An Effectiveness-Implementation Trial of SPIRIT in ESRD (Short title: SPIRIT Trial)

National Clinical Trial (NCT) Identified Number: NCT031385464

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Summary of Changes from Previous Version:

Affected Section(s)	Summary of Revisions Made	Rationale
4.2 Scientific Rationale for Study Design 5.1 Inclusion Criteria 5.5 Recruitment 10.1.1.2 Conflict of Interest Policy	Inclusion of a new recruitment site.	Expanding recruitment locations to meet target sample size.

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STATEMENT OF COMPLIANCE

The trial will be carried out in accordance with International Conference on Harmonisation Good Clinical Practice (ICH GCP) and 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, 21 CFR Part 312, and/or 21 CFR Part 812)

  National Institutes of Health (NIH)-funded investigators and clinical trial site staff who are responsible for the conduct, management, or oversight of NIH-funded clinical trials have completed Human Subjects Protection and ICH GCP Training.

  The protocol, informed consent form(s), recruitment materials, and all participant materials have been approved by the Institutional Review Board (IRB) at:

  Emory (Study No.: IRB0094859; approved on 3/3/2017)
  University of New Mexico (Study No: 17-357 approved on 10-27.17)
  University of Pittsburgh (Study No.: PRO07070106; approved on 09/08/17)
  University of North Carolina at Chapel Hill (Study #: 17-1295; approved on 7/28/2017)

  RRI Carolina Dialysis approval (08/03/2017)
  FMC approval 4.1.18
  DCI approval & IRBAA 1.22.18

  Any amendment to the protocol requires review and approval by the IRB before the changes are implemented to the study. In addition, all changes to the consent form will be IRB-approved.

1 PROTOCOL SUMMARY

1.1 SYNOPSIS

Title: An Effectiveness-Implementation Trial of SPIRIT in ESRD

Study Description: This multicenter, clinic-level cluster randomized trial will evaluate the effectiveness of SPIRIT, an advance care planning (ACP) intervention, delivered by dialysis care providers as part of routine care in free-standing outpatient dialysis clinics compared to usual care. Simultaneously, we will evaluate the implementation of SPIRIT, including its sustainability.

Objectives:

Primary Aim 1. Examine the effectiveness of SPIRIT compared to usual care on preparedness outcomes for end-of-life decision making (defined as dyad congruence on goals of care, patient decisional conflict, and surrogate decision-making confidence) at 2 weeks post-intervention

Aim 2. Evaluate the process outcomes of SPIRIT implementation: acceptability, fidelity, intervention costs, and sustainability during the initial and delayed implementation of SPIRIT (Descriptive aim to generate data for translation)

Aim 3. Examine the effectiveness of SPIRIT and usual care on surrogates' post-bereavement distress (anxiety, depression, and post-traumatic distress symptoms) at 3 months after the patient's death

Aim 4 (exploratory): Examine the effectiveness of SPIRIT and usual care on end-of-life treatment intensity (healthcare utilization; percentages of patients hospitalized, having ICU admission, and having intensive procedures and length of hospital stay) during the final month of life

In a supplement study, we will pilot test SPIRIT adapted for patients with ESRD plus dementia as a model for determining whether patients with dementia superimposed on complex multimorbidity can fully participate in an advance care planning discussion.

Supplement Aim 1. Estimate the effects of the SPIRIT-dementia intervention on 1) the preparedness outcomes 2-3 days post intervention, 2) care decisions assessed at 6 months post intervention or the patient's death.

Supplement Aim 2. Estimate the effects of the SPIRIT-dementia intervention on surrogates' post-bereavement distress at 1 months after the patient's death.

Supplement Aim 3. Explore the relationships among patients' cognitive status, decision-making capacity and their ability to express end-of-life wishes.

A new supplement study is a longitudinal cohort study leveraging the parent study. The objective is to assess the effect of the pandemic on the stability of end-of-life care preferences and on our key outcomes (dyad congruence on goals of care, patient decisional conflict, and surrogate decision-making confidence).

Aim 1. Compare the stability of patients' goals-of-care preferences over time, from pre-outbreak to during-outbreak, by group (SPIRIT vs control) and estimate effect by race (Blacks and Whites).

Aim 2. Assess the stability in the preparedness outcomes (dyad congruence, patient decisional conflict, and surrogate decision-making confidence) comparing pre-outbreak to during-outbreak by group, and estimate race effect.

Aim 3. Examine the associations of the COVID-19 Related Stress questionnaire, sex,

race/ethnicity, and other sociodemographic characteristics (e.g., education level, income) to change in the outcomes and the stability of patients' goals-of-care preferences after the COVID-19 outbreak.

Endpoints:	Primary Endpoints (Aim 1): Dyad congruence on goals of care, patient decisional conflict, and surrogate decision-making confidence at 2 week post-intervention Secondary Endpoints (Aim 3): Surrogate HADS and PTSS scores at 3 months after the patient's death; Exploratory (Aim 4): EOL treatment intensity Supplement Aim: Dyad congruence on goals of care, patient decisional conflict, and surrogate decision-making confidence at 2-3 day post-intervention
Study Population:	400 patients and 400 surrogates of the patients participate as pairs (400 patient-surrogate dyads); adults (>=18 y); both genders; all race and ethnicity; ESRD/chronic dialysis population For the supplement aims: 30 patients with ESRD + cognitive impairment, including early stages of dementia, who are not eligible for the parent study due to cognitive impairment, and 30 surrogates of the patients as pairs Supplement cohort study: ~100 dyads who completed the baseline assessment and post-intervention assessment prior to the pandemic lockdown.
Phase:	**Phase III effectiveness trial** **For the supplement aims, NIH Stage 1 biobehavioral intervention research**
Description of Sites/Facilities Enrolling Participants:	Participants recruited from outpatient dialysis centers located in GA (Emory), NC (UNC-CH), VA (UVA) and PA (U of Pitt).; dialysis centers owned and managed by Emory Healthcare, Fresenius Medical Care (FMC), Renal Research Institute (RRI), and Dialysis Clinic Inc (DCI). A total of 29 free-standing dialysis centers. For the supplement aims, only Emory dialysis centers will serve as study site. Supplement cohort study: no new participant recruitment from the clinic. Current study participants who are eligible for the cohort study will be contacted via phone.
Description of Study Intervention:	**SPIRIT** (**S**haring **P**atient's **I**llness **R**epresentation to **I**ncrease **T**rust), a patient and family-centered ACP intervention based on the Representational Approach to Patient Education, is to establish a testable model of how end-of-life care discussions could occur between a dialysis patient and his/her chosen surrogate (usually a spouse or adult child). The discussions, which are facilitated by a trained care provider, are framed around addressing each individual's representations of

(beliefs about) the illness and views of life-sustaining measures at the end of life. SPIRIT follows a six-step learning objective over two-sessions, which together take about 60 minutes.

Study Duration: 60 months

For supplement aims, up to 2 years.

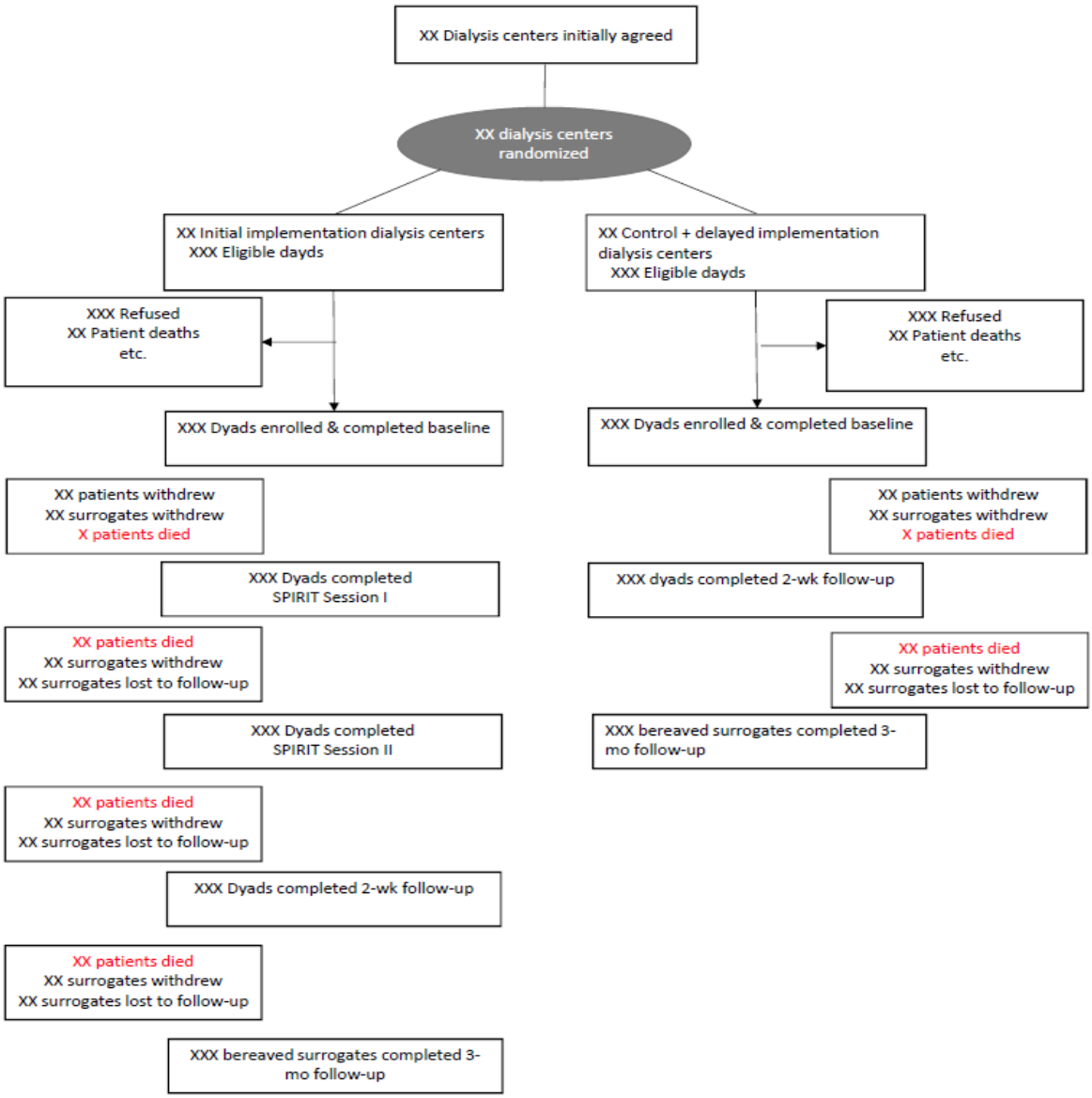
Supplement cohort study: 2 years

Participant Duration: For patients, baseline and 2-week follow up (active participation), and then an observational period for 9 months (or until death). We will request extension of 12 additional months at completion of 9 month time point.
For surrogates, baseline and 2-week follow-up (active participation), and then a 9 month observational period. We will request extension of 12 additional months if patient is still living. A post-death follow-up survey at 3 months after the patient death (if the patient death occurs during the observational period).

For supplement aims,
Patients: a brief survey at baseline and a follow-up at 2-3 days after the intervention, and then an observational period for 12 months.
Surrogates: a brief survey at baseline and a follow-up at 2-3 days after the intervention, and then a post-death follow-up survey at 1 month after the patient's death (if the patient death occurs during the observational period).

Supplement cohort study: ~ 6 months once enrolled.

1.2 SCHEMA


XX Dialysis centers initially agreed
XX dialysis centers randomized
XX Initial implementation dialysis centers
XXX Eligible dayds
XX Control + delayed implementation dialysis centers
XXX Eligible dayds
XXX Refused
XX Patient deaths
etc.
XXX Refused
XX Patient deaths
etc.
XXX Dyads enrolled & completed baseline
XXX Dyads enrolled & completed baseline
XX patients withdrew
XX surrogates withdrew
X patients died
XX patients withdrew
XX surrogates withdrew
X patients died
XXX Dyads completed SPIRIT Session I
XXX dyads completed 2-wk follow-up
XX patients died
XX surrogates withdrew
XX surrogates lost to follow-up
XX patients died
XX surrogates withdrew
XX surrogates lost to follow-up
XXX Dyads completed SPIRIT Session II
XXX bereaved surrogates completed 3-mo follow-up
XX patients died
XX surrogates withdrew
XX surrogates lost to follow-up
XXX Dyads completed 2-wk follow-up
XX patients died
XX surrogates withdrew
XX surrogates lost to follow-up
XXX bereaved surrogates completed 3-mo follow-up

1.3 SCHEDULE OF ACTIVITIES (SOA): Randomization occurs at the clinic level

Days offset	Procedure	Note
Patients and surrogates	Patient referrals[a]	Screened and willing patients
	Patient screened (by research staff) [b]	Linked to eligibility checklist
Day -14 to Day -7	Obtaining patient informed consent in person[b]	Scan and upload signed consent pdf
	Obtaining contact information[b]	
	Medical record review: clinical characteristics[b]	To be linked to "pt consent"
	Usual care review 1[b]	To be linked to "pt consent" & separate Every 6 months
Day 0	Surrogate verbal consent[b]	
	Surrogate verbal consent received[b]	
	Scheduling baseline (T1) appointment	If control, schedule both T1 & T2
	Reminder call for T1	
Day 14 (+/- 7)	**Baseline (T1)-patient completion**	Link to the measures
	Baseline (T1)-surrogate completion	Link to the measures
	Payment (T1) mailed to patient	With thank-you note
	Payment (T1) mailed to surrogate	With thank-you note
	Scheduling SPIRIT Session I & II and 2-wk F/U[b]	Need to coordinate with the care provider for SPIRIT sessions
	SPIRIT Session I[a]	
	SPIRIT Session II reminder call[b]	Two days prior
	SPIRIT Session II[a]	
	SPIRIT Interview Guide Checklist[b]	Care provider interventionist completes and the Site Coordinator enters to REDCap
	Reminder call for T2	Central
	2-week follow-up (T2)-patient completion	2 weeks from SPIRIT; including acceptability survey and SPIRIT components
	2-week follow-up (T2)-surrogate completion	2 weeks from SPIRIT; including acceptability survey and SPIRIT components
	Payment (T2) mailed to patient	With thank-you note
	Payment (T2) mailed to surrogate	With thank-you note
	Monthly check-in call 1	1 month from T2
	Monthly check-in call 2	
	Monthly check-in call 3	
	Monthly check-in call 4	
	Monthly check-in call 5	
	Usual care review 2[a]	May need one more
	Monthly check-in call 6	
	Monthly check-in call 7	
	Monthly check-in call 8	
	Monthly check-in call 9	With note on study completion
	Mailing sympathy card	Upon patient death
	Contacting surrogate & scheduling a 3-month post-death F/U	
	Postcard reminder 2 weeks before the F/U	
	Reminder call for 3-month F/U	
	F/U 3 month post death	
	Payment (F/U 3M) mailed to surrogate	With thank-you note
	Clinic-level contextual data[b]	At the end of each implementation
Care providers	Informed consent[b]	At the end of each implementation
	Acceptability assessment[b]	Brief survey and interview
	SPIRIT care provider interview-sustainability[b]	

[a] Performed locally by the chosen care provider; [b] Procedures performed locally by research personnel

2 INTRODUCTION

2.1 STUDY RATIONALE

End-stage renal disease (ESRD) currently affects nearly 662,000 people in the U.S.[1] While dialysis is the treatment of choice for over 90% of patients with ESRD and is universally covered by Medicare regardless of patient age or means, the likelihood that dialysis can restore health or prolong life is limited; only 50% of dialysis patients are alive 3 years after the onset of ESRD.[1] Thus many dialysis patients and their family members or surrogate decision-makers have to face difficult end-of-life decisions. Although advance care planning (ACP), in which patients and surrogate decision-makers discuss future health states and treatment options, is a central tenet of dialysis care,[2-5] the vast majority of dialysis patients (>90%) report never engaging in ACP discussions with their care providers.[6,7] The lack of effective ACP to prepare patients and their surrogates for end-of-life decision making with sufficient time before death has deleterious consequences at all levels of society. Consequences have been well documented: prolonged use of futile treatment at the end of life, which misuses the healthcare system, high levels of surrogate distress during decision making, which emanates from not having a clear understanding of the patient's wishes, and surrogates experiencing later sequelae of psychosocial morbidities, such as depression and family discord.[8-14]

SPIRIT (**S**haring **P**atient's **I**llness **R**epresentation to **I**ncrease **T**rust), a patient and family-centered ACP intervention based on the Representational Approach to Patient Education,[15,16] was designed by our team to establish a testable model of how end-of-life care discussions could occur between a dialysis patient and his/her chosen surrogate (usually a spouse or adult child). The discussions, which are facilitated by a trained care provider, are framed around addressing each individual's representations of (beliefs about) the illness and views of life-sustaining measures at the end of life. SPIRIT follows a six-step learning objective over two-sessions, which together take about 60 minutes. The care provider, who is value-neutral, guides the patient in examining his/her values related to end-of-life care, helps the surrogate understand the patient's illness progression, and prepares the surrogate for his/her role as a surrogate in a highly emotionally charged medical setting. Over the last decade, we have iteratively tested SPIRIT to establish feasibility, patient-surrogate acceptability, and efficacy.[17-20] In these explanatory trials carried out in dialysis clinics, SPIRIT was delivered by trained research nurses. Patients and surrogates in SPIRIT showed significant improvement in preparedness for end-of-life decision making, including the extent to which: a) the patient and surrogate agreed on end-of-life care goals, b) the patient had reduced conflict about the benefits and burdens of life-sustaining treatments, and c) the surrogate had increased confidence about the role of surrogate. Key to establishing the utility of this approach for broader generalizability, surrogates who received SPIRIT reported significantly improved post-bereavement psychological outcomes after the patient's death compared to those who did not. The logical, critical next step is to ask: Will SPIRIT be effective as part of routine care in real-world clinical settings with less control? To address this very issue, we will conduct a real-world effectiveness-implementation study, an essential step prior to widespread implementation of SPIRIT.

