

**NCT 01485627**

**Ronald M. Epstein, M.D.**

**Randomized Controlled Trial of Patient, Caregiver &  
Physician Communication Coaching in Advanced Cancer  
(THE CANCER COMMUNICATION STUDY)**

**Acronym: VOICE - Values and Options in Cancer Care**

## I. PURPOSE OF THE STUDY AND BACKGROUND

### Purpose of the Study

The purpose of this study is to (a) determine whether a combined intervention for patients, caregivers and physicians improves communication regarding prognosis and treatment choices in advanced cancer, (b) to determine whether the intervention improves patient and caregiver well-being, quality of life and sense of peace, and (c) to determine whether the intervention affects health services utilization.

### Background and Rationale

Crafting care that is concordant with the patient's wishes in the context of serious illness requires clear, patient-centered communication.<sup>1,2</sup> We aim to test a potentially powerful, two-component intervention – targeting oncologists as well as patients and their caregivers – to improve four communication behaviours related to prognosis and treatment choices in advanced cancer: ENGAGING patients to participate in the consultation and decisions regarding their care; RESPONDING to patients' concerns; INFORMING patients about treatment choices; and balanced FRAMING of prognosis information. Patient-physician communication research is often theoretical, and frequently focuses exclusively on individual communication behaviors or psychological processes.<sup>1</sup> Our aims, intervention, and outcomes are based on Street's ecological theory<sup>3,4</sup> – which has provided insights into communication in serious illness by addressing the mutual and reciprocal influences between patients and physicians, and the social and illness contexts within which they occur.

### Overview of the VOICE Study

This is a behavioral research study, run in parallel at the University of Rochester Medical Center (URMC) and University of California – Davis (UCD). This protocol only applies to the URMC site; a separate protocol and IRB submission to the UCD IRB for the UCD site will be completed.

The URMC study site will recruit oncologists from Highland Hospital, Interlakes Oncology, Rochester General Hospital, Unity Health Systems, Buffalo Practice Group, Roswell Park, Century Medical Associates, P.C. and Pluta Cancer Center as needed to meet the recruitment goal.

All interviews and in-person meetings with research team members at all recruitment sites will be conducted in a private area based on the subject's comfort and preference (e.g. meeting room, office, infusion suite, your home, by phone).

The study includes **two phases** and involves adult human subjects.

- **Phase 1** is observational only.
- **Phase 2** will be a cluster randomized trial with oncologists as the unit of randomization. Human subjects will be randomized into two groups.

Study subjects will include:

- **Oncologists** (n= up to 26), who will participate in both phases) and will be randomly assigned to a behavioral intervention or control. Oncologists will help the study team identify eligible patients.
- **Phase 1 patients** (n= up to 81) will complete two sets of surveys. They will also agree to have a clinical consultation with an oncologist audio-recorded. Patients will all have advanced cancer and various levels of functional status. Phase 1 patients will be asked to identify a caregiver who may choose to participate in the study; having a willing caregiver is **not** a requirement for patients to participate in the study.

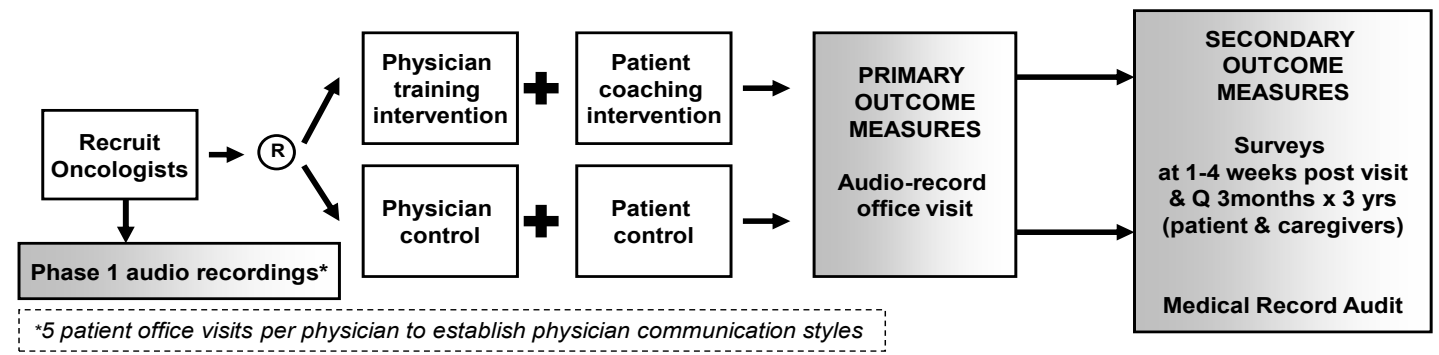
Caregiver is defined as a key person in the patient's life (e.g. family member, partner, friend, actual caregiver) age 21 or older with whom the patient discusses their health and well-being or someone who can be helpful in health-related matters.

- **Phase 1 caregiver** (n = up to 75), who will complete surveys and, if they are present at the patient-oncologist consultation, will agree to having the consultation audio-recorded.
- **Phase 2 patients** (n= up to 220) will be assigned to a behavioral intervention or control, complete surveys and agree to have one consultation with an oncologist audio-recorded. Phase 2 patients will be assigned to the intervention group if their oncologist has been randomly assigned to the intervention or they will be assigned to the control group if their oncologist has been randomly assigned to control. Phase 2 patients will be asked to identify a caregiver who may choose to participate in the study; having a willing caregiver is **not** a requirement for patients to participate in the study.
- **Phase 2 caregiver** (n = up to 170), who will be asked to accompany the patient to the behavioral intervention or control, complete surveys and, if they are present at the patient-oncologist consultation, agree to having the consultation audio-recorded.

The study will compare the effectiveness of a control condition with a two-component intervention; both the physician component and the patient-caregiver component are designed to promote discussions about prognosis and treatment choices. Based on preliminary studies, we hypothesize that the intervention will have positive effects on patient-caregiver-oncologist communication, patients' and caregivers' self-reported well-being and health care utilization. We will not administer any drugs, devices, or clinical procedures to any subject. The Phase 2 will use intention-to-treat analyses.<sup>5</sup> The study design and all consent forms will be approved by the RSRB.

