Study Protocol and Statistical Analysis Plan

Protocol: Planning for the Care you Want
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PI: Ramona Rhodes, MD

NCT: 02320123

The University of Texas Southwestern Medical Center at Dallas
Institutional Review Board

Title: Planning for the Care You Want

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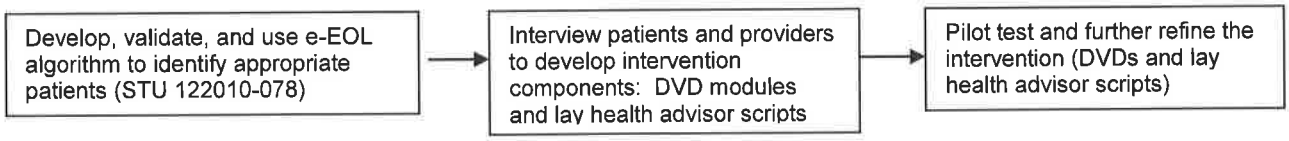
1. **Introduction and Purpose:** The goal of this patient-centered project is to develop and pilot test a multicomponent intervention to increase intent to discuss end-of-life (EOL) care options among African American (AA) patients with life-limiting illness. This will be accomplished through the following specific aims, which are to: 1) Develop and refine a culturally sensitive intervention to increase knowledge about, reduce barriers, and promote intention to discuss EOL care options among AA patients hospitalized with advanced illness who are ≥ 55 years of age; and 2) Test the feasibility and acceptability of a theory-based, multi-component pilot program that will identify older AA patients hospitalized with advanced illness via the e-EOL algorithm and then deploy a culturally sensitive, patient-centered intervention to change knowledge and barriers about and intent to discuss EOL care options.

   A separate aim is also included in the overall study, which has been funded by the Agency for Healthcare Research and Quality (AHRQ) and the Palliative Care Research Cooperative Group. The entire 3-aim study is Project 2 in the AHRQ-funded UT Southwestern Center of Patient-Centered Outcomes and Research. The first aim mentioned above, serves as a precursor to the aims described in this protocol. This aim, which uses applied medical informatics and chart review methods to develop an EMR-enabled (e-EOL) algorithm to identify patients hospitalized with advanced breast, lung, and colorectal cancer appropriate for EOL care counseling was approved in IRB submission STU 122010-078. It will be referred to at times in this protocol. Figure 1 shows the flow of the chronological flow of the entire proposal.

Figure 1



For the purposes of this IRB protocol, Aims 2 and 3 of the overall project will be referred to as Aim 1 and Aim 2 moving forward.

This IRB submission is intended to combine both Aim 1 and Aim 2. For Aim 1, we will conduct semi-structured interviews with AA patients and their caregivers, and focus groups with expert physicians to create and refine new culturally sensitive DVD modules and lay health advisor scripts to communicate messages about EOL care and overcome key barriers. For Aim 2, we will use the e-EOL algorithm (described above) to identify participants to pilot the intervention, which will consist of EOL education and counseling via DVD modules and a culturally identifiable lay health advisor. This will be done to assess the feasibility and acceptability of the intervention. This will provide the groundwork for a future R01 application for a fully powered, randomized controlled trial of the multi-component, patient-centered intervention to increase intent to discuss EOL care options among AAs with advanced illness. This innovative approach uses multiple methods (medical informatics, shared decision making, patient-centered outcomes research, and behavioral intervention design and development) to address a significant need for increasing awareness and use of EOL care options for groups who have been found to underutilize them.

2. **Background:** Racial differences in health care are documented across the health care continuum, and persist in aging and EOL care. AAs and other underrepresented minorities often choose more aggressive therapies at the end of life and are less likely to utilize hospice care in the terminal stages of their illness; potential reasons for these disparities include: lack of knowledge of and misperceptions about palliative and hospice care, spiritual beliefs, and mistrust in the health care system, among others. Despite the literature on disparities in EOL care, reasons for underuse and the presence of national EOL care guidelines, attempts to address this problem have been limited and often not rigorously evaluated. The majority of interventions to promote EOL care were done in majority populations and focused predominantly on trying to change physician awareness of patient's pain, symptoms, and values or to change physician communication behavior. While these early studies made tremendous contributions to the study of EOL care and the needs of the terminally ill, the interventions associated with these studies did not reach their desired effectiveness. We propose a different strategy that would focus specifically on previously identified barriers to utilization of advance directives, palliative care, and hospice care among African Americans – including physicians' difficulty and discomfort with prognostication, AA patients' knowledge, attitudes and beliefs towards hospice and palliative care, conflict between patients' spiritual beliefs and the general hospice and palliative medicine philosophy of care, and medical mistrust. The goal of this project is to improve methods of prognostication for physicians and increase awareness of EOL care options for AAs. To overcome the dual challenges of physicians' reluctance to discuss EOL care and patients' discomfort in engaging in such conversations, we will use the electronic medical record (EMR) to automatically identify AA patients with life-limiting illness who are eligible for counseling about EOL care options. To change knowledge and attitudes toward EOL care options among AA patients, we will design a culturally sensitive intervention that will combine multimedia materials and a culturally concordant lay health advisor who will deliver tailored education and counseling.

