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Fred Hutch Cancer Center

TITLE: Latinos' Beliefs and Communication about Advance Care Planning

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Confidentiality Statement

This document is confidential and is to be distributed for review only to investigators, potential investigators, consultants, study staff, and applicable independent ethics committees or institutional review boards. The contents of this document shall not be disclosed to others without written authorization from FHCC.

Fred Hutchinson Cancer Center

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Institution Name

Weill Cornell Medicine

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Institution Name

UT Southwestern

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Institution Name

Confluence Health

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Institution Name

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Principal Investigator's Name	**Principal Investigator's Signature**	**Date**

List of Abbreviations

AE	Adverse Event
CFR	Code of Federal Regulations
CRF	Case Report Form
CTSC	Clinical Translational Science Center
DSMP	Data Safety Monitoring Plan
FDA	Food and Drug Administration
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act of 1996
HRBFA	Human Research Billing Analysis Form
HUD	Humanitarian Use Device
ICF	Informed Consent Form
IDE	Investigational Device Exemption
IND	Investigational New Drug
IRB	Institutional Review Board
PLAN	Planning for Your Advance Care Needs
PHHS	Parkland Hospital and Health Systems
PHI	Protected Health Information
PI	Principal Investigator
REDCap	Research Electronic Data Capture
SAE	Serious Adverse Event
SUSAR	Suspected Unexpected Serious Adverse Reaction
UIRTSO	Unanticipated Problem Involving Risks to Subjects or Others
UT Southwestern	University of Texas Southwestern
WCM	Weill Cornell Medicine
FHCC	Fred Hutchinson Cancer Center

1. Protocol Summary

Full Title:	Latinos' Beliefs and Communication about Advance Care Planning
Short Title:	PLAN (Planning For Your Advance Care Needs) Intervention
Principal Investigator:	Megan Shen, PhD
Study Description:	The goal of this study is to develop and pilot test a culturally competent communication intervention designed to enhance Latino advanced cancer patients' engagement in advance care planning (ACP).
Sample Size:	N=50 advanced cancer patients
Study Population:	Latino advanced cancer patients
Enrollment Period:	12 months
Study Design:	Pilot randomized controlled trial (RCT)
Description of Sites/ Facilities Enrolling Participants:	Fred Hutchinson Cancer Center Alliance UT Southwestern Confluence Health
Study Duration:	November 1, 2021 to April 30, 2024
Participant Duration:	4 to 6 weeks

Primary Objective:	To determine the feasibility, acceptability, and potential efficacy of the culturally competent communication to improve engagement in ACP (i.e., end-of-life discussions with providers and families, completion of advance directives) for Latino patients with advanced cancer.
Secondary Objectives:	Not applicable
Exploratory Objectives:	Not applicable
Endpoints:	Feasibility will be measured by intervention completion (Benchmark: ≥ 70% complete the intervention sessions). Acceptability will be measured by a single-item question assessing helpfulness of the intervention (1 = not at all helpful, 5 = very helpful) as well an open-ended question about helpfulness of the intervention ("What was helpful about the intervention?") (Benchmark: ≥ 70% rate it as "helpful" or "very helpful"). Advance Care Planning Readiness will be measured using the Advance Care Planning Engagement Survey, which is a validated 49-item scale (α=.94)[1] designed to assess knowledge, readiness/motivation, and self-efficacy of ACP. Engagement in ACP will measure two key elements of ACP. First, *EOL care discussions* will be measured by asking patients to self-report whether they have discussed any of the following: (1) wishes they have about the care they would like to receive if they were dying and/or (2) advance care directives, with an oncology provider or family member: DNR orders, living wills, durable powers of attorney for health care, assignments of health care proxies (yes/no format). Second, *completion of advance directives* will be assessed by examining the medical chart for completed advance directive documents (DNR order, living will, durable power of attorney, health care proxy).
Analytic Plan:	SPSS version 23.0 will be used to conduct all quantitative statistical analyses. Participants (N=50) will be randomly assigned to the culturally competent communication intervention group or PLAN (n=25) or the control group (n=25). They will then complete measures of engagement in ACP post-intervention. Preliminary analyses will utilize t-tests to compare the two groups on baseline characteristics (e.g., education, age). Using a criterion of $p < .10$, any variables that are different among the groups will be included in the final logistic regression models as potential confounders. Five separate logistic regression models will be run in which ACP outcomes (end-of-life care discussions with family and providers; and the completion of advance directives DNR, health care proxy, and living will) will be predicted by the group variable (intervention vs. control). The statistical power of the proposed logistic regressions to detect a minimum odds ratio of 2.0 for dichotomous outcome measures of ACP, for a two-tailed test with power $(1 - \beta)$ equal to 0.80, and $\alpha = 0.05$, requires a sample size of 113. Our proposed sample size of n=50 will be underpowered if the effect size is small but adequately powered if it is large.

1.1 Study Objectives

1.1.1 Objectives

To determine the feasibility, acceptability, and potential efficacy of the culturally competent communication to improve engagement in ACP (i.e., end-of-life discussions with providers and families, completion of advance directives) for Latino patients with advanced cancer.

1.1.2 Hypotheses / Research Questions

The culturally competent communication intervention will be feasible, acceptable, and result in greater engagement in ACP than those in the control condition.

2. Background and Significance

Latino/non-Latino, white disparities are prevalent in ACP and quality of EOL care. Cancer is the leading cause of death among US Latinos.[2] This highlights the importance of addressing advance care planning (ACP) for Latino cancer patients. So do recent U.S. Census Bureau statistics indicating that Latinos are the fastest growing minority group in the U.S., with expected growth rates of 57% from 2015 to 2050 (totaling to 103 million).[3]. Latino/white disparities are prevalent in end-of-life care planning and outcomes. For instance, terminally ill Latinos are less likely than non-Latino, whites (hereafter referred to as "whites") to engage in ACP.[4-8] ACP enables patients to achieve their preferred EOL goals of care. Latinos are significantly less likely than whites to engage in two main forms of ACP: (1) end-of-life discussions (32% vs. 85%)[4] and (2) completing advance directives such as having a living will (9% vs. 67%) or naming a health care proxy (4% vs. 59%).[4] Engaging in ACP is critical to receiving preferred end-of-life care. Among all groups, patients who engage in ACP have been shown to be significantly more likely to receive care in line with their end-of-life care wishes (86% vs. 30%)[9] and to die in their preferred place (85% preferred home).[10] The absence of ACP, in turn, is linked to higher rates of death in the Intensive Care Unit (ICU). ICU death is linked to greater physical and emotional distress and poorer quality of life.[11,12] Latino patients are more likely than their white counterparts to receive aggressive care (e.g., CPR, ICU stays) at the end of life.[13-15] They are also less likely to use hospice services.[14,16-18] The aggressive care that Latinos often receive is generally contrary to their preferences and values,[19-24] associated with poorer quality of life,[12,19,25,26] and very costly.[13]

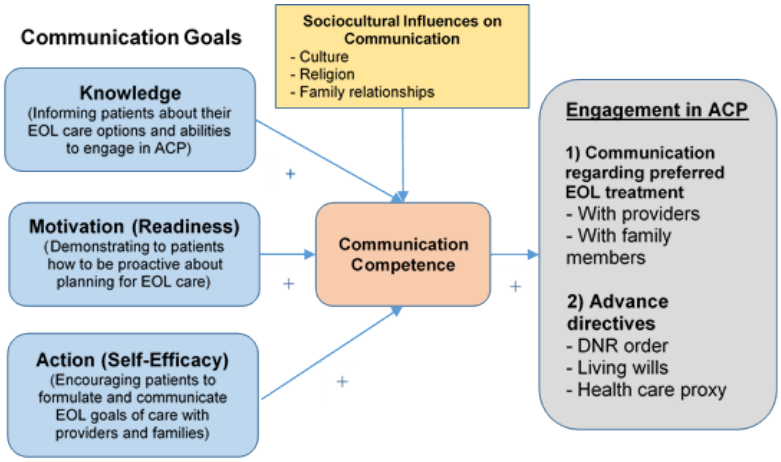


Figure 1. Conceptual model of the role of communication competence and social psychological influences on engagement in ACP among Latinos.