For Supplement Aims:
Cognitive impairment, including dementia, is common among individuals with ESRD but is a poorly recognized problem. The prevalence ranges from 16-38% and up to 70% depending on the sample,[5-8] but only less than 4% are formally diagnosed.[7,9] Prevalence rates of dementia for dialysis patients are threefold higher than the age-matched general population.[7] The most common type of dementia among patients with ESRD is **vascular dementia followed by Alzheimer's disease**.[7]

ESRD is never a single disease but accompanied by other complex chronic conditions, such as diabetes, hypertension, coronary artery disease, congestive heart failure, and peripheral vascular disease.[10] When dementia is superimposed on ESRD, the risk for poor outcomes, including disability, hospitalization and death, sharply increases.[11,12] Similarly, initiating dialysis in older adults with multiple comorbidities, including dementia, does not offer survival benefit; a study of 3,700 nursing home residents found that half of the residents died within 6

months and more than 70% died by 12 months after the start of dialysis.[13] Nevertheless, the vast majority of dialysis patients (>90%) across all age groups and comorbid conditions report never engaging in advance care planning (ACP) discussions with their care providers.[14,15] The lack of ACP to prepare patients and their surrogates for end-of-life decision making is particularly problematic for those with dementia and complex multimorbidity given their poor prognosis and the limited window of opportunity before decision-making capacity is lost.

In an on-going study ("SPIRIT in Dementia," R01AG057714) which is now running in parallel to the parent SPIRIT in ESRD study, we carefully adapted **SPIRIT for persons with mild to moderate dementia and their surrogates**. As part of the NIH Stage I behavioral intervention development trial,[16] we pilot tested the feasibility of the adapted SPIRIT intervention with 23 dyads (74% white; mean age = 74 years) recruited from the Emory Brain Health Center. The goal of SPIRIT is to promote cognitive and emotional preparation for end-of-life decision making for patients with a serious or life-threatening illness and their surrogates. SPIRIT is based on the Representational Approach to Patient Education.[17,18] We demonstrated that, by using the adapted SPIRIT intervention, persons with dementia (PWD) were able to engage in an ACP discussion meaningfully and exchange authentic dialogue with their surrogates about experiences surrounding illness and values. While the sample was small, our team was able to conclude that meaningful ACP conversations were possible even for individuals with moderate dementia and that decision-making capacity might be the more important mental faculty than global cognitive functioning in ACP discussion. It is important to note that in most studies of ACP, including our own previous SPIRIT studies[1-4] and the current parent SPIRIT-ESRD study,[19] PWD (regardless of their cognitive impairment level) are routinely excluded from clinical trials, largely because investigators assume that PWD do not have the cognitive capability to appreciate the complexity of ACP.

As a next step we are now conducting a full-scale RCT of the adapted SPIRIT intervention for PWD and surrogates to examine preliminary efficacy on immediate outcomes, including preparedness for end-of-life decision making. In the SPIRIT-dementia study, we are targeting people with early stages of Alzheimer's disease and related dementia. Therefore, in contrast to the patients in the ESRD study, PWD in the dementia study have a longer life expectancy (~10 years) and, for the most part, do not have complex multimorbidity. For patients with ESRD who have cognitive impairment, including dementia, the urgency for ACP is time sensitive because care decisions (e.g., discontinuation of dialysis, hospice enrollment) and surrogates' bereavement are rather imminent.

In this supplement study, we will pilot test the adapted SPIRIT intervention (SPIRIT-dementia) for patients with ESRD plus dementia as a model for determining whether patients with dementia superimposed on complex multimorbidity can fully participate in ACP discussion. The pilot randomized trial will include 30 dyads of patients with ESRD plus dementia and their surrogates from Emory dialysis clinics that are currently participating in the parent study.

Supplement cohort study:

For patients with complex multimorbidity (e.g., ESRD), COVID-19 infection results in much worse outcomes even after ICU admission and aggressive life-sustaining treatment.[5,6] With the high risk of hospitalization and death in the context of scarce healthcare resources caused by the COVID-19 pandemic, experts in the field have urged the public to make their end-of-life wishes known especially if they have serious chronic illness and prefer to forgo prolonged life support measures.[7] The COVID pandemic has brought fear and uncertainty to all aspects of life and to medical care in particular. Research has shown that after experiencing a natural disaster, people exhibit more risk averse behaviors, and that belief systems can change, i.e., people "update" their perception of background risk and perceive the world to be a much riskier place.[8,9]

We have spent the past decade studying how to help individuals with a range of illnesses (and their caregivers /surrogates) clarify their end-of-life care preferences and prepare for end-of-life decision making to minimize unnecessary or unwanted end-of-life treatments in the face of life-limiting illnesses. We, through this body of

work, and others have shown that values and preferences for end-of-life care are stable over time especially after individuals made an effort to actively think about their end-of-life preferences, such as engaging in ACP.[2,4,10] On the other hand, another body of literature suggests that abrupt and disturbing social changes, such as disasters, can affect the psychological mechanisms underlying cognitive performance.[11] A disaster like the COVID-19 pandemic evokes fear, anxiety, acute panic, and uncertainty surrounding access to resources, including medical care, which can cause irrational behaviors.[12] The relationship between fear and demand for aggressive treatment has been debated since 1955.[13] Generally, fear reinforces reflexive decision making in multiple domains.[14] For instance, stockpiling toilet paper during COVID-19 is a behavior reflective of a need to regain a sense of control.[15] Lerner *et al*.[9] found that experimentally induced fear caused people to express more pessimistic risk perceptions and to make more risk-averse choices in hypothetical scenarios. We are interested in assessing the effects of a disaster, such as the COVID pandemic, on the stability of end-of-life care preferences and outcomes of ACP in patients with ESRD so that we can gather evidence to revise/update our conceptual model to integrate best practices for ACP in the settings of disasters.

2.2 BACKGROUND

Dialysis patients experience high end-of-life treatment intensity that may not reflect their wishes. Despite advances in dialysis, adjusted all-cause mortality rates are 6-8 times greater for dialysis patients than for individuals in the general age-matched Medicare population.[1] Only 50% of dialysis patients are alive 3 years after the onset of ESRD.[1] End-of-life treatment intensity in this population is also substantially greater than that reported for other Medicare beneficiaries with life-limiting illnesses.[21] For instance, in a study of older Medicare beneficiaries (≥ 65 years; N≅100,000) those on dialysis experienced significantly higher rates of hospitalization (76% vs 61% in cancer), ICU admission (48.9% vs 29% in cancer), and use of intensive procedures (29% vs 9% in cancer) during the final month of life.[22]

Dialysis patients and their surrogates are not knowledgeable about the natural course of ESRD. Although withdrawal of dialysis precedes 1 in 4 deaths of patients with ESRD,[23] withdrawal from dialysis and aggressive treatment is very rarely (< 6%) discussed by patients and their surrogates with sufficient time to consider alternatives such as hospice or dying at home.[23-26] In a study of over 530 chronic dialysis patients, only 19% indicated that they would want to continue dialysis if severely cognitively or functionally impaired, and 65% stated that they prefer to die at home or in hospice rather than in a hospital.[27] Patients' preferences for end of life care are significantly influenced by the patients' illness representations (e.g., perceived illness severity).[28] That is, when patients understand their illness severity and progression, they are likely to forgo futile end-of-life treatment, such as mechanical ventilation and CPR. In our work we have discovered that because so many dialysis patients are unaware that they are likely to die from an acute illness or complication (e.g., stroke, infection) rather than die from ESRD per se, they endorse the notion that with dialysis they can live as long as those without ESRD.[18,29] Similarly, surrogates are equally unaware of patients' likely illness progression and comorbidities; surrogates report that prior to the time of end-of-life decision making they have not been told that the patient's illness cannot be cured.[9] Studies indicate that spouses' judgments about dialysis patients' preferences for continuation of dialysis were only modesty correlated with patients' preferences (r = .33),[30,31] and spouses do not have intimate knowledge of whether or how long the patient would want to pursue life-sustaining measures.[32,33] Our previous work demonstrated that surrogates are overly confident about their ability to act as a surrogate in that they have little understanding of the patient's preferences and yet report confidence in understanding the patient's wishes and their role as a surrogate.[34]

Lack of preparedness for end-of-life decision-making can have a detrimental effect on patients and surrogates. There are predictable psychological and emotional consequences of lack of preparedness for end-of-life decision making. These include: high levels of conflict brought on by having to make life or death decisions (e.g., whether to withhold or withdraw mechanical ventilation, prolonging use of life sustaining measures that are deemed

futile); regrets over missed opportunities to benefit from palliative care or hospice; excessive distress for family members during decision making due to interfamily conflict, time pressure to make important decisions, lack of knowledge about options; and well documented psychosocial sequelae for family members (e.g., depression, anxiety, post-traumatic stress disorder) and complicated bereavement after the patient's death.[8,13,35-43] Numerous studies, including ours, indicate that families experience greater difficulty in decision making when they are uncertain about the patient's wishes, when they feel unprepared for their role because they have never discussed it, and when they are called on to make decisions in a short period of time.[29,37,43-48] Evidence shows that this distress contributes to a high prevalence of psychiatric illness among family decision makers: in one study nearly 40% of bereaved families who experienced a loved one's death in the ICU 3 to 12 months previously had at least one psychiatric illness meeting DSM-IV criteria, such as anxiety disorder or major depression.[42] Even at 6-12 months after the patient's death, family members may experience intrusive thoughts of regret, guilt or search for evidence that they made the right decision.[8,43,45,49,50] We will test the hypothesis that surrogates' post-bereavement psychosocial distress will be reduced by SPIRIT, a patient and family-centered ACP, in a real-world setting.

Usual care does not prepare patients and surrogates for end-of-life decision making. Usual ACP in free-standing dialysis facilities is based on the Centers for Medicare & Medicaid (CMS) requirements[51] that written information on advance directives (ADs) is provided on a patient's first day of dialysis, and a member of the dialysis team (e.g., social worker) reviews the written information with patients and encourages them to complete an AD. If completed, the AD is documented on the Plan of Care forms. If a patient expresses a desire not to be resuscitated in the dialysis unit, a do-not resuscitate (DNR) order is written by a nephrologist and placed in the clinic record. If there is no DNR order in the record, a full code is presumed. CMS has recently issued two new billing codes (CPT 99497 and 99498) effective in 2016 that can be used to report the first 30 minutes and each additional 30 minutes of face-to-face services between a physician or other qualified healthcare professional and a patient, family member and/or surrogate in discussing ADs, with or without completing relevant legal forms.[52] Although this is encouraging, CMS provides neither ACP tools nor guidance to ensure consistency and quality in ACP services. CMS recommends that ACP discussions be conducted during annual wellness visits at a doctor's office to which these codes can be added; ACP discussions occurring outside of these visits are subject to patient co-pay or deductibles, which limits utility of the policy in other care settings. Further, ACP in these codes is narrowly defined as "including the explanation and discussion of ADs" and thus it may reinforce a common pitfall in ACP, i.e., a sole focus on AD completion.[53]

SPIRIT, a patient and family-centered ACP, has beneficial effects on a range of psychosocial outcomes for dialysis patients and their surrogates. The goal of SPIRIT is to promote cognitive and emotional preparation for end-of-life decision making for patients with ESRD and their surrogates. SPIRIT is based on the Representational Approach to Patient Education.[15,16] This approach melds two theories: Leventhal's common sense model[54] and the conceptual change model.[55] The common sense model proposes that individuals have representations of their illness or health problems. Because representations are based on an individual's everyday experiences, traditional or cultural information, or media, they may not be medically accurate. However, it is critical to understand the representations because they serve as the cognitive framework that affects whether or not individuals accept or reject new information,[15] and whether knowledge is translated into behavior change.[56,57] The conceptual change model proposes that the likelihood of learning increases when the individual has an opportunity to reflect and comment on current ideas and their consequences, when the individual is dissatisfied with current ideas or recognizes their limitations, and when alternative information is seen as beneficial.[15,16,55,58] Learning/change can occur through integrating new information into existing representations to fill in gaps in understanding, through clarifying existing representations to reduce confusion, or through exchanging existing representations with new information.[58,59] The Representational Approach to Patient Education requires a care provider to elicit the patient's pre-existing illness representations before providing new information.[15,16] Then, both the care provider and the individual have an opportunity to recognize gaps or confusions in the patient's representations, and the

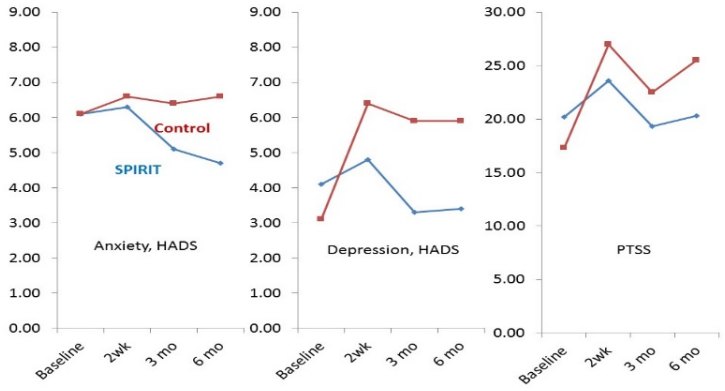
care provider can provide new information that is specific and relevant to the person. Thus, the patient is likely to understand and act on the new information.

SPIRIT is a two-session, 60-minute, structured psychoeducational intervention, targeting both patient and surrogate. Using a provider manual, the care provider follows six steps: 1) assessing illness presentation, 2) identifying gaps and concerns, 3) creating conditions for conceptual change, 4) introducing replacement information, 5) summarizing, and 6) setting goals and planning (See **Appendix**).[60] SPIRIT first establishes an understanding of the cognitive, emotional and spiritual aspects of the patient's representation of his/her illness. This understanding enables the care provider to provide individualized medical information and to assist the patient in examining his/her own values related to life-sustaining treatment at the end of life. In this way, the patient can more readily express his/her treatment preferences to the surrogate. SPIRIT also enables the surrogate to understand the patient's illness experiences and values and to be prepared for the responsibility and emotional turmoil that can arise during decision making at the end of life. Each element of SPIRIT is designed to enhance the quality and authenticity of exchanges between patient and surrogate about experiences surrounding illness and values. During the process, the patient discovers his/her own representations about illness and dialysis and examines thresholds and/or conditions for (dis)continuing life support measures. The surrogate gains an understanding of the patient's illness experience and begins to see his/her limited life expectancy. The surrogate also validates similarities or differences with the patient in regard to life support measures and examines his/her own ability to follow the patient's wishes. This process is critical to preparation for end-of-life decision making.[20,60] To deliver SPIRIT sessions, care providers are trained in communication skills and end-of-life planning. Over 12 years of conducting iterative trials of SPIRIT with diverse dialysis patient populations, we have developed a structured protocol to assist providers in addressing the unique challenges and complexities in ACP with dialysis patients and surrogates. This evidence-based guide promotes quality, consistency, and fidelity in ACP delivery[60] in this pragmatic trial of SPIRIT.

Preliminary data to support feasibility of the proposed cluster randomized trial in dialysis clinics.
Three RCTs testing SPIRIT[18-20] were conducted in free-standing outpatient dialysis settings and established the feasibility, patient and surrogate acceptability, preliminary effects (R21NR009662), and efficacy of SPIRIT delivered in those settings by trained research nurses. Dialysis facilities varied in type, including profit and non-profit ownership, urban and rural, and academic affiliation and community. The PI (Dr. Song) has the intimate knowledge of implementing SPIRIT in these complex health care systems. Recruitment rates have consistently been over 80% with a very low dropout rate (<4%). Throughout these trials, we have tested strategies and procedures related to recruitment, retention, data collection, and SPIRIT training, fidelity, and measurement.

In a full-scale multicenter RCT (R01NR011464), we formally tested the efficacy of SPIRIT compared to usual care in preparation for end-of-life decision-making: Measured at 2, 6, and 12 months, primary outcomes were dyad congruence, patient decisional conflict, and surrogate decision-making confidence.[20] We also tested whether SPIRIT reduced post-bereavement distress for surrogates (at 2 wks., 3 and 6 months). For the RCT, 210 dyads of seriously ill dialysis patients and their surrogates from 20 free-standing dialysis facilities (mean age 62, 57% women, 67% African Americans, 96% on hemodialysis) were randomized to SPIRIT or usual care. Intention-to-treat analysis showed that, adjusting for time and baseline values, dyad congruence on goals of care (*OR*=1.89 [95% *CI*, 1.1 to 3.3]; p=.029) and surrogate decision-making confidence (β=0.13 [*CI*, 0.01 to 0.24]; *p*=.027) were significantly better in SPIRIT. Patient decisional conflict was significantly lower in SPIRIT at 12 months (β=-0.19 [*CI*, -0.33 to -0.04]; *p*=.011). We also created a composite outcome combining dyad congruence and surrogate decision-making confidence because surrogates can feel highly confident even if they misunderstand patients' wishes.[18,34] Thus, to differentiate surrogates who understand the patient's wishes and feel confident in their role from those who do not (i.e., understand the wishes but lack confidence, misunderstand the wishes but feel confident, or neither understand nor feel confident), dyads were grouped as congruent in both scenarios and surrogate decision-making confidence ≥ 3 ("confident" to "very confident"), or not.[18] SPIRIT's effect on the composite outcome was also significant (*OR*=1.82 [95% *CI*, 1.0 to 3.2]; *p*=.041).