3. **Concise Summary of Project:**

Aim 1:

A. We will create additional DVD segments that will address previously identified barriers to EOL care for AAs that are not addressed in the available materials, including: 1) spiritual/religious conflict; 2) medical mistrust; and 3) lack of knowledge about EOL care alternatives. The communication messages and proposed intervention strategies are detailed in Table 1 below. We will obtain feedback on the newly developed segments from 6-10 patients recruited from the Parkland Cancer/Tumor Registry (focus group), the Patient Centered Outcome Research (PCOR) Center Community Advisory Panel, (focus group) or 6-8 AA religious leaders (focus group) recruited from local churches if available. Separate focus groups will also be conducted with Palliative Care and Geriatric faculty at UT Southwestern and Parkland Hospital as well. Informed consent will be obtained prior to conducting the interviews and focus groups. All will last up to 60 minutes.

Table 1. Communication Messages and Intervention Strategies

Theoretical Construct	Communication Message	Intervention Strategy
Lack of Knowledge About EOL Care Alternatives	1) Palliative and curative care can be complementary. 2) Hospice and palliative care can help with pain, symptoms	1)Information session led by an AA lay health advisor (LHA) that includes: 2) DVD segments explaining EOL care options, including advance care planning, palliative care, and hospice care.
Conflict with Spiritual Beliefs	1) Advance care planning is not "giving up" or "losing faith." 2) Choosing palliative care /hospice is not going against God's plan.	1) Information session led by an AA LHA that includes: 2) DVD segments that address this conflict. (testimonial from an AA clergy person with personal and/or professional experience in hospice/palliative medicine)

Mistrust in the Health Care System/Providers	1) Many AA patients have had positive experiences with hospice and palliative medicine and its providers.	1) Information session led by an AA LHA that includes: 2) DVD segments addressing mistrust (testimonials from AA palliative care /hospice patients and AA physicians with personal /professional experience with EOL care)

B. A lay health advisor (LHA) will be recruited from the community to provide counsel about EOL care to patients who will receive the intervention. The LHA will undergo training in how to provide culturally sensitive EOL care for AAs via the APPEAL (A Progressive Palliative Care Educational Curriculum for the Care of AAs at Life's End) Curriculum created at Duke University, the Respecting Choices® Advance Care Planning curriculum, or other appropriate training program depending on availability. After training, the LHA will participate in in-service work with the Parkland Palliative Care Team and the PI.

Aim 2:
We will use the e-EOL algorithm (IRB #: STU 122010-078) to identify AA patients hospitalized at Parkland who have advanced breast, lung, and colorectal cancer to identify potentially eligible candidates for the intervention (See Aim 1 eligibility criteria); however, if sufficient numbers are not identified, patients with other advanced cancers will also be considered. Once eligibility is confirmed the PI or her designee (research assistant, coordinator, or LHA) will introduce the study to the patient, and obtain informed consent. Each patient will be asked to identify a primary caregiver who may be able to participate in the intervention. Of note, if a caregiver cannot be identified, is not eligible, or cannot participate in the intervention for other reasons (scheduling difficulties, etc.), the patient will still be allowed to participate. Caregivers are not required to participate in the intervention (i.e. watch the DVD segments), though it will be encouraged. The PI or her designee (research assistant, coordinator, or LHA) will contact the patient to confirm participation in the study, and arrange a time to meet to conduct the intervention. We anticipate that 48 patients (and their caregivers if available) will be enrolled in the study (16 for each type of cancer). We plan to conduct a small, pilot randomized controlled trial with up to 24 patients (and their caregivers if available) in the intervention arm, and up to 24 patients (and their caregivers if available) in a usual-care control group. The PI will randomize every other eligible patient (and caregiver if available) to the usual-care control group.