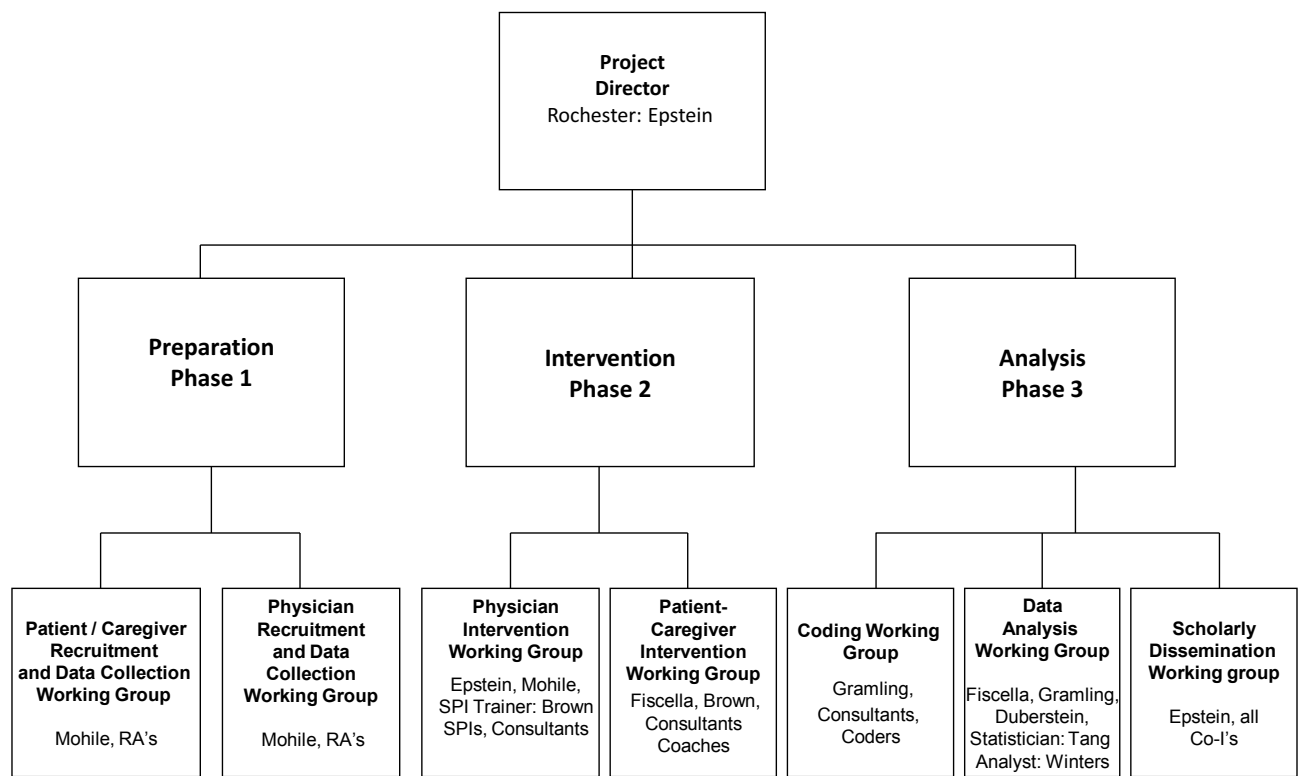
**Table 1: VOICE Study Hypotheses and Outcomes**

Primary outcome	Aim 1a	Improved patient-physician-caregiver communication about prognosis and treatment choices (higher frequency of key pre-specified communication behaviors, coded from audio-recorded patient-caregiver-oncologist office visits)
Secondary outcomes	Aim 1b&c	Improved patient-perceived patient-physician-caregiver communication about prognosis and treatment choices, fewer unmet needs for information and support, greater shared understanding (survey measures).
	Aim 2	Greater patient and caregiver well-being, including quality of life and sense of peace (survey measures).
	Aim 3	Changes in health care utilization. Fewer aggressive interventions in the last week of life and more palliative care and hospice consultations following the intervention (chart audit).



The study will be organized into teams and will occur over five years. There will be three teams, and seven working groups as depicted in the organizational chart below. In addition, the study is organized into three phases. Phase 1 of the project is preparatory, and includes collection of Phase 1 patient and oncologist data. Phase 2 consists of the implementation of the randomized control trial, including baseline data, the intervention and follow-up surveys. Phase 3 is for chart audits, data coding, analysis and dissemination.

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**Methodological fidelity** (implementation of coaching protocols, blinded allocation, etc.), will be achieved by following clear protocols and holding weekly teleconferences between key study project staff and coordinators to ascertain that details of the study are being implemented consistently. All randomization, data management and analyses will be coordinated and conducted by the Rochester biostatistics team. Data sharing between and within sites will be via SharePoint, a secure, encrypted web-based data sharing service.

## **Additional Caregiver Aims**

Paul Duberstein, PhD at the University of Rochester and Holly Prigerson, PhD, at the Dana-Farber/Harvard Cancer Center are dual PIs for the added caregiver aims supported by additional funding from NCI. Paul Maciejewski, PhD at Brigham and Women's Hospital will provide statistical analysis support. We will assess caregivers while the patients are alive as well as 2 and 7 months after the patients' deaths. As patient quality of life and caregiver mental health dynamically influence each other over time<sup>70-72</sup>, we designed these aims to enable collection of data from caregivers to coincide with prospective patient data collection in Phase 2 of the VOICE study. In addition, the 1-month post-mortem assessment includes an audio taped interview to explore caregivers' experiences with key elements of decision-making, information exchange (e.g., inadequate, overload), deliberation (e.g. indecisiveness, outcome uncertainty, regret), and relationships (e.g. coercion, abandonment).

Phase 2 patients and caregivers consented prior to the additional caregiver aims, will be asked to re-consent at the next in-person assessment. For patients that are deceased, caregivers will be asked to re-consent at the 1 month post mortem visit which is conducted in person.

The additional caregiver aims are:

**Aim 1:** *Examine whether a health care communication intervention for oncologists, patients, and caregivers leads to better mental health outcomes in caregivers following patient death.* **Hypothesis:** Compared with control, intervention group caregivers will have lower levels of prolonged grief symptoms on the PG-13<sup>68</sup> (Primary outcome), depression, anxiety, and thoughts of death 7 months after the patient's death.

**Aim 2:** *Determine whether the intervention leads to better physical health outcomes in caregivers following patient death.* **Hypothesis:** Intervention group caregivers will have better physical health summary scores on the SF-12<sup>73</sup> (Primary outcome) and lower levels of self-reported disability 7 months after the patient's death.

**Aim 3:** *Contextualize these findings by conducting mediational analyses and qualitative analyses.* We will examine whether caregiver outcomes are mediated by patient-reported quality of life and patient health care utilization (quantitative). We will explore caregiver perspectives on decision-making and communication processes to link bereavement outcomes with VOICE study communication outcomes (qualitative).

**Table 2: Proposed 7-Month Caregiver Bereavement Outcomes**

	<b>Aim</b>	<b>Domain</b>	<b>Caregiver Outcome</b>
<b>Primary Outcomes</b>	1	Mental Health	Prolonged grief symptoms <sup>68</sup>
	2	Physical Health	Physical health-related function <sup>73</sup>
<b>Secondary Outcomes</b>	1	Mental Health	Depression, <sup>102, 103</sup> anxiety, <sup>104</sup> thoughts of death, <sup>105</sup> decisional regret, <sup>106</sup> purpose-in-life <sup>107</sup>
	2	Physical Health	Self-reported disability <sup>108</sup>

**Table 3. Key VOICE Patient and Caregiver Assessments**

<b>VOICE Study</b>		
Assessment Instrument	Completed by:	Construct
McGill Quality of Life	Pt	Pt's Psychological and existential well-being, plus overall quality of life
FACT-G	Pt	Pt's Physical well-being, social/family well-being.

PEACE	Pt	CG's Peaceful acceptance of terminal illness
PEPPI	CG	CG's Self-efficacy in interacting with oncologist
Mishel Uncertainty	CG	CG's uncertainty about pt's illness and treatment
HCCQ	CG	CG's view of oncologist as autonomy-supporting
<b>VOICE Caregiver Assessments</b>		
PHQ-9	CG	Depression
SF-12	CG	Emotional and physical functioning
Health Questionnaire	CG	Chronic disease
BFI	CG	Personality
Regret Scale	CG	Decisional Regret
PIL	CG	Sense of purpose/meaning

Key: Pt=Patient self-report; CG=Caregiver self-report. FACT-G=Functional Assessment of Cancer Therapy; PEACE=Peace, Equanimity and Acceptance in the Cancer Experience; PEPPI=Perceived Efficacy in Patient-Physician Interactions; HCCQ=Health Care Climate Questionnaire; PHQ-9=Patient Health Questionnaire-9; SF-12=Short Form-12; BFI=Big Five Inventory; PIL=Purpose in Life.