Mortality rates between the groups were similar. Among 45 bereaved surrogates, adjusting for time and baseline values, those in the SPIRIT had less anxiety (β=-1.13 [*CI*, -2.23 to -0.03]; p=.044), depression (β=-2.54 [*CI*, -4.34 to -0.74]; p=.006), and post-traumatic distress (β=-5.75 [*CI*, -10.9 to -0.64]; p=.027) than did controls.



Our qualitative thematic analysis of post-bereavement interviews with surrogates (**Box 1**) helps explain how SPIRIT reduced surrogates' post-bereavement distress.[61] Our data revealed that surrogates reported gaining insight about the life-limiting nature of the patient's illness and that death might be near; notably, no prognostic information was provided during the SPIRIT sessions. An important outcome was that the steps of SPIRIT helped raise prognostic awareness for participants without prognostic estimates having been conveyed.[61]

Box 1. Perceived impact of SPIRIT: Themes

SPIRIT…

a) was an eye-opening experience, acquiring knowledge and understanding of the patient's illness, prognosis, and end-of-life care
b) helped strengthen relationships between patients and surrogates
c) helped surrogates feel prepared during the time leading up to end-of-life decision-making
d) helped surrogates have peace of mind during and after actual end-of-life decision-making

For Supplement Aims:

Adaptation of SPIRIT for dementia and pilot testing: In contrast to people with ESRD, participants in the ongoing parallel trial ("SPIRIT in Dementia," R01AG057714) do not have complex multimorbidity and are expected to live for ~10 years after a diagnosis of dementia. We have completed the iterative process of adaptation for persons with mild to moderate dementia and their surrogates and recently pilot tested the adapted SPIRIT with a sample of 23 PWD (a Montreal Cognitive Assessment [MoCA] score, M=17.7, SD=4.0, range, 13-25; 74% non-Hispanic white; 50% male; mean age=74 years) and their surrogates (65% female, 74% spouse). The PWDs also were assessed for their decision-making capacity using a screening test, the University of California San Diego Brief Assessment of Capacity to Consent (UBACC),[38] at enrollment (M=13.2, SD=2.1, range 9-16 out of 18). As part of the analysis, using a "quantitizing" technique of qualitative data analysis,[39] we reviewed SPIRIT session transcripts focusing on the values of treatment outcomes and the goals of care discussions, and rated the level of PWD's articulation of end-of-life care preferences on a 3-point scale (from 3=expressed wishes very coherently to 1=unable to express wishes coherently).

Preliminary findings: Of the 23 PWD, 14 PWD (60.9%) had moderate dementia (MoCA=13-17). Of note, all 23 PWD were able to articulate their values and end-of-life wishes somewhat or very coherently; 20 of them expressed their wishes very coherently (rating=3). While MoCA (global cognitive functioning) scores did not differ by the level of articulation of wishes, the UBACC (decision-making capacity) scores did, Kruskal-Wallis H = 5.57, df = 1, p = 0.02, with a mean rank score of 3.50 for a rating of 2 (somewhat coherent, n = 3) and 13.28 for a rating of 3 (very coherent, n = 20).

Our finding that meaningful ACP conversations were possible even for those with moderate dementia and limited decision-making capacity is an important finding because Hirschman et al[40] found that as PWD's cognitive impairment becomes advanced, family members use the best interest standard (what a reasonable person would do) more often than substituted judgement (what my loved one would have wanted). The primary reason for using the best interest standard was that there had been no previous discussion about the PWD's preferences.[41] Our data also show that decision-making capacity may be the more important mental faculty than global cognitive functioning in ACP discussion, particularly for eliciting end-of-life wishes. However, the relationships among cognitive functioning, decision-making capacity, and ability to express wishes need future evaluation. As part of the supplement, we propose to replicate the examination of one's ability to express wishes about end-of-life care in a sample of patients with ESRD plus dementia to assess 1) if these patients have more severe cognitive

impairment and how that impacts the ACP conversations, and 2) if complex multimorbidity, i.e., ESRD, impacts the ACP conversation across a range of dementia severity. The supplement also gives us the opportunity to evaluate the adapted SPIRIT with a largely African American sample who are disproportionately represented in conditions with multimorbidity and dementia.

The adapted SPIRIT intervention (SPIRIT-dementia) sessions lasted 100 minutes on average (range, 51-122). The main reasons for the longer duration compared to earlier SPIRIT studies (on average 82 minutes) were that the interventionist was required to: a) speak slowly, b) repeat questions for the PWD, and 3) ask clarifying questions whenever the PWD's response was vague. As is typical with PWD there is slowing of speech and the PWDs often paused to come up with words or collect their thoughts, and the interventionist was prohibited from rushing, interrupting, or finishing the sentence for the PWD. Although the intervention could have been broken down to two sessions, as in previous SPIRIT with other patient populations, we determined that a single session approach would be more appropriate due to PWD's limited or absent short-term memory.

Supplement Cohort Study:

End-of-life preferences of patients with serious illnesses are generally stable. A recent systematic review[10] of evidence on the stability of end-of-life preferences over time found that more than 70% of patients' preferences for end-of-life care were stable over time, and preference stability was generally greater among inpatients and seriously ill outpatients than among older adults without serious illnesses ($p<.002$; N=55 studies; 24 studies for metanalysis). Further, patients who completed advance directives had more stable preferences than those who did not, suggesting that efforts to engage patients in actively thinking about these decisions can augment stability of preferences for treatment over time. These findings support that previously stated preferences for end-of-life care may be sufficiently stable to guide current care.

Disasters, psychosocial impact, and decision making behaviors: According to the National Oceanic and Atmospheric Administration,[19] over the past 4 decades, the U.S. has been affected by 219 natural disasters where the overall damage costs exceeded in inflation-adjust $1 billion, and 10,000 lives were lost. Recently, the COVID-19 pandemic, one of the most devastating disasters, has killed 100,000 Americans in less than 4 months (as of May 2020)[20] and caused 4 million job losses nationwide.[21]

Because disasters are typically unexpected, sudden, and overwhelming, it is common for people who have experienced one to have strong psychological responses, and their behaviors are affected in the short and possibly longer term.[22,23] Studies[24,25] have shown that following disaster, people frequently feel disoriented or unable to integrate distressing information, and once these initial reactions subside, people can experience a variety of thoughts and behaviors, such as intense or unpredictable feelings of nervousness or grief, disruptive sleep and eating patterns, strained interpersonal relationships with increased conflict and disagreements with family members, and disengagement from seeking social support. Shortly after the 9/11 terrorist attack, a national survey[26] found that heightened levels of posttraumatic stress were not limited to New York city and surrounding areas but across the country, suggesting that the psychological impact of a disaster may not require direct exposure to the disaster.

There is great interest in elucidating the effects of disaster for different racial groups especially in light of the disproportionate health disparities in COVID-related hospitalization rates and deaths in Blacks across the US. We briefly discuss 2 studies that did not concern disasters but that sheds light on why race is an important consideration in our proposed aims. Rosen et al.[27] found that Blacks, compared to Whites, were more risk tolerant even after adjusting for educational status. Specifically, Blacks were more willing to live with the risks of their underlying disease and undergo fewer procedures and that Blacks would accept much larger risks to avoid an invasive procedure compared to Whites. They also found that White race, lower education, and female sex were associated with a higher likelihood of risk aversion. On the other hand, from a different study, Blacks and Hispanics are far less likely to invest in the stock market (more risk averse in terms of investing behaviors) than

Whites, and low-income Whites are far more likely to invest in the stock market than Blacks or Hispanics regardless of income.[28]

Although the literature on economical and psychosocial impact of disasters is growing, we have very little empirical data to guide ACP with our sickest patients during a disaster. Via this new research, we seek to learn whether a disaster would make patients with a serious chronic illness more or less likely to want aggressive treatment. We posit that the effects of a disaster bring doubt to clinicians as well as families regarding how to interpret an advance directive or end-of-life care preferences expressed some time ago before the pandemic. We will generate empirical data on the impact of the COVIDE-19 pandemic on patients' end-of-life preferences, to address whether the stability of preferences is disrupted by the pandemic, and to identify patient characteristics, including race/ethnicity, associated with pre-/post-pandemic changes.

2.3 RISK/BENEFIT ASSESSMENT

2.3.1 KNOWN POTENTIAL RISKS

As the SPIRIT intervention has proven to be safe and efficacious, this Phase III pragmatic trial involves very minimal or low risk. Patient and surrogate participants may experience an emotional reaction (e.g., anxiety) or fatigue during the intervention or data collection. In our previous studies,[17-20] intervention dyads were less apprehensive and more satisfied with the quality of communication than control dyads. It is expected that psychological burden caused by the SPIRIT intervention will be less than or equal to that of usual care.

2.3.2 KNOWN POTENTIAL BENEFITS

Findings from our previous studies indicate benefits of the SPIRIT interventions for participants in the intervention group, including meeting needs to plan for future medical care and sharing values and beliefs. In addition, in our recent study, surrogates in the intervention group perceived the intervention to be highly beneficial during end-of-life decision making for their loved ones and surrogates showed significantly lower post-bereavement distress symptom scores.

2.3.3 ASSESSMENT OF POTENTIAL RISKS AND BENEFITS

As described above, it is expected that psychological burden caused by the SPIRIT intervention will be less than or equal to that of usual care. Previous studies have demonstrated the potential benefits of SPIRIT.

3 OBJECTIVES AND ENDPOINTS

The objective of this multicenter, clinic-level cluster randomized trial is to evaluate the effectiveness of SPIRIT delivered by dialysis care providers as part of routine care in free-standing outpatient dialysis clinics compared to usual care plus delayed SPIRIT implementation. Simultaneously, we will evaluate the implementation of SPIRIT, including sustainability. We will use a Type I effectiveness-implementation hybrid approach[62,63] that combines testing intervention effectiveness and gathering information about implementation of an efficacious intervention in a real world setting. The short-term goal is to generate sufficient evidence to accelerate the integration of SPIRIT into dialysis practice and policy. We will recruit 400 dyads of patients at high risk of death in the next year and their surrogates from 30 dialysis clinics in 4 states.

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS
Primary		

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS
Examine the effectiveness of SPIRIT compared to usual care on preparedness outcomes for end-of-life decision making (defined as dyad congruence on goals of care, patient decisional conflict, and surrogate decision-making confidence) at 2 weeks post-intervention.	Dyad congruence on goals of care (binary); Patient decisional conflict (scale); Surrogate decision-making confidence (scale) Composite outcome (goals-of-care congruence with confident surrogate; binary)	The primary goal of SPIRIT is to prepare the patient and surrogate for end-of-life decision making. The preparedness outcomes will indicate whether or to what extent SPIRIT accomplished the goal.
Secondary		
Examine the effectiveness of SPIRIT and usual care on surrogates' post-bereavement distress	Anxiety symptom score (HAS-anxiety); Depression symptom score (HAS-depression); Post-traumatic distress symptom score (PTSS)	Surrogate prepared by SPIRIT for EOL decision making should experience less post-bereavement distress.
Evaluate the process outcomes of SPIRIT implementation: during the initial and delayed implementation of SPIRIT	Acceptability, fidelity, intervention costs, and sustainability	Descriptive aim to generate data for translation
Tertiary/Exploratory		
Examine the effectiveness of SPIRIT and usual care on EOL treatment intensity	Health care utilization (percentages of patients hospitalized, having ICU admission, and having intensive procedures, and LOS)	To examine whether SPIRIT reduces aggressive EOL treatment
Supplement		
Estimate the effects of the SPIRIT-dementia intervention on the preparedness outcomes and care decisions	Dyad congruence on goals of care (binary); Patient decisional conflict (scale); Surrogate decision-making confidence (scale) Composite outcome (goals-of-care congruence with confident surrogate; binary) Care decisions (withdrawal from dialysis, Do-Not-Resuscitate order, hospice enrollment)	The primary goal of SPIRIT is to prepare the patient and surrogate for end-of-life decision making. The preparedness outcomes will indicate whether or to what extent SPIRIT accomplished the goal. Care decisions will reflect the effects of SPIRIT on end-of-life decision making.
Estimate the effects of the SPIRIT-dementia intervention on surrogates' post-bereavement distress	Anxiety symptom score (HAS-anxiety); Depression symptom score (HAS-depression)	Surrogate prepared by SPIRIT for EOL decision making should experience less post-bereavement distress.
Supplement cohort study (non-clinical trial)		
Assess the effect of the pandemic on the stability of end-of-life care preferences and on our key outcomes (dyad congruence on goals of care, patient decisional conflict, and surrogate decision-making confidence).		

Measurement and data collection time points

Outcome	Measure	Completed by			Time points
		pt	srgt	prov	
Effectiveness outcome evaluation					
Preparedness					
Dyad congruence	Goals-of-Care Tool (2 end-of-life scenarios)	√	√		Baseline and 2 wks
Patient decisional conflict	Decisional Conflict Scale (range, 1-5)	√			Baseline and 2 wks
Surrogate decision-making confidence	Decision Making Confidence Scale (range, 0-4)		√		Baseline and 2 wks
Overall preparedness	Preparedness for End-of-Life Decision Making (range, 26-104)	√	√		Baseline and 2 wks
Post-bereavement distress	HADS (each subscale range, 0-21) PTSS-10 (range, 10-70)		√		Baseline and 3 mo. after patient death
End-of-life care intensity	Percentages of patients hospitalized, having ICU admission, and having intensive procedures and length of hospital stay				Medicare claims data after patient death
Initial implementation process evaluation					
Care provider acceptability	Dialysis care provider's perceived acceptability (range, 7-28); Semi-structured interview			√	End of the initial implementation
Patient & surrogate acceptability	Patient and surrogate acceptability (range, 10-40 each)	√	√		2 wks
Fidelity	SPIRIT provider's coverage of the SPIRIT components and durations; Brief patient and surrogate survey	√	√	√	SPIRIT provider after each SPIRIT completion Patient and surrogate at 2 wks
Intervention costs	The actual time the care provider spent in carrying out SPIRIT, multiplied by hourly wage (+benefits), plus costs of materials				End of the early implementation
Sustainability	Brief semi-structured interview			√	End of 12 mo.post 9-month follow-up
Delayed implementation process evaluation					
Care provider acceptability	Dialysis care provider's perceived acceptability (range, 7-28); Semi-structured interview			√	End of the delayed implementation
Fidelity	SPIRIT provider's coverage of the SPIRIT components durations			√	SPIRIT provider after each SPIRIT completion
Intervention costs	The actual time the care provider spent in carrying out SPIRIT, multiplied by hourly wage (+benefits), plus costs of materials				End of the delayed implementation
Descriptors and potential covariates					
Sociodemographics	Sociodemographic Profile	√	√		Baseline for patients and surrogates
				√	End of the initial implementation for clinicians
Clinical characteristics	Medical Profile				Baseline
Clinic-level contextual data	Contextual Data Collection Form				End of each implementation
Usual care	Documented AD completion on the Plan of Care form; presence of DNR, POLST, or MOST (from EMR)				Baseline and 6 mo.

Pt, patient; Srgt, surrogate; Pro, care provider
Data collection highlighted in yellow is performed locally.

For supplement aims:

Measurement and data collection time points

Outcome	Measure	Completed by		Time points
		pt	srgt	
Estimating the effects of SPIRIT-dementia				
Preparedness				
Dyad congruence	Goals-of-Care Tool (2 end-of-life scenarios)	√	√	Baseline and 2-3 days
Patient decisional conflict	Decisional Conflict Scale (range, 1-5)	√		Baseline and 2-3 days
Surrogate decision-making confidence	Decision Making Confidence Scale (range, 0-4)		√	Baseline and 2-3 days
Overall preparedness	Preparedness for End-of-Life Decision Making (range, 26-104)	√	√	Baseline and 2-3 days
Post-bereavement distress	HADS (each subscale range, 0-21)		√	Baseline and 1 mo. after patient death
Care decisions	Percentages of patients hospitalized, having ICU admission, and having intensive procedures and length of hospital stay	CMS form 2746		After patient death

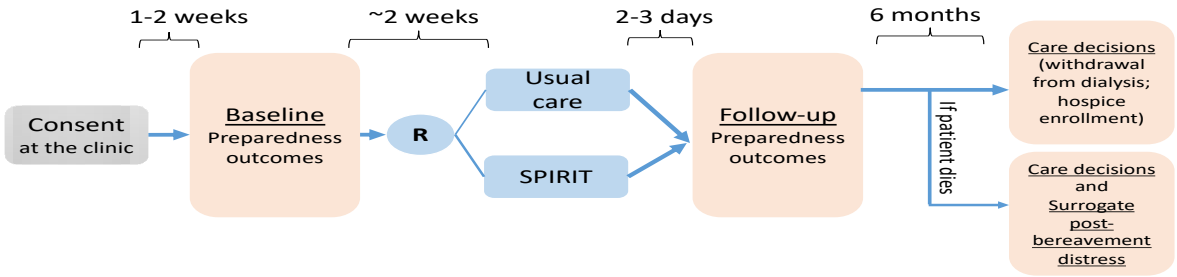
4 STUDY DESIGN

4.1 OVERALL DESIGN

We will conduct a dialysis clinic-level cluster randomized trial with two groups, SPIRIT versus usual care followed by delayed SPIRIT. We will recruit 400 dyads of patients on chronic ("prevalent") dialysis who are at high risk of death in the next year and their surrogate decision-makers (total 800 individuals) from 30 free-standing dialysis clinics in 4 states. The primary outcomes are patient and surrogate self-report preparedness for end-of-life decision making. The implementation evaluation data will be obtained throughout the study course. Upon patient death (anticipate 20% of patients; n = ~ 80), we will assess surrogates' post-bereavement distress. Patient participation will end at 9 months (to allow for obtaining Medicare claims data during the study period) or death, whichever occurs first; surrogate participation will end at 9 months or at the completion of 3-month post-death follow-up. If patient is still living at 9 months, we will ask for an extension of follow up period to include 12 more months. Medicare claims data for end-of-life treatment intensity will be obtained quarterly. Clinics assigned to usual care will receive the delayed implementation, SPIRIT, in Year 4, Q1. This is a Phase III trial of an intervention that involves minimal risks and has proven to be efficacious, and thus no interim analysis is planned.