The LHA will meet with eligible patients and available caregivers in the intervention arm and assist them in watching the developed DVD segments. Afterward, the LHA will answer questions and provide additional information. They will tailor the discussion to the patient's values, preferences, concerns, and clinical circumstances. The patients who are enrolled in the usual care arm will not receive the intervention.

The primary process outcome tested will be the feasibility and acceptability of the intervention. Feasibility success will be measured by the number and rates of patients/caregivers who complete the intervention and follow-up interviews. The primary decision-making outcome is change in intent to discuss EOL care options based on the Transtheoretical Stages of Change Model (i.e., pre-contemplation, contemplation, preparation, and action). Secondary outcomes measured will include: 1) knowledge of prognosis and EOL care options; 2) quality of life, which will be measured by the McGill QOL Questionnaire, a well-validated 20 item scale developed to measure quality of life at the end of life; 3) health care utilization, such as outpatient visits, ER visits, hospitalizations, use of hospice services; and 4) date and place of death if applicable. Other patient and treatment variables will also be collected. The study variables, data sources, time frame of measurement, and references for the validated instruments are outlined in Table 2.

Table 2. Study Variables, Data Sources, and Time Frame Measurements

Variable	Source	Index Admit	Time Frame		
			1 month	3 months	6 months
Sociodemographics, clinical, treatment data	Chart review	X			
Knowledge of prognosis, EOL care options	Interview	X	X	X	
Feasibility and acceptability of the intervention	Interview	X	X	X	
Mistrust and spirituality	Interview	X	X	X	
Intent to consider EOL care options	Interview	X	X	X	X
Quality of life	Interview	X	X	X	
Healthcare and EOL utilization	Interview, chart	X	X	X	X

4. Study Procedures:

For Aim 1:

The PI and/or research assistant will conduct one interview with each interview participant (patient and caregiver). The visit will last 30-45 minutes. No medications are involved. The PI and/or research assistant will conduct focus groups with expert providers that will be 1 hour in duration. Again, no medications are involved. The PI and/research assistant will also conduct focus groups with AA religious leaders, community members, patients and/or caregivers that will be 45 – 60 minutes in duration.

For Aim 2:

The PI or her designee will conduct a pre-assessment interview with eligible patients to assess their knowledge of advance care planning, hospice, and palliative care. The PI or her designee will also attempt to contact identified caregivers to conduct an assessment of caregivers' knowledge of their loved one's prognosis, perceived quality of life, treatment plan, physical symptoms, and preferences for aggressive treatment. Verbal consent will be obtained, and caregivers will be given the option of completing the interview in person or by phone. The LHA will conduct an in-hospital visit with patients (and their caregivers if available) randomized to the pilot intervention. During this visit, the LHA will assist them in watching the EOL care DVD segments. If a patient's caregiver is unable to be present for viewing, they will be given the option of watching the video via a password protected website. Afterward, the LHA will answer questions and provide additional information as needed. The LHA will then use counseling scripts created by the PI and research team to probe in more depth about the patient's goals of care, understanding of their clinical condition, prognosis, and treatment options, mistrust and spirituality, decisional conflict, quality of life and healthcare utilization. All participants will be asked about their intent to consider EOL care options, and their stage of decision-making will be noted (pre-contemplation, contemplation, preparation, or action). The LHA will tailor the discussion to the patient's values, preferences, concerns, and clinical circumstances. Those who express interest in hearing more about EOL care options will be encouraged to discuss this with their doctor. The LHA will offer to update their attending physician on the discussion and help communicate the patient's desire for a palliative care consult or advance directive if applicable. Specific questions about prognosis will be referred to the treating physician. Formal palliative care consults will be ordered and performed in the usual fashion if requested. This visit will be no more than 2 hours in length. A follow-up visit will also be conducted to address any questions that participants may have with regard to the study.

The patients and available caregivers enrolled in the study will participate in follow-up phone interviews at 1, 3, and 6 months post discharge (if applicable). At that time, patients and available caregivers will be asked similar questions that will examine the primary and secondary outcomes

noted in Table 2 about knowledge of prognosis/EOL care options, mistrust, spirituality, quality of life, health care utilization, and intent to consider EOL care options. These interviews will last 30 minutes to 1 hour.

5. Sub-Study Procedures: None.

6. Criteria for Inclusion of Subjects:

Aim 1 patients must: 1) receive their care at Parkland 2) be diagnosed with advanced cancer (breast, lung, or colon) 2) self-identify as AA; 3) be proficient in English; 4) be competent to give informed consent; and 5) have no evidence of cognitive impairment (Mini-Cog score of ≥3 or 1-2 with normal clock draw).