**Caregiver Aims Timeline** The NCI funding for the Caregiver aims will extend funding for the VOICE Study until December 31, 2017. Dedicated resources for more extensive assessments of the caregivers themselves, including follow-up and post-mortem assessments, are unavailable in VOICE. The final 7 month-postmortem assessment for the additional caregiver aims will be conducted in the fall of 2016 to leave sufficient time (7 months) for data cleaning, analysis, and manuscript preparation.

## CHARACTERISTICS OF THE RESEARCH POPULATION

### Oncologists

We will enroll a total of up to 26 oncologists at the University of Rochester Medical Center (URMC) site. The oncologists will participate in two phases of the study.

- **Phase 1.** Oncologists will complete surveys. Up to five of their patients will be recruited. ("Phase 1 patients", see below) One consultation with each of the patients will be audio-recorded.
- **Phase 2.** Oncologists will be randomized to a behavioral intervention or control by a statistician blinded to physician identities.

**Gender of subjects.** There are no gender-based enrollment restrictions.

**Age of Subjects.** Adults age 21 and over.

**Racial and ethnic origin.** There are no racial or ethnic origin enrollment restrictions.

**Inclusion criteria.** Eligible oncologists will be in an active clinical practice of medical, gynecologic or radiation oncology. Oncologists will consent to participate in the intervention, complete surveys and have visits with consenting patients audio-recorded. Physicians will be asked to identify patients by means of the "surprise question"; if he/she "would not be surprised if the patient died within the ensuing 12 months". This criteria generally identifies patients with a median prognosis of 9-12 months. **Exclusion criteria.** Oncologists who intend to move or retire within the ensuing six months will be *excluded*.

**Vulnerable Subjects.** No vulnerable physician subjects will be targeted for inclusion in the study.

### Patients

We will enroll up to a total of 300 patients; up to 15 patients per each participating oncologist. **Patients will participate in either Phase 1 or Phase 2 of the study.** From their perspectives, Phase 1 and Phase 2 patients are participants in separate studies.

**Phase 1 patients** are enrolled to assess physician-patient communication behaviors prior to randomization of oncologists to intervention or control arms of the study. Up to five patients per participating oncologist (up to 81 Phase 1 patients total) will consent to participate. Phase 1 patients:

- Will allow one office visit with their oncologist to be audio-recorded.
- Will receive \$15 for completion of each of two sets of orally-administered survey measures. Completed in person at enrollment and immediately following the audio-recorded office visit.
- Will **not** complete any further follow-up measures; their study participation ends upon completion of these two sets of surveys.
- Will be asked to identify up to three people as a key “*family member, partner, friend or caregiver [age 21 or older] with whom the patient discusses or gets help in health-related matters*”; patients who cannot identify such a person (“caregiver”) can be eligible for the study.

**Phase 2 patients** are being enrolled to test the effectiveness of the combined intervention. Phase 2 patients will be recruited after their oncologist has completed up to five audio-recorded Phase 1 patient visits, the post-visit surveys, and has completed the oncologist intervention or control. Up to ten patients per participating oncologist (up to 220 Phase 2 patients total) will consent to participate in Phase 2, a combined patient-caregiver-physician communication intervention (vs. control). Phase 2 patients:

- Will be assigned to intervention or control depending on oncologist assignment. Patients of oncologists who are assigned to the physician intervention will participate in the patient intervention. Patients of oncologists who are assigned to control will be assigned to the control condition.
- Will allow one office visit with their oncologist to be audio-recorded.
- Will receive \$15 for completion of each set of orally-administered survey measures – in person at enrollment, right after the doctor visit, approximately 1 week following the visit, and then either by telephone or in-person every three months for up to four years.
- Will be asked to identify one key “*family member, partner, friend or caregiver [age 21 or older] with whom you discuss or who can be helpful in health-related matters*”; patients who cannot identify such a person (“caregiver”) can be eligible for the study.
- Will allow follow-up phone calls from the coach, if appropriate at approximately 1 month intervals for up to 6 months depending on the needs and wishes of each patient, this is to reinforce the coaching intervention and address patients’ concerns.<sup>30</sup>
- Phase 2 patients will also consent to having relevant data extracted from their medical records regarding health care utilization.

**Recruitment and retention strategies.** Phase 1 patients and Phase 2 patients will be identified by research assistants working closely with participating physicians and their clinic staff by reviewing the clinic roster in detail to ascertain that all potentially eligible patients are identified. Potentially eligible patients will receive a brochure that describes the study and opt-out post card (see attached study brochure). They will be asked if a research assistant can call them within two weeks to find out if they might be interested in participating in the study. Patients who do NOT want to be contacted about the study will be asked to return an enclosed stamped, addressed opt-out card to the study office within 4 days of receiving the study brochure. A research assistant will only call patients who have not returned the opt-out card within the stated time period. Patients who express an interest in the study will be screened for eligibility and provide written consent.

**Gender of subjects.** There are no gender-based enrollment restrictions.

**Age of Subjects.** Adults age 21 and over.

**Racial and ethnic origin.** There are no racial or ethnic origin enrollment restrictions.

**Inclusion criteria.** Eligible patients will be:

- Will be age 21 years or older.
- Will be able to understand spoken English (the coach will read materials to low literacy patients)
- Will have advanced cancer, defined as stage III or IV.
- Will **not** have to forego any anti-cancer treatments to participate.
- Will have a limited prognosis as assessed by using the “surprise question”. This method is used in numerous studies of patients with advanced cancer. Physicians are asked to identify patients who meet the above criteria **and** also if he/she “would not be surprised if the patient died within the ensuing 12 months.” This criterion generally identifies patients with a median prognosis of 9-12 months. This has become standard methodology in part due to oncologists’ reluctance to estimate an individual’s life expectancy directly.

**Exclusion criteria.** Patients will be excluded if they or their caregivers state that they are unable to complete orally-administered surveys in English language due to health, sensory or cognitive impairment; if they are hospitalized or in hospice care at the time of recruitment; or if they have had prior involvement in coaching interventions. Patients anticipating bone marrow transplantation or diagnosed with leukemia or lymphoma also will be excluded; they are likely to have a more unstable clinical course and long hospitalizations, complicating data collection and generalizability.

**Vulnerable Subjects.** No person with decisional incapacity will be enrolled. Patients with advanced cancer who are terminally ill will be included. Elderly persons (persons over age 65) with decisional capacity who meet other enrollment criteria will be included. No other vulnerable subjects will be targeted for inclusion in the study.

**Caregivers.** We will enroll a maximum of 245 caregivers.

Caregivers will be identified by enrolled Phase 1 (n= up to 81) and Phase 2 (n=up to 220) patients, as described above. Not all patients will have an identified caregiver; the presence of an available caregiver who agrees to participate is not a prerequisite for patient participation.

**Gender of subjects.** There are no gender-based enrollment restrictions.

**Age of Subjects.** Adults age 21 and over.

**Racial and Ethnic Origin.** There are no racial or ethnic origin enrollment restrictions.

**Inclusion Criteria.** A caregiver can be anyone age 21 or over who is able to understand spoken English and understand the study process and provide informed consent. One caregiver for each Phase 1 and Phase 2 patient will be eligible.

**Exclusion Criteria.** Caregivers unable to understand the consent form due to cognitive, health, or sensory impairment will be excluded.

**Vulnerable Subjects.** No person with decisional incapacity will be enrolled. Elderly persons (persons over age 65) with decisional capacity who meet other enrollment criteria will be included. No other vulnerable subjects will be targeted for inclusion in the study.