Engaging in ACP is critical to having quality and value-consistent EOL care. Prior research as well as our pilot data show that engaging in ACP is critical to improving end-of-life care among Latinos. For example, one of our prior studies found that among Latino advanced cancer patients who completed a do not resuscitate (DNR) order and/or had an end-of-life discussion, none received aggressive care at the end of life.[27] More recent findings from *our recent publication*[28] demonstrate that when Latino patients had an end-of-life discussion, it increased their odds of completing a DNR order tenfold, nearly eliminating the pre-existing Latino/white disparities in DNR order completion. Thus, it is critical to develop an intervention that will increase engagement in ACP to improve quality of

care at the EOL among Latino advanced cancer patients.

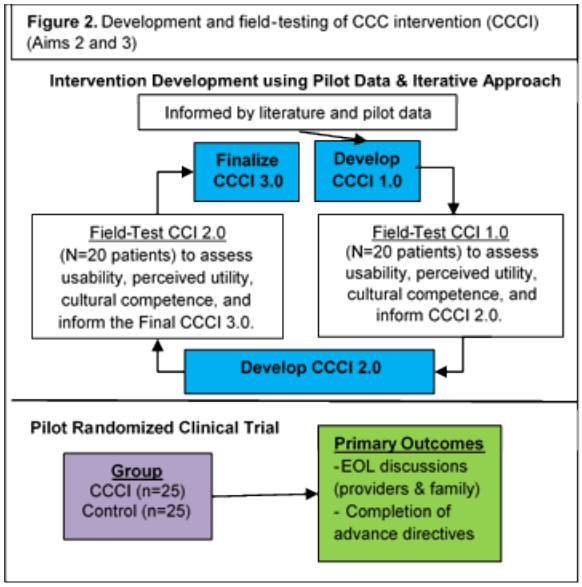
An effective intervention to increase Latinos' engagement in ACP should *incorporate* communication competence and cultural values. In designing an effective intervention for increasing Latinos' engagement in ACP, it is necessary to consider what contributes to Latinos' low rates of ACP. First, as highlighted by a narrative review of the literature (33 empirical studies), lack of knowledge about advance directives[29] contributes to less engagement in ACP. Second, Latinos prefer a family-centered approach to determining end-of-life goals of care.[29] Finally, distinct cultural and religious beliefs about end-of-life care also reduce engagement in ACP.[15,17,18,20,21] Based on these findings, an effective intervention should target communication and knowledge of ACP while also *incorporating* cultural, religious, and familial beliefs about ACP.

A patient-targeted "coaching" intervention may be the most effective approach for Latinos. Prior research in other clinical contexts indicates that clinicians give more information and achieve a better understanding of patients' goals of care when patients engage in a more participatory consultation style (asking more questions, stating preferences).[30-33] Patients' participation has been shown to benefit disadvantaged and minority groups most, indicating its importance among Latinos.[32] One way to improve patient participation and communication in medical consultations is to utilize a patient-targeted coaching intervention (demonstrated to be effective across 137 intervention trials).[34] Because Latinos' beliefs surrounding ACP are also influenced by specific cultural, familial, and religious beliefs,[15,17,18,20,21] an effective intervention should communicate about ACP in a culturally sensitive manner. Communication that focuses on *incorporating* social and cultural context in communication as a way to reduce racial and ethnic disparities in quality care[35] is referred to as *culturally competent communication*.[36] Social psychological theories, such as sociocultural theory[37] which examines how social and culture influence behaviors, provides a useful framework for understanding the influence of social relationships and culture on engagement in ACP. In short, a patient-targeted coaching intervention that is culturally competent may be the most effective intervention for improving Latinos' engagement in ACP. Despite the great promise of the effectiveness of a culturally competent communication coaching intervention, little research has focused on identifying effective strategies for improving Latino advanced cancer patients' engagement in ACP. The proposed K07 aims to address this gap in the literature through developing and examining the feasibility, acceptability, and efficacy of a theoretically-guided, culturally competent communication intervention that will coach Latinos on how to engage in ACP and communicate their preferred end-of-life goals of care. This intervention will be developed based on current literature grounded in models of communication competence.[38,39] The proposed work will make a significant contribution by developing an effective, low-resource intensive intervention designed to improve Latino advanced cancer patients' engagement in ACP, ultimately leading to a reduction in disparities in end-of-life care. Results from this study will also guide the development of a future, multisite study (R01) examining the efficacy of the culturally competent communication intervention among various sub-groups of Latinos.

3. Study Design and Methods

3.1 Overall Design

Following Phase IIb of the ORBIT model,[40] we will pilot test the developed intervention (PLAN) to demonstrate feasibility, acceptability, and preliminary effectiveness at improving patients' engagement in ACP. To assess this, 50 Latino advanced cancer patients will be recruited and randomly assigned to the intervention group (n=25) or the control group (n=25). After completing the intervention/control, patients will fill out measures of completion of end-of-life discussions and advance directives (confirmed via medical charts). Phase III (of the ORBIT model)[40] (Efficacy) will be tested in a future R01 RCT.



Because this is a protocol being transferred from Weill Cornell to FHCC, the PI (Shen) requested that two additional sites (UT Southwestern and Confluence Health) be added to the protocol to ensure the proper number of Latino patients can be enrolled in this study. Confluence Health reports a base rate population of 58% Latino patients. UT Southwestern (UTSW) has been a prior collaborator of the PI and her collaborators at Weill Cornell on R01 projects examining advanced cancer patients over time. In this prior work, they have consistently recruited several Latinx advanced cancer patients successfully and met all recruitment goals (often n=50 to 75 patients within 12 to 18 months), Additionally, Dr. Paulk has collaborated on this research and has several publications in the area of end-of-life care. Finally, the current number of eligible Latinx advanced cancer patients at this site is n=15 to 20 patients per week. Finally, of great importance, UT Southwestern has trained and devoted bi-lingual research staff to assist with study recruitment. These features of the site and the lead collaborator, Dr. Paulk, make it a highly feasible collaborative site for this multi-site project. Dr. Paulk is the founder of palliative medicine programs at UTSW and currently serves as the Medical Director of ambulatory and inpatient palliative medicine programs for the Parkland Health and Hospital System (PHHS). Additionally, this site is expected to serve as a site for future R01 submissions, thus inclusion at this point will enhance the ability to demonstrate feasibility. This request was approved by the NCI PO for this K07 award.

3.2 Study Population

Patient subjects with an advanced cancer diagnosis who meet the inclusion and exclusion criteria will be eligible for this study.

3.3 Inclusion Criteria

Patient eligibility criteria: (1) identifying ethnically as Latino; (2) locally advanced or metastatic cancer and/or have experienced disease progression on at least first-line chemotherapy and (3) ability to provide informed consent.

3.4 Exclusion Criteria

Patient exclusion criteria: (1) not fluent in English or Spanish; (2) severely cognitively impaired (as measured by Short Portable Mental Status Questionnaire scores of ≥ 6 to be delivered by trained study research staff during screening);[41] (3) too ill or weak to complete the interviews (as judged by interviewer); (4) currently receiving hospice at the time of enrollment (to allow prediction of ACP); (5) children and young adults under age 18; and (6) patients deemed inappropriate for the study by their treating oncologist. Because the primary outcomes include both completion of advance care planning documentation as well as conversations around ACP, we have chosen not to add exclusion criteria around completion of advance directives. The goal of PLAN is two-fold – which is to increase completion of these documents but also to increase engagement in conversations around ACP with loved ones and providers (which can be present or not present despite completion of documents).