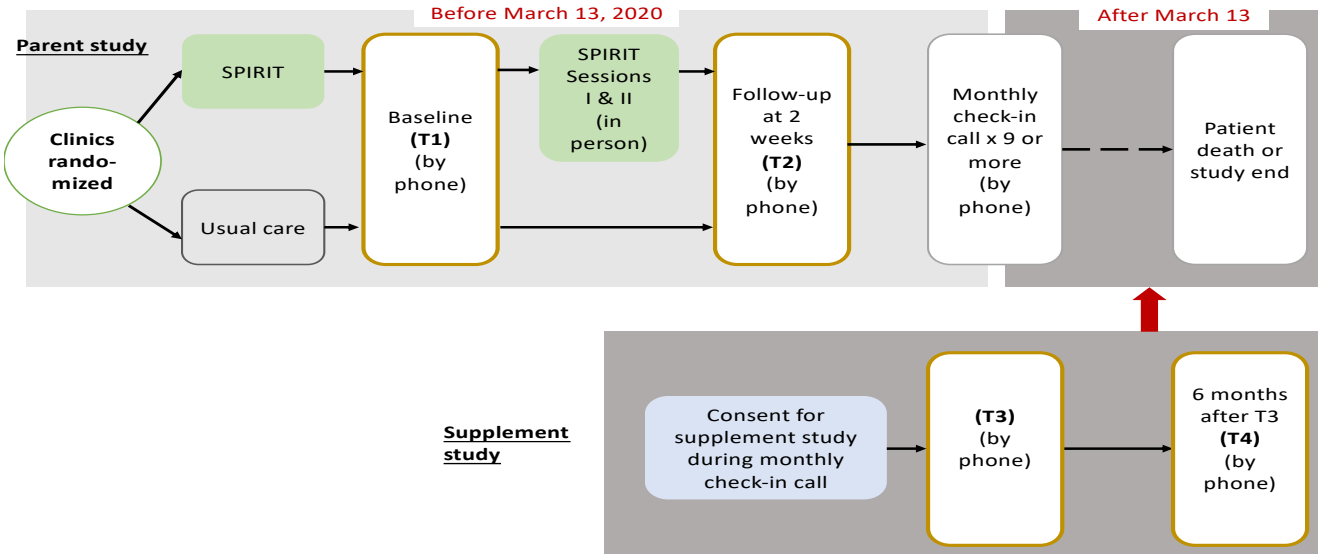
For Supplement Aims:

Figure 1. Design Overview



We will use a randomized controlled trial design with two groups: SPIRIT-dementia and usual care. From the pool of screened but excluded ESRD patients, we will recruit 30 dyads of patients with mild to moderate dementia and their surrogates. The groups will be stratified by race (white vs non-white). Patient and surrogate self-reported preparedness for end-of-life decision making will be measured at baseline and shortly after the intervention (by phone in the next 2-3 days) as done in the pilot test of SPIRIT-dementia. Additionally, we will review the patient's medical record to examine care decisions at 6 months or after the patient's death, whichever occurs first. In the case of patient death, we will also assess surrogates' post-bereavement outcomes (anxiety and depression symptoms) at 1 month after the patient's death. Based on previous research,[13] we anticipate about 50% of the supplement sample will die within 12 months of enrollment. All data collection from study participants will be telephone-based.

Supplement cohort study:



4.2 SCIENTIFIC RATIONALE FOR STUDY DESIGN

We chose cluster over individual randomization for the benefits of increased efficiency and decreased risk of experimental contamination, while recognizing potential loss in statistical precision from the effects of variance inflation.[64] However, cluster effects are usually small and can be controlled in analysis. Cluster randomization is also a favorable design strategy for the Type I hybrid effectiveness-implementation approach to test clinical effectiveness while gathering information on implementation.[62] Hybrid designs are increasingly used to expedite the sequential process, "efficacy to effectiveness to preliminary implementation[63] and are recommended when there is strong evidence of the intervention effects and the intervention is low risk for participants.[62]. To maximize data on the implementation process and sustainability, we chose a delayed intervention design[65] in which clinics are randomized either to implement SPIRIT immediately after randomization (i.e., initial implementation) or to maintain usual care for a comparison condition and then implement the intervention in Year 4 (i.e., delayed implementation). The delayed implementation group will effectively serve as control for effectiveness evaluation. The process outcomes from the initial implementation of SPIRIT will be used to determine if any modifications to SPIRIT are necessary. We anticipate that we will make clinic-specific adaptations to improve implementation in the delayed implementation phase. Clinics in the delayed implementation phase will be evaluated on the process outcomes, which will provide data on the iterated version of SPIRIT without having to conduct another trial. The

delayed implementation is more ethical than not providing SPIRIT at all because its demonstrated efficacy would preclude equipoise.

Virtually no trials are purely pragmatic or explanatory; based on the PRECIS Tool and key characteristics of pragmatic trials,[66,67] the proposed study is more pragmatic than explanatory in the pragmatic-explanatory continuum because it will include diverse patient populations, multiple heterogeneous settings, few inclusion and exclusion criteria, and the comparison condition is a real-world alternative (i.e., usual care), not a placebo. Further, the study is built around normal dialysis care operations as much as possible with flexible study protocols that minimize intrusion in daily work flow at the dialysis facilities. Of direct relevance to dialysis care, the intervention will be implemented by dialysis care providers, such as nurses and social workers.

For Supplement Aims:

As in our previous studies of SPIRIT, we chose individual randomization because intervention spillover to the control condition is very unlikely. The intervention will be delivered by a trained interventionist, not a care provider, in a private room at the clinic, or virtually due to the COVID-19 pandemic, and thus it is nearly impossible for care providers to obtain the knowledge and skill related to SPIRIT to change their ACP practice. We chose race (white vs non-white) as a stratification factor to ensure equal allocation of race to each condition to control for race as a confounding variable.[49]

The follow-up time point (2-3 days post intervention) is to evaluate the impact of SPIRIT on preparedness outcomes while minimizing the potential influence of the patient's impaired ability to recall what was discussed during the SPIRIT session. We considered measuring the outcomes immediately following the intervention, but this would increase subject burden as SPIRIT sessions tend to last longer with PWDs than those without cognitive impairment. The time point for care decision reviews (6 months post intervention) was chosen to help maximize the number of patients whose conditions progress within the study period so that we can explore the impact of SPIRIT-dementia on care decisions. As in earlier SPIRIT trials and the parent study with ESRD patients and the parallel study with dementia patients, we will use telephone-based data collection to reduce participants' travel burden.

Supplement cohort study:

We posit that reflexive decision-making in response to the pandemic could discount previously expressed preferences for end-of-life care, thereby affecting the stability of those preferences. We postulate that such alterations in decisions may be more prevalent among patients and families who have not had ACP to explore own values and beliefs about end-of-life care (such as dyads in the control group in the parent study), and also among Blacks, a racial group that is thought to embrace more aggressive treatment at the end of life.[29] This is especially important now in light of recent findings[30] that counties in the U.S. with higher Black populations account for more than half of all COVID-19 cases and almost 60% of deaths even though Blacks represent only 13.4% of the American population. We have an opportunity to address these complicated but urgent questions about end-of-life decision making when people fear a dangerous virus and are alarmed about scarce lifesaving resources, such as ICU beds and ventilators.

4.3 JUSTIFICATION FOR INTERVENTION

The SPIRIT intervention is a one-time advance care planning intervention that has been rigorously tested and has demonstrated its efficacy. The details about the intervention, including the rationale, are described above (2.2 Background).

4.4 END OF STUDY DEFINITION

Because the study uses a delayed intervention design to maximize implementation data collection, the end of the study will be the completion of care provider acceptability, fidelity and cost data collection.

For Supplement Aims:
We will review the patient's medical record to examine care decisions at 6 months or after the patient's death, whichever occurs first. In the case of patient death, we will also assess surrogates' post-bereavement outcomes (anxiety and depression symptoms) at 1 month after the patient's death. Based on previous research,[13] we anticipate about 50% of the supplement sample will die within 12 months of enrollment.

Supplement cohort study:
Completion of 6 month follow-up (T4) after T3.

5 STUDY POPULATION

5.1 INCLUSION CRITERIA

Patient eligibility criteria:
a) 18 years or older
b) on either hemodialysis or peritoneal dialysis
c) able to understand and speak English.

Surrogate eligibility criteria:
a) 18 years or older (to serve as a surrogate decision-maker, the individual must be an adult)
b) being chosen by the patient.

Roughly 76 providers at the 29 clinics, including all medical directors, nurse managers, social workers, and those who are selected to conduct SPIRIT sessions will participate in the implementation evaluation.

For Supplement Aims:

Patient eligibility criteria:
a) Receiving in-center hemodialysis at Emory or UVA dialysis clinics.
b) Diagnosed with dementia of any etiology (or those for whom their care providers, either MD or APRN, are suspicious of dementia) with having mild to moderate cognitive impairment based on a Montreal Cognitive Assessment (MoCA) score of 13 or higher,[54,55] or a Saint Louis University Mental Status (SLUMS) score of 21 or higher (high school education) or 20 or higher (less than high school education)[56]
c) Able to understand and speak English
d) A UBACC (decision-making capacity screening test) score $\geq$ 11. Because dementia is largely under-diagnosed in the clinical setting for patients with ESRD, to identify additional patients with possible dementia, a trained research assistant will administer the MoCA or SLUMS to patients who are suspected (by dialysis clinicians) of having dementia. MoCA or SLUMS will take about 10 minutes to complete.

Surrogate eligibility criteria:
a) 18 years or older (to serve as a surrogate decision-maker, the individual must be an adult)
b) being chosen by the patient.

For supplement cohort study:

Dyads who completed the parent study's baseline (T1) and 2-week follow-up (T2) before March 13, 2020.

5.2 EXCLUSION CRITERIA

Patient exclusion criteria:

a) lack of an available surrogate,
b) too ill or cognitively impaired to participate based on clinicians' judgment*,
c) already enrolled in hospice.

Surrogate exclusion criterion:

a) Those who cannot complete questionnaires due to physical or cognitive limitations will be excluded.

For Supplement Aims:
Patient exclusion criteria:

a) lack of an available surrogate,
b) uncompensated hearing deficits,
c) already enrolled in hospice.

***Patients who are excluded from the parent study will be considered for the supplement study.**

5.3 LIFESTYLE CONSIDERATIONS

Not applicable

5.4 SCREEN FAILURES

Because patients are approached first at the dialysis center, it is possible that patients provide written consent to participate in the study with the assumption that their surrogates would be willing to participate with them (however, patients cannot complete the baseline without willing surrogates), and then the surrogate actually declines to participate. Because randomization occurs at the clinic level, not the individual level, these cases will be reported under "not eligible" with reason.

5.5 STRATEGIES FOR RECRUITMENT AND RETENTION

Recruitment and Consent procedures:
The dialysis care provider who has been selected by the clinic as one responsible for SPIRIT delivery at each clinic (so-called, "SPIRIT clinician champion") in both groups will generate a list of patients each quarter who meet the inclusion criteria. **Depending on the clinic's structure and workflow, the care provider who determines patients meeting these criteria may not be the same care provider, i.e., SPIRIT clinician champion who is responsible for SPIRIT delivery.**

From this list, the care provider will then assess the patient's willingness to meet with a recruiter from the research team. The recruiter will then approach willing patients during their scheduled dialysis clinic appointment to explain the study purposes and procedures. In a private room, written consent will be obtained from the

patient after the study is reviewed and understanding is established. The recruiter will then provide the patient with a study brochure and encourage him/her to talk to the surrogate regarding the study within the next 2-3 days (to avoid a cold call). Several days later, the recruiter will telephone the surrogate to assess his/her willingness to participate. **Using a Surrogate Verbal Consent script and form, the site coordinator will document time and date. Upon this verbal consent, the research staff at the Emory Study Coordination Center will conduct baseline data by phone.** For surrogates in the SPIRIT implementation clinics, the recruiter (at each study site) will schedule the first SPIRIT session to take place at the clinic 2 weeks hence, as is possible.

Recruitment will occur over 24 months beginning at the end of Year 1. We are highly experienced in recruiting seriously ill ESRD patients and their surrogates for research. Consent rates in our previous studies have been consistent at approximately 84% despite the studies' focus on end-of-life, the requirement that both patient and surrogate participate, and long-term follow-up. We expect a similar if not higher consent rate because the study involves a shorter follow-up time and minimal data collection directly from patients and surrogates. Based on our previous studies,[18-20] we conservatively anticipate that 427 patients (20%) will be *eligible and willing* to participate. To reach 400 dyads, we expect to enroll 21-22 dyads per cluster on average. These clinics each accept 10-70 new patients each year (total 700 additional patients), and thus our recruitment goal is readily achievable.

To Maximize Participant Retention, strategies found effective in retaining dyads over 12 months (dropouts, 3.8%) in our efficacy trial[20] will be used: we will

a) obtain two backup contacts from each member of the dyad in the event that we cannot reach them by telephone and mail
b) make confirmation phone calls 2 days prior to each follow-up
c) make monthly check-in calls
d) send holiday cards
e) assign the same data collector whenever possible
f) compensate each member of the dyad with gift cards ($15 at baseline, $15 at 2 weeks for the preparedness outcome assessment; $20 at 3 months for the post-bereavement outcome assessment). Consistent with a pragmatic trial, participants will not be compensated for participating in the intervention. The Emory Study Coordination Center will be responsible for disbursement.

For Supplement Aims:
Participants will be recruited from the Emory dialysis centers and the UVA dialysis centers . First, patients who have been diagnosed with an early stage of dementia (mild to moderate) or are suspected of having cognitive impairment by a care provider will be referred by the dialysis APRN. The medical records of those patients will be reviewed to preliminarily determine eligibility by a research staff member. During the patient's dialysis treatment session at the center, the patient's care provider will gain permission for the staff member to explain the study. With the patient's permission, the staff member will approach the patient, briefly explain the study, obtain verbal consent to conduct the MOCA or SLUMS and UBACC screening. If the patient has met the criteria for both early stages of cognitive impairment and decision-making capacity, the research staff member will provide detailed study information and confirm his/her surrogate decision-maker. Written consent will then be obtained from the patient. The research staff member will obtain the name and phone number of the surrogate (or confirm with the medical record as necessary) and call the surrogate in 2-3 days to assess the surrogate's willingness to participate. Verbal consent will be obtained from the surrogate. At the time of surrogate consent, the staff member will schedule a telephone-based data collection session for baseline assessment in about 2 weeks.

To minimize in-person contacts, we will screen patients remotely/via phone whenever possible. Patients who are deemed eligible will be approached by a social worker during their dialysis treatment session or by phone to ask them about their willingness to be contacted via telephone by Emory research staff. Patients who agree to be contacted, a research staff member will call the patient, briefly explain the study, obtain verbal consent to conduct the cognitive screening using the MoCA and UBACC. Verbal consent will then be obtained from the

patient if screening occurred over the phone. The research staff member will obtain the name and phone number of the surrogate (or confirm with the medical record as necessary) and call the surrogate in 2-3 days to assess the surrogate's willingness to participate. Verbal consent will be obtained from the surrogate. At the time of surrogate consent, the staff member will schedule a telephone-based data collection session for baseline assessment in about 2 weeks.

For supplement cohort study:
At the next monthly check in phone call (as part of the parent study protocol), the research staff member will proceed with the procedures for the parent study and then introduce the participant to the supplement study, including the purpose and procedures and obtain verbal consent. After both members of the dyad have consented, the recruiter will schedule two data collection calls (T3 within 1 week and T4 at 6 months). If additional subjects are needed, we will contact those who already completed the study before the pandemic.

To Maximize Participant Retention, we will

a) obtain two backup contacts from each member of the dyad in the event that we cannot reach them by telephone and mail
b) make confirmation phone calls 2 days prior to the baseline and/or the SPIRIT session (intervention group)
c) make scripted monthly check-in calls
d) send holiday cards
e) assign the same data collector whenever possible
f) provide transportation support ($20) for the SPIRIT session in person at the center (intervention group)
g) compensate each member of the dyad with gift cards ($20 at baseline; $25 at post-intervention follow-up; and surrogates who complete post-bereavement assessment will receive $30 at 1 month after the patient's death).
   For supplement cohort study, each member of the dyad will receive an additional $20 at the completion of T3 and $30 at T4.

Recruitment of Care Providers for Implementation data collection, we will obtain a list of dialysis care providers from each dialysis center, who are willing to be contacted by the study staff for participating in implementation related data collection. This data collection is to obtain inputs from the care providers regarding SPIRIT implementation as part of routine dialysis care. Research study staff at the study site will contact care providers on the list using their preferred contact numbers or emails. Verbal Care Provider Informed Consent will be used in consenting process. Survey/Interviews will be scheduled to be conducted over the phone or in person at the convenience of the Care Provider. There will be no compensation for care provider's participation.

6 STUDY INTERVENTION(S)

6.1 STUDY INTERVENTION(S) ADMINISTRATION

6.1.1 STUDY INTERVENTION DESCRIPTION

SPIRIT Intervention:
All care providers responsible for SPIRIT delivery will follow the structured SPIRIT Interview Guide. All sessions will be conducted in a private room in the clinic. The goals of SPIRIT are to assist patients clarify their end-of-life preferences and to help surrogates understand the patient's wishes and prepare for the surrogate role. SPIRIT has two face-to-face sessions with patient and surrogate together. These sessions may occur using teleconferencing

software (Zoom) when surrogate decision makers live or work outside a 50-mile radius of patient's clinic. We project the monthly caseload for SPIRIT delivery will be 1-2 dyads per cluster on average.