Aim 2 Patients Must: 1) be hospitalized at Parkland 2) be diagnosed with advanced cancer (breast, lung, colon, or other advanced cancers if sufficient numbers are not identified) 2) self-identify as AA; 3) be proficient in English; 4) be competent to give informed consent; and 5) have no evidence of cognitive impairment (Mini-Cog score of ≥3 or 1-2 with normal clock draw.

All Caregivers (Aim 1 and 2) must be: 1) identified by the selected patients as their primary caregiver, 2) 21 years of age or older, 3) English proficient, and 4) competent to give informed consent.

For the expert provider focus group, participants must be a health care provider (physician, nurse practitioner, chaplain, social worker, nurse) who works within hospice and palliative medicine.

7. Criteria for Exclusion of Subjects:
For patients: 1) identify with a race other than African American; 2) have a diagnosis other than advanced cancer.

8. Sources of Research Material: Clinical and treatment data: clinical diagnosis (type, stage), Karnofsky performance status (measure of functional status in increments of 10, where 0 = death, and 100 = perfect health), reason for admission, advance directive status, inpatient and outpatient provider details (specialty, presence of a primary care provider, usual source of care) will be obtained from the patients' Parkland medical record. Other information data will be obtained from questionnaires and interviews (group and individual).

9. Recruitment Methods and Consenting Process: Aim 1: The PI and research assistant will work with the attending physicians in the Parkland Palliative Care Clinic, Amelia Court Geriatrics Clinic, the Parkland inpatient Geriatrics and General Internal Medicine services, and researchers at the Simons Cancer Center to identify eligible candidates for semi-structured interviews and focus groups. Information will also be obtained for patient's caregivers, and they will be contacted by phone and regular mail to assess their interest in participation.

Palliative Care providers will be recruited via professional contacts. Providers will be approached via email and phone to assess their interest in participating in the focus group.

AA Religious leaders will be recruited from the African American Pastors Coalition and/or local AA churches. They will be approached by email (if available) and phone to assess their interest in participating in the study.

Aim 2: Patient participants will be recruited via development of a computerized algorithm using EMR data to identify hospitalized patients with advanced illness appropriate for EOL care discussion according to national guidelines. Development and validation of this algorithm is currently in process and has already received IRB approval (STU 122010-078: Evaluation of Racial Differences in Palliative and End-of-Life Care among Persons with Life-Limiting Illness). The algorithm will run once every day to flag potentially eligible candidates using an IT protocol used successfully in previous research at Parkland. The PI or her designee (research assistant or research coordinator) will contact the attending physicians of those identified by the algorithm to confirm eligibility and get permission to introduce the study to those patients. Creation of the algorithm is actually Aim 1 of an AHRQ-funded study that includes all three aims; consequently, the algorithm will be complete enough to use for recruitment in Aim 2 described here.

The PI or her designee (research assistant, research coordinator, or LHA) will contact each patient's primary caregiver by phone to confirm their participation in the study.

The PI will be responsible for all recruitment. Verbal informed consent will be obtained from all study participants. The PI, Co-Investigators, and study personnel will be authorized to obtain informed consent from participants. Waiver of documentation of informed consent can be justified because the research presents no more than minimal risk to subjects—study participation is limited to responding to survey questions—and because the research involves procedures for which written consent is not normally required outside the research context Participants will be informed that they do not have to participate and can stop their participation at any time.

10. **Potential Risks:** Risks associated with this research include a potential minimal risk of loss of confidentiality. Every effort will be made to keep patient information confidential as described below. Some of the questions could be upsetting to patients, as these questions probe the patients' knowledge of their diagnosis and level of spirituality. Additional risk includes psychosocial concerns such as anxiety. Should the LHA be encounter a patient who has an unexpected reaction or becomes upset during the interview, the PI (a physician trained in geriatrics, hospice, and palliative medicine) will be contacted to assist. Additionally, pastoral care, psychiatry, and psychology services will be made available to participants should they desire it. Patients will have access to the inpatient consult services and outpatient follow-up should the need arise. There are no questions that would pose a risk to the patients' reputations, residency status, or employment.

11. **Subject Safety and Data Monitoring:** This is a minimal risk protocol involving only the potential risk of loss of confidentiality. All medical and other identifying information will be kept in a secure location, only accessible to the PI and/or her designee. Processes to maintain data integrity will be followed. After data collection is completed, all patients will be assigned a unique identifier, all data will be de-identified, and no protected health information will be stored. The database will be stored on a secure server with access limited to the research team. Interview forms will be locked in a secure location with access provided only to the research team. All computers used for this project will be password protected.