3.5 Strategies for Recruitment and Retention

To recruit patients at FHCC, trained bi-lingual, bi-cultural research staff will review the electronic health record to identify potentially eligible patients. And will contact the treating oncologist to confirm initial eligibility and obtain permission to approach these patients about the study. Using the eligibility criteria outlined, study staff will screen participating oncologists' clinic schedules for patients that meet the inclusion criteria (e.g., cancer diagnosis and treatment status). Alternatively, oncologists will refer their patients directly to the study.

To recruit patients at Confluence Health, a clinical roster will be reviewed daily by oncologists or clinical team members. Potentially eligible patients will be identified and forwarded in a list to FHCC study staff. Trained bi-lingual, bi-cultural FHCC research staff will approach, determine eligibility, and consent eligible patients.

To recruit PHHS patients by UTSW study staff, the site PI (Dr. Paulk) or trained bi-lingual, bi-cultural staff at UTSW will obtain verbal consent either in-person or over the phone from Parkland patients eligible for the study. All consented patients will then be given assessments/surveys. For patients randomized to the intervention condition, they will receivethe telephone-based intervention by the FHCC study staff. These approaches are outlined and will be approved by the participating site's local IRB.

Recruitment and retention. We will recruit advanced cancer patients from three sites: FHCC, UT Southwestern, and Confluence Health. To maximize recruitment rates and ensure timely completion of the proposed study, we will use multiple methods and processes used in our prior (R01-CA106370, PI: Prigerson) and current work (K07-CA207580, PI: Shen; R21-CA224874, PI: Shen) outlined below. Our team of investigators, most notably Dr. Shen (PI), Dr. Prigerson (Co-Investigator), and Dr. Paulk (Co-Investigator) have a long track record of success recruiting advanced cancer patients to research studies. Sampling and recruitment procedures to be utilized in the present study, as noted, have been used for similar NCI-funded studies (e.g., CwC I, II, and III; PI: Prigerson: Site PI: Paulk). Recruitment across these studies (e.g., R01-CA106370, PI: Prigerson) have indicated recruitment rates of 70-80% for an advanced cancer patient population with the same eligibility criteria outlined in this application. As such, we project a conservative estimate of 70% of eligible patients. The average number of new advanced cancer patients seen annually at FHCC (based on solid tumors included in the proposed study) is n= 2,405, of whom n=372 identify as Latinx (based on 2019 numbers from formerly Seattle Cancer Care Alliance). Given this projected

patient flow, the allowed year for active recruitment is a highly feasible timeline for recruiting n=50 patients at FHCC.

Although our prior studies have successfully recruited 70% of advanced cancer patients, we acknowledge that recruitment to the present study may pose different and unique challenges. As such, we outline here the specific measures we will take to maximize rates of recruitment and retention to ensure timely and full completion of the study at each site.

At FHCC, study staff will review FHCC clinic schedules twice weekly to identify advanced cancer patients who meet the eligibility criteria. Study staff will confirm the potential eligibility of all identified patients through medical record review. Once a potentially eligible patient is identified, research study staff will email the patient's treating oncologist or other clinical team member to confirm eligibility and request permission to approach the patient. When an eligible patient is identified and confirmed to be eligible by the patient's treating oncologist or clinical team member, the research study member will approach the patient in the clinic and describe the study to the patient in person. If the research study member is unable to meet the patient during his/her clinic appointment, the study member will mail a letter out describing the study, which includes contact information for the study team. The letter will instruct the patient to call the study team either to learn more about the study or indicate he or she is not interested. If no contact is made by the patient, the study team member will follow up with a phone call to provide additional information about the study and assess interest in participating. Once the patient has expressed interest and is deemed eligible, they will each be given an introductory letter, a study information sheet, and consented to the study. Once consented, the assessments and telephone-based intervention will be conducted by FHCC study staff.

At UTSW, Dr. Paulk and other providers within the PHHS palliative care clinic will refer potentially eligible patients to UTSW research study members. A Form HH HIPPA supplement and waiver of authorization has been sent and approved by Fred Hutch and UTSW IRB in order to review EMRs to determine eligibility for recruitment purposes. When an eligible patient is identified and confirmed, the UTSW study member will either approach the eligible patient in person, during a clinic visit, or mail out recruitment material, if they are unable to approach the patient in person. If approaching the eligible patient in person, the study member will coordinate with the clinic staff to find an appropriate time to approach the patient. When approaching the patient, the study member, will proceed to describe the study and give the patient a study flyer. If the research study member is unable to meet the patient during their clinic visit, they will mail the patient an envelope containing a study flyer and information sheet. An information sheet is a UTSW form used to provide study information to potential participants and used for guiding the verbal consenting process. Two weeks after mailing out the letters, UTSW study staff will contact the participant over the phone to gauge interest for study participation. A Form HH Waiver of Consent documentation has been sent and approved by Fred Hutch and UTSW IRB in order to waive documentation of consent (signed form) in order to obtain verbal consent.

If the patient is interested after the in person or telephone call approach, the patient will give verbal consent for participation to the UTSW study member. Once verbal consent has been obtained the UTSW research assistants, will notify the Fred Hutch coordinator. The Fred hutch coordinator and social worker will then carry out the rest of the study procedures with the UTSW participants over the phone. Since the Fred Hutch Coordinator and social worker conduct the remaining study procedures, they will mail out the gift cards to participants who

have completed the surveys. Due to workflow, timing, scheduling and sessions/surveys conducted over the phone, Fred Hutch will take responsibility to compensate the participants, as UTSW staff will not be involved in the downstream of study procedures. To avoid any delays and to ensure timely compensation, once the participant has completed the survey with the participant over the phone, the Fred Hutch team will mail out the gift card to the participant. For each completed survey, the compensation will be a gift card in the amount of $25.00. Participants are eligible to receive up to $50.00 for completed both first and last survey.

At Confluence Health, oncologists within the cancer clinic will refer potentially eligible patients directly to the FHCC study team. Dr. Overton (Co-Investigator, Confluence Health) will directly assist in this process by communicating with and overseeing oncologist referrals at Confluence. When an eligible patient is identified and referred to FHCC study staff, staff members will be responsible for approaching the participant with an introductory letter and a study information sheet via mail. If interested, the patient will be consented to the study. All consented patients will then be given assessments as well as the telephone-based intervention by FHCC study staff.

Each of these methods for approaching and consenting methods have been used successfully previously at Weill Cornell (PI's previous institution) to recruit advanced cancer patient.

Additionally, the following measures will be taken to improve retention. Follow up calls or texts (depending on participant preference) to participants will be utilized to remind patients of upcoming study activity (interviews, assessments, etc.). A social worker interventionist and "coach" has been included as the study interventionist to improve patients' access to needed resources throughout the study intervention, which has been shown in our prior work to improve retention to intervention studies. Throughout the study period, accrual and retention rates will be monitored at weekly study meetings through CONSORT flow diagrams reporting reasons for missed approaches, study refusal, and loss to follow up. This will allow the PI and study team members to notice quickly issues in accrual and/or retention and the potential reasons for it so that proper action can be taken to resolve the issue. This approach has previously helped similar studies which had fallen to 50% accrual to improve to 90% accrual through a targeted approach system that addressed the specific reasons for refusal (e.g., accommodating schedules, fatigue, etc.). Finally, all attempts have been made to keep interviews and questionnaires brief and flexible in order to reduce burden on the patients.

Patients at the FHCC and Confluence sites, who are approved for contact by the treating oncologist will be sent a letter in the mail that includes a brief description of the study and contact information of study staff. Research staff will then meet these patients in the clinic, introduce themselves, and provide the patient with a study information sheet and consent form. Patients who indicate they want to participate will be consented at that time or provided a pre-paid postmarked return envelope in which to return the consent form and contacted within one week via telephone for follow-up. Patients who study staff are unable to meet during clinic appointments will be contacted by study staff over the telephone and will be provided with information on the study and administered informed consent. Once consented, participants will be enrolled in the study.