During the first session (~45 min.), the care provider will assess the patient's and surrogate's cognitive, emotional, and spiritual/religious representations of the patient's illness, prognosis, and end-of-life care. This will allow the care provider to provide individualized information about topics, such as the effectiveness of life-sustaining treatment for people with end-organ failure, and assist the patient to examine his/her values about life-sustaining treatment at the end of life. The care provider will help the surrogate prepare for end-of-life decision-making and for the emotional burden of decision-making by actively involving the surrogate in the discussion. If the surrogate is someone out of the order of the hierarchical compensatory model[71] (e.g., a sibling is chosen instead of a spouse), the care provider will explore potential family conflicts and encourage the dyad to talk with other family members and complete a healthcare power of attorney. A Goals-of-Care document will be completed at the end of the session to indicate the patient's preferences.

A brief second session (~15 min.) will be delivered about **approximately 2 weeks later, if possible**. **For PD patients who scheduled dialysis is varying, the second session of the SPIRIT Intervention can be scheduled to occur approximately 2-4 weeks hence, if possible**. This session is a follow-up to address remaining or new concerns and questions raised after the first session. The patient's Goals-of-Care document will be reviewed and assessed for the need for clarification or correction. The provider will document the patient's end-of-life preferences and the surrogate's name and relationship to the patient in the medical record. If the patient desires a DNR order, POLST, or MOST, the care provider will discuss with the patient's nephrologist and arrange a meeting to complete a treatment order form. We will track completion of these forms.

For Supplement Aims: the SPIRIT intervention will include one session only due to the patient's limited or absent short-term memory. During the COVID-19 pandemic, all SPIRIT sessions will be done via zoom whenever possible.

Usual Care

As required by CMS,[51] written information on ADs is provided to a patient on the first day of dialysis, and a social worker reviews this information with patients and encourages them to complete an AD. This typically takes about 10 minutes. If completed, the presence of an AD is documented on the Plan of Care form. If a patient expresses a desire not to be resuscitated in the dialysis unit, a DNR order is written by a nephrologist and placed in the clinic record. If there is no DNR order in the record, a full code is presumed. A social worker or charge nurse reviews code status and updates it annually. Currently, all four states endorse the physician orders for life-sustaining treatment (POLST) paradigm; NM MOST (medical orders for scope of treatment), NC MOST, PA POLST, VA POST and GA POLST; these forms may be completed to complement ADs. None of the clinics employ routine identification of patients at high risk for death or structured ACP sessions targeting those patients.

6.1.2 DOSING AND ADMINISTRATION

Described above (6.1.1).

6.2 PREPARATION/HANDLING/STORAGE/ACCOUNTABILITY

6.2.1 INTERVENTIONIST TRAINING AND ACCOUNTABILITY

Care Provider Training for SPIRIT

The ideal individual to conduct ACP discussions is still unknown, but we believe it is not the profession per se but rather the willingness and appropriate training that make an individual suitable for conducting the discussions. Each dialysis clinic has identified a care provider designated to conduct SPIRIT sessions (e.g., ANP, RN, MSW). SPIRIT training will occur shortly after randomization for the initial implementation clinics and in early Year 4 for

the delayed implementation clinics. The SPIRIT trainers, trained and certified by the PI at the Study Coordination Center (at Emory), will conduct SPIRIT training for all four sites based on the manualized curriculum.

Care provider training will consist of a 1½-day, competency based program that has been used in our previous trials:

- Module 1 (1/2 day) to ensure understanding of end-of-life care issues and communication as key to improving end-of-life care and the Representational Approach (theoretical underpinnings of SPIRIT);
- Module 2 (1/2 day), as skill-base session to gain understanding of the SPIRIT intervention and delivery, including role plays. A 2-week practice period will be scheduled for integration of skills and exploration of additional learning needs; and
- Module 3 (1/2 day) for skill-demonstration and certification. These training sessions will be conducted in collaboration with the Emory Nursing Professional Development Center.

For Supplement Aims:
An RN who has been trained and certified for SPIRIT-dementia will deliver the intervention, who is currently working as the interventionist for the SPIRIT-AD study (IRB #00099738). SPIRIT sessions will be conducted in a private room at the dialysis center or virtually with ZOOM. At the beginning, the interventionist will administer the MoCA or SLUMS (depending on which test was used at enrollment), which should take about 10 minutes. The interventionist will begin the SPIRIT session by assessing the patient's and surrogate's cognitive, emotional, and spiritual/religious representations of the patient's illness, prognosis, and end-of-life care. This will allow the interventionist to provide individualized information about topics, such as the effectiveness of life-sustaining treatment for people with end-organ failure, and assist the patient to examine his/her values about life-sustaining treatment at the end of life. The interventionist will help the surrogate prepare for end-of-life decision-making and for the emotional burden of decision-making by actively involving the surrogate in the discussion. If the surrogate is someone out of the order of the hierarchical compensatory model[59] (e.g., a sibling is chosen instead of a spouse), the care provider will explore potential family conflicts and encourage the dyad to talk with other family members and complete a healthcare power of attorney. A Goals-of-Care document will be completed at the end of the session to indicate the patient's preferences. The delivery of SPIRIT-dementia incorporates so-called "enhanced consent techniques," such as reducing information load by proceeding in manageable segments or chunks, offering repetition of material, opportunity for rehearsal, and using targeted questioning to verify adequate comprehension prior to eliciting preferences for goals of care.[60-62] All sessions will be audio-recorded and transcribed. At the end of the session, the dyad will receive $20 to compensate travel costs. The interventionist will schedule a follow-up call for the outcome assessment in the next 2-3 days.

6.2.2 FORMULATION, APPEARANCE, PACKAGING, AND LABELING

Not applicable.

6.2.3 PRODUCT STORAGE AND STABILITY

Not applicable.

6.2.4 PREPARATION

Not applicable.

6.3 MEASURES TO MINIMIZE BIAS: RANDOMIZATION AND BLINDING

Clinics covered by the same care provider who will deliver SPIRIT sessions will be combined to one cluster to avoid risk of contamination; this results in clusters (4 in GA, 3 in NC, 8 in NM, 5 in PA and 8 in VA). Because the numbers of available patients substantially vary across the clusters, to minimize group imbalance clusters will be stratified to three sizes: small (patient census ≤ 52), medium (53-105), and large (≥ 106). We will randomize clusters to either SPIRIT or usual care plus delayed SPIRIT, with randomly permuted blocks (sizes of 2 and 4) within cluster size stratum nested in each state, using a pseudo-random-number generator, by the Study Coordination Center.

Before the study starts, the Study Coordination Center will inform the group assignment for each cluster to the site PIs, with a unique ID consisting of abbreviations for state and cluster size stratum. While the heterogeneity in minority race/ethnicity across clusters improves the study's generalizability, stratification or pairing clusters by race/ethnicity is not feasible because some clinics uniquely serve one race with no comparable clinics within state. Group imbalances on race/ethnicity and other potential confounding factors will be examined and adjusted for in the analyses. The cluster randomized design prevents blinding patient-surrogate dyads and dialysis care providers to group allocation. However, research staff assessing effectiveness outcomes will be blind to group assignment.

For Supplement Aims:
Dr. Paul (biostatistician/Co-I) will generate a randomization scheme using stratified (by race), permuted block randomization with block size 5, using a random-number generator. Dyads will be randomized with equal allocation (1:1) to SPIRIT or usual care. Due to the nature of the intervention, blinding dyads to their group allocation is impossible, but the research staff assessing outcomes will be blind. Immediately after the completion of the baseline assessment by phone, the data collector will open a sealed envelope to identify group assignment and schedule an intervention session to take place ~2 weeks hence for SPIRIT as well as a follow-up data collection session in the next 2-3 days.

6.4 STUDY INTERVENTION COMPLIANCE

To maintain internal validity, certain components of the intervention will be standardized: standardized care provider training using the training modules (described above); Session 1 will be delivered via face-to-face; the SPIRIT Interview Guide will be used during each session to promote consistency and quality of intervention delivery. We will develop a template of procedures related to SPIRIT implementation for each clinic to customize and use as a resource.

To assess fidelity, we will use two independent data sources.

1) The SPIRIT Interview Guide will direct the care provider to document performance data after each patient-surrogate dyad encounter (the data will be entered into REDCap by each site coordinator). The Guide has a checklist of SPIRIT components, including start and finish times and brief self-evaluation.
2) At the 2-week post-intervention follow-up, a research assistant will query patients and surrogates about the SPIRIT sessions using the checklist of SPIRIT components. After the first 50 dyads (~first 4 months) have been seen, clinics with <80% adherence on both data sources will receive feedback and another orientation meeting by the Site PI and the SPIRIT trainer.

We considered replacing clinics with <80% adherence, but this approach would not be consistent with the pragmatic nature of the study to test SPIRIT in a real-world setting. We also considered recording a sample of SPIRIT sessions, but this approach would likely be considered intrusive by the dialysis care providers and is unrealistic in a pragmatic trial.

For Supplement Aims:
To promote consistency and quality of intervention delivery, the SPIRIT Interview Guide will be used during each session. To monitor fidelity, we will use two data sources. 1) The SPIRIT Interview Guide will direct the interventionist to document performance data after each patient-surrogate dyad encounter; these data will be

entered into the Research Electronic Data Capture (REDCap) by the research coordinator. The Guide has a checklist of SPIRIT components, including start and finish times, and brief self-evaluation. 2) All intervention sessions will be audio-recorded. Every 2 months, 50% of sessions randomly selected will be reviewed by the PI. Using the Treatment Fidelity Assessment Tool, the interventionist's adherence to intervention content, process, and duration will be evaluated on a 3-point scale (1=appropriate, 3=skipped). Problems detected including drift from protocol will be discussed with the interventionist and re-training will be provided if adherence is <80% based on the Fidelity Assessment Tool.

6.5 CONCOMITANT THERAPY

Not applicable (all patients receive usual care related to advance care planning).

6.5.1 RESCUE MEDICINE

Not applicable.

7 STUDY INTERVENTION DISCONTINUATION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

7.1 DISCONTINUATION OF STUDY INTERVENTION

SPIRIT is a one-time intervention with two sessions. If patient-surrogate dyads is not able to complete Session I or II, the reason or circumstances (e.g., the patient became too ill) will be documented and reported. Session II cannot be offered without Session I completed; that is, it is possible that a patient-surrogate dyad completes Session I but not Session II. Dyads who never complete Session I and dropout will be replaced by enrolling a new dyad.

7.2 PARTICIPANT DISCONTINUATION/WITHDRAWAL FROM THE STUDY

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

- If the participant meets an exclusion criterion that precludes further study participation.

The reason for participant discontinuation or withdrawal from the study will be recorded on the study REDCap. Subjects from the dialysis center randomized to initial SPIRIT who sign the informed consent form but do not receive the study intervention may be replaced. Subjects in the initial SPIRIT who sign the informed consent form and receive the study intervention, and subsequently withdraw, or are withdrawn or discontinued from the study will not be replaced.

7.3 LOST TO FOLLOW-UP

Patients lost to follow-up will not be applicable in this trial since all patients must come to the dialysis center for their treatment and thus can be contacted at the center.

A surrogate participant will be considered lost to follow-up if he or she fails to complete the scheduled 2-week follow-up (after the receipt of the intervention) and is unable to be contacted by the study site staff until the end of the 9-month follow-up period. Or, a surrogate participant will be considered lost to follow-up if he or she fails

to complete the scheduled 3-month follow-up (after the patient's death) and is unable to be contacted by the study site staff.

The following actions must be taken if a participant is determined to be lost to follow-up:

- The site will attempt to contact the participant and reschedule the missed appointment for 4 weeks and ascertain if the participant wishes to continue in the study.
- Before a participant is deemed lost to follow-up, the investigator or designee will make every effort to regain contact with the participant (where possible, 3 telephone calls and, if necessary, a certified letter to the participant's last known mailing address or local equivalent methods, or speak to the patient at the dialysis center). These contact attempts will be documented in the participant's record in REDCap.
- Should the participant continue to be unreachable, he or she will be considered to have withdrawn from the study with a primary reason of lost to follow-up.

8 STUDY ASSESSMENTS AND PROCEDURES

8.1 OUTCOME ASSESSMENTS

Collecting effectiveness outcome data will be centralized; research staff at the Study Coordinating Center will collect the data from patients and surrogates by phone. Telephone-based collection minimizes participants' travel burden. Centralized data collection maintains data collectors being blind to group assignment. The preparedness outcomes will be assessed at 2 weeks post-intervention, as in our R21 trial.[18] We expect roughly 40% of study patients (~160) to die by the 9-month follow-up; deaths are readily identifiable through dialysis clinics and will trigger post-bereavement surveys with surrogates at 3 months and staggered CMS data collection. Post-bereavement assessment at 3 months is based on our efficacy data showing that distress symptoms sharply rose in both groups 2-weeks post-bereavement and then stabilized at 3 months.

Effectiveness Outcomes

Preparedness for end-of-life decision making (measured at baseline and 2 wks post-Session II):

- **Dyad congruence** will be assessed using the Goals-of-Care Tool,[18,20] which includes two scenarios describing medical conditions commonly occurring in ESRD patients. In the first, the patient develops a severe complication and cannot speak for himself/herself; the medical team believed recovery unlikely and continuing life-sustaining treatment, including dialysis, would no longer be beneficial. In the second scenario, the patient develops advanced dementia. Each scenario has three response options: "The goals of care should focus on delaying my death, and thus I want to continue life-sustaining treatment", "The goals of care should focus on my comfort and peace, and thus I do not want life-sustaining treatment, including dialysis", and "I am not sure". Patients and surrogates complete this tool independently and their responses are then compared to determine dyad congruence -- either congruent in both scenarios or incongruent. If both members of the dyad endorse "I am not sure", they are considered incongruent.
- **Patient decisional conflict** will be measured using the 13-item Decisional Conflict Scale (DCS), a validated measure in the context of end-of-life decision making[17]; higher scores indicate greater difficulty in weighing benefits and burdens of life-sustaining treatments and decision making (range 1-5; Cronbach's α = 0.8 – .93[17,18,20,72]).
- **Surrogate decision-making confidence** will be measured using the 5-item Decision Making Confidence (DMC) scale (Cronbach's α = 0.81-0.90[18,34]) on which higher scores reflect greater comfort in performing as a surrogate (range 0, not confident at all-4, very confident). DMC is a self-report of a surrogate's confidence in: knowledge of the patient's wishes, ability to make treatment decisions even in a highly stressful situation, ability to seek information about risks and benefits of medical choices, ability to handle unwanted pressure from others, and ability to communicate with health care providers about the patient's wishes.

- **Composite outcome**: We will also create a composite outcome combining dyad congruence and surrogate DMC to differentiate surrogates who understand the patient's wishes and feel confident in their role from those who don't (understand the wishes but lack confidence, misunderstand the wishes but feel confident, neither understand nor feel confident).[18,34]
- We will also assess **the overall preparedness for end-of-life decision making** using the 26-item investigator-developed measure. The measure assesses the level of preparedness for end-of-life decision making in the cognitive, emotional, and behavioral dimensions on a 4-point scale (4=strongly agree to 1=strongly disagree) with higher scores indicating higher levels of preparedness. Patient and surrogate each will complete this measure separately.

During the supplement cohort study, the participating dyads will complete the same measures above twice, at enrollment and 6 months after.
In addition, they will complete the COVID-19 Stress Scale. **COVID-19 Stress Scale**[35] is a 35-item measure to assess pandemic related emotional responses (i.e., COVID-19 stress and anxiety symptoms) on a 5-point scale ranging from 0 (not at all) to 4 (extremely). The subscales are (1) danger and contamination fears, (2) fears about economic consequences, (3) xenophobia, (4) compulsive checking and reassurance seeking, and (5) traumatic stress symptoms about COVID-19. The scale has demonstrated excellent internal consistency reliability (Cronbach's α>.8 for all subscales) and convergent and discriminant validity. We will also add an overall rating to assess how much respondents worry about COVID-19, which recently was used by Wang *et al*.,[36] "Please rate the level of your current worry toward COVID-19" on a scale ranging from 1 (very mild) to 10 (very severe).

Surrogates' post-bereavement psychological distress (at baseline and 3 mo. post patient death):
Symptoms of anxiety, depression, and post-traumatic distress[42,73] will be measured using the Hospital Anxiety and Depression Scale (HADS)[74]; subscale scores range from 0 to 21 with higher scores indicating greater symptom severity. Internal consistencies and test-retest reliabilities are 0.88–0.90 and 0.84–0.94, respectively.[75] Intensity of post-traumatic distress symptoms will be assessed using the Post-Traumatic Symptoms Scale-10 (PTSS-10).[76] Higher scores indicate more intense symptoms (range 10-70).[77] The PTSS-10 has been shown to have high sensitivity and specificity.[76,78,79]

Implementation Process Outcomes
For the initial SPIRIT intervention, after the final dyads have completed the SPIRIT sessions (~Year 3, Q1), care providers will complete a survey and an interview.

- **Care provider acceptability** will be evaluated using the 7-item Care Providers' Perceived Acceptability Survey to assess their perceptions about SPIRIT implementation, including the time required, impact on interactions with patients, and whether they would recommend SPIRIT to other clinics.[80] Response options range from 1=strongly disagree to 4=strongly agree; higher scores indicate greater acceptability.
- **A brief (~15 min.) semi-structured interviews (face-to-face or by telephone; audio-recorded) will obtain providers' perspectives** on whether the implementation of SPIRIT is compatible with their setting and the workflow, it's perceived utility, their willingness to continue using it after the study, factors influencing implementation (barriers, logistical constraints, and facilitators), and suggestions for improvement.
- **Patient and surrogate acceptability** will be assessed using the 10-item ACP Acceptability Questionnaire developed from our previous trial,[24] Participants are asked how strongly they agree or disagree (4 to 1) with statements about their experience with SPIRIT sessions, including duration, interactions with the care provider, level of comfort and satisfaction. Higher scores indicate greater acceptability. Each patient and surrogate will complete this survey at the 2-week post-intervention follow-up.
- **Fidelity/adherence** will be assessed using two independent data sources, (a) the SPIRIT Interview Guide, Checklist, and self-evaluation completed by the care provider after each SPIRIT session and (b) patient and surrogate responses to the SPIRIT components coverage during the 2-week post-intervention follow-up as described above. The number of SPIRIT components covered, the minutes required for the care provider

to complete the sessions, the number of dyads who complete SPIRIT sessions, and the number of incomplete or interrupted sessions will be aggregated.