## II. METHODS AND PROCEDURES

### Methods and procedures

**Randomization.** Enrollment is completed when Phase 1 baseline data are obtained, oncologists will be randomized to either the intervention or control arm of the study by a statistician blinded to their identities. This is a cluster randomized controlled trial. Thus, patients of oncologists in the intervention arm and their caregivers will be assigned to the intervention arm; patients of oncologists in the control arm and their caregivers will be assigned to the control arm.

### Oncologist component: control and intervention



## ***Oncologist Control.***

Control oncologists will meet with the research assistant and will receive no specific training.

## ***Oncologist Intervention - In-office Coaching.***

Oncologists randomized to the intervention arm will have *two educational outreach sessions*<sup>6,7</sup> – a 60-minute training session and a 45-minute booster session one month later.<sup>8,9</sup> Sessions will be conducted at the oncologist's clinical office. The sessions will be conducted by Standardized Patient-Instructors (SPIs). SPIs are study personnel who are highly trained to portray the role of a patient with sufficient realism that physicians cannot distinguish them from real patients. Furthermore, they are trained to provide concise, focused educational feedback about communication skills and other physician behaviors. SPIs are used extensively in medical education. **The SPI roles** for the in-office coaching sessions will be of a patient with metastatic colon, lung or kidney cancer with progression despite state-of-the-art treatment – with an expected prognosis of 12 months or less – who will be facing important treatment decisions over the next few weeks. SPIs will report moderate uncontrolled pain, weight loss and fatigue, and, as is common in such situations, will not have a clear idea of the prognosis.

At the first of the two in-office oncologist coaching sessions, the SPIs will:

- Introduce the session (5 minutes) and the patient question prompt lists (QPLs). QPLs are materials used in the patient-caregiver intervention that help patients to formulate and ask relevant questions about their illness.
- Show a 15-minute DVD<sup>10</sup> which presents actual clinical examples to outline key skills in discussing prognosis and treatment choices with patients and their caregivers. They will also give physicians *laminated checklist cards* prompting them to discuss topics that appear in the QPLs (e.g., prognosis, symptoms).
- Introduce the role-playing exercise. They will give physicians a medical “chart” containing prior consultation, radiographic and laboratory reports that provide the context for the (simulated) patient visit to review.
- Conduct the role-playing exercise. During the exercise (approximately 20 minutes), the SPIs will enact the role of a patient with advanced cancer and a spouse during which the physician will have the opportunity to practice the communication skills demonstrated in the DVD.
- Provide *specific tailored feedback* on the key communication skills; physicians will have the opportunity to rehearse areas of difficulty.
- Provide evidence-based communication guidelines in advanced cancer.<sup>11</sup>

**The 45-minute booster session** – approximately one month later – will have a similar format, using an SPI role portraying a different site of cancer, gender and ethnicity. The DVD will not be shown again, though.

**Key communication skills** highlighted in the DVD and SPI feedback were chosen based on ecological theory and evidence that they a) promote discussions of prognosis and treatment choice, b) can be taught in brief interventions, and c) are associated with patient trust and lower anxiety.<sup>11-17</sup>

- **ENGAGING.** Physicians will be coached to a) clarify the patient's concerns early in the visit<sup>18</sup> – this corrects the tendency to address the first concern mentioned at the expense of more important issues,<sup>19</sup> b) acknowledge the QPL to increase its effectiveness,<sup>20</sup> c) encourage questions, and d) encourage participation in decisions regarding their care.<sup>20-22</sup>
- **RESPONDING.** Emotional expression and empathy are uncommon in oncology consultations,<sup>16;23;24</sup> therefore physicians will be coached to respond to the emotional components of patients' concerns with empathy and support.
- **INFORMING.** Based on recent studies,<sup>10;25</sup> physicians will be coached to use an “Ask-Tell-Ask” protocol – asking patients about their wishes regarding information about prognosis and treatment choices, providing desired information in a desired format, and then checking patient understanding.

- **FRAMING.** Based on recent studies,<sup>10;26</sup> physicians will be trained to present both optimistic (“best-case”) and pessimistic (“worst case”) information. Balanced information appears to better align patients’ and physicians’ efforts by reducing bias introduced by one-sided presentation of data.

**SPI recruitment and training** will use successful protocols from prior studies. In our pilot, two SPIs were trained to perform their roles (patient and caregiver) and give feedback with >95% fidelity with 12 oncology fellows. For the proposed study, experienced SPIs and trainers will be drawn from SP programs at UPMC and local actors organizations, and undergo intensive role training. Training will include an interactive cultural competency module.

**SPI monitoring and fidelity** will be approached similarly to our prior studies. All SPI sessions will be audio-recorded. A 100-item SPI Fidelity Checklist will be completed by the SPI trainer via review of the audio-recording within 2 days of the SPI visit to assess role performance as well as feedback. During weekly conference calls, trainers at Rochester and UC-Davis will discuss any deviations from protocol. SPIs will be given feedback following each visit; additional training will be scheduled as necessary. As in prior studies, we will exclude visits that have <95% fidelity. Physicians will be offered copies of their audio-recordings of the training sessions with SPIs (not their office visits with real patients).

### **Patient and caregiver component: control and intervention**

#### ***Patient-caregiver control.***

Once recruited and assigned to the control group, control patients and caregivers (when they are available and consent) will complete surveys, then will arrange to meet with a research assistant 30 minutes before the patient’s next scheduled visit with an oncologist, and will receive brochures from the National Cancer Institute that are in the cancer center library. These brochures are for patients and family members with advanced cancer and have information about treatments, coping and helpful resources. They will be introduced to other readily available written and video material in the Cancer Center or office where they receive their care.

#### ***Patient-caregiver coaching (intervention).***

Once recruited, consented and assigned to the intervention group, **patients** will complete surveys then arrange to meet 1 hour before their next consultation with an oncologist or at a different private location/time that is more convenient for the patient.

**Caregivers**, when they are available and consent, will also complete surveys and participate in the intervention. We base our protocols on previous successful QPL and coaching studies.<sup>20;27</sup>

Intervention patients and caregivers will meet with a patient coach 60 minutes before the patient’s scheduled visit, anticipating an intervention of 30-45 minutes. Coaches are study personnel who are highly trained to elicit patients’ concerns, help them formulate questions that are important to their care, help them be assertive when their questions are not answered to their satisfaction and help them form effective working relationships with their oncologist and other members of the care team. During the coaching session, the coach will give each patient and caregiver a Question Prompt List (QPL). Question prompt lists contain common questions asked by patients with advanced cancer about their illness, available treatments, palliative care, psychosocial issues, impact on family and advance directives. Then the coach will help patients a) identify personally relevant and important questions on the list, b) ask questions during the visit, c) ask for clarification when they do not understand, d) express desire to participate more actively in discussions about prognosis and treatment choices, and e) prepare for the future.<sup>20;21;27-29</sup> These skills promote the same goals as the physician intervention. Patients interested in a palliative care consultation will be encouraged to discuss this further with their care team. The coach will make follow-up phone calls to patients (and caregivers, if appropriate) at approximately 1 month intervals for up to 3 months, to reinforce the coaching intervention and address patients’ concerns.<sup>30</sup> Coaches will not provide disease-specific information.

**Recruitment, training and fidelity of patient coaches.** Lay health educators, and others with a health

care background will be recruited as coaches, similar to prior studies.<sup>27</sup> All coaches will participate in intensive training, similar to our previous studies. Training includes a 1-day cultural competency module. All intervention sessions and follow-up telephone calls will be audio-recorded and reviewed by supervisors for the coaches. Patients will be offered copies of audio-recordings from their coaching sessions (not their clinical visits).