3.6 Interviews, Focus Groups, Surveys, and/or Observations

A. Administration

- *Timing and Frequency*
  Pre-interview/baseline assessment, intervention, and post assessment follow up post-intervention (within a week).
- *Location*
  Telephone-based delivery of the intervention and in person or over the phone assessments. Cancer patients may opt to have their interview(s) during infusion at participating sites (FHCC, UT Southwestern/PHHS, Confluence Health).

  ***Additional measures to protect participants in the in-person interviews or usability testing from COVID-19 related exposure and infection**. In-person interviews will only be conducted in line with all the safety regulations and recommended procedures for vulnerable and at-risk patient populations. As such, no in person approaches will happen prior to the appropriate approval and authorization at each participating site. In the even in person approaches are approved, study personnel will ensure proper PPE is worn by approaching study staff, proper social distancing is observed, and that all patients consent to and are comfortable with in person interviews. Due to potential risks, telephone-based interviews will be promoted among participating patients, when available.

- *Person Identifiers*
  Clinical variables will be collected from medical records and will include the following: cancer diagnosis and stage, treatment received, co-morbid conditions (i.e., Charlson Comorbidity Index, CCI), and Karnofsky performance status.

B. Study Instruments

Feasibility will be measured by intervention completion (Benchmark: ≥ 70% complete the intervention sessions). Acceptability will be measured by a single-item question assessing helpfulness of the intervention (1 = not at all helpful, 5 = very helpful) as well an open-ended question about helpfulness of the intervention ("What was helpful about the intervention?") (Benchmark: ≥ 70% rate it as "helpful" or "very helpful"). Demographics will be measured via self-report assessing: age, gender, race, ethnicity, marital status, employment status, education, income, religion, insurance coverage, national origins (e.g., Mexican), cultural heritage, and acculturation.[42] Clinical variables will be assessed using records from medical charts and will include the following: cancer diagnosis, treatment, site, and stage; co-morbid conditions, and Karnofsky[43] performance status.
Quality of life will be measured using the validated, 27-item Functional Assessment of Cancer Therapy-General (FACT-G) scale.[44] Cultural beliefs will be measured using three brief scales developed for the present studies (included in the R01). *Fatalismo*[45] will be measured using a 4-item scale assessing the acceptance of belief that all events are predetermined and inevitable. *Personalismo*[46,47] will be measured using a 4-item scale assessing the existence of a warm, personal relationship with the medical professional and trust based on mutual respect. *Respeto*[48] will be measured using a 4-item scale assessing the degree to which patients endorse the role of authority in following doctor's orders. Familial beliefs will be measured using two brief scales developed for the present studies (included in R01). *Familismo*[61,62]

will be measured using a 5-item scale assessing the degree of family loyalty and cohesion. Related to *familismo*, *filial duty*[49] will be measured with a 6-item scale assessing the degree to which children should be involved in caring for their elderly parents. Religious/spiritual beliefs will be measured with two scales: (1) *Religious coping* will be measured using *Pargament's brief RCOPE*,[50] which is a validated 14-item scale (α > .80[50]) assessing the extent to which patients engage in 7 types of positive and 7 types of negative religious coping. (2) *Religious beliefs about EOL medical care* will be measured using a 9-item scale. We have recently begun to validate this scale among advanced cancer patients in our prior studies.[51] Potential confounders to be measured include *terminal illness acceptance,* which will be assessed using our validated, single-item question,[19,52] which asks patients how they would define their current health status and *illness understanding*, a single item measure that assesses understanding of incurability of illness. We will use the Advance Care Planning Engagement Survey, which is a validated 49-item scale (α=.94)[1] designed to assess knowledge, readiness/motivation, and self-efficacy of ACP. Engagement in ACP will measure two key elements of ACP. First, *EOL care discussions* will be measured by asking patients to self-report whether they have discussed any of the following: (1) wishes they have about the care they would like to receive if they were dying and/or (2) advance care directives, with an oncology provider or family member: DNR orders, living wills, durable powers of attorney for health care, assignments of health care proxies (yes/no format). Second, *completion of advance directives* will be assessed by examining the medical chart for completed advance directive documents (DNR order, living will, durable power of attorney, health care proxy). Patient's Medical Status**.** Patients' current and past cancer diagnoses, the dates of each, patients' Karnofsky performance score[43] and the number and type of oncology providers seen at that clinic will be obtained from the patient's medical chart. Advance Directives and Referrals for Palliative Care**.** Patient's medical charts will be reviewed for documentation of advance directives and referrals for palliative care during the study observation period (consent to interview).

3.7 Intervention (PLAN)

The intervention for this study, Planning For Your Advance Care Needs (PLAN), is a coaching-based communication information designed to be culturally competent, In PLAN, all coaching sessions will occur over the phone and be a maximum of 45 minutes to reduce patient burden. These sessions will focus on creating individualized messages and skill-building exercises based on patients' learning needs, goals, and values (as indicated on the intake form). The intervention will be delivered across three sessions, with the following modules, as based on prior communication competence coaching interventions:[53] (1) *Assessment* of current knowledge, motivation, and self-efficacy (action) as well as cultural and religious preferences/values surrounding EOL care (tablet-based intake questionnaire); (2) *clarification and correction of misconceptions* about EOL care and ACP; (3) *teaching* of relevant concepts (education about ACP and EOL care options); (4) *planning* (identifying goals of care, creating achievable goals of care, and creating strategies to communicate goals of care to providers and family members); (5) *rehearsal* of communication skills using role play exercises (practice question-asking, etc.); (6) *portrayal* of learned skills (patient applies learned skills in their oncology visit and/or with family members).

3.8 Interviewer Training and Instrument Administration

Interviewer Training. Staff working on this protocol have extensive experience interviewing

patients with advanced cancer in an end-of-life care settings from our previous NCI-funded studies. These fully trained, experienced interviewers will train new interviewers. Training will consist of learning the interview question prompts/guides, practice sessions, and instruction in administration of surveys, including IRB approved procedures for approaching potential study participants. Newly trained interviewers will be required to have a high degree of inter-rater-reliability (e.g., κ=0.85) with fully-trained, experienced interviewers on core assessments (e.g., religious beliefs about end-of-life medical care) before they will be allowed to collect data for the study.

Scheduling of Assessments. Study staff will contact enrolled patient study participants to schedule their interviews. Patients will be given the option to communicate about their assessments and the scheduling of the assessments via phone calls, emails, and/or text messages. Patient assessments will be scheduled to occur at the earliest convenient time for the participant following study enrollment. All baseline assessments will be given first. Then, patients will engage in their first intervention session within one week of completing a baseline assessment. The three intervention sessions will then be given approximately a week a part, taking approximately four weeks to complete. After completion of the intervention, patients will complete a post-intervention assessment within one week. Finally, a brief three month follow up will occur that extracts data from their EHR on healthcare utilization. For those in the control condition, they will receive a baseline assessment and then a “post-intervention” session four weeks later, which is the expected span of time between baseline and post-intervention assessments for those in the experimental condition. Three month follow up data extraction will occur for subjects in experimental and control conditions.

Conduct of Patient Assessments. Patients’ assessments will be conducted either in person in clinic or at home, or over the telephone depending on the wishes of the patient. Interviews will be conducted in English or Spanish depending on the preference of the patient. We have previously validated all measures to be used in samples of English- and Spanish-speaking advanced cancer patients, and all assessments will be translated into Spanish through Datagain, a professional translation service which utilizes HIPAA compliant procedures and has been used in prior studies by the PI. We will document the language in which the interview was conducted. Each interview will be conducted alone with the patient to permit greater freedom of expression and will be approximately 45 minutes in length. If patients appear depleted or otherwise unable to be interviewed at that time, the interviewer will reschedule the interview at a time and place of their choosing within a few days. Considerable care has been taken to ensure that the interviews are as brief as possible. All Spanish translated materials will be submitted for IRB approval after receiving approval for the English documents.