12. **Procedures to Maintain Confidentiality:** No identifying information will be included in the transcription of the focus groups or on any instruments. The instruments will be coded and the master list that links the individual and the code will be maintained by a member of the research staff under lock and key or on a password-protected computer. At the end of the study, the recorded information and the document linking participant with his/her code will be destroyed.

13. **Potential Benefits:** The benefits to the human subjects identified in this research are as follows. They will receive information about options for care that they might otherwise not have known about. This will be done by a culturally sensitive EOL counselor with specific training in providing counsel to AA with chronic illnesses. There is also potential benefit to future patients requiring end-of-life care and to society. Data collected for this research will allow the PI and research team to identify persons from underrepresented groups who may not be aware of their options for EOL care, and consequently design multifaceted interventions to reduce previously identified disparities.

Study Title: Aim 1 (Development of the intervention)

Total Planned Enrollment: 68

TARGETED/PLANNED ENROLLMENT: Number of Subjects			
Ethnic Category	**Sex/Gender**		
	Females	**Males**	**Total**
Hispanic or Latino	0	0	0
Not Hispanic or Latino	34	34	68
Ethnic Category: Total of All Subjects *	34	34	68
Racial Categories			
American Indian/Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American**	26	26	52
White***	8	8	16
Racial Categories: Total of All Subjects *	34	34	68

*** Patient/caregiver pairs, and AA religious leaders ***Palliative care Providers*

Study Title: Aim 2 (Pilot test of the intervention)

Total Planned Enrollment: 96

TARGETED/PLANNED ENROLLMENT: Number of Subjects			
Ethnic Category	**Sex/Gender**		
	Females	**Males**	**Total**
Hispanic or Latino	0	0	0
Not Hispanic or Latino	48	48	96
Ethnic Category: Total of All Subjects *	48	48	96
Racial Categories			
American Indian/Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	48	48	96
White	0	0	0
Racial Categories: Total of All Subjects *	48	48	96

Statistical Analysis Plan:

The PI will use descriptive statistics to characterize study participants and proportion of intervention elements and follow-up assessments completed. The specificity and positive predictive value of the e-EOL algorithm operating in real world practice will be assessed using methods described for Aim 1 with physician chart review as the criterion standard. Acceptability and feasibility process data will be tallied. The main decision making outcome will be *change in the stage of intent to discuss EOL care options* from baseline through all follow-up intervals. Movement to an adjacent stage is a 1 point change. The PI will assess several aspects of stage change based on the proportion of patients at each time interval showing: 1) *any* stage pro/regression, and 2) *full progression to* the action stage of discussion EOL care options. Mean and range of progression at each interval will also be reported. The proportions above and means for *persistent* change will also be defined as the difference between baseline and 6 months (or 3 months if no 6 month contact or patient deceased). The PI will similarly examine pre- and post-intervention changes over time in knowledge, attitudes, and beliefs about EOL care and prognosis, decisional conflict, and QOL using non-parametric tests among the intervention group versus controls. Pre-specified subgroup analyses will stratify change in outcomes by: condition, mistrust, and spirituality. To achieve sensitivity of around 50% (with 10% confidence intervals, e.g. CI: 40% to 60%) in the outpatient algorithm, the PI will need to review 150 charts of patients diagnosed with metastatic (Stage III or IV) breast, lung and colorectal cancer (75 "test positive" and 75 "test negative" cases). The controlled pilot study in Aim 3 is designed to establish: feasibility, acceptability, detect preliminary efficacy signals (changes in behavioral intent, knowledge, attitudes, beliefs, decisional conflict), and generate point/variance estimates to be used to in power calculations for a future fully-powered RCT. The PI proposes a small pilot RCT that will include 24 patient-caregiver pairs in each arm (intervention versus a usual care control group). This will yield greater than 80% power to detect a large intervention effect defined as an absolute difference in desired primary outcome of 40% (across a range of different point estimates), and between 60-70% power to detect a more modest absolute difference of 30% between the two groups (across a range of point estimates). To ensure the ability to recruit the additional patient-caregiver pairs for the study, the PI will extend the enrollment period from 15 months to 18 months. Parkland Hospital providers care for more than 900 breast, lung and colon cancer patients per year, and roughly 40% are African American; consequently the PI believes that she will able to successfully enroll this number of participants within an 18-month timeframe.