A Communication Tool to Assist Older Adults Facing Dialysis Choices
NCT04466865

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Best Case/Worst Case: A Multisite Randomized Clinical Trial of Scenario Planning for Patients with End-Stage Kidney Disease
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Contents

Introduction

Background and rationale

Almost half of all patients starting dialysis are now over age 65.[1] Although there is a modest survival advantage for older patients treated with dialysis, for patients with serious comorbidity, dialysis may not improve survival at all.[2] For example, for patients age 80-85 median survival after starting dialysis is 15.6 months, yet 20% of patients will die within three months of dialysis initiation.[3] While mortality for older patients receiving dialysis is high, even patients who achieve a survival advantage will experience treatment burdens and distressing symptoms. These include time spent in dialysis; repeat hospitalizations; vascular access complications; and symptoms including pain, sleep disturbance, itching, edema, constipation, nausea and loss of appetite.[4] For patients who forgo dialysis, there are fewer treatment-associated burdens, but symptoms are similarly formidable. Whether patients choose to initiate or forgo dialysis, older patients with life-limiting ESRD would benefit from receipt of palliative care to alleviate symptoms and clarify goals.[5]

Older adults who initiate dialysis often do so by passively accepting dialysis without making an active commitment to life-supporting treatment. Anthropologists Ann Russ and Sharon Kaufman report that this leads to confusion about treatment goals and questions such as *"Do I really need this? Can I ever get off? When will this end?"*[6] In one Canadian study, more than 60% of older adults regretted their decision to start dialysis.[7] Furthermore, nephrologists have financial incentives to avoid placing catheters for dialysis access, which promotes early fistula creation and generates a clinical momentum to treat kidney failure without consideration of the patient's overall health status or goals.[8] These systems forces likely promote use of dialysis, inhibit consideration of "no dialysis" and limit receipt of palliative care with or without dialysis.

Older patients with ESRD have an urgent need for palliative care throughout their illness trajectory, not simply at the end of life. Fewer than 6% of patients on dialysis have had the opportunity to discuss end-of-life wishes.[9] Yet studies show most of these patients would prefer not to die in a hospital and to stop dialysis if they were to become cognitively or functionally impaired.[9] As compared to patients with terminal cancer and heart failure, patients with ESRD are more than twice as likely to be admitted to the ICU and less than half as likely to be admitted to Hospice in the final month of life.[10-12] Palliative care concurrent with usual treatment has clearly-demonstrated benefits for patients throughout the course of illness by promoting advance care planning, symptom relief and less invasive treatments near death without increasing mortality.[13,14] (Figure 1)