Medical Chart Extraction. Study staff will review participating patients’ medical charts during the course of the study to extract information about patients’ health and disease status, healthcare, documentation of advance care directives, and referrals for palliative care during the study observation period.

Reducing Missing Data. To reduce missing data, following all assessments study staff will review the contents and scan for missing information. If missing information is found, the staff member will contact the subject or review the medical chart to fill-in missing data.

3.9 Intervention Administration

A total of 50 Latino advanced cancer patients will be enrolled in this study and randomly assigned to the intervention (n=25) or control (n=25) condition. Pre-intervention, patients’

communication goals will be assessed. Then, patient will participate in the intervention or a usual care control condition. After participating in the intervention or control condition, patients' engagement in ACP will be assessed to determine if the intervention improved ACP engagement and planning.

The intervention itself will be administered by a fully trained, licensed social worker via telephone. This interventionist will use a culturally competent communication intervention to "coach" patients in how to be motivated for and to actually engage in ACP, and will be bi-lingual in Spanish and English.

Patients randomized into the control group will receive usual care. For usual care, patients will engage in standard care with no modifications. Thus, ACP discussions will only occur as they do in usual clinical care (i.e. brought up in clinical encounters).

3.10 Special Concerns

Patients who agree to participate in the study and provide informed consent will be asked to complete an intervention and post-intervention assessment. Assessments will occur within a few weeks of study enrollment. Each patient assessment will be scheduled to take place at a time and a location that is convenient for the participant, and will take approximately 30 minutes to complete. Patient assessments are designed to be focused and brief. The assessment batteries are less lengthy than those for a prior, similarly designed study (Coping with Cancer), for which rates of incomplete assessments were extremely low, with no interviews of patients requiring rescheduling, and with minimal missing data.

3.11 Compensation

Patient participants will each receive $25 (gift card) compensation for each completed survey assessments (2) for a total of up to $50. The issue of compensation is addressed in the respective consent forms. This amount was selected to compensate patients for their time without coercion to enrollment in the study. UTSW participants will receive their gift cards via mail, by the Fred Hutch team following survey and assessments completed over the phone.

4. Registration Procedures

4.1 Subject Registration (FHCC and Sub-sites)

Subjects will be registered within OnCore CTMS as per the standard operating procedure for Subject Registration.

5. Study Procedures

5.1 Schedule of Assessments

Table 1. Schedule of trial events

	Baseline	*Post-intervention (with 1 week of completing intervention)*	*3 mos. after completion of intervention*	*Off Study*
Informed consent	X			
Demographics	X			
Clinical variables				X
Acceptability		X		
Usability		X		
Feasibility		X		
Quality of life	X	X		
Cultural beliefs (Fatalismo, personalismo, respeto)	X	X		
Familial beliefs (Familismo, filial duty)	X	X		
Religious/spiritual beliefs (Religious coping, religious beliefs about end-of-life medical care)	X	X		
Terminal illness acceptance	X	X		
Illness understanding	X	X		
Readiness for ACP	X	X		
Engagement in ACP	X	X		
Healthcare utilization	X	X	X	
Goal-concordant care	X	X	X	

6. Data Reporting / Regulatory Considerations

6.1 Data Collection

The source of the data to be collected will be verbally administered surveys and (with patient consent) extraction of data from medical records. All materials outlined here will be used specifically for the purposes described in this proposal and not for any other purpose. All data collected during the study will be de-identified. Participants will be informed that all responses will be kept confidential. Data will be linked to participants' names only by means of an assigned study identification number. Authorized study staff are the only individuals who will have access to participants' identification numbers and personal information. This information will be stored in a password protected database on the secure FHCC server as well as in hard copy format in a locked file cabinet in a locked office that is only accessible to the study PI and relevant study staff. The files linking participant study identification numbers to participant names will be destroyed after study completion. All necessary precautions will be taken to ensure that there is no breach of confidentiality.

Participants' completed interviews and self-report measures will be saved in a password protected file on the secure FHCC network server (electronic format) or stored in a locked file cabinet in a locked office (hard copy format) accessible only to the PI and relevant study staff. Participants' responses will be entered into a password-protected electronic database for analytic purposes. This database will be stored on the secure FHCC network server that is password protected.

Data will be obtained by experienced research staff trained in interviewing study participants. All study staff involved in the research will be educated on the protection of human research participants, including attending formal training in the Responsible Conduct of Research provided at FHCC (for FHCC study staff) and UT Southwestern (for UT Southwestern study staff). All personnel involved in the proposed protocol will be educated regarding HIPAA regulations and will fully understand their responsibility to safeguard the personal health information of every participant involved in the research. The data will be used specifically for the purposes outlined in this proposal or a subsequently IRB approved protocol and not for any other purpose.

***Additional measures to protect participants in the in-person interviews or usability testing from COVID-19 related exposure and infection**. In-person interviews will only be conducted in line with all the safety regulations and recommended procedures for vulnerable and at risk patient populations. As such, no in person approaches will happen prior to the appropriate approval and authorization at each participating site. In the even in person approaches are approved, study personnel will ensure proper PPE is worn by approaching study staff, proper social distancing is observed, and that all patients consent to and are comfortable with in person interviews. Due to potential risks, telephone based interviews will be promoted among participating patients.

6.1.1 REDCap

All data will be entered and stored securely on FHCC REDCap servers.

6.2 Regulatory Considerations

6.2.1 Institutional Review Board/Ethics Committee Approval

As required by local regulations, the Investigator will ensure all legal aspects are covered, and approval of the appropriate regulatory bodies obtained, before study initiation.

Before initiation of the study at each study center, the protocol, the ICF, other written material given to the patients, and any other relevant study documentation will be submitted to the appropriate Ethics Committee. Written approval of the study and all relevant study information must be obtained before the study center can be initiated or the IP is released to the Investigator. Any necessary extensions or renewals of IRB approval must be obtained for changes to the study, such as amendments to the protocol, the ICF, or other study documentation. The written approval of the IRB together with the approved ICF must be filed in the study files.

The Investigator will report promptly to the IRB any new information that may adversely affect the safety of the subjects or the conduct of the study. The Investigator will submit written summaries of the study status to the IEC/IRB as required. On completion of the study, the IRB will be notified that the study has ended.

The Investigator will not modify or alter this protocol without the agreement of the IRB. All agreed protocol amendments will be clearly recorded on a protocol amendment form and will be signed and dated by the original protocol approving signatories. All protocol amendments will be submitted to the relevant institutional IRB for approval before implementation, as required by local regulations. The only exception will be when the amendment is necessary to eliminate an immediate hazard to the trial participants. In this case, the necessary action will be taken first, with the relevant protocol amendment following shortly thereafter.

Once protocol amendments or consent form modifications are implemented at the lead site, FHCC, updated documents will be provided to participating sites. FHCC must approve all consent form changes prior to local IRB submission.

Relevant study documentation will be submitted to the regulatory authorities of the participating countries, according to local/national requirements, for review and approval before the beginning of the study. On completion of the study, the regulatory authorities will be notified that the study has ended.

6.2.2 Ethical Conduct of the Study

The Investigators and all parties involved should conduct this study in adherence to the ethical principles based on the Declaration of Helsinki, GCP, ICH guidelines and the applicable national and local laws and regulatory requirements.

This study will be conducted under a protocol reviewed and approved by the applicable ethics committees and investigations will be undertaken by scientifically and medically qualified persons, where the benefits of the study are in proportion to the risks.

6.2.3 Informed Consent

The investigator or qualified designee must obtain documented consent according to ICH-GCP and local regulations, as applicable, from each potential subject or each subject’s legally authorized representative prior to participating in the research study. Subjects who agree to participate will sign the approved informed consent form and will be provided a copy of the signed document.

The initial ICF, any subsequent revised written ICF and any written information provided to the subject must approved by IRB prior to use. The ICF will adhere to IRB requirements, applicable laws and regulations.

Informed Consent will occur under the IRB of FHCC and UT Southwestern.

