stepped wedge trial design: a systematic review. BMC Med Res Methodol. 2006;6:54.
150. Abraham C, Michie S. A taxonomy of behavior change techniques used in interventions. Health Psychol. 2008;27(3):379-87.
151. Williams RM, Bambara J, Turner AP. A Scoping Study of One-to-One Peer Mentorship Interventions and Recommendations for Application With Veterans With Postdeployment

Syndrome. The Journal of Head Trauma Rehabilitation. 2012;27(4):261-73 10.1097/HTR.0b013e3182585cb6.
152. Alspach JG. Weighing the evidence on patient safety: Strategies to implement now. Crit Care Nurs. 2013;33(3):9-12.
153. Reese PP, Mgbako O, Mussell A, Potluri V, Yekta Z, Levsky S, et al. A Pilot Randomized Trial of Financial Incentives or Coaching to Lower Serum Phosphorus in Dialysis Patients. Journal of Renal Nutrition.
154. Simmons D, Prevost AT, Bunn C, Holman D, Parker RA, Cohn S, et al. Impact of Community Based Peer Support in Type 2 Diabetes: A Cluster Randomised Controlled Trial of Individual and/or Group Approaches. PloS one. 2015;10(3):e0120277.
155. Linda Lindsey D, Broome ME, Cox RP. Maximizing retention in community-based clinical trials. Journal of Nursing Scholarship. 2002;34(1):47-53.
156. Robinson KA, Dennison CR, Wayman DM, Pronovost PJ, Needham DM. Systematic review identifies number of strategies important for retaining study participants. J Clin Epidemiol. 2007;60(8):757-65.
157. Mody L, Miller DK, McGloin JM, Freeman M, Marcantonio ER, Magaziner J, et al. Recruitment and Retention of Older Adults in Aging Research. Journal of the American Geriatrics Society. 2008;56(12):2340-8.
158. McNeely EA, Clements SD. Recruitment and Retention of the Older Adult into Research Studies. J Neurosci Nurs. 1994;26(1):57-61.
159. Steinhauser KE, Clipp EC, Hays JC, Olsen M, Arnold R, Christakis NA, et al. Identifying, recruiting, and retaining seriously-ill patients and their caregivers in longitudinal research. Palliat Med. 2006;20(8):745-54.
160. Little RJA, Rubin DB. Statistical analysis with missing data. Hoboken, N.J.: Wiley; 2002. xv, 381 p. p.
161. Emerson RM, Fretz RI, Shaw LL. Writing ethnographic fieldnotes. Chicago: University of Chicago Press; 2011.
162. Perlman RL, Finkelstein FO, Liu L, Roys E, Kiser M, Eisele G, et al. Quality of life in chronic kidney disease (CKD): a cross-sectional analysis in the Renal Research Institute-CKD study. Am J Kidney Dis. 2005;45(4):658-66.
163. Norris K, Nissenson A. Racial disparities in chronic kidney disease: tragedy, opportunity, or both? Clinical Journal of the American Society of Nephrology. 2008;3(2):314-6.
164. Hall YN, Choi AI, Chertow GM, Bindman AB. Chronic kidney disease in the urban poor. Clinical Journal of the American Society of Nephrology. 2010;5(5):828–35.

SUPPLEMENTS/APPENDICES

Supplements and Protocol Appendices

- *Data Assessment and Flow (section 44 of IRB application)*
    - *Implementation Assessment Plan*
    - *Patient Data Flow: Plan for Linking Peer Mentoring Records to UM-KECC Patient Data*
    - *Data Flow Diagram*
- *Consent Process*

- *Opt out process*
- *Informed Consent Document*
- *Patient Information Sheet distribution script*
- *Script for UM Study Coordinator to use when calling patients to offer them Peer Mentoring*
- *Help Line Scripts*

- *Staff Incentive Plan for Checklist completion*
- *Data elements list*
- *Executed Data Use agreement/Business Associate Agreement*
- *Surveys*
  - *Peer Mentee Satisfaction Survey*
  - *Peer Mentor Satisfaction Survey*
  - *Practice Patterns Survey - Medical Directors*
  - *Practice Patterns Survey - Nurse Managers*

Related Documents

- *HIPAA Compliance of Dialysafe Tools*
- *Study Intervention Materials*
  - *Patient activation intervention materials*
    - *Patient Story Videos (by peer mentoring session; uploaded separately in IRB application per instructions)*
    - *Patient Education Sessions 1-5 (section 44 of IRB application)*
  - *Peer Mentor Training (section 44 of IRB application)*
    - *Dialysafe Peer Mentor Emergency Procedures*
    - *Peer Mentor Training Fidelity Checklist*
    - *Peer mentoring fidelity checklists*
  - *Provider intervention materials (section 44 of IRB application)*
    - *Staff training modules, parts 1-4*
    - *Provider Educational Intervention Advanced Practitioners (Physician, NP and PA training modules)*
    - *Provider training fidelity checklists*
    - *Checklist Application Overview*
- *Schedule of Events*

1. Murphy SL, Kochanek KD, Xu J, et al. Mortality in the United States, 2020. National Center for Health Statistics Data Brief. 2021;427.
2. United States Renal Data System (USRDS). The 2021 USRDS Annual Data Report (ADR) Available: https://adr.usrds.org/2021. Accessed February 28, 2022.
3. Gilbertson DT, Solid C, Collins AJ. A Comparison of Projected ESRD Incidence and Prevalence with Recent Data. American Society of Nephrology Kidney Week 2011.
4. Foley RN, Parfrey PS, Sarnak MJ. Epidemiology of cardiovascular disease in chronic renal disease. Journal of the American Society of Nephrology. 1998;9(12 Suppl):S16-23.
5. Green D, Roberts PR, New DI, et al. Sudden cardiac death in hemodialysis patients: an in-depth review. Am J Kidney Dis. 2011;57(6):921-929.
6. Unruh ML, Weisbord SD, Kimmel PL. Psychosocial factors in patients with chronic kidney disease: Health-related quality of life in nephrology research and clinical practice. Seminars in Dialysis. 2005;18(2):82-90.
7. Caplin B, Kumar S, Davenport A. Patients' perspective of haemodialysis-associated symptoms. Nephrology Dialysis Transplantation. 2011;26(8):2656-2663.
8. Kimmel PL, Cohen SD, Weisbord SD. Quality of life in patients with end-stage renal disease treated with hemodialysis: survival is not enough! J Nephrol. 2008;21 Suppl 13:S54-58.
9. Kimmel PL, Cukor D, Cohen SD, et al. Depression in end-stage renal disease patients: a critical review. Adv Chronic Kidney Dis. 2007;14(4):328-334.
10. Kimmel PL. Psychosocial factors in dialysis patients. Kidney Int. 2001;59(4):1599-1613.