- **Intervention cost**s will be estimated based on the actual time the care provider spent in carrying out SPIRIT, multiplied by hourly wage (+benefits), plus costs of materials. Overhead (e.g., facility) costs and research staff's time will not be included.
- We define **sustainability** as the extent to which a newly implemented intervention is maintained within a service setting's ongoing, stable operations.[81] In Y4, Q4, we will conduct a brief interview with SPIRIT care providers to ask about sustainability: (a) Is SPIRIT on-going (and at what frequency)? (b) What components of the SPIRIT protocol have been retained? and (c) Has SPIRIT implementation been evaluated at the clinic level? If so, how?[82]

For the delayed SPIRIT implementation, the process evaluation will involve care providers only since patient and surrogate study participation will have ended at the end of 9-month follow-up or patient death. Care provider acceptability, fidelity, and intervention costs will be determined as described above.

End-of-life treatment intensity (upon patient death)

We will link study data to publicly available USRDS data. The USRDS captures inpatient and outpatient Medicare claims on all treated U.S. ESRD patients and releases these data annually free of charge. Medicare claims data are the most complete and reliable source of data on end-of-life care intensity because patients on dialysis are Medicare beneficiaries. The USRDS data are far superior to that which could be obtained through individual hospitals because data collection at the latter is extremely difficult and highly likely to result in missing data. From the inpatient and outpatient claims data, we will obtain dates and attributed causes of death; dates of hospital, skilled nursing facility, and hospice admissions and discharges; dates of outpatient encounters (including dialysis sessions and ED visits); and diagnostic and procedure codes for all inpatient and outpatient encounters. Thus, we will be able to determine hospitalization, ICU days, days hospitalized, use of intensive procedure, (dis)continuation of dialysis (also from CMS Form 2746), and hospice use during the final month of life. We will consider the following to be intensive procedures: mechanical ventilation, feeding tube placement, dialysis, and cardiopulmonary resuscitation.[22] These intensive procedures will be identified using HCPCS and ICD-9-CM codes (e.g., ICD-9 codes for intubation and mechanical ventilation: 96.04, 96.05, 96.7X).[83]

Descriptors and Potential Covariates

- Patients and surrogates will complete a **Sociodemographic Profile** which includes age, gender, race and ethnicity, type of relationship between patient and surrogate, marital status, religious affiliation, education, household income, previous end-of-life decision-making experience, and previous participation in an ACP discussion or AD completion.
- To describe the sample, **the patient's clinical characteristics**, including dialysis modality, years on dialysis, comorbid conditions will be abstracted from the patient's EMR.
- **Care providers' sociodemographic data** will include age, gender, race and ethnicity, education, and years of practice.
- At baseline, we will collect **clinic-level contextual data**[84] that could facilitate understanding study results, including staffing, patient census, rural-urban status,[85-89] palliative care and hospice availability, and proximity of hospitals.

For Supplement Aims,

- **The preparedness outcomes measures** will be assessed at baseline and 2-3 days after the intervention.
- **Surrogates' post-bereavement psychological distress** will be assessed using the HADS, which will be completed at baseline and 1 month post patient death.
- **Patients' level of articulation of end-of-life wishes:** Using a "quantitizing" technique of qualitative data analysis,[39] two raters will independently review SPIRIT session transcripts focusing on the values of

treatment outcomes and the goals of care discussions and rate the level of patient's articulation of end-of-life care preferences on a 3-point scale (3=expressed wishes very coherently, 2=somewhat coherently, 1=unable to express wishes coherently). Inter-rater reliability (percent agreement) will be established, targeting ≥ 90%.

- **Care decisions (assessed at 6 months post intervention or after the patient's death, whichever occurs first):** Stopping dialysis, DNR order, and hospice enrollment are major care decisions that must involve the treating physician (or APRN) and social worker. These decisions are also required to be documented in the CMS Form 2746 in the event of a dialysis patient's death. On a monthly basis, the research coordinator will check in with the outpatient dialysis APRN to track these care decisions and will be aggregated at 6 months.
- **Descriptors and Potential Covariates (collected at baseline):** Patients and surrogates will each complete a Sociodemographic Profile which includes demographic information and previous end-of-life decision-making experience. Patients' clinical characteristics (e.g., date of dementia diagnosis, etiology of dementia, and comorbid conditions) will be abstracted from the patient's medical records.

8.2 SAFETY AND OTHER ASSESSMENTS

SPIRIT is a one-time psychoeducational intervention. The study involves very low risk and the potential risk may include fatigue or emotional upset during the session.

Fatigue

As part of outcome assessment, HADS and PTSS-10 will be completed. Although these measures are not diagnostic tools, if a surrogate's HADS-Depression is high (≥ 15), the data collector will ask the surrogate if she/he is aware of the mood state and encourage to speak to his/her primary care provider. If a surrogate expresses suicidal ideation, the data collector will immediately notify the local site coordinator who will confer with the Site PI. This Site PI will determine if referral to the local mental health clinic (during hours) or the 24-hour Emergency Psychiatry Service (after hours) for evaluation of mental health or emergency intervention is necessary.

8.3 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

8.3.1 DEFINITION OF ADVERSE EVENTS (AE)

SPIRIT is a one-time psychoeducational intervention. The study involves very low risk and the potential risk may include fatigue or emotional upset during the session, neither of which is a "medical occurrence". SPIRIT has been extensively tested in previous trials and no safety concerns have ever arisen. The present trial is to generate data to accelerate translation of the intervention into clinical practice.

8.3.2 DEFINITION OF SERIOUS ADVERSE EVENTS (SAE)

The trial targets ESRD patients on dialysis who already have serious life-threatening medical conditions and are likely to die within a year (by clinician's judgment). SPIRIT is an advance care planning intervention to prepare these patients and their surrogates for end-of-life decision making. SPIRIT's safety and beneficial effects (e.g., reducing psychological distress) have been consistently demonstrated. Participants' deaths or hospitalizations (or other events described above) during the trial are expected (and needed to answer the scientific questions) and will occur as part of the illness course. These events will not be considered as SAE in this trial. However, any participant's death will be reported to IRB through annual progress report and included in the NIH annual progress report.

8.3.3 CLASSIFICATION OF AN ADVERSE EVENT

8.3.3.1 SEVERITY OF EVENT

Not applicable.

8.3.3.2 RELATIONSHIP TO STUDY INTERVENTION

Not applicable.

8.3.3.3 EXPECTEDNESS

There are no known expected adverse reactions. SPIRIT has been tested in 5 RCTs with various patient populations with serious chronic conditions and in 3 different regions and settings. Although possible adverse reactions to the intervention may include fatigue or emotional distress during the intervention session, no such reactions have been observed in the previous studies. Thus, these reactions are very unlikely to occur and will be considered “unexpected.” Intervention sessions will stop if any of these events occurs.

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

Not applicable.

8.3.5 ADVERSE EVENT REPORTING

The possible adverse reactions (fatigue, emotional distress during the intervention session), if ever occurs, will be tracked (documented in the study REDCap) and the aggregated numbers will be reported at the upcoming biannual DSMB meeting.

Any disease-related events (DREs) common in the study population (e.g., expected) such as death will not be reported per the standard process of reporting but will be monitored so that surrogates’ post-bereavement outcomes and end-of-life treatment intensity data (Medicare claims data) can be collected timely. However, any participant’s death will be reported to IRB through annual progress report and included in the NIH annual progress report.

8.3.6 SERIOUS ADVERSE EVENT REPORTING

Not applicable.

8.3.7 REPORTING EVENTS TO PARTICIPANTS

Not applicable.

8.3.8 EVENTS OF SPECIAL INTEREST

Not applicable.

8.3.9 REPORTING OF PREGNANCY

Not applicable.

8.4 SUBJECT SAFETY

Any unexpected problem related to the Research that negatively affects the rights, safety or welfare of subjects and is not described as such in the materials describing risks associated with the study.

8.4.1 DEFINITION OF UNANTICIPATED PROBLEMS (UP)

Unanticipated problems are defined by DHHS 45 CFR part 46 as any incident, experience, or outcome that meets all of the following criteria:

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

It will be extremely unlikely in this study that the events of fatigue and emotional distress would meet the all of the criteria above.

8.4.2 UNANTICIPATED PROBLEM REPORTING

If we encounter any adverse event that meets the definition above and that is related to the intervention, the PI will notify the Emory IRB and NINR Program Official and the DSMB within 24 hours of the event being reported to the PI. The expedited report will be followed by a detailed, written SAE report as soon as possible.

8.4.3 REPORTING UNANTICIPATED PROBLEMS TO PARTICIPANTS

Not applicable.

9 STATISTICAL CONSIDERATIONS

9.1 STATISTICAL HYPOTHESES

- Primary Endpoint(s):
  1) The number of SPIRIT dyads who are congruent on goals of care at 2 weeks post-intervention will be significantly higher than that of control dyads.
  2) Patient decisional conflict scores at 2 weeks post-intervention will be significantly lower than those of control dyads.
  3) Surrogate decision making confidence (DMC) scores at 2 weeks post-intervention will be significantly higher than those of control dyads.

4) The number of SPIRIT dyads who are congruent on goals of care and confident surrogate (DMC=3 or higher) at 2 weeks post-intervention will be significantly higher than that of control dyads.

- Secondary Endpoint(s):
  1) HAD-anxiety scores in SPIRIT surrogates will be significantly lower than those of control surrogates at 3 months after the patient's death.
  2) HAD-depression scores in SPIRIT surrogates will be significantly lower than those of control surrogates at 3 months after the patient's death.
  3) PTSS-10 scores in SPIRIT surrogates will be significantly lower than those of control surrogates at 3 months after the patient's death.

- Exploratory: Among patients who have died,
  1) The percentage of patients hospitalized during the final month of life in the SPIRIT group will be significantly lower than that in the control group.
  2) The percentage of patients admitted to an ICU during the final month of life in the SPIRIT group will be significantly lower than that in the control group.
  3) The percentage of patients having intensive procedures during the final month of life in the SPIRIT group will be significantly lower than that in the control group.
  4) The length of hospital stay during the final month of life in the SPIRIT group will be significantly shorter than that in the control group.

For Supplement Aims:

- Aim 1:
  1) The number of SPIRIT dyads who are congruent on goals of care at 2-3 days post-intervention will be higher than that of control dyads.
  2) Patient decisional conflict scores at 2-3 days post-intervention will be lower than those of control dyads.
  3) Surrogate decision-making confidence (DMC) scores at 2-3 days post-intervention will be higher than those of control dyads.
  4) The number of SPIRIT dyads who are congruent on goals of care and confident surrogate (DMC=3 or higher) at 2-3 days post-intervention will be significantly higher than that of control dyads.
  5) The proportion of decisions made at 6 months (e.g. stopping dialysis, DNR order, and hospice enrollment etc.) follow-up or death of patient will be higher in the intervention dyads than that of control dyads.

- Aim 2:
  1) HAD-anxiety scores in SPIRIT surrogates will be lower than those of control surrogates at 1 month after the patient's death.
  2) HAD-depression scores in SPIRIT surrogates will be lower than those of control surrogates at 1 months after the patient's death.

Supplement cohort study:

Aim 1. Changes in patient's goals of care preferences over time (T2-T3 and T2-T4) in the intervention group will be smaller than those in the control group.
Aim 2. Changes in the preparedness outcomes over time in the intervention group will be smaller than those in the control group.
Aim 3. The COVID-19 Related Stress and race/ethnicity will be significantly associated with changes in goals of care stability and the preparedness outcomes.

9.2 SAMPLE SIZE DETERMINATION

We have an adequate sample size to detect clinically meaningful differences between SPIRIT and usual care for our primary outcomes. Statistical power is based on a random effects models: a generalized linear mixed model for binary outcomes (e,g., dyad congruence) and a linear mixed model for continuous outcomes (e.g., patient decisional conflict).

Power for comparing SPIRIT and usual care with 19 clusters

Aim 1	Percent or min. difference	*OR* or variance	ICC[a]	Estimated power
Dyad congruence	48%	*OR*=2.0	0.02	0.92
			0.04	0.84
Patient DCS	*d*=0.24	0.23	0.01	0.98
			0.10	0.81
Surrogate DMC	*d*=0.22	0.20	0.01	0.99
			0.10	0.80
Composite outcome	47%	*OR*=2.0	0.02	0.93
Aim 3				
Anxiety	*d*=1.35	7.0	0.01	0.84
			0.03	0.80
Depression	*d*=1.60	10.0	0.01	0.85
			0.03	0.79
PTSS-10	*d*=4.75	90.0	0.01	0.85
			0.03	0.78

[a] observed ICCs in our prior work; *d*=1/2 *SD*.
DCS, decisional conflict scale; DMC, decision-making confidence.

We conducted a simulation study to estimate power with 2-sided significance level alpha=.05, corrected for anticipated dropout and potential intraclass correlations (ICCs) ranging .01-.04, based on ICCs observed in our prior work. To estimate the power more conservatively, we used the effect sizes observed at 2 months[20] rather than those at 2 weeks,[18] which are larger (e.g., for the composite outcome, *OR*=1.8 at 2 months, *OR*=4.4 at 2 weeks). The overall power to detect clinically meaningful differences is excellent for the primary outcomes and good for the post-death outcomes.

For Supplement Aims:
Because this is a pilot study, prior estimates of effect sizes were not available; thus a traditional sample size calculation was not performed. Instead we focused on calculating the minimum effect size that can be detected with adequate power (>=80%). Based on preliminary calculations, we found that a sample size of 30 will achieve 80% power to detect an effect size (Cohen's f^2) of 0.28 (moderate-high), attributable to the treatment group indicator using an F-test at a 5% significance level. We will use the estimates of effect sizes obtained from this study for sample size calculations in future larger studies.

Supplement cohort study:

Due to the exploratory nature of the study, a traditional sample size calculation was not performed. Instead, our goal was to provide estimates of effect sizes (standardized mean differences between pre- and during- COVID-19 study points) for the outcomes in aims 1-3. Preliminary power calculations based on a two-sample t-test, indicate that a sample size of 72 in the SPIRIT intervention and 35 in the usual care group achieve 80% power to detect a difference in mean changes of 0.5 between the groups. This calculation assumes a repeated measures design with a standard deviation of 1.0 at both time points, a between measurement correlation of 0.2 and a 5% significance level.

9.3 POPULATIONS FOR ANALYSES

Patient-surrogate dyads will be the primary unit of analysis; all analyses will be intent to treat with all available data from all participants.

9.4 STATISTICAL ANALYSES

9.4.1 GENERAL APPROACH

The preliminary analysis will include summarizing variables with standard descriptive statistics and graphical displays or frequency tables. Distributional assumptions will be assessed and the data will be transformed as necessary. Clinic characteristics (e.g., rural-urban status) will be compared using χ^2 tests for categorical variables and t-tests for continuous variables. We will compare SPIRIT and usual care participants on baseline characteristics (e.g., age, race/ethnicity) to explore possible between-group differences using generalized estimating equation (GEE) methods, accounting for the observed correlation within the same cluster.[90,91] In our previous work SPIRIT has no effect on patient mortality[20]; however, we will compare survival time between SPIRIT and usual care using Cox proportional hazards models, adjusted for cluster effects. If imbalanced, we will consider adjustment for the group difference.

9.4.2 ANALYSIS OF THE PRIMARY ENDPOINT(S)

SPIRIT effectiveness on the preparedness outcomes: Dyad congruence and the composite outcome (binary variables) will be analyzed by fitting a generalized mixed effects model for each, where the binary outcome is modeled in terms of a logit link[90] with both a random intercept and random slope to control for variation within and between subjects and clusters. The model also includes the intervention SPIRIT, cluster size and their interaction. For patient DCS and surrogate DMC scores, we will replace the logit link by the identity link with an additional error term. These models will allow us to examine whether SPIRIT was superior to usual care in the primary outcomes at 2 weeks and whether the effect of SPIRIT varies by cluster size. The analysis will be adjusted for potential covariates, such as race/ethnicity, and rural-urban status, in the model, including interaction between treatment and race/ethnicity.

For Supplement Aims:
To account for small sample size, resampling methods will be used for all analyses and 95% bootstrap confidence intervals of the differences in outcome scores will be reported.

1) Aim 1. SPIRIT effects on the preparedness outcomes: For testing the effect of the intervention on dyad congruence, a paired binary outcome (congruent or not congruent), Mcnemar's test will be used. In addition, a logistic regression model will be used to test for differences in post-intervention outcomes by groups after adjusting for potential covariates. The adjusted ratio of odds of congruence in the intervention group versus the control group will be evaluated and reported as an effect size estimate.

2) Aim 1. SPIRIT effects on care decisions: Differences in proportion of decisions made (e.g. stopping dialysis, DNR order, and hospice enrollment etc.) at 6-month follow up or death of patient will be described across groups and used as effect size. We will also explore time to event analysis to assess the difference in rate of risks between the two groups using non-parametric and semiparametric methods.

3) Aim 2. Surrogate post-bereavement distress (HADS scores): Differences in the HADS subscale scores between the intervention and control groups will be assed using t-tests. Because, we estimate a 50% rate of death during the study, the number for this analysis would be n=15. A standardized difference between groups will be used as an effect size estimate.