At UTSW, verbal consent will be obtained from recruited participants who give consent. A waiver for documentation has been approved by Fred Hutch and UTSW IRB.

6.2.4 Compliance with Trial Registration and Results Posting Requirements

The following refers to the proposed project, which will be considered a clinical trial according to NIH standards. This dissemination plan is consistent with NIH Guide Notice NOT-OD-16-149. Dr. Shen (PI) will register the proposed trial on ClinicalTrials.gov prior to recruiting and consenting the first participant. All study results from the trial will be submitted to ClinicalTrials.gov no later than 12 calendar months after the trial's primary completion date. Dr. Shen (PI) will review all ClincalTrials.gov entries for accuracy and comprehensiveness prior to submission for review.

Compliant with NIH policy, all informed consent documents for the pilot trial will include a statement that these results will be made available at the ClinicalTrials.gov website after the initial analysis is complete. Additionally, all participants will be informed that study findings will be presented in aggregate form and that participant-level and identifying information will not be included to ensure confidentiality.

FHCC has an internal policy to ensure that clinical trials registration and results occur in compliance with policy requirements. Specifically, the FHCC Clinicaltrials.gov administrator will facilitate the Principal Investigator's dissemination of study results through ClinicalTrials.gov registration and reporting. Dr. Shen will be responsible for handling ClinicalTrials.gov requirements for this project according to FHCC Clinicaltrials.gov policy. Once a record is established, Dr. Shen will confirm accuracy of record content; resolve problems; and maintain records including content update and modifications. Dr. Shen will also be responsible for results reporting and Adverse Events reporting at the conclusion of the project.

6.2.5 Record Retention

Essential documents are those documents that individually and collectively permit evaluation of the study and quality of the data produced. After completion of the study, all documents and data relating to the study will be kept in an orderly manner by the Investigator in a secure study file. Essential documents should be retained for 2 years after the final marketing approval in an ICH region or for at least 2 years since the discontinuation of clinical development of the IP. In addition, all subject medical records and other source documentation will be kept for the maximum time permitted by the hospital, institution, or medical practice.

7. Statistical Considerations

Participants (N=50) will be randomly assigned to the intervention group (n=25) or the control group (n=25). They will then complete measures of engagement in ACP post-intervention. Feasibility and acceptability will be examined with frequency and descriptive statistics (i.e., mean, median, standard deviation, range) for enrollment rates, number of sessions completed, number of weeks required to complete the intervention, and Likert-scale items assessing satisfaction with the intervention and perceived helpfulness. Because this is a pilot study, in accordance with published standards for pilot feasibility clinical trials,[54] inferential statistics on measures of feasibility (≥70% intervention completion rates) and acceptability (≥70% rate it as "helpful" or "very helpful") are not recommended. Rather, we will examine the average rates of completion

as well as satisfaction and helpfulness ratings to determine feasibility and acceptability based on those values being equal to or greater than 70%. We will also conduct qualitative analyses on the open-ended questions related to helpfulness. Thematic analysis using an iterative process will be conducted for all qualitative analyses.[55-59] A coding scheme and codebook will be created to analyze transcripts of the responses to the open-ended question. Transcripts will be coded separately by two individual coders for manifest (e.g., frequencies) and latent (e.g., underlying themes) variables. If discrepancies occur, a third coder will resolve these conflicts. Interviews will continue until thematic saturation is achieved.[60,61] Based on our prior field testing of interventions with patients with advanced illness, we anticipate reaching saturation with n=10 participants. Thus, n=25 in the experimental condition should be well powered to reach thematic saturation.

To examine potential efficacy, preliminary analyses will utilize t-tests to compare the two groups on baseline characteristics (e.g., education, age). Using a criterion of $p < .10$, any variables that are different among the groups will be included in the final logistic regression models as potential confounders. To test the study aim, five separate logistic regression models will be run in which ACP outcomes (yes/no to EOL discussions with family and providers; and the completion of advance directives DNR, health care proxy, and living will) will be predicted by the group variable (CCC intervention vs. control). The statistical power of the proposed logistic regressions to detect a minimum odds ratio of 2.0 for dichotomous outcome measures of ACP, for a two-tailed test with power $(1 – \beta)$ equal to 0.80, and $\alpha = 0.05$, requires a sample size of 113. Our proposed sample size of n=50 will be underpowered if the effect size is small but adequately powered if it is large. However, this study is a preliminary pilot and the main focus and goal of this is to determine feasibility, acceptability, and to provide preliminary data to inform a fully-powered RCT in future research (R01 submission).

7.1 Randomization. We will utilize stratified randomization at the level of each site to ensure balance across the interventional and control groups at the level of each site. To randomize, we will employ a random number generator to randomize participants to study arms at the level of each site. To ensure randomization was effective, separately for each binary outcome, we will perform a two-sample proportions test to test if the rate of outcomes is significantly different between intervention and control groups. Separately for each continuous outcome, we will perform a two-sample unpaired t-test or unpaired Wilcoxon test (as appropriate) to test if the rate of outcomes is significantly different between intervention and control groups.

7.2 Missing data. To reduce missing data, study staff will conduct interviews rather than relying on written self-reports. This approach has been used previously in our prior work to help reduce data that is missing due to patients accidentally overlooking or missing items or requiring clarification of certain terms (e.g., what is an advance directive). Due notice is taken to ensure that patients know that they are free to skip items they prefer not to answer.

8. Adverse Event Reporting Requirements

8.1 Potential Adverse Events

Potential adverse events (AEs) for this project are all non-medical in nature. Participants may experience mild distress when discussing the status of the patients' cancer, decision-making, or care. Study staff may become aware of adverse events through participant self-report, routine study assessments, or study staff interactions with participants.

We will use standard NIH definitions of AEs/SAEs and UPs as follows:

Adverse Event (AE): Any untoward or unfavorable medical occurrence in a human study participant, including any abnormal sign (e.g. abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the participants' involvement in the research, whether or not considered related to participation in the research. The most likely event for the present study is elevated psychological distress.

Serious Adverse Event (SAE): Any adverse event that: Results in death; Is life threatening, or places the participant at immediate risk of death from the event as it occurred; Requires or prolongs hospitalization; causes persistent or significant disability or incapacity; Results in congenital anomalies or birth defects; Is another condition which investigators judge to represent significant hazards. An example in the present study is a hospitalization or institutionalization or suicidal ideation.

Unanticipated Problem (UP): Any incident, experience, or outcome that is: Unexpected, in terms of nature, severity, or frequency; related or possibly related to participation in the research; and suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

We will use the following grading and relatedness scales in use at FHCC, UT Southwestern, and Confluence Health for severity rating and relatedness raring:

Grading scale:

0. No adverse event
1. Mild AE – No treatment needed
2. Moderate AE – Resolved with treatment
3. Severe AE – Inability to carry on normal activities, required professional medical attention
4. Life-threatening or disabling AE
5. Fatal AE

Relatedness scale:

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

To summarize, potential adverse events (AEs) for this project are all non-medical in nature and are expected to be graded as mild to moderate. Participants may experience mild distress when discussing the status of the patients' prognosis or advance care planning. Serious adverse events (SAE) will include the following: suicidal ideation and/or discussing plans to harm another individual. Study staff may become aware of adverse events through participant self-report, routine study assessments, or study staff interactions with participants.

An unanticipated problem (UP) in the present study would include physical harm of any form to patients, as the proposed study only poses to potentially increase distress. As outlined in NIH policy, the AEs are expected to be mild to moderate in severity; the SAEs are expected to be serious in severity; and the UPs are expected to be mild to moderate in severity.