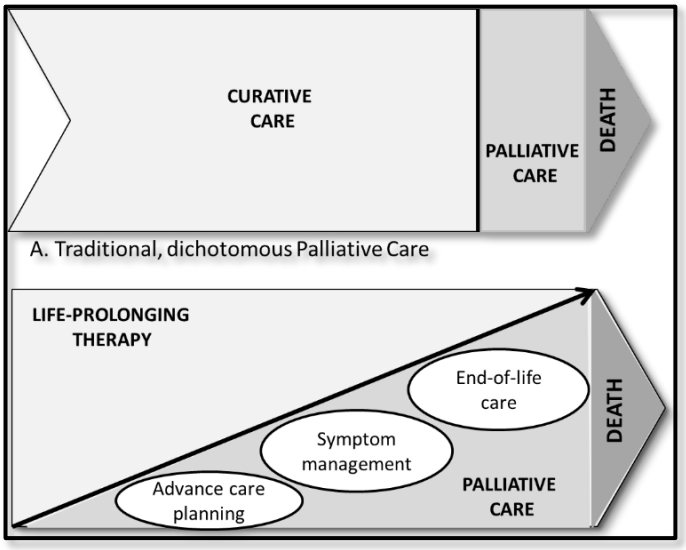

Figure 1: Use of palliative care over time

Current communication practices do not provide the critical information patients need to decide between dialysis and no dialysis, or recognize the value of palliative care regardless of treatment choice. Nephrologists routinely focus on electrolyte management, blood pressure medications and "treatment for when the kidneys fail," rather than engaging patients in a discussion about overall prognosis and goals.[15-19] This makes it difficult for patients to associate their personal values with the likely consequences of starting dialysis. We have documented that nephrologists rarely present "supportive care" as a choice, and consideration of "no dialysis" is typically initiated by patients.[20,21] By describing dialysis as "kidney replacement" nephrologists do not reveal how a patient might experience dialysis, or expected downstream outcomes, such as predictable changes in functional status or long-term prognosis.[22] Improving conversations about dialysis may help patients to receive palliative care consultation and to support subsequent treatment decisions that align with personal goals. Although palliative care for patients with poor prognosis is supported by the American Society of Nephrologists,[23,24] barriers to palliative care include (1) patient lack of awareness about the life-limiting nature of ESRD and (2) an illness trajectory typified by a slow overall decline with interval catastrophic events and partial recovery, not a sharp and obvious deterioration.[25] These barriers cannot be overcome by simply referring patients to palliative care. Uptake of palliative care is limited when patients who have frequent contact with clinicians are unable to comprehend the value of an additional clinical visit. Patients who are more informed about the experience of dialysis and their overall health trajectory might take advantage of palliative care earlier in their course of illness.

Older adults need information to make decisions about life-sustaining treatments (dialysis) contextualized into their personal story. Using a strategy called scenario planning and Elwyn's conceptual model for shared decision making,[26,27] we have developed the Best Case/Worst Case communication tool. It is designed specifically for face-to-face clinical interactions to promote dialogue and to generate goal-concordant treatment decisions in the context of life-limiting illness. This tool is distinct from other decision aids that educate and activate patients for decision making before meeting with a clinician.[28,29] The Best Case/Worst Case communication tool uses *scenario planning* to facilitate decision making in the setting of uncertainty. Scenario planning was originally developed in the 1950s by the Department of Defense and the RAND Corporation for military planning. It was then popularized for broader use by Pierre Wack[30,31] an economist at Shell Oil, to translate vast probabilistic information into narrative description to facilitate strategic decisions. Rather than emphasizing precise isolated risks, this technique generates multiple plausible futures, prompting decision makers to visualize what might happen under different sets of assumptions. Scenario planning is distinct from standard-practice risk prediction and prognostication. By highlighting the interaction between forces that drive change and providing an organized way to consider alternative futures, it promotes insight.[32] Although it has been successfully applied to a wide range of decisions in business and government, scenario planning is not widely used in the clinical setting.

We have adapted the practice of scenario planning for healthcare decision making in the Best Case/Worst Case communication tool.[33] We posit that well-constructed scenarios (personalized stories about possible futures) will appeal to the deeply held concerns of patients, encourage them to comprehend a new,

previously unimaginable reality and prepare for major shifts in a way that simple prognostication (forecasting) cannot.

How the Best Case/Worst Case tool works: The clinician verbally describes the "best case," "worst case," and "most likely" stories about the experience of each treatment option—incorporating rich narrative from clinical experience and patient-specific relevant outcomes—while drawing a graphic aid of those options (Figure 2). Vertical bars represent treatment options; their length shows the range of outcomes and the magnitude of the difference between the "best case" (star), the "worst case" (box) and a "most likely case" (oval). The clinician also writes short notes about each option on the diagram, which helps the patient recall details of the conversation later. The narrative description and graphic aid help the patient formulate and express preferences. From this exchange, the clinician can then provide a treatment recommendation that is grounded in the relevant clinical context and reflects the patient's values. A copy of the graphic aid is stored in the patient's chart. Patients also retain the graphic aid to discuss options with family and to support future conversations with their nephrologist and other clinicians. This approach—using a personalized information and a graphic aid—are best practices to improve understanding of complex health information, especially for persons with low health literacy.[34,35]

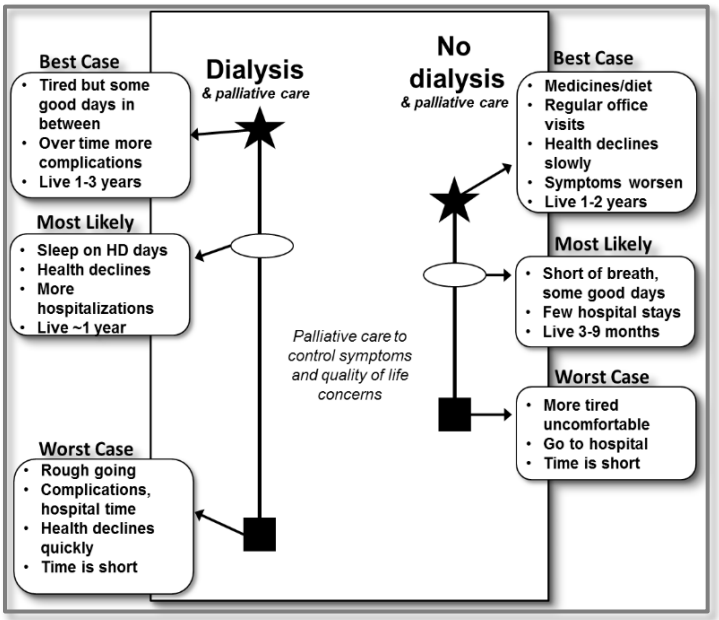

Figure 2: Example graphic aid for "Best Case/Worst Case"