4) Aim 3. **Relationships among patients' cognitive status, decision-making capacity and their ability to express end-of-life wishes:** For patients in the SPIRIT intervention arm (n=15), associations between patients' cognitive status (continuous), decision-making capacity (continuous) and their ability to express end-of-life wishes (categorical) will be analyzed using one-way analysis of variance (ANOVA). We will also explore ordinal logistic regression to obtain the proportional odds ratios defined by the odds of "expressing wishes very coherently" or

"expressing wishes somewhat coherently" versus the odds of "unable to express wishes coherently" for a unit increase in cognitive status or decision-making capacity.

Supplement cohort study:

As in the parent R01, we will use the Research Electronic Data Capture (REDCap) to create and update study participants' data. During data entry, automated checks will be performed that will immediately flag problematic data (e.g., missing, out of range, inconsistent). Preliminary analyses will include summarizing variables with descriptive statistics and graphical displays. We will assess distributional assumptions of the outcomes and apply appropriate transformations to remedy any violations. Any differences in patient characteristics (e.g. age, sex, education level, household income) across groups will be adjusted when modeling the outcomes. As observed in the parent R01 (< 1% missing data), we expect very little missing data. Nonetheless, we plan to use restricted maximum likelihood (REML) method for estimating the repeated measures analysis to minimize the impact of missing data. This will make it possible to retain cases with partial data while making less restrictive assumptions about missing data patterns.

Aim 1. Compare the stability of patients' goals-of-care preferences over time, from pre-outbreak to during-outbreak, by group and estimate effect by race: We will use mixed effects modeling to assess differences in patients' goals of care over time, from pre- to post-lockdown time points. We will sequentially build a longitudinal model that will include time, treatment group and race as fixed effects; then 2-way interactions of time x group, time x race, treatment x race, and finally a 3-way interaction of time x group x race, if the sample size permits. We will select the most parsimonious model using Akaike information criterion (AIC) and Bayesian information criterion (BIC). We will use contrasts to test whether participants demonstrated significant change in goals-of-care preferences across different combinations of treatment and race.

Aim 2. **Assess the stability in the three preparedness outcomes, from pre-outbreak to during-outbreak by group, and estimate race effect:** We will perform analyses similar to those described in Aim 1. In addition, for non-normal outcomes (binary, count) a generalized mixed effects model will be used. Appropriate contrasts will be used to assess differences in the outcomes over time by treatment groups, race and groups x race.

Aim 3. Examining the associations of the COVID-19 Related Stress, sex, race/ethnicity, and other sociodemographic characteristics to the level of changes in the preparedness outcomes and patient's goals-of-care preference stability: We will use analysis of covariance to assess the relationship between COVID-19 related stress and changes in outcomes from T2 to T3 and T3 to T4, after controlling for the corresponding baseline values of the outcomes (i.e., T2 and T3 respectively). Using similar methods, we will evaluate whether there are disparate effects of sex, race/ethnicity and other sociodemographic factors on outcome changes and goals-of-care preference stability from T2 to T3 and T3 to T4, respectively

9.4.3 ANALYSIS OF THE SECONDARY ENDPOINT(S)

Analysis of secondary endpoints are not dependent on findings of primary endpoints.

SPIRIT effectiveness on surrogates' post-bereavement psychological distress: We will use the same approach as in the analysis of the primary endpoints to compare anxiety, depression, and post-traumatic distress symptoms in SPIRIT vs usual care among surrogates of patients who die during the initial implementation and 9-month (or extended) follow-up.

Implementation process outcomes: Quantitative data on acceptability, fidelity, and costs of SPIRIT will be summarized using descriptive statistics. SPIRIT will be determined to be acceptable to care providers and patients and surrogates if over 75% of responses exceed an average summative score ≥ 3 (of 4) on the acceptability measures. Cost estimates will be used to ascertain resources needed to implement or replicate SPIRIT in the

future.[92] We will also explore the relationships of these quantitative data with characteristics of settings and stakeholders. Transcripts of acceptability interviews will be transferred to ATLAS.ti for analysis. Content analysis techniques[93] will be used without preconceived categories.[94] Open coding will be applied[95] and disagreements on coding will be resolved by consensus. We will examine the data for patterns or differences in themes between those with acceptability scores >=3 and scores <3 and setting characteristics. This analysis will be facilitated by creating matrixes that organize textual and numeric data for comparing and contrasting[96] so that what contributed to acceptability scores that are positive and less than positive may be identified. We will use a similar approach, content analysis, to evaluate the sustainability data.

9.4.4 SAFETY ANALYSES

Not applicable.

9.4.5 BASELINE DESCRIPTIVE STATISTICS

See 9.4.1 General Approach.

9.4.6 PLANNED INTERIM ANALYSES

Not applicable.

9.4.7 SUB-GROUP ANALYSES

In order to evaluate whether the SPIRIT has differential effects according to demographic factors such as age, sex, race/ethnicity we consider the same generalized mixed effects model in the context of protocol design, mentioned in Section 9.4.1. Our approach is first to consider each factor one at a time. We will fit the same generalized mixed model by additionally including a subject level factor (e.g., race) and its' interaction with the SPIRIT. If the interaction is significant the analysis will indicate that SPIRIT effect changes according to race. We will report p-values and importantly, standard errors and confidence intervals by recognizing the fact that we may not have power to detect significant interaction effects for examining all demographic factor combinations.

For Supplement Aims: no subgroup analyses will be possible due to the small sample size.

Supplement cohort study: no subgroup analyses will be possible due to the small sample size

9.4.8 TABULATION OF INDIVIDUAL PARTICIPANT DATA

Individual participant data will be listed by measure and time point.

9.4.9 EXPLORATORY ANALYSES

SPIRIT effectiveness on end-of-life treatment intensity: Among patients who die during the initial SPIRIT implementation and follow-up, percentages of patients hospitalized, having ICU admission, having intensive procedures and length of hospital stay in the final month of life will be summarized using descriptive statistics, 95% CIs, and graphical displays. The exploratory examination of SPIRIT's effectiveness on improving these outcomes, we will use the same analytic approach as in the analysis of the primary endpoints (See 9.4.2).

10 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1 REGULATORY, ETHICAL, AND STUDY OVERSIGHT CONSIDERATIONS

10.1.1 INFORMED CONSENT PROCESS

10.1.1.1 CONSENT/ASSENT AND OTHER INFORMATIONAL DOCUMENTS PROVIDED TO PARTICIPANTS

Consent forms describing in detail the study intervention, study procedures, and risks are given to the participant and written documentation of informed consent is required prior to starting intervention/administering study intervention. The following consent materials are submitted with this protocol.

- Patient Consent Form-SPIRIT
- Patient Consent Form-Usual Care
- Surrogate Verbal Consent Form –SPIRIT
- Surrogate Verbal Consent Form – Usual Care
- Care Provider Verbal Consent Form
- VERBAL Consent Addendum – Patient
- VERBAL Consent Addendum - Surrogate

For Supplement Aims, the following consent materials will be used:

- Patient Verbal Consent for Screening (cognitive impairment level)
- Patient Consent Form
- Surrogate Verbal Consent Form

Supplement cohort study:

- Verbal Consent Addendum for Cohort – Patient
- Verbal Consent Addendum for Cohort - Surrogate

10.1.1.2 CONSENT PROCEDURES AND DOCUMENTATION

Participating dialysis centers/clinics will be randomized first (see the study flow diagram). The care team member who has been selected by the clinic as a care provider responsible for SPIRIT delivery at each clinic in both groups (e.g., nurse or social worker) will generate a list of patients each quarter based on the inclusion criteria. This staff member may differ from clinic to clinic depending on who is qualified, comfortable and able to assess each potential participant. The medical director of the dialysis unit (and/or the attending physician as required) approves the list if required by the dialysis center. From this list, one of the care providers will then assess the patient's willingness to meet with a recruiter from the research team. The recruiter (e.g., site coordinator) will then approach willing patients during their scheduled dialysis clinic appointment.

Consent forms have been Institutional Review Board (IRB)-approved and the participant will be asked to read and review the document. In a private room, a verbal explanation will be provided in terms suited to the patient's comprehension of the purposes, procedures, and potential risks of the study and of their rights as research participants. Patient participants will have the opportunity to carefully review the written consent form (including HIPAA authorization from) and ask questions prior to signing. The patient participants should have the opportunity to discuss the study with their family or surrogates or think about it prior to agreeing to participate. The patient participant will sign the informed consent document prior to any procedures being done specifically for the study. Patient participants must be informed that participation is voluntary and that they may withdraw from the study at any time, without prejudice. A copy of the informed consent document will be given to the

participants for their records. The informed consent process will be conducted and documented in the source document (including the date), and the form signed, before the participant undergoes any study-specific procedures. The rights and welfare of the participants will be protected by emphasizing to them that the quality of their medical care will not be adversely affected if they decline to participate in this study. The recruiter will then provide the patient participant with a study brochure and encourage him/her to talk to the surrogate regarding the study within the next 2-3 days (to avoid a cold call).

Several days later, the recruiter will telephone the potential surrogate participant to assess his/her willingness to participate. Following the Surrogate Verbal Consent Form, a verbal explanation will be provided in terms suited to the surrogate's comprehension of the purposes, procedures, and potential risks of the study and of their rights as research participants. Upon the surrogate's verbal consent using the IRB approved script/form, the research staff at the Emory Study Coordination Center will schedule and conduct a baseline data collection session. All surrogates will provide verbal consent only with a waiver of written consent and a Surrogate Verbal Consent form will be signed by the recruiter.

For Supplement Aims:
Participants will be recruited from the Emory dialysis centers and UVA dialysis centers. First, patients who have been diagnosed with an early stage of dementia (mild to moderate) or are suspected of having cognitive impairment by a care provider will be referred by the dialysis APRN. The medical records of those patients will be reviewed to preliminarily determine eligibility by a research staff member. During the patient's dialysis treatment session at the center, the patient's care provider will gain permission for the staff member to explain the study. With the patient's permission, the staff member will approach the patient, briefly explain the study, obtain verbal consent to conduct the MOCA or SLUMS and UBACC screening. If the patient has met the criteria for both early stages of cognitive impairment and decision-making capacity, the research staff member will provide detailed study information and confirm his/her surrogate decision-maker. Written consent will then be obtained from the patient. The research staff member will obtain the name and phone number of the surrogate (or confirm with the medical record as necessary) and call the surrogate in 2-3 days to assess the surrogate's willingness to participate. Verbal consent will be obtained from the surrogate.

Supplement cohort study:

At the upcoming scheduled monthly check-in call with the participant (in the parent study, a check-in telephone call [scripted] is made to each member of the dyad after the 2-week follow-up call), the research staff member will proceed with the procedures for the parent study and then introduce the participant to the supplement study, including the purpose and procedures and obtain verbal consent. After both members of the dyad have consented, the recruiter will schedule two data collection calls (baseline/T3 and 6 months/T4).

10.1.2 STUDY DISCONTINUATION AND CLOSURE

It is very unlikely that this study may be suspended or prematurely terminated sine the SPIRIT intervention has been extensively tested, including its safety and efficacy. Also, this study aim includes collecting implementation data and no planned interim analysis and stopping rules. Nonetheless, if suspension or termination occurs, written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to study participants, investigator, dialysis organizations, and regulatory authorities. If the study is terminated or suspended, the Principal Investigator (PI) will promptly inform study participants, the Institutional Review Board (IRB), and sponsor and will provide the reason(s) for the termination or suspension. Study participants will be contacted, as applicable, and be informed of changes to study appointment schedule.

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

- Determination of unexpected, significant, or unacceptable risk to participants
- Insufficient compliance to protocol requirements

Study may resume once concerns about safety, protocol compliance, and data quality are addressed, and satisfy the sponsor and IRB.

10.1.3 CONFIDENTIALITY AND PRIVACY

Participant confidentiality and privacy is strictly held in trust by the participating investigators, their staff, and the sponsor. The study documentation, data, and all other information generated will be held in strict confidence. No information concerning the study or the data will be released to any unauthorized third party without prior written approval of the sponsor.

All research activities will be conducted in as private a setting as possible.

The study monitor, other authorized representatives of the sponsor, representatives of the Institutional Review Board (IRB), regulatory agencies may inspect all documents and records required to be maintained by the investigator, including but not limited to, medical records (office, clinic), for the participants in this study. The clinical study site will permit access to such records.

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

Study participant research data, which is for purposes of statistical analysis and scientific reporting, will be directly entered into and stored in REDCap study database. Individual participants and their research data will be identified by a unique study identification number. All information collected during the study will be secured and password protected. At the end of the study, all study databases will be de-identified and archived at the Emory Study Coordination Center.

10.1.4 FUTURE USE OF STORED SPECIMENS AND DATA

Data collected for this study will be analyzed and stored at the Emory Study Coordination Center. After the study is completed, the de-identified, archived data will be transmitted to and stored in the REDCap study archive for use by other researchers including those outside of the study. When the study is completed, access to study data will be provided through the Emory Study Coordination Center.

10.1.5 KEY ROLES AND STUDY GOVERNANCE

Study Coordination Center	**Principal Investigator** Mi-Kyung Song, PhD, RN Professor Emory University, School of Nursing 1520 Clifton Rd NE, Atlanta, GA 30322 404-727-3134 *mi-kyung.song@emory.edu*	**Project Director** Mary Laszlo Project Manager Emory School of Nursing 404-727-2882 Mary.laszlo@emory.edu
Study Site	**Site PI**	**Site Coordinator**
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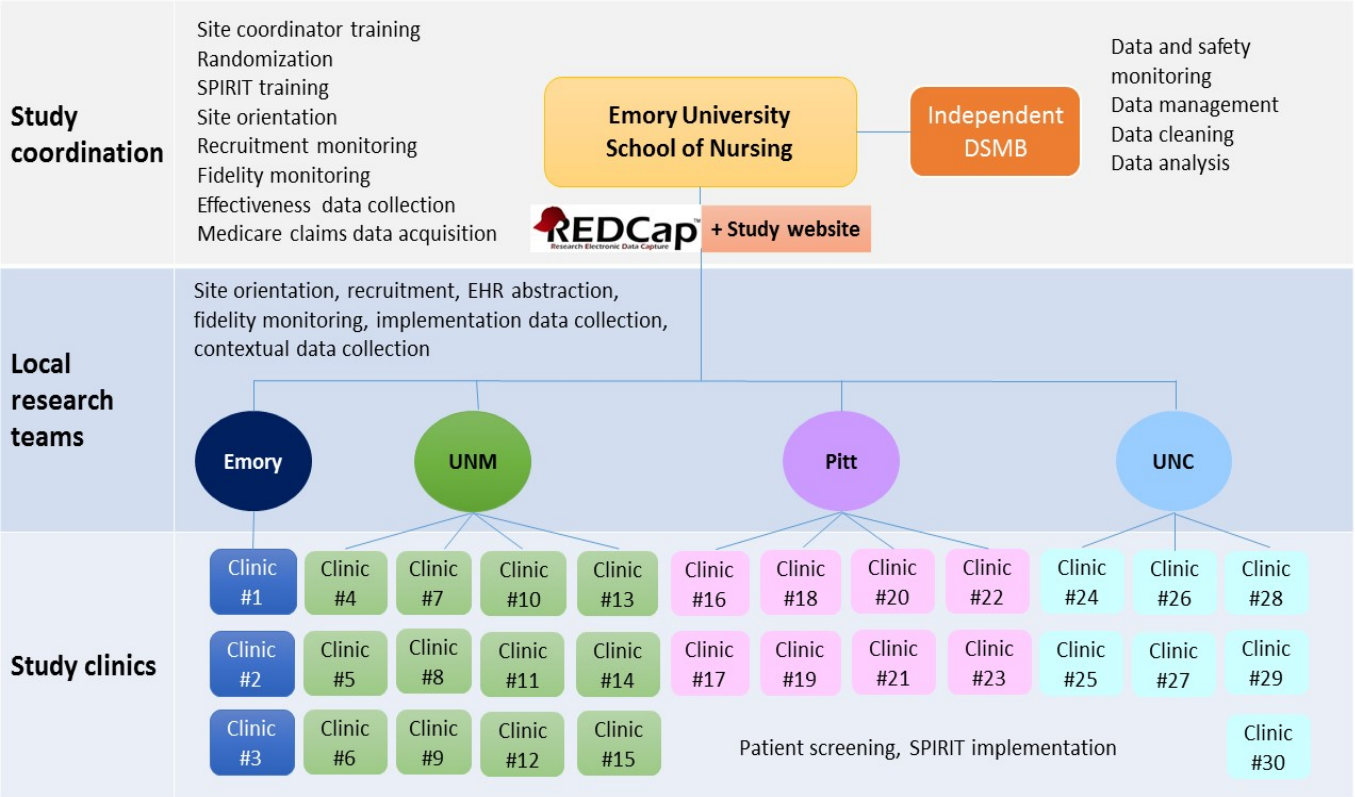
Study organization and coordination



For Supplement Aims:

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Supplement cohort study:

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10.1.6 SAFETY OVERSIGHT

Safety oversight will be under the direction of a Data and Safety Monitoring Board (DSMB) composed of 5 individuals with the appropriate expertise, including dialysis care, advance care planning, palliative care, clinical trials, intervention testing, and biostatistics. Members of the DSMB are independent from the study conduct and free of conflict of interest (see signed disclosure forms).