Based on our prior work, we anticipate that AEs will occur rarely (in less than 2% of cases based on prior studies); SAEs to be 0% (based on prior work); and UPs to be less than 1% based on prior work. In most cases, only an AE of distress is expected to be directly related to study procedures whereas SAEs and UPs are rarely linked to study procedures directly in similar work

8.2 AE/SAE Reporting

To identify possible AEs and SAEs, all study staff will be trained in identifying possible AEs or SAEs and will be required to keep a written log after each participant completes study procedures. In the event an AE or SAE is noticed, study staff will notify the PI either within 24 hours (for SAEs) or within five days (for AEs). Additionally, the PI will review all study materials, including recording interviews and answers to study questions to ensure that no AEs or SAEs go undetected.

All SAEs noted by study staff will be discussed with the PI or designee and reported within 24 hours of discovery by study staff to the IRB and the NCI Program Officer. The PI is required to report adverse events to the Institutional Review Board (IRB) on an ongoing basis. In addition, yearly IRB renewal submissions require detailed adverse event reporting, which will also be sent to the NCI Program Officer and the grant PI (Dr. Shen). Adverse events are also reported as part of the progress reports in the non-competitive and competitive renewals for the NIH. All study staff will complete the NIH required training in participation and conduct of studies that involve human subjects. If study staff discover any untreated physical conditions, they will refer participants to appropriate treatment immediately.

Some participants will be receiving active treatment at the time of study participation; therefore, fluctuations in cancer-related symptoms will not be considered adverse events related to the study. The PI will discuss safety concerns, adverse events, participant complaints and, if any, protocol violations with co-investigators as well.

Meetings with co-investigators will be used to determine if any additional procedures are needed to augment data and safety monitoring. When SAEs occur that are unanticipated, they will be reported to and verified by Dr. Shen, and reported to the IRB and the NCI Program Officer.

After reporting to the IRB, the PI will determine necessity for further reporting and next steps, which will include the following:

- No further reporting of a “definitely not related” AE (but not SAE) will occur.
- All deaths will be reported to the IRB and NCI Program Officer within 24 hours of learning about this event.

- All adverse events that are both serious (SAE) and unexpected (i.e., have not been previously reported for the study's intervention) will be reported to the IRB and NCI Program Officer as well as the PI within 48 hours of the study's knowledge of the SAE. (All deaths within 24 hours, as per above.)
- The summary of all other SAEs will be reported to NIA Program Officer and SO, quarterly.

Few AEs or SAEs are expected for this slightly greater than minimal risk study of a behavioral intervention. As such, it is possible based on the high morbidity and multimorbidity of this population (i.e., advanced cancer patients) that there will occur one or more hospitalizations and/or other moderate to severe illness-related events during the study period that are unrelated to study participation. Nonetheless, if these occur, they will be reported as AEs or SAEs and the appropriate steps as outlined above will be taken.

Below are the specific events that will trigger reporting to the parties described above:
Acute alerts/Serious Adverse Events (SAEs)

- Hospitalization of study participant
- Institutionalization of participant
- Emergency room visit of participant
- Death of participant

Safety Alerts/Adverse Events

- Severe medical problem of participant
- Participant threatens to harm him or herself or others
- Evidence of abuse to participants

8.3 Plans for Assuring Compliance Regarding Adverse Events Reporting

All serious adverse events noted by study staff will be discussed with the PI or designee and reported within 24 hours of discovery by study staff to IRB. The PI is required to report adverse events to the IRB on an ongoing basis. In addition, yearly IRB renewal submissions require detailed adverse event reporting, which will include logs of adverse events. Adverse events are also reported as part of the progress reports in the non-competitive and competitive renewals for the NIH. All study staff will complete the NIH required training in participation and conduct of studies that involve human subjects. If study staff discover any untreated physical conditions, they will refer participants to appropriate treatment immediately. Some participants will be receiving active cancer treatment at the time of study participation; therefore, fluctuations in cancer-related symptoms will not be considered adverse events. The PI will discuss safety concerns, adverse events, participant complaints and, if any, protocol violations with co-investigators. These meetings will be used to determine if any additional procedures are needed to augment data and safety monitoring.

8.4 Plans for Assuring that Action Resulting in Suspension of Trial is Reported

The PI is responsible for contacting the NIH grant program director in the event that any action resulting in temporary or permanent suspension of the trial/study occurs. Because this trial/study does not involve any investigational medication, the action would be limited to an IRB-or investigator-initiated suspension.

8.5 Plans for Assuring Unanticipated Problems are Managed and Reported

The PI will meet with study staff on a weekly basis to review study progress and discuss unanticipated problems in subject recruitment, data collection, randomization, and intervention administration. Further, the PI will be available to study staff on a continuous basis (i.e., between scheduled meetings) to discuss and address unanticipated problems. Unanticipated problems that result in protocol deviations will be reported to the IRB, consistent with IRB policy. Further, the PI will report unanticipated problems to all study investigators and will obtain their input on and approval of solutions to these problems.

8.6 Plans for Assuring Data Accuracy and Protocol Compliance

Study data will be entered by a research assistant trained to enter data into a password-protected, secure database. A percentage (5%) of overall data entry will be entered a second time, by a different study team member to assure data accuracy. The PI will oversee first and second pass data entry and will generate reports based on data entered. The reports enable the PI to oversee data entry and level of accuracy as well as percentage of error in data entry. These reports will be generated on a regular basis and discussed with Co-Investigators.

Protocol compliance will be monitored at the weekly project staff meetings. The PI will meet with the study staff, convened via conference call, on a weekly basis to train and ensure adherence to the intended protocol. The PI will be responsible for updating all investigators regarding any study related issues that arise of that need to be addressed.

9. Unanticipated Problems Involving Risks to Subjects or *Others*

9.1 Potential Risks: The risks involved in this study are minimal. There are no risks of physical injury. We anticipate that there may be questions in the interview that some study participants find upsetting. However, based on interviewing patients with advanced cancers in prior NCI-funded studies, we do not anticipate that this will be problematic. Should participants become exceedingly upset, overwhelmed or fatigued, or need to attend to matters of personal care during the interview, interviewers will be instructed to ask the participant if he or she would like to take a break or reschedule the interview for another time. However, across all prior studies (PI: Shen), distress caused by engaging in these conversations has been minimal.

In addition, participants may find engagement in the intervention to be upsetting, particularly due to the potential for family conflict to arise. In addition, discussing advance care planning and end-of-life goals of care can be difficult. Patients will be in weekly contact with study interventionists who will be licensed social workers with experience working with medically ill patients and their families. These social workers will have the skills to assess exacerbations in distress in study participants and provide appropriate support. Additionally, the social workers will provide patients with continued support throughout the intervention. In the event a study participant requires a higher level of care than provided in this study, a FHCC licensed on call psychiatrist or mental health professional, UT Southwestern Licensed Clinical Psychologist, or a Confluence Health licensed on call psychiatrist or mental health professional will be consulted and the participant will be referred to the appropriate level of care. Dr. Shen (PI) will also be contacted if a patient endorses suicidal ideation. If additional intervention is necessary, Dr. Shen will coordinate with FHCC's clinical team for referral and care, Dr. Paulk will coordinate with UT Southwestern's Psychiatry Department, and Dr. Overton will coordinate with a mental health professional at Confluence Health. Study participants

who express a desire following the post-intervention interview to talk at greater length about issues raised during the study will be encouraged to call study staff at the telephone number provided, and should they want a referral for psychological counseling, study staff will provide them with a referral to a mental health professional at a location that is convenient for them.

9.2. Adequacy of Protection against Risks

9.2.1 Recruitment

Study staff will review medical records and consult with the treating oncologists to identify patients who may be eligible for the proposed study. When a potentially eligible patient is identified and study staff have received permission from the treating oncologist to contact the patient, a research staff member will send the patient a brief letter describing the study. The letter will encourage patients to contact the study team if they are interested in receiving more information about the study or if they would prefer not to be contacted further. Study staff will then attempt to meet the patient during their next clinic visit in order to introduce him/herself to the patient, and provide the patient with a study information sheet and consent form. Research staff will review study aims and procedures and answer any questions that prospective participants might have regarding the study at that time. If research staff are not able to meet the patient during their clinic appointment, research staff will call the patient to provide additional information about the study and review the consent form. All consent forms will receive proper IRB approval. Treating oncologists may also refer patients to the study.