**Audio-recordings of oncologist-patient visit.** A research assistant will audio-record the first patient-oncologist consultation after recruitment (for the up to five Phase 1 patients) and after coaching or control interventions (for the up to 10 Phase 2 patients) for further analysis. Patients, caregivers and physicians will ***not*** receive copies of these recordings.

### **Sources of materials and measures**

**Surveys** will be completed by oncologists, patients and caregivers. The tables below list all measures. We use the following code letters to indicate timing of the surveys:

*A = baseline, at study entry (e.g. enrollment) (patient, caregiver and physician surveys)*  
*B<sub>1</sub> = immediately after the office visit (patient, caregiver and physician surveys)*  
*B = 0 – 10 days after the office visit [aim for 2-4days](patient and caregiver surveys only)*  
*C<sub>1</sub> = 1st three-month follow-up only (patient and caregiver surveys)*  
*C = every three months for up to four years (patient surveys only)*  
*D = 1month (four weeks) postmortem (caregiver surveys only)*  
*E = end of study (physician surveys only)*

**Oncologist surveys.** Oncologists will complete orally-administered in-person surveys at the beginning and the completion of the study. Baseline demographic data will include age, sex, race, ethnicity and years in practice. Surveys will also ask about their comfort with discussing prognosis and end of life issues and shared decision-making style. Oncologists will report on their satisfaction with the intervention and the study. There will be no questions that relate to the oncologist's own health status or well-being.

In addition, after each enrolled patient visit, oncologists will complete brief surveys about clinical features (cancer type, metastasis, etc.), treatment intent (curative, palliative, etc.) and estimated prognosis (e.g., for survival and quality of life) of the enrolled patient. Please see the appended oncologist surveys.

Aim	Measure	Items	Administration
Aim 1b	Treatment intent and prognosis	3	B <sub>1</sub> – In-person questionnaire
Aim 2	Peace, Equanimity, and Acceptance in the Cancer experience (about patient)	5	B <sub>1</sub> – In-person questionnaire
Moderators	Assessment of skills with discussing prognosis and end-of-life issues	19	A – In-person questionnaire E – In-person questionnaire
	Comfort with shared decision making	5	A – In-person questionnaire E – In-person questionnaire
Other	Patient Disease Status	6	B <sub>1</sub> – In-person questionnaire
Other	Patient's Preferences for Life Extending Treatment	3	B <sub>1</sub> – In-person questionnaire
	Affective Forecasting	1	B <sub>1</sub> – In-person questionnaire
	Your thoughts about the training sessions	12	– on-line survey completed after training

Note. A = baseline, B<sub>1</sub> = immediately after office visit, E = end of study

**Patient surveys.** Enrolled patients in the **Phase 1 group** will complete in-person orally-administered surveys at enrollment (baseline visit 00) and immediately after the audio-recorded office visit. They include scales that measure shared understanding, prognosis, hopes, treatment preferences, affective forecasting, unmet needs for information and support, self-efficacy, quality of life, peaceful acceptance and decision quality. Because we are sensitive to respondent burden in patients who may be quite ill, we have used short forms of surveys whenever possible.

Enrolled patients (designated as enrolled at the baseline visit) in the **Phase 2 group** will complete the same measures as the Phase 1 group. **In addition**, they will complete surveys 0-10 days after the office visit and every three months thereafter for a maximum of four years. Survey questions will be administered orally to patient participants. The first two sets of surveys will be administered in-person, at baseline and immediately following the audio-recorded doctor visit. If greater than 4 weeks elapse between the baseline survey and visit01 (audiorecorded visit), repeat the single McGill QOL question. If greater than 8 weeks elapse between baseline and visit01 then repeat the entire baseline surveys. Most of the time, this happens when patients are scheduled with longer intervals between their oncology doctor visits. Subsequent surveys will be in-person or over the telephone, whatever the patient prefers and is feasible for research staff (e.g., patients who live considerable distance from the medical center and are not receiving active treatment in Rochester will tend to have telephone surveys). Because we are sensitive to respondent burden in patients who may be quite ill, we have used short forms of surveys whenever possible. Please see the appended patient surveys.

Aim	Measure	Items	Administration
Aim 1b	Understanding of prognosis	3	A – In-person interview B – In-person or phone interview
	The Human Connection (THC)	16	A – In-person interview B – In-person or phone interview C <sub>1</sub> – In-person or phone interview
Aim 2	McGill Quality of Life Questionnaire (MQOL)	14	A – In-person interview C – In-person or phone interview
	Peace, Equanimity, and Acceptance in the Cancer experience (PEACE)	5	A – In-person interview C <sub>1</sub> ,C – In-person or phone interview
	FACT-G	14	A – In-person interview C <sub>1</sub> ,C – In-person or phone interview
Moderators	Perceived efficacy (PEPPI)	5	A – In-person interview B – In-person or phone interview C <sub>1</sub> – In-person or phone interview
	Physician-patient interaction (HCCQ)	5	B <sub>1</sub> – In-person or phone interview
	Preferred decision role (Control Preferences Scale)	4	A – In-person B – In-person or phone interview
	Achievement of preferred decision role (Actual Decision Role Scale)	3	B <sub>1</sub> – In-person or phone interview
	Preferences for life-extending treatment	4	A – In-person interview B – In-person or phone interview

			C – In-person or phone interview
Other	Hopes for Treatment	2	A – In-person interview C <sub>1</sub> – In-person or phone interview
	Affective Forecasting	3	A – In-person interview B <sub>1</sub> – In-person or phone interview C <sub>1</sub> – In-person or phone interview
	Out of Area Care Form	4	A – In-person or at next follow-up; update as needed
	Survey Completion	2	A,B <sub>1</sub> ,C <sub>1</sub> ,C – In-person or phone interview
	Comments	1	A,B <sub>1</sub> ,C <sub>1</sub> ,C – In-person or phone interview
	Demographics Patient Status Form	13 16	A – In-person interview Withdrawal form as needed
Chart Abstraction	Hospice and Palliative Care Utilization	4	D
	Chemotherapy Utilization Form	6	D
	30-Day Pre-mortem Hospital Abstraction	56	D

Note. A = baseline, B<sub>1</sub> = immediately after office visit, B = 0 – 10 dys [aim for 2-4] after office visit, C<sub>1</sub> = 1<sup>st</sup> 3 month follow-up C = every 3-month follow-up D = Post-mortem

**Caregiver surveys.** Enrolled caregivers in the **Phase 1 group** will complete in-person orally-administered surveys at enrollment, and immediately after the audio-recorded office visits. These surveys will include demographic information and assessments of the patient's quality of life as well as their understanding of the patients' hopes and understanding of their illnesses. The first two surveys will be administered in-person. Because we are sensitive to respondent burden, we have used short forms of surveys whenever possible.

**Caregivers in the Phase 2 group** will complete all of the measures noted above, and will also complete brief orally-administered surveys at three months. Measures include assessments of the patient's quality of life, as well as their own quality of life, dependency and bereavement. In addition, if the patient dies within the four years of follow-up, the caregiver will be interviewed about the patient's quality of life during the final weeks of life and where the patient received care in the final month of life. The three-month follow-up surveys will be in-person or over the telephone, whatever the caregiver prefers and is feasible for research staff (e.g., those who live considerable distance from the medical center and are not coming in for patients' treatments and appointments in Rochester will tend to have telephone surveys). The post-mortem survey will be in person whenever possible, unless the caregiver expresses a preference that the survey be conducted by telephone. Due to the open ended nature of the qualitative questions the caregiver will be asked if these can be recorded; refusing does not affect their participation in the study. Please refer to the caregiver surveys.