We expect that use of the Best Case/Worst Case communication tool will help nephrologists and patients identify the need for palliative care whether or not patients choose to initiate dialysis. Nephrologists can use this tool to illustrate treatment options, acknowledge uncertainty, and convey a clear message about prognosis. By using scenario planning to translate evidence about the patient's overall health—including symptoms, events like hospital admissions and prognosis— within narratives about different possible futures, nephrologists can elicit patient preferences about specific health states and recommend goal-concordant treatment. *Moreover, scenario planning allows patients to anticipate unwanted events, thus enabling nephrologists to facilitate a palliative care consultation to alleviate symptoms and clarify care goals regardless of the patient's dialysis decision.*

Teaching nephrologists to use the Best Case/Worst Case communication tool has potential to increase receipt of palliative care and reduce intensive treatments at the end of life via multiple pathways. (Figure 3): first, via direct provision of information about prognosis and health trajectory, second, through improving the quality of communication about options and outcomes, and third, via improving decision making about dialysis initiation. Our primary outcome is receipt of palliative care and intensity of treatment at the end of life. We will assess whether patients' palliative care needs were met by measuring the patient's change in health-related quality of life over time. We will measure the impact of upstream outcomes and events that may mediate receipt of palliative care including patient and caregiver-reported assessment of quality of communication and the patient's decision to initiate or forgo dialysis.

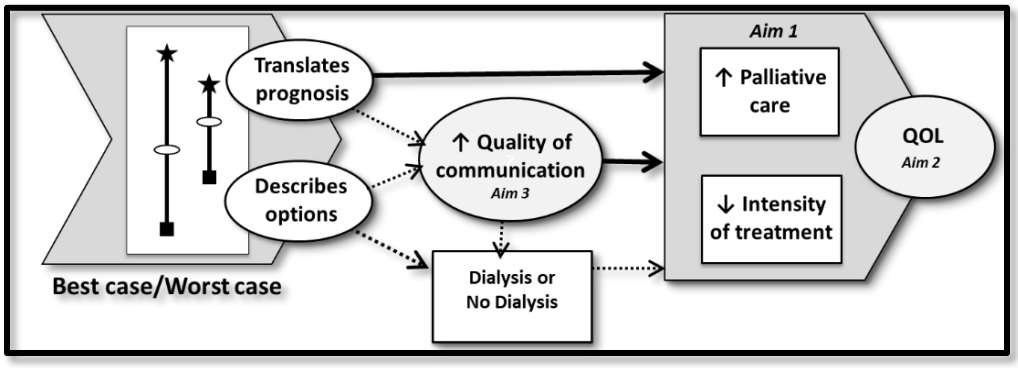

Figure 3: Theoretical framework behind the Best Case/Worst Case intervention and this proposal

Specific aims

- Aim 1: To test the effect of the Best Case/Worst Case intervention on (1) receipt of palliative care and (2) intensity of treatment at the end of life for older patients with ESRD. We will compare (1) receipt of palliative care within 12 months of enrollment and (2) intensive care unit admissions, hospitalizations and emergency department visits in the last 30 days of life. Receipt of palliative care is the primary outcome for this study.
- Aim 2: To test the effect of the Best Case/Worst Case intervention on quality of life of older patients with ESRD. We will use the Functional Assessment of Chronic Illness Therapy – Palliative Care scale to measure quality of life at baseline, and every three months for up two years after study enrollment.
- Aim 3: To test the effect of the Best Case/Worst Case intervention on the quality of communication between nephrologists and patients. We will use the Quality of Communication scale, which includes measurement of end-of-life communication. We will also use this patient and caregiver-reported measure to explore the mediating effect of provider communication on downstream health outcomes.