The DSMB will meet bi-annually to evaluate the study progress, including assessment of data quality, timeliness, participant recruitment, rates of eligibility and ineligibility across study clinics and sites/states, accrual and retention, participant risk versus benefit, performance of trial sites, patient deaths, and any adverse events or care providers' concerns that can affect study outcome. Consistent with prior end-of-life communication interventions, including our prior trials, we do not expect that the intervention will alter mortality rates. Nonetheless, this will be one of the measures monitored by the DSMB. The DSMB will compare recruitment rate and sample characteristics to assumptions used for power calculations. The DSMB will monitor the design factor, intra-cluster correlation coefficient, to assess whether the study will have expected power. Formal interim analyses are not planned for several reasons: (a) the SPIRIT efficacy has been established, (b) risks associated with SPIRIT are very minimal, (c) the control condition is usual care, not a placebo, and (d) the proposed study also aims to gather implementation data, including sustainability, that are critical for widespread implementation. Finally, the DSMB will not monitor fidelity/adherence data and make recommendations for ways to improve adherence because of the pragmatic nature of the proposed trial (i.e., seeking real world answers). The DMSB will operate under the rules of an approved charter that will be written and reviewed at the organizational meeting of the DSMB.

See DSMB Charter.

For Supplement Aims:
Although the proposed study involves minimal risk, we will implement a data and safety monitoring plan at multiple levels to ensure the safety of participants and the validity and integrity of the data:

(1) The PI/Dr. Song will convene weekly meetings with staff to review progress, subject accrual, and any anticipated and unanticipated problems. The weekly progress information will be aggregated for reports and presented at bi-monthly or monthly all investigators meetings.
(2) The PI/Dr. Song will convene a videoconference with the study investigators monthly. At these meetings the investigators will assess study performance related to subject recruitment, review the quality of the data, and discuss any adverse events. The investigators will determine any need for re-training of study staff.

(3) We will set up a Data and Safety Monitoring Committee (DSMC) responsible for reviewing trial data on an ongoing basis to ensure the safety of study participants and validity and integrity of the study data. The DSMC will include 3 experts who are independent, with no vested interest in SPIRIT or trial outcomes (to-be-named; e.g., investigators in the field and academic institutions, and biostatistician).

The DSMC will meet with the PI twice during the study or as needed to evaluate the study progress, including informed consent procedures, participant recruitment, rates of eligibility and ineligibility, assessment of data quality, timeliness, and retention, participant risk versus benefit, breaches in confidentiality, patient deaths, and any adverse events or care providers' concerns that can affect the protection of human subjects and study outcome.

The first meeting will occur at the beginning of the trial. At this meeting, the committee will review the study protocols, including consenting procedures, recruitment and retention procedures for practicality and protection of human subjects and make recommendations as needed. At the subsequent annual meetings, the DSMC will review:

a. Timeliness in meeting the goals for recruitment and retention
b. Adherence to the study protocols
c. Adherence to the intervention protocol
d. Data related to adverse events
e. Quality, completeness, and timeliness of the data collected
f. Factors that could affect the outcome or compromise data or confidentiality
g. Other factors outside the study, such as therapeutic developments, agency related to policies that could impact the safety of participants or the ethical conduct of the study

In general, recommendations the DSMC may make include:

a. Continue the study without change
b. Modifications to the study protocol
c. Suspension or early termination
d. Alternative approaches to consider (e.g., if there is a failure to accrue participants as planned)

The information about adverse events that occur during the study will be sent to the DSMC chairperson, who will distribute it to the other members of the committee. The relatedness of the event to the study would be provided at the time of presentation of the information. In addition, the Emory University IRB and the NIH Program Officer will be notified within one week of the event by the PI.

10.1.7 CLINICAL MONITORING

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

All study data will be directly entered into REDCap. The data entry forms in REDCap will be set up such that out-of-range values are not accepted, which will minimize data entry error. Although HADS (anxiety and depression symptom scales) and PTSS-10 (post-traumatic distress symptom screening) are not diagnostic tools, when a surrogate's HADS score is abnormal (Depression score ≥15), the REDCap data entry form will flag the research staff to notify the surrogate that the local research staff member may confer with the Site PI so that the participant can be referred to a local mental health if necessary.

- The PI and Project Director will conduct centralized monitoring quarterly throughout the study. A random review of 10% primary endpoint data and secondary endpoint data (HADS and PTSS-10) will be performed. A monitoring report will be generated at completion of review and will be shared with the study site teams.
- Independent audits will not be conducted as this trial does not collect clinical data after baseline (as descriptors).

10.1.8 QUALITY ASSURANCE AND QUALITY CONTROL

We will use centralized training of research staff for recruitment and data collection activities as appropriate. The PI and Project Director will train staff in all study procedures. All project staff will complete university sponsored research integrity training, including modules on the protection of human subjects, HIPAA, and Good Clinical Practice. All roles, responsibilities, and a protocol with scripted subject contacts will be clearly delineated in the study Standard Operating Procedures (SOPs). These SOPs will be accessible via REDCap.

Data collectors/recruiters will attend a competency based, one-day training session that the PI and Project Director will convene. Following a demonstration by the PI or Project Director on how to recruit participants and obtain informed consent, the recruiters will be expected to perform three satisfactory practice recruitment sessions before actual performance. The final practice sessions will be audio- or video-recorded and reviewed for adherence to the protocol. After demonstrating satisfactory performance of consenting sessions, the recruiters will be authorized to recruit and enroll participants.

Training for data collection will include scripted data collection techniques with special attention to assessing participant fatigue or discomfort during the data collection session. Data collectors will conduct a series of three practice baseline and follow-up data collections using volunteers. After demonstrating satisfactory performance on data collection, they will be authorized to perform data collection activities with enrolled participants. They will also need to demonstrate completeness of data collection activities using REDCap.

Each study site will perform internal quality management of study conduct, data collection, documentation and completion. In general the following strategies will be employed:

- Use of data collection and data entry SOP
- Before ending the data collection session, review the data entry form in REDCap for any missing data
- Each data collector signs his/her work
- Audit research staff members' performance (e.g., consenting and data collection) Biannually.

We will also employ systematic checking of data quality: The project director at the Emory Study Coordination Center will run quality control checks on the database quarterly; any missing data or data anomalies will be reported to the PI and communicated to the site(s) for clarification/resolution.

The PI/Dr. Song will convene weekly meetings with staff to review progress, subject accrual, and any unanticipated problems at the Emory site. Site PIs will do the same at their respective study sites. The weekly progress information will be aggregated for reports and presented at bi-monthly or monthly all study sites meetings.

To ensure compliance with the monitoring plan and reporting requirements across study sites, the PI/Dr. Song at the Study Coordination Center will convene a videoconference (using Adobe Connect or Zoom) with the study investigators, project director, SPIRIT trainer, and site coordinators monthly. At these meetings the investigators will assess study performance related to subject recruitment across the study sites (at least 1 dyad per month in a small cluster and 3 dyads in a larger cluster), review the quality of the data, and discuss any adverse events.

10.1.9 DATA HANDLING AND RECORD KEEPING

10.1.9.1 DATA COLLECTION AND MANAGEMENT RESPONSIBILITIES

The School of Nursing at Emory University, the Emory site, will be the Study Coordination Center and will maintain close contact with every entity within the study and will monitor study activities. All study sites will use a common study web-portal using the Research Electronic Data Capture (REDCap) created and managed in Emory SON. Each site will create and update study participants' data through REDCap. During data entry, automated checks will be performed that will immediately flag problematic data (e.g., missing, out of range, inconsistent), allowing for the sites to address any discrepant data promptly thus increasing data quality. Data entered into the web-based form are immediately stored in a study database and tracked through a journaling process where they are accessible for review by the study team. Social Security numbers are entered directly into REDCap and not listed on paper forms. Suspicious data can be flagged through a query management system, and automated alerts provided to the sites. A complete audit trail is stored for each database modification. Any discrepant data identified through analytic manipulations will be communicated to the sites. Once all queries have been resolved and the database has been deemed "clean", it will be officially locked. All permissions to make changes (append, delete, modify or update) to the database by the sites will be removed at that time.

Record keeping and data collection (recruitment data, patient medical record review at enrollment, clinic-contextual data, SPIRIT implementation data) are the responsibilities of the research staff at the site under the supervision of the site investigator. The investigator is responsible for ensuring the accuracy, completeness, legibility (if hardcopies of worksheets are used), and timeliness of the data reported.

10.1.9.2 STUDY RECORDS RETENTION

All study's written records will be stored in a locked cabinet for 5 years. Study data will be de-identified and shared with future researchers per written request and IRB approval (Resource and Data Sharing Plans).

10.1.10 PROTOCOL DEVIATIONS

A protocol deviation is any noncompliance with the clinical trial protocol, International Conference on Harmonisation Good Clinical Practice (ICH GCP), or Manual of Procedures (MOP) requirements. The noncompliance may be either on the part of the participant, the investigator, or the study site staff. As a result of deviations, corrective actions are to be developed by the site and implemented promptly.

It is the responsibility of the site investigator to use continuous vigilance to identify and report deviations within 7 working days of identification of the protocol deviation. See Protocol Deviation/Violation Report Form and the related SOP. All deviations will be addressed in study source documents, reported to the Study Coordination Center. The site investigator is responsible for knowing and adhering to the reviewing IRB requirements.

10.1.11 PUBLICATION AND DATA SHARING POLICY

This study will be conducted in accordance with the following publication and data sharing policies and regulations:
National Institutes of Health (NIH) Public Access Policy, which ensures that the public has access to the published results of NIH funded research. It requires scientists to submit final peer-reviewed journal manuscripts that arise from NIH funds to the digital archive PubMed Central upon acceptance for publication.
This study will comply with the NIH Data Sharing Policy and Policy on the Dissemination of NIH-Funded Clinical Trial Information and the Clinical Trials Registration and Results Information Submission rule. As such, this trial has

been registered at ClinicalTrials.gov, and results information from this trial will be submitted to ClinicalTrials.gov. In addition, every attempt will be made to publish results in peer-reviewed journals.

Authorship determination: Authorship confers credit and has important academic, social, and financial implications. Authorship also implies responsibility and accountability for published work. We will follow the recommendations by the International Committee of Medical Journal Editors (ICMJE) to determine authorship (vs. non-author contributors). http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html

Authorship will be based on the following 4 criteria:

1. Substantial contributions to the conception or design of the work or the acquisition, analysis, or interpretation of data for the work; AND
2. Drafting the work or revision it *critically for important intellectual content* (simply participating in writing or technical editing of the manuscript is insufficient for authorship); AND
3. Final approval of the version to be published; AND
4. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Those who do not meet all 4 of the above criteria will be acknowledged as non-author contributors.

Data sharing:
We will make the final data from the study, including a codebook, available to researchers after acceptance for publication of the main findings from the final dataset. The final data will be a complete and cleaned data set free of identifiers. We will make the research data available to users with a data-sharing agreement that includes: (1) a commitment to using the data only for research purposes, (2) a commitment to securing the data using appropriate computer technology, (3) a commitment to destroying the data after analyses are completed and not redistributing to third parties, and (4) IRB approval and clear research questions. Data request and sharing procedures, data request forms, and a data-sharing agreement will be accessible through the website of Center for Nursing Excellence in Palliative Care, Nell Hodgson Woodruff School of Nursing. The requester will be able to download final dataset and codebook. Also, care providers or administrators who wish to use the SPIRIT intervention in their practice and care setting can place a request through the Center's website and will be able to download the SPIRIT intervention manual.

10.1.12 CONFLICT OF INTEREST POLICY

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

10.2 PROTOCOL AMENDMENT HISTORY

Version	Date	Description of Change	Brief Rationale
1	29-June-2017	Original draft	

2	25-September-2017	From: waiver of written consent for surrogates from the control clinics To: waiver of written consent for all surrogates From: audio-recording surrogate verbal consent To: no audio-recording surrogate verbal consent	To make the consent process consistent between the intervention and control groups and the intervention's safety has been proven, involving no greater than minimal risk. This change will also reduce the risk of breach of confidentiality by only mailing 1 copy signed by coordinator.
		From: the SPIRIT clinician champion will determine whether the patient meets the SQ criterion To:	Procedure for dialysis clinic identification of potential participants with "no" to SQ question will be determined by the staff who is thought to be most qualified and suitable in making assessment by the clinic. The culture and workflow of the dialysis clinic should be respected.
		For PD patients who have to travel far to visit the clinic, SPIRIT Session II may be scheduled to occur approximately 4 weeks after Session I.	To coincide with the next monthly clinic visit and thus reduce the travel burden.
		Severe depression symptom scores (HADS-Depression ≥ 15) score given procedure for referral. Add response to suicidal ideation With a high HADS-depression score, the surrogate should be informed and encouraged to consider talking to the primary care provider. If suicidal ideation is expressed, site coordinator is notified and he/she will address with Site PI.	Subject safety
3	25 January-2018	Remove: copy of verbal consent will be mailed. Changed name of Site Coordinator at Univ. of Pittsburgh	Unnecessary according to IRB policy. For information purposes only.
4	31 July 2018	Addition of DCI and Emory Decatur to Emory University Sites	In order to meet recruitment goals
5	4 December 2018	Deletion of Surprise Question inclusion criterion and addition of teleconferencing for SPIRIT session	Broadening the recruitment base in order to meet recruitment goal by proposed timeframe.
		Delete: Surprise Question- "would I be surprised if the patient died in the next year?"	Renal community has been promoting timely advance care planning for every patient on dialysis regardless of their current health condition because of their high comorbidity and unpredictable prognosis. Because the SPIRIT intervention has extensively tested and demonstrated its safety and efficacy, the investigators have

		Allow for teleconferencing for Intervention delivery (Using Zoom, LITS approved platform)	decided to broaden the inclusion criteria by not using the SQ any longer. This change will also help ensure the study meets the target sample size within the proposed timeline. Chosen Surrogates may not live locally and this would allow their participation in a secure and private setting and alleviate transportation and schedule demands.
6	21 January 2019	Add: University of Virginia as study site	Additional University site added to increase recruitment to meet study milestones and targets.
7	27 February 2019	1.1 Synopsis 4.1 Overall study design 9.4.3 analysis of secondary endpoint(s) 9.4.9 Exploratory analysis 10.1.1.1 Consent/Assent Study Duration: Patients & Surrogates participation duration of 9 months post data collection; we will request an extension of 12 months by Informed Consent addendum for both patients and surrogates	We have had very few patient deaths (less than 4% of recruited population) and we run the risk of not meeting secondary aims unless we can extend the follow up period. This will be done by informed consent addendum for both patient and surrogate at completion of 9 month time point
8	05 August 2019	Note: Below revisions are all related to the supplement study, and the parent study is not affected. 3 Aims, endpoint, phases, Emory only sites, duration ~ 2 years Supplement study to include dementia patients Preliminary study results from SPIRIT-AD for the supplement study Objectives, endpoints, justification and measures. Randomization to two groups Single SPIRIT session Follow up period up to 12 months ESRD plus dementia – use of MoCA, SLUMS and UBACC Same; patients previously excluded will have opportunity under supplement Transportation support offered Single session due to patients limited short-term memory Addition of MoCA and SLUMS	We request approval for a modification to the current protocol to evaluate the effects of SPIRIT in patients on dialysis who have an early stage of cognitive impairment or dementia and thus would be ineligible for the current parent study. This additional evaluation of SPIRIT added to the current protocol has been funded by the NIH. Dialysis patients will continue to be assessed for their eligibility for the parent study. If they meet the inclusion criteria for the current parent study, they will move along with the existing pathway. If they are determined to be ineligible due to cognitive impairment, those patients may be qualified for this sub-study. Having these two pathways, patients who are excluded from the parent study but still able to consent for study participation and able to express their wishes will have an

		Randomization by dyad into one of two groups; SPIRIT or usual care. Addition: Audio recording of sessions and sequent qualitative analysis 1 month post-death HADS for surrogate, medical records review at 6m or death AIMS 1 & 2, sample size = 30 AIM 1: Preparedness and Care decisions; AIM 2: Srgt post-bereavement distress: AIM3: Decision making capacity Pt written consent, Srgt verbal consent and Screening HIPAA. Limit to Emory Sites. Use of MoCA and SLUMS Add: Dr. Paul, biostatisitian, Linda Turberville-Trujillo ANP, and Drenna Waldrop-Valverde, PhD	opportunity to participate. This sub-study will involve Emory dialysis centers only. If patients are eligible for the pathway of the sub-study, they will be randomized either to receive usual care only or to receive SPIRIT adapted for those with cognitive impairment. We have brought in additional investigators who have expertise in neuroscience and cognition.
9	July 29, 2020	Changes in 5.5. Strategies for recruitment and retention and 6.0 Study intervention Supplement study procedures to be done remotely/via phone During the pandemic, SPIRIT sessions will be conducted via zoom whenever possible.	To avoid or minimize in-person contacts.

5.5. Strategies for recruitment and retention **6.0 Study intervention**	**July 29, 2020**	**Supplement study procedures to be done remotely/via phone** **During the pandemic, SPIRIT sessions will be conducted via zoom whenever possible.**	**To minimize in-person contacts**
10 1.1 Synopsis 2.1 Study rationale 2.2 Study background 4.1 Overall study design 4.2 Scientific rationale for study design 4.4 End of study definition 5.1 Inclusion criteria 5.5 Strategies for recruitment and retention 8.1 Outcome assessments 9.1 Statistical hypotheses 9.2 Sample size determination 9.4 Statistical analyses 10.1 Regulatory, ethical, and study oversight considerations	8/12/20	New Changes are related to a new supplement, COVID-19 related, study and do not affect the parent study.	A new supplement study is a longitudinal cohort study leveraging the parent study. The objective is to assess the effect of the pandemic on the stability of end-of-life care preferences and on our key outcomes (dyad congruence on goals of care, patient decisional conflict, and surrogate decision-making confidence).
11	10-.22.2020	5.1 Inclusion Criteria: ***Changes are related to supplemental aim (SPIRIT in ESRD plus ADRD), and do not affect the parent study.**	**Supplement study: Adjusting the MoCA and SLUMS criterion to meet target sample size.**
12	1/8/2021	5.5 Recruitment: Care Providers recruitment and consent procedures	Recruitment involves email contacts and phone calls. Current informed consent for Care Providers is not changing.

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