Aim	Measure	Items	Administration
Aim 1b	Understanding of Prognosis	4	A – In-person interview B – In-person or phone interview
Aim 2	McGill Quality of Life Questionnaire (MQOL), caregiver report about patient	1/5	A, C – In-person or phone interview

	Peace, Equanimity, and Acceptance in the Cancer experience (PEACE), caregiver report about patient (single item)	1	A – In-person or phone interview
	PEACE, caregiver report about patient, post-mortem	3	D – In person interview preferred/or phone interview
	FACT-G (select items)	2,5,6	A, C, D – In-person or phone interview
	Quality of Death/Dying, caregiver report about patient (Qualitative questions - due to the open ended nature of these question the caregiver will be asked if they can be recorded; QOD-LTC-C, and Distress Survey)	29	D – In person interview preferred/or phone interview
	Physician Caregiver Interaction (HCCQ)	5	B – In-person or phone interview
Aim 3	Health services utilization	3	D – In person interview preferred/or phone interview
Moderators	Perceived Efficacy in Caregiver-Physician Interactions (PECPI)	5	A – In-person interview C <sub>1</sub> – In-person or phone interview
	Preferences for life-extending treatment, caregiver report about patient	3	A – In-person interview C <sub>1</sub> – In-person or phone interview
Other	Hopes for Treatment, caregiver report about patient	2	A – In-person interview
	Mischel uncertainty in Illness Scale (Adult)	1	B – In-person or phone interview
	Mischel uncertainty in Illness Scale (Community), Purpose in Life Scale (PIL)	11	C <sub>1</sub> – In-person or phone interview
	Affective Forecasting, caregiver report about patient	3	A,B <sub>1</sub> ,C <sub>1</sub> – In-person or phone interview
	Satisfaction with coaching	11	B – mailed
	Comments	1	A,B,C <sub>1</sub> – In-person or phone interview
	BFI	44	A – In-person interview or phone
	SF-12	12	A,C <sub>1</sub> ,C – In-person interview or phone
	Physician Health Questionnaire	15	A – In person
	PHQ-8 plus 1	9	A,C <sub>1</sub> ,C,D – In person interview preferred/or

		phone interview
Decision Uncertainty and Regret Scale	8	C1– In person or phone interview
The Human Connection Scale	18	B, D – In person interview preferred/or phone interview
Demographics	7	A – In-person interview
Caregiver Status Reporting Form	9	Withdrawal form as needed

Note. A = baseline, B= 0 to 10 days [aim for 2-4] after office visit, C<sub>1</sub> = 1st 3-month follow-up; C = every 3-months, D = 4 weeks postmortem

**Heath care utilization data.** Chart audit, including electronic medical records, will allow examination of healthcare utilization. We will extract data about utilization and disease characteristics from outpatient and inpatient charts and home care organizations using standard methods.<sup>31-33</sup> We will extract the following information: emergency department visits, hospital stays, intensive care use, outpatient visits, hospice referrals, palliative care consultations, use of oral and intravenous cytotoxic chemotherapy in the last month of life, hospital and ICU length of stay, use and duration of mechanical ventilation and attempted cardiopulmonary resuscitation. Under supervision by study investigators, a research assistant will access charts from outpatient and inpatient encounters at the main hospitals and clinics where the patient receives care. In addition, in the post-mortem interview with caregivers, the research assistant will ask the caregiver to identify additional sites where the patient has received care and perform audits at those sites as well when possible. Please refer to the 30-Day Abstraction Form and the Hospice-Chemo Form.

**Audio-recordings.** The primary study outcome measures are derived from audio-recordings of oncologist-patient visits (often with a caregiver present). All enrolled patients (Phase 1 and Phase 2 groups) will have one office visit with their participating oncologist audio-recorded. All parties present for recorded office visits, including: enrolled patients; any accompanying caregivers, family or friends; the oncologist; and any other physicians or health care providers not participating in the study will be fully aware that the conversation is being audio-recorded and will provide verbal assent immediately before any recording begins, in addition to the prior written consent of enrolled subjects. All enrolled patients, caregivers and physicians will agree to have their coaching and educational outreach sessions audio-recorded to assess fidelity of the intervention.

For our Primary Aim (Aim 1), we will use four validated and reliable indicators of communication about prognosis and treatment choices. The primary outcome measures encompass all of the communication domains in our conceptual model based on ecological theory: RESPONDING to patients' concerns; INFORMING patients about treatment choices; balanced FRAMING of prognosis information, and ENGAGING patients to participate in decisions. Our team has experience with all of the study measures. All measures have satisfactory psychometric properties. If all four indicators show clinically significant improvement (at least 0.5 standard deviation), we will consider that physician-patient dyads have responded completely to the intervention. Clinically significant improvement in one, two or three measures will be considered a partial response. **Coders** will undergo extensive training and supervision by developers of the scales, will not be involved in any other aspects of the study, and will be blind to study hypotheses and assignment to intervention vs. control. Control patients have contact with research staff and receive brochures; thus, conversational elements will be unlikely to unblind coders.

### Primary Outcome Measures (Aim 1)

<b>Construct / Measure</b>	<b>What it measures</b>	<b>Characteristics</b>	<b>Validation</b>
<b>ENGAGING</b>	<i>Sequences between: a) patients' assertive behaviors, and b)</i>	<i>Patient question-asking, assertive</i>	<i>Patients' active</i>

<b>The Active Patient Participation Coding Scheme (APPC)</b> <sup>34-42</sup>  <i>Both physician and patient behaviors</i>	<i>facilitative physician behaviors promoting patient participation.</i>	<i>responses and expressions of concern.</i>  <i>Physician facilitation of patients to express opinions, ask questions, talk about feelings, and participate in decision-making.</i>	<i>participation associated with clinicians' facilitation behaviors. Mutual interactions associated with health outcomes.</i>  <i>ICCs = .52 to .79.</i> <i>Cronbach's <math>\alpha</math> = .90</i>
<b>RESPONDING</b>  <b>Exploring and Validating Concerns (EVC)</b> <sup>15;43</sup>  <i>Physician behaviors</i>	<i>Depth of physician exploration and validation of (i.e. empathic and supportive response to) each specific patient concern.</i>	<i>Response to each patient concern given 1 point for preliminary exploration, 1 for further exploration, and 3 for validation. Based on the Measure of Patient-Centered Communication.</i> <sup>14;44;45</sup>	<i>Associated with prescribing behavior, health care costs and patient trust.</i>  <i>Cronbach's <math>\alpha</math> = .78. Intra-class correlations (ICCs) &gt;.80.</i>
<b>INFORMING</b>  <b>Prognosis and Treatment Choices Coding (PTCC)</b> <sup>43</sup>  <i>Physician behaviors</i>	<i>Physicians' efforts to address patients' wishes for information and support regarding prognosis and treatment choices.</i>	<i>7-item scale, e.g., "Doctor asks if patient wants to know more about his or her diagnosis" and "Doctor assesses patient's understanding of his or her diagnosis." Scored similarly to the EVC.</i>	<i>Developed for cancer contexts based on Braddock et al.</i> <sup>46</sup>  <i>Cronbach's <math>\alpha</math> = .80. ICC = .81</i>
<b>FRAMING</b>  <b>Framing of prognostic information: Optimism / pessimism subscale</b> <sup>26</sup>  <i>Physician behaviors</i>	<i>Degree to which physicians balance optimistic and pessimistic framing.</i>	<i>Statements coded as optimistic or pessimistic, then sub-coded past/present or future, e.g., "Your tumor has responded very well..." (optimistic, past-present); "Very few patients respond to ..." (pessimistic/future).</i>	<i>More balanced framing associated with greater shared understanding about likelihood of cure.</i>  <i>Inter-rater reliability (kappa).78.</i>
<b>Exploratory measures</b>	<i>Number of questions asked by patients and caregivers, the degree to which physicians encourage patient question-asking</i> <sup>20;21</sup> ; <i>OPTION shared decision-making measure,</i> <sup>47;48</sup> <i>visit duration.</i>		

### **Caregiver 2 and 7 month Postmortem Assessments**

This is designed to examine whether the VOICE health communication intervention can lead to better caregiver mental health (Aim 1) and physical health (Aim 2) 7-months after the death of the patient. Mixed methods will be used to contextualize these findings (Aim 3). Specifically, qualitative analyses will link caregiver bereavement outcomes with VOICE study communication outcomes (e.g., communication quality) and mediational analyses will explore whether caregiver bereavement outcomes are associated with patient-reported quality of life and healthcare utilization.