Study design

This is a multi-site, cluster-randomized clinical trial supported by the infrastructure of the Palliative Care Research Cooperative Group (PCRC). It is a parallel randomization trial with a wait-list control, randomizing nephrologists within each site to receive the intervention at study initiation or after study completion. We will enroll a total of 320 pre-dialysis patients with an estimated glomerular filtration rate (eGFR) of less than 20mL/min/1.73M^2 who are age 60 and older and have an estimated survival of 18 months or less.[36] We expect eight sites are required to ensure complete enrollment (one enrollment plan for example, 8 sites x 4 nephrologists per site with 10 patients per nephrologist = 320). (Note: two sites were added in 2022, for a total of ten sites.) We will follow patients for up to two years after study enrollment. At the start of the study, within each site, nephrologists are randomized to the control or intervention group in a ratio of 1:1. A block randomization scheme will be utilized with blinded block size. Nephrologists assigned to the intervention group will receive training on how to use the Best Case/Worst Case communication tool. Patients in the control group will receive usual care; patients in the intervention group will receive care from their nephrologist trained to use the Best Case/Worst Case communication tool. Palliative care will be available to all patients.

Table: Outcomes Measures for Each Aim				
Construct	Specific Measure	Type; range	Source	Timing
Aim 1: receipt of palliative care and intensity of treatments received at the end of life				
Receipt of palliative care	Any palliative care consult within 12 months of enrollment	Binary; 0/1	Chart review	T0 to 12 mo
Intensity of treatment	ICU admission within 30 days of death	Binary; 0/1	Chart review	$T3_{minus}$ 30d.
Aim 2: Health-related Quality of Life				
Health related quality of life	Functional Assessment of Chronic Illness Therapy-Palliative Care Version 4 (FACIT-Pal)	Continuous; 0-184	Patient	T2a…. T2h
Aim 3: Quality of Communication				
Quality of Communication	Quality of Communication Questionnaire (QOC)	Continuous; 0-10	Patient	T1
Secondary Outcomes and Follow-up Measures				
Receipt of palliative care	Receipt of any palliative care during study period Hospice enrollment New documentation of advance care planning	Binary; 0/1 Binary; 0/1 Binary; 0/1	Chart review Chart review Chart review	T0 to 2 yr. T0 to 2 yr. T0 to 2 yr.
Intensity of treatment	ER visit, ICU or hospitalization within 30 days of death Surgical procedures within 30 days of death	Binary composite; 0/1 Count	Chart review Chart review	$T3_{minus}$ 30d. $T3_{minus}$ 30d.
Dialysis	Initiation of dialysis, Withdrawal of dialysis	Binary; 0/1	Chart review	T0 to 2 yr.
Death	Patient death	Time to event	Chart review and family report	T3
Bereavement	Quality of Dying and Death (QODD) survey	Continuous; 0-100	Caregiver	T4
Health related quality of life	Cambridge Palliative Audit Schedule (CAMPAS-R) (Caregiver QOL)	Continuous; 0-100	Caregiver	T2a…. T2h
Quality of Communication	Quality of Communication Questionnaire (QOC) (Family member version)	Continuous; 0-10	Caregiver	T1
Practitioner Opinion Survey	Nephrologist perceptions of the communication tool	Continuous; 0 - 15	Nephrologist	Study Completion

mo. = months, yr. = year, d. = day, T0 = enrollment, T1 = 48 hours after enrollment, T2 is every 3 months for up to 2 years, 2_a-2_h = repeated measures every 3 months, T3 = patient death, T4 = 3 months after patient death.

Blinding

Patients and caregivers will be blinded to the objectives of this study. They will be told that the study goal is to evaluate doctor-patient communication. Nephrologists will not be blinded to study group. We will inform all participating nephrologists about the goals of this study. Specifically, this is a study testing an intervention to improve communication about dialysis initiation and to support patient access to palliative care. We will make every effort to blind study staff, yet it is impossible to ensure that study staff will be completely blinded to intervention group. To reduce the possibility of study staff exposure to the nephrologist's randomization assignment we will coordinate the intervention allocation centrally through UW and provide regular reminders to nephrologists that they should avoid revelation of their training to study staff. To decrease ascertainment bias, study staff will adhere to a strict study script during interactions with nephrologists and during survey administration with patients and caregivers. To standardize chart abstraction, we will create a detailed abstraction protocol with data dictionary, and the UW team will train study staff to use the REDCap electronic database. We will ensure data quality by

independent abstraction and double data entry of 10% by the site PI or a suitable designee. We will compare the two abstractions and correct and retrain as needed.

Data and Safety Monitoring Plan

No formal interim analyses are planned during this study, and all study outcomes will be assessed at the completion of study follow-up.

Meetings of the DSMB will be held at least two times a year at the call of the Chairperson. DSMB interim report templates will be prepared by a study statistician with assistance from the PCRC and the Data, Informatics and Statistics Core (DISC), to be reviewed by the DSMB members at the first meeting.