9.2.2 Informed Consent

Informed consent is a process, not a one-time event. During the informed consent process, the study staff obtaining consent will review the study in detail allowing the participant to interject with questions at any time during the discussion. It is extremely important that the participant has an opportunity to have his/her questions addressed as well as ample time to read the consent document and determine whether or not they would like to participate in the study. Study staff conducting informed consent will be trained by the PI on techniques for effective administration of informed consent. Study staff will also be trained on HIPAA regulations and will fully understand their responsibility to safeguard the personal health information of study participants.

The main points that will be addressed by study staff obtaining informed consent include explaining why the current research study is being conducted, the source of funding for the project, and what purpose the proposed research serves. Additionally, the subject will be made aware of who is responsible for conducting the research, what other sites are involved as well as how participants, including themselves, are selected for participation in the research.

The study staff will explain in explicit detail what will be asked of the participants if they agree to participate in the study and estimate the potential time commitment involved. Participants will know what their responsibilities will entail, what risk or benefit may be involved and what potential costs could be incurred should they agree to participate. The study staff will underscore the importance placed upon maintaining participant confidentiality as well as their rights while involved in the study, which includes the right to withdraw participation at any

time during the research due to the fact that their participation is entirely voluntary in nature. The informed consent will also contain a section dedicated to explaining what constitutes protected health information and how this information remains confidential per HIPAA (Health Insurance Portability and Accountability Act) guidelines. Additionally, it will contain the necessary language to indicate that the aggregate data resulting from the study will be made available on ClinicalTrials.gov.

Finally, the informed consent will provide contact information for the Principal Investigator as well as the Office for the Protection of Research Subjects. All informed consent processes will adhere to the policies set forth by the Institutional Review Board. All informed consent forms will be stored in a locked file cabinet or locked computer file in a locked office to maintain the privacy of all study participants. In summary, the consent form will include a description of all study procedures, information regarding the risks and benefits of participation, contact information for study staff who can answer participants' questions, and alternatives to participation in the study. The consent form will also state that: (1) participation is voluntary, (2) participants can refuse to answer any questions, (3) participants can withdraw from the study at any time, (4) all responses will remain confidential, and (5) participation in the study is not related to care received at the cancer center. The consent form will also describe circumstances justifying a breach of confidentiality in the event of a psychological emergency. All patients will be given a hard copy of the consent document. This hard copy will be mailed to participants who provide oral consent.

9.2.3 Protection against Risks

The potential risk of this study is emotional distress and family conflict. In the event that a participant is actively suicidal and/or at risk of harming self or others, a FHCC licensed mental health professional, UT Southwestern clinical psychologist or psychiatrist, or Confluence Health mental health professional will be contacted immediately to determine the appropriate level of acute care. In the event of a psychiatric emergency, confidentiality may be suspended. Participants will be informed of the limits of confidentiality during the consent process and will be provided with the PI's contact information should they have additional questions. In the event family conflict arises from using the intervention (PLAN), the social worker interventionist will determine and provide the appropriate level of care and guidance to resolve the conflict and handle any undue distress. Should the resulting distress be severe, the above procedures outlined will be conducted.

Measures taken to protect study participants include the exclusion of patients who would be too weak to participate in the interviews, the curtailed length of the interviews, and the option for administration of the interviews over the telephone. All interviews will be designed to be brief, focused, and of minimal burden to participants. Only essential information will be asked of participants. Similarly, the intervention is designed to be brief and focused only on information relevant to the patients' current situation. Additionally, specific measures have been taken to reduce and oversee potential family conflict, including close monitoring of participants in the intervention. The inclusion of a licensed social worker as the interventionist was made to ensure proper study design, monitoring of participants, and handling of any potentially resulting distress or family conflict.

Thorough training of project interviewers is also designed to ensure adequate protection of human subjects. All project interviewers will receive all required training and certification in FHCC's or UT Southwestern's human subjects in research. Project interviewers will be required to participate in a training program designed to ensure that they administer the interviews and evaluate participant responses in a sensitive manner. Interviewers will begin each interview with a series of statements that remind participants of their right to refuse to answer a question, to stop the interview at any time, or to continue at a later date. Interviewers will be trained to speak clearly and audibly and let participants determine the pace of the interview. In addition, study interventionists will be licensed social workers. Study interventionists will be provided with thorough training on administration of the intervention in a manner that recognizes the difficult nature of the ACP decision-making process in the context of advanced cancer.

Should participants become upset, disoriented or fatigued or need to attend to matters of personal care during study procedures, interviewers and interventionists will ask the participants if they would like to take a break or reschedule the interview/session for another time. Participants who express a desire following the final interview to talk at greater length about issues raised during the study will be encouraged to call study staff at the telephone number provided, and should they want a referral for additional psychological counseling, staff will provide them with a referral to a mental health professional at a location that is convenient for them.

To ensure protection against study risks, the IRB will review and approve the study procedures, materials, and consent form prior to study initiation. Consistent with previously approved IRB protocols, the following procedures will be implemented to minimize the potential risk of loss of confidentiality: (1) all study data will be coded with unique participant identification numbers; (2) participant names and other identifying information will not be recorded on study measures; (3) study data will be stored either in secure databases (digital copies) or in locked file cabinets in a locked office; (4) all information saved on the FHCC secure network will be password protected; and (5) only authorized study staff will have access to the study data. These procedures have been utilized in other studies managed by the PI and Co-Investigators with no breaches of confidentiality or other risks to participants, indicating their effectiveness.

Study participants will be assured that all responses will be kept confidential. All data collected during the interview process will be de-identified. To ensure confidentiality, data collected will be linked to participants' personal information only by means of an assigned study identification number. Authorized study staff will be the only individuals who have access to participants' personal information. This information will be stored in a password protected computer file on the secure FHCC server and/or in a locked file cabinet in a locked office. De-identified study data will be stored in REDCap, a secure HIPAA-compliant data management system supported by FHCC IT services. All necessary precautions will be taken to ensure that there is no breach of confidentiality.

All study staff involved in the research proposed are required to be educated on the protection of human research participants and the proposed research will comply with the regulations set forth in 45 CFR Part 46, Protection of Human

Subjects. All personnel involved in the proposed protocol have been educated regarding HIPAA regulations and fully understand their responsibility to safeguard the personal health information of every participant involved in the study.

The following steps will be taken to minimize participant burden. First, significant effort will be made to coordinate in-person study contacts (e.g., to provide information on the study and administer informed consent) with existing appointments to minimize the number of trips to FHCC, UT Southwestern/Parkland Hospital, or Confluence Health required of participants. Second, with the participant's permission, study visits can be conducted during scheduled chemotherapy infusions (if applicable, as some advanced cancer patients will no longer be receiving chemotherapy). Chemotherapy infusion appointments are often long (multiple hours) and patients are unable to leave the clinic during the appointment. In our previous NCI-funded studies (PI: Dr. Shen) of patients with advanced cancer, patients often elected to conduct research meetings during infusion appointments to provide activity during the appointment and reduce the overall time spent at the hospital. Prior to conducting visits during infusion appointments, participants will be reminded that infusion clinics are often not private and their permission to conduct the visit during infusion will be obtained. Participants will also be informed that they can discontinue at any time if they become uncomfortable due to the setting. If participants are not comfortable conducting visits during infusion appointments, separate appointments will be scheduled over the telephone. Third, participants will be given the option to complete administration of all study measures over the telephone, if preferred. This method will eliminate the need for participants to travel to the clinic to complete study measures. Any subject participating in the study may decline to continue participation and may withdraw from the study at any time. If they do not wish to participate but are interested in exploring other options such as counseling or support groups, we will provide appropriate referrals.

9.2.4 Vulnerable Subjects

Vulnerable subjects will not be involved in the proposed project.

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