<b>Additional Caregiver Assessments</b>	<b>2 Mo.</b>	<b>7 Mo.</b>
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If needed finish the Qualitative Interview from 1 Month postmortem visit		C <sub>1</sub>	
PG-13 <sup>68</sup>	13	C <sub>2</sub>	C <sub>3</sub>
PHQ-9 <sup>103</sup> ( <i>original 10 ques + 10 additional</i> )	20	C <sub>3</sub>	C <sub>6</sub>
SF-12 Health Survey <sup>73</sup> /MOS Brief Disability	19	C <sub>4</sub>	C <sub>4</sub>
Affective Forecasting [MOOD]	3	C <sub>5</sub>	
GAD-7 <sup>104</sup>	8		C <sub>5</sub>
Purpose in Life <sup>107</sup> (+ 1 ques.)	7		C <sub>2</sub>
Decision Uncertainty and Regret Scale <sup>110</sup> ( <i>original scale only</i> )	8		C <sub>1</sub>
The Human Connection Scale(THC)>about Phys	12	C <sub>6</sub>	C <sub>7</sub>

## **VOICE Data analysis and monitoring**

**Overview.** This is a cluster-randomized trial, where our primary communication outcomes (Aim 1a) are measured at the level of the physician-patient dyad and our secondary outcomes (Aims 1b, 2 & 3) are measured at the level of the patient. Analyses are based on published guidelines for group (cluster) randomized controlled trials.<sup>49</sup>

**Prior to hypothesis-testing,** we will conduct preliminary analyses to estimate whether random assignment of physicians produces comparable patient groups. Any departure from comparability will be addressed in the analyses of hypotheses. Data for these analyses will be provided by a “Phase 1 sample” of five patients per physician who will not be enrolled in the Phase 2 part of the study. These patients and their physicians will provide audio-recorded office visits with study physicians analyzed using the same communication measures as in the Phase 2 part of the study. These patients will also complete surveys at study entry. We will compare physician factors from the audio-recordings and patient factors from the surveys at study entry across the two randomized arms using t-tests, chi-square and nonparametric methods, as appropriate. These comparisons will identify any potential confounders requiring further attention via stratified and multiple regression analyses. We will also assess use of specific intervention-related behaviors by physicians and patients in the Phase 1 sample.

**Hypothesis testing** will involve comparisons of the two randomized groups. Since the patients are nested within oncologists, methods for panel data will be applied. We will use both generalized estimating equations (GEE) and mixed-effects model (MM) for analysis of these clustered data. GEE provides more robust inference since it does not require a parametric distribution assumption. Our primary outcomes (Aim 1a) are unlikely to require substantial attention to attrition, since measurement occurs shortly after randomization, and will not require methods for repeated measures.

For the secondary outcomes that are measured repeatedly (Aims 1b, 2 & 3), hierarchical linear models with nested random coefficients will be applied. Missing values are likely in this study. Since there is no one standard way of handling missing data, we describe our approach in detail. The patients in this study have advanced cancer; one likely reason for attrition is the progression of disease, which may also be associated with decreases in quality of life. Thus, missing data will tend to occur more frequently in those with poorer quality of life. Because death (or survival time) is not a primary outcome of the study, we will treat death as missing data for the survey measures. Since death is often (but not always) preceded by a decline in quality of life, then death might similarly be associated with quality of life. GEE requires the “missing completely at random” (MCAR) assumption for valid inference, which may not be met for some outcomes in this study, including quality of life and quality of death. Therefore, we will apply the response-dependent missingness – or the missing at random (MAR) assumption when outcomes and missing data are less likely to be independent. In addition, we will examine the nature of the missing data and use weighted GEE (WGEE), or multiple imputation and sensitivity analyses, if necessary. Data suggest that end-of-life conversations do not affect survival. However, if we observe that death rates differ substantively between control and intervention groups, then we will conduct sensitivity analyses, assuming a range of QOL values to evaluate this potential bias.

Generalized linear models will be applied to model the treatment mean response for each group. A significant group effect will indicate difference between the two groups. Time by treatment group interaction will be included in the models as appropriate for repeated measures. Any factors identified as potential confounders in the pre-hypothesis testing phase of analysis will be considered for inclusion in all subsequent multivariate analyses – based on the effect that its removal has on the estimate of association. In assessing significance, we will use the false discovery rate (FDR) to control for type I error.<sup>50;51</sup> All analyses will be conducted using the latest version of SAS, which includes procedures for GEE and WGEE. If discrepancies in MM and GEE (WGEE) analyses occur, GEE (WGEE) will be recommended as they generally provide more robust inference.

### **Analysis of VOICE Specific Aims**

- **Aim 1 (Primary). To determine whether a combined intervention for patients/caregivers and physicians improves communication regarding prognosis and treatment choices in advanced cancer.** The physician-patient dyad will be the unit of analysis, as measured in a single audio-recorded clinical encounter. Because patients are clustered within physicians, in the data analysis, we may add random effects for physicians to account for the within-physician correlation of each dyad. If analysis of the Phase 1 data identifies plausible confounding by physician (communication style) or patient factors (demographic, clinical status), these factors will be eligible for inclusion in final analyses as described above. GEE will be applied to test differences in communication between the intervention and control groups. The log link function will be used. If there are excessive zeroes, the zero inflated Poisson (ZIP) model will be deployed. We will then determine if the response to the intervention is complete (clinically significant improvement in all four measures), partial (improvement in one, two or three measures), or nil.
- **Aims 1b and 2 (secondary). To determine whether the intervention group has fewer unmet needs, greater shared understanding and improved well-being.** Because repeated patient measurements are nested by oncologists, hierarchical linear models will be applied. Identity link functions will be applied for continuous responses and log link functions will be applied for count responses. For count responses, if there are excessive zeroes, the zero inflated Poisson model will be used.
- **Aim 3 (secondary). To determine whether the intervention affects health services utilization.** Cochran-Mantel-Haenszel test will first be applied to examine whether there is difference between the two intervention groups in the binary health service utilization variable (no utilization vs. any utilization), followed by GEE (or WGEE) with log link functions, similar to Aim 2. The outcomes for Aim 3 will be patients' use of mechanical ventilation, resuscitation, and ICU admission during the last week of life, and palliative care consultations and hospice enrollment at any point after the intervention. The logit link function will be used. In *exploratory* analyses, we will assess whether these effects are mediated by communication behaviors.