Analysis of Primary Outcome

The sample size estimate, 320 patients (160/group), is based on the primary hypothesis that patients in the intervention arm will be more likely to receive palliative care and will have fewer intensive treatments at the end of life. We aim to recruit 32 nephrologists, each treating on average 10 study patients. We estimate a 10% attrition rate for study participation and that 80% of patients will die during the 2-year study period. This study is powered to detect a 10-15% absolute difference in the care patients receive, consistent with other interventions designed to effectively increase access to palliative care.[37-40] Smaller differences are unlikely to be considered meaningful to clinicians, patients or researchers.[41] We desire a two-sided type I error rate of 0.05 and estimate that the between-physician variance is around 10%. We plan to use fixed effects to account for clustering by site because it is faithful to our study design and controls for confounding related to imperfect randomization due to site imbalances better than a random effects model. Assuming the baseline rate of palliative care is 10%,[42,43] we will have a power of 90% to detect a 14.7% increase and a power of 80% to detect a 12.9% increase in the rate of palliative care received.

General Analysis Plan

Primary Outcome

1. For receipt of **palliative care consult within 12 months of study enrollment**, for each treatment arm, we will report the sample counts and percentages. The denominator for each proportion will include all randomized subjects to the respective treatment arm. The treatment effect will be assessed using a Likelihood Ratio Test (LRT) of the fixed effect from the proportional odds cumulative incidence model, incorporating the competing risk of death.[44] The model will include a random-intercept for physician, and will include fixed effects for: site, comorbidity, and baseline functional status.

   Null Hypothesis: After accounting for baseline differences, there is no difference in the receipt of palliative care consult within 12 months of study enrollment between control patients and Best Case/Worst Case intervention patients.

Alternative Hypothesis: After accounting for baseline differences, there is a difference in the receipt of palliative care consult within 12 months of study enrollment between control patients and Best Case/Worst Case intervention patients.

Secondary outcomes:

1. For **receipt of palliative care during 2-year follow up**, for each treatment arm, we will report the sample counts and percentages (this outcome is in addition to the primary outcome). The denominator for each proportion will include all subjects randomized to their respective treatment arm. The treatment effect will be assessed using a LRT of the fixed effect from the proportional odds cumulative incidence model, incorporating the competing risk of death. The model will include a random-intercept for physician, and will include fixed effects for: site, comorbidity, and baseline functional status.

   Null Hypothesis: After accounting for baseline differences, there is no difference in the proportion of receipt of palliative care between control patients and Best Case/Worst Case intervention patients.

   Alternative Hypothesis: After accounting for baseline differences, there is a difference in the proportion of receipt of palliative care between control patients and Best Case/Worst Case intervention patients.

2. For proportion of **ICU admissions within 30 days of death**, for each treatment arm, we will report the sample counts and percentages. The denominator for each proportion will include subjects randomized to their respective treatment arm that died within the study period. The treatment effect will be assessed using a LRT of the fixed effect from the logistic mixed-effects model. The logistic mixed-effects model will include a random-intercept for physician, and will include fixed effects for: site, comorbidity, and baseline functional status.

   Null Hypothesis: After accounting for baseline differences, there is no difference in the proportion of patients with an ICU admissions within 30 days of death between control patients and Best Case/Worst Case intervention patients.

   Alternative Hypothesis: After accounting for baseline differences, there is a difference in the proportion of patients with an ICU admissions within 30 days of death between control patients and Best Case/Worst Case intervention patients.

3. For the **FACIT-Pal total score patient reported health related quality of life** (score range 0-184, 46 items, survey questions 1-46), for each treatment arm, we will report the mean and standard deviation of the **FACIT-Pal total score at last follow-up** (either 2 years of follow-up or last administered survey prior to death, whichever occurs first). The treatment effect will be assessed using a LRT of the fixed effect from the linear mixed-effects model. The linear mixed-effects model will include a random-intercept for physician, and will include fixed effects for: baseline FACIT-Pal total score, site, comorbidity, and baseline functional status.

   Null Hypothesis: After accounting for baseline differences, there is no difference in the average FACIT-Pal total score at last follow-up between control patients and Best Case/Worst Case intervention patients.

Alternative Hypothesis: After accounting for baseline differences, there is a difference in the average FACIT-Pal total score at last follow-up between control patients and Best Case/Worst Case intervention patients.

4. For the **FACIT-Pal total score patient reported healthy quality of life** (score range 0-184, 46 items, survey questions 1-46), for each treatment arm, we will report the mean and standard deviation of the **score slopes** (difference in baseline and either 2 years of follow-up or last administered survey prior to death, whichever occurs first, divided by the length of follow-up). The treatment effect will be assessed using a LRT of the fixed effects from the linear mixed-effects model. The linear mixed-effects model will include a random-intercept for physician, and will include fixed effects for: site, comorbidity, and baseline functional status.

   Null Hypothesis: After adjusting for baseline differences, there is no difference in the slope of the FACIT-Pal total score between control patients and Best Case/Worst Case intervention patients.

   Alternative Hypothesis: After adjusting for baseline differences, there is a difference in the slope of the FACIT-Pal total score between control patients and Best Case/Worst Case intervention patients.

5. For the **FACT-G total score patient reported health related quality of life** (score range 0-108, 27 items, survey questions 1-27), for each treatment arm, we will report the mean and standard deviation of the **FACT-G total score** at last follow-up (either 2 years of follow-up or last administered survey prior to death, whichever occurs first). The treatment effect will be assessed using a LRT of the fixed effect from the linear mixed-effects model. The linear mixed-effects model will include a random-intercept for physician, and will include fixed effects for: baseline FACT-G score, site, comorbidity, and baseline functional status.

   Null Hypothesis: After accounting for baseline differences, there is no difference in the average FACT-G score at last follow-up between control patients and Best Case/Worst Case intervention patients.

   Alternative Hypothesis: After accounting for baseline differences, there is a difference in the average FACT-G score at last follow-up between control patients and Best Case/Worst Case intervention patients.

6. For the **FACIT-Pal palliative care subscale (PalS) patient reported health related quality of life** (score range 0-76, 19 items, survey questions 28-46) for each treatment arm, we will report the mean and standard deviation of the subscale composite scores for **PalS** at last follow-up (either 2 years of follow-up or last administered survey prior to death, whichever occurs first). The treatment effect will be assessed using a LRT of the fixed effect from the linear mixed-effects model. The linear mixed-effects model will include a random-intercept for physician, and will include fixed effects for: baseline Pal score, site, comorbidity, and baseline functional status.

   Null Hypothesis: After accounting for baseline differences, there is no difference in the average PalS score at last follow-up between control patients and Best Case/Worst Case intervention patients.

Alternative Hypothesis: After accounting for baseline differences, there is a difference in the average PalS score at last follow-up between control patients and Best Case/Worst Case intervention patients.

7. For overall **Quality of Communication (QOC)** within 48 hours of enrollment, for each treatment arm, we will report the mean and standard deviation of the 13-item composite scores. The treatment effect will be assessed using a LRT of the fixed effect from the linear mixed-effects model. The linear mixed-effects model will include a random-intercept for physician, and will include fixed effects for: site, comorbidity, and baseline functional status.

   Null Hypothesis: After accounting for baseline differences, there is no difference in average overall QOC scores between control patients and Best Case/Worst Case intervention patients.

   Alternative Hypothesis: After accounting for baseline differences, there is no difference in average overall QOC scores between control patients and Best Case/Worst Case intervention patients.

8. For the **general Quality of Communication (QOC)** within 48 hours of enrollment, for each treatment arm, we will report the mean and standard deviation of the 6-item general subscale composite scores. The treatment effect will be assessed using a LRT of the fixed effect from the linear mixed-effects model. The linear mixed-effects model will include a random-intercept for physician, and will include fixed effects for: site, comorbidity, and baseline functional status.

   Null Hypothesis: After accounting for baseline differences, there is no difference in average general QOC scores between control patients and Best Case/Worst Case intervention patients.

   Alternative Hypothesis: After accounting for baseline differences, there is a difference in average general QOC scores between control patients and Best Case/Worst Case intervention patients.

9. For the **end-of-life Quality of Communication (QOC)** within 48 hours of enrollment, for each treatment arm, we will report the mean and standard deviation of the 7-item end-of-life subscale composite scores. The treatment effect will be assessed using a LRT of the fixed effect from the linear mixed-effects model. The linear mixed-effects model will include a random-intercept for physician, and will include fixed effects for: site, comorbidity, and baseline functional status.

   Null Hypothesis: After accounting for baseline differences, there is no difference in average end-of-life QOC scores between control patients and Best Case/Worst Case intervention patients.

   Alternative Hypothesis: After accounting for baseline differences, there is a difference in average end-of-life QOC scores between control patients and Best Case/Worst Case intervention patients.

10. For **hospice enrollment during 2-year follow up**, for each treatment arm, we will report the sample counts and percentages. The denominator for each proportion will include all subjects randomized to their respective treatment arm. The treatment effect will be assessed using a LRT of the fixed effect from the logistic mixed-effects model. The logistic mixed-effects model will include a random-intercept for physician, and will include fixed effects for: site, comorbidity, and baseline functional status.

Null Hypothesis: After accounting for baseline differences, there is no difference in the proportion of patients with hospice enrollment between control patients and Best Case/Worst Case intervention patients.

Alternative Hypothesis: After accounting for baseline differences, there is a difference in the proportion of patients with hospice enrollment between control patients and Best Case/Worst Case intervention patients.

11. For **documentation of new advance care planning during 2-year follow up**, for each treatment arm, we will report the sample counts and percentages. The denominator for each proportion will include all subjects randomized to their respective treatment arm. The treatment effect will be assessed using a LRT of the fixed effect from the logistic mixed-effects model. The logistic mixed-effects model will include a random-intercept for physician, and will include fixed effects for: site, comorbidity, and baseline functional status.

    Null Hypothesis: After accounting for baseline differences, there is no difference in the proportion of documentation of new advance care planning between control patients and Best Case/Worst Case intervention patients.

    Alternative Hypothesis: After accounting for baseline differences, there is a difference in the proportion of documentation of new advance care planning between control patients and Best Case/Worst Case intervention patients.

12. For **treatment intensity at the end of life**, for each treatment arm, we will report the sample counts and percentages of patients who experience any ER visits or ICU stays or hospitalization as determined by chart review or patient or caregiver report within 30-days of death. The denominator for each proportion will include all subjects randomized to their respective treatment arm that died within the study period. The treatment effect will be assessed using a LRT of the fixed effect from the logistic mixed-effects model. The logistic mixed-effects model will include a random-intercept for physician, and will include fixed effects for: site, comorbidity, and baseline functional status.

    Null Hypothesis: After accounting for baseline differences, there is no difference in the proportion of treatment intensity at the end of life between control patients and Best Case/Worst Case intervention patients.

    Alternative Hypothesis: After accounting for baseline differences, there is a difference in the proportion of treatment intensity at the end of life between control patients and Best Case/Worst Case intervention patients.

13. For **surgical treatment intensity**, for each treatment arm, we will report the sample counts and percentages of patients who experience any surgical procedures within 30-days of death. The denominator for each proportion will include all subjects randomized to their respective treatment arm that died within the study period. The treatment effect will be assessed using a LRT of the fixed effect from the logistic mixed-effects model. The logistic mixed-effects model will include a random-intercept for physician, and will include fixed effects for: site, comorbidity, and baseline functional status.

Null Hypothesis: After accounting for baseline differences, there is no difference in the proportion of surgical treatment intensity between control patients and Best Case/Worst Case intervention patients.

Alternative Hypothesis: After accounting for baseline differences, there is a difference in the proportion of surgical treatment intensity between control patients and Best Case/Worst Case intervention patients.

14. For **initiation of dialysis during 2-year follow up**, for each treatment arm, we will report the sample counts and percentages. The denominator for each proportion will include all subjects randomized to their respective treatment arm. The treatment effect will be assessed using a LRT of the fixed effect from the proportional odds cumulative incidence model for competing risks, incorporating the competing risk of death.[44] The model will include a random-intercept for physician, and will include fixed effects for: site, comorbidity, and baseline functional status.

    Null Hypothesis: After accounting for baseline differences, there is no difference in the proportion of initiation of dialysis between control patients and Best Case/Worst Case intervention patients.

    Alternative Hypothesis: After accounting for baseline differences, there is a difference in the proportion of initiation of dialysis between control patients and Best Case/Worst Case intervention patients.

15. For **time to on-study death**, for each treatment arm, we will report survival rates by six month intervals, every 6 months from baseline to 2-years. Risk groups will include all patients all subjects randomized to their respective arms. The treatment effect will be assessed using a LRT of the fixed effect from the logistic mixed-effects model. The mixed-effects Cox regression model will include a random-intercept for physician, and will include fixed effects for: site, comorbidity, and baseline functional status.

    Null Hypothesis: After accounting for baseline differences, there is no difference in the 2-year survival rate of on-study death between control patients and Best Case/Worst Case intervention patients.

    Alternative Hypothesis: After accounting for baseline differences, there is a difference in the 2-year survival of on-study death between control patients and Best Case/Worst Case intervention patients.

16. For **caregiver-reported Quality of Dying and Death** (QODD) within 3 months of patient death, for each treatment arm, we will report the mean and standard deviation of the QODD composite scores. Only patients who died within the study period will be analyzed in the treatment arms they were randomized. The treatment effect will be assessed using a LRT of the fixed effect from the linear mixed-effects model. The linear mixed-effects model will include a random-intercept for physician, and will include fixed effects for: site, comorbidity, and baseline functional status.

    Null Hypothesis: After accounting for baseline differences, there is no difference in average caregiver-reported quality of dying and death scores between control patients and Best Case/Worst Case intervention patients.

Alternative Hypothesis: After accounting for baseline differences, there is a difference in average caregiver-reported quality of dying and death scores between control patients and Best Case/Worst Case intervention patients.

17. For the **Cambridge Palliative Audit Schedule** (CAMPAS-R) caregiver reported health related quality of life, for each treatment arm, we will report the mean and standard deviation in composite score at last follow-up (either 2 years of follow-up or last administered survey prior to death, whichever occurs first). The treatment effect will be assessed using a LRT of the fixed effect from the linear mixed-effects model. The linear mixed-effects model will include a random-intercept for physician, and will include fixed effects for: baseline CAMPAS-R score, site, comorbidity, and baseline functional status.

    Null Hypothesis: After accounting for baseline differences, there is no difference in average CAMPAS-R score at last follow-up between control patients and Best Case/Worst Case intervention patients.

    Alternative Hypothesis: After accounting for baseline differences, there is a difference in average CAMPAS-R score at last follow-up between control patients and Best Case/Worst Case intervention patients.

18. For **caregiver-reported general Quality of Communication** (QOC) within 48 hours of enrollment, for each treatment arm, we will report the mean and standard deviation of the general 6-item subscale composite scores. The treatment effect will be assessed using a LRT of the fixed effect from the linear mixed-effects model. The linear mixed-effects model will include a random-intercept for physician, and will include fixed effects for: site, comorbidity, and baseline functional status.

    Null Hypothesis: After accounting for baseline differences, there is no difference in average general QOC scores between control patients and Best Case/Worst Case intervention patients.

    Alternative Hypothesis: After accounting for baseline differences, there is a difference in average general QOC scores between control patients and Best Case/Worst Case intervention patients.

19. For **caregiver-reported end-of-life Quality of Communication** (QOC) within 48 hours of enrollment, for each treatment arm, we will report the mean and standard deviation of the general 7-item subscale composite scores. The treatment effect will be assessed using a LRT of the fixed effect from the linear mixed-effects model. The linear mixed-effects model will include a random-intercept for physician, and will include fixed effects for: site, comorbidity, and baseline functional status.

    Null Hypothesis: After accounting for baseline differences, there is no difference in average end-of-life QOC scores between control patients and Best Case/Worst Case intervention patients.

    Alternative Hypothesis: After accounting for baseline differences, there is a difference in average end-of-life QOC scores between control patients and Best Case/Worst Case intervention patients.

Exploratory analyses

1. Per-protocol analysis:

   The study team will assess adherence to the Best Case/Worst Case intervention using ascertainment and review of the Best Case/Worst Case graphic aid. Primary outcomes for aims 1 through 3 will be repeated removing those in the intervention group that did not adhere to the protocol, specifically removing those who did not receive the Best Case/Worst Case intervention.

2. Heterogeneity of Treatment Effect (HTE):

   To determine the impact of the intervention on different subgroups of interest, heterogeneity of treatment effects will be explored. Mixed-effects models with random-intercepts for nephrologist will be fit for each primary outcome in Aim 1 to 3. These models will be fit with a fixed-effect interaction term between intervention status and the following subgroup variables: gender, race/ethnicity (minority/non-minority), health literacy (low/high), age (less than 80/older than 80), insurance status (Medicaid (dual eligible)/no Medicaid), and nephrologist background (MD/advance practice provider (PA/NP)). Significance in interaction fixed-effects will indicate heterogeneity of treatment effect. Caregiver outcomes (secondary analysis outcomes 9-12) will also be explored for HTE in a similar manner.

3. Casual Mediation Analysis:

   To determine if the effect that Best Case/Worst Case intervention has on receipt of palliative care and intensity of treatment at the end of life (Aim 1; Outcomes 1 and 2) is mediated by improved quality of communication and decreased usage of dialysis, casual mediation analysis will be implemented. For each primary outcome, we will fit separate models for both mediating factors (improved QOC and decreased usage of dialysis). For the 4 sets of models, we will follow the procedure of Baron & Kenny to estimate the direct and indirect effects. To determine significance of the mediating factors, we will use the bootstrapping procedure for mediation analysis.

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