### **VOICE Sample size (power) calculations**

This is a nested study, with the physician as the unit of randomization. There is no standard method for calculating power in nested studies (i.e. accounting for clustering), so we describe our approach in detail. Based on prior studies, we have made the following assumptions: physician attrition 0-3%, patient attrition <5% for audio-recordings and 10%, 30% and 35% for the 1 week, 3 and 6-month post-visit patient surveys,<sup>31;52</sup> 80% patient mortality during 2-year follow up, availability of >80% caregiver post-death interviews,<sup>53;54</sup> availability of >90% medical records for audit,<sup>54-56</sup> no differential attrition between the intervention and control groups, and intra-cluster correlations of <0.1 for all measures.<sup>57-59</sup>

Prior work found that activation training increases physician communication behaviors two to three fold.<sup>4;20;60-63</sup> Conservatively, for our primary outcome (Aim 1), we expect effect sizes for each of the measures to be 2.0 SD; 0.5 SD is clinically significant. Because these measures are moderately correlated ( $r$  = approximately 0.3 - 0.4), and the primary outcome is achievement of clinically significant changes in all measures, we are powering the study conservatively at 0.7 SD. Power is based on a single measurement of these behaviors in the post-intervention physician visit. With 15 oncologists in each group and 10 patients per oncologist, the minimum detectable effect size is 0.46 SD. Sensitivity analyses assuming ICC of .3 yields a minimum effect size of .65 SD.

For our survey outcomes (Aims 1b & 2), we rely on observational data from Curtis et al<sup>64</sup> indicating correlations between quality of life and communication of 0.4 to 0.7 standard deviation. With an intervention we would

expect these differences to be larger. The power analysis takes advantage of a repeated measures design, derived using the method of Frison and Pocock.<sup>65</sup> For patient data, we assume one pre-intervention measure and two post-intervention QOL measures, and an average correlation among repeated measures of 0.5. Using this approach, our proposed sample size is sufficient to detect an effect size of 0.42 with power of .80. For our utilization outcomes, we rely on data that suggest 3- to 8-fold differences in use of aggressive treatments during the final week of life between patients who have had discussions compared to those who have not.<sup>54;56</sup> Thus, the study will be adequately powered, even considering attrition.

**Caregiver Data Analytic Plan** Analyses will be based on published guidelines for group (cluster) RCTs<sup>111</sup>. Prior to hypothesis-testing, we will evaluate whether random assignment of intervention arms to physicians produces comparable physician, patient, and caregiver groups. Any departure from comparability will be addressed in the analyses of hypotheses. We will compare physician, patient, and caregiver factors at entry across the two randomized arms using t-tests, chi-square and nonparametric methods, as appropriate. These comparisons will identify any potential confounders for consideration in our multi-level regression analyses. Additionally, we will evaluate the distributions of caregiver outcome variables to ensure that the regression models we fit to test our primary hypotheses are suitable. This will allow us to decide whether these data should be transformed prior to further analysis, or if we should consider fitting non-linear models. We will also evaluate the extent to which caregiver health outcomes are correlated with each other. Caregiver outcomes that are highly correlated will be treated as multivariate dependent variables. We will test our primary hypotheses via hierarchical linear<sup>112</sup> or, if need be, hierarchical non-linear<sup>113</sup>, modeling. Consistent with the cluster-randomized design of the VOICE study with caregivers nested within physicians, our hierarchical models will represent caregiver outcomes at the caregiver level (Level 1) and the effect of the intervention at the physician level (Level 2). The hierarchical structure of these models will allow us to account for both within-cluster and between-cluster variation in caregiver outcomes in our tests of the effects of the intervention. We will fit these hierarchical models using *HLM 7*<sup>113</sup>, commercially available software designed to fit hierarchical linear and hierarchical non-linear models. *HLM 7* can also be used to fit hierarchical multivariate linear models. Potentially confounding variables can be included in hierarchical models without difficulty.

**Aim 1:** *Examine whether a health care communication intervention for oncologists, patients, and caregivers leads to better mental health outcomes in caregivers following patient death.* Means-as-outcomes hierarchical linear models will be used to test hypotheses that caregivers in the intervention group, as compared to those in the control group, will have lower levels of prolonged grief symptoms (primary outcome) and better mental health outcomes on the other measures. Group differences at 7 months will be our key comparison. Caregiver mental health outcomes will be represented at Level 1 and the effect of the intervention will be represented at Level 2. Prior to model-fitting, we will confirm that scores on mental health measures are only modestly correlated. If they are correlated >.5, analyses will be repeated by a) controlling for each outcome with which it is correlated and b) creating a latent outcome variable derived by multilevel factor analysis<sup>114</sup>.

**Aim 2:** *Determine whether the intervention leads to better physical health outcomes in caregivers following patient death.* Means-as-outcomes hierarchical linear models, similar to those to be employed to test hypotheses for Aim 1, will also be used to test hypotheses that caregivers in the intervention group, as compared to those in the control group, will have better physical health summary scores on the SF-12 (primary outcome) and better function on the MOS Brief Disability Scale

**Aim 3:** *Contextualize these findings by conducting mediational analyses and qualitative analyses.* We will explore whether intervention effects are mediated by patient-reported quality of life and patient health care utilization (quantitative). We will explore caregiver perspectives on decision-making and communication processes to link bereavement outcomes with VOICE communication outcomes (*qualitative*).

Further analysis details include:

1. Explore relationships between patient survey data and chart abstraction, such as the degree of accuracy of patients' and doctors' survival prognosis estimates.
2. Assess the fidelity and impact of patient coaching and physician training using notes written by coaches and trainers outlining what happened during the coaching and training sessions to understand better the mechanisms for the observed effects of the intervention on patient-oncologist communication.

3. Analyze patients' affective forecasts for how they will feel in three months time compared with their reported quality of life.
  4. Analyze using qualitative methods patient responses to survey questions regarding their hopes for treatment, and the evolution of those hopes over time.
- See Appendix III for a current list published papers, abstracts and presentations.

**Mediation:** Means-as-outcomes and intercept-and-slopes-as-outcomes hierarchical linear (for continuous outcome) and hierarchical non-linear (for dichotomous outcome) models employing criteria for mediation will be used. To establish mediation, the intervention must be significantly predictive of the patient-related factor near the end of life, significantly predictive of the caregiver health outcome post-loss without adjustment for the patient-related factor, and less related to the caregiver health outcome post-loss adjusting for the patient-related factor. When the outcome is binary, we will use the appropriate adaptation of the indirect effect measure<sup>115</sup>. Inference for indirect effects will be based on bootstrapped variance estimates<sup>116</sup>. Mediation effects will be quantified using the mediated proportion<sup>117</sup>.

**Qualitative:** Interview data will be transcribed verbatim<sup>118</sup>. A research assistant will review each transcript for accuracy, correct errors, and note extended pauses, emotional displays, or disruptions (e.g., people leaving the room, telephone calls). All identifying information will be excised and replaced with de-identified demographic information. The corrected transcript will be time stamped and entered into Atlas.ti 6.2.

Dimensional analysis, an inductive technique, will be used to identify and describe the most salient ways that individual cases vary<sup>119</sup>. By identifying dimensions of content, process, and structure as well as their individual variations, we will be sensitized to how elements of our working model may be expressed and will have identified other significant characteristics that vary across interviews. We will explore the following sensitizing concepts<sup>120</sup>: information exchange (e.g., tailored, inadequate, overload), deliberation (e.g. collaboration, indecisiveness, outcome uncertainty, regret), and relationships (e.g., partnership, coercion, abandonment). Following this first round of analyses, we will have developed a provisional coding scheme in Atlas-ti in which major types of content, process, and structure have been identified.

Criterion based purposeful sampling<sup>121</sup> will be used in the second round of analyses, to make deliberate comparisons linking the VOICE study and these caregiver aims based on 3 criteria: group assignment in the VOICE study (intervention or control), caregiver reported communication at 3 months after the index visit in the VOICE study (specifically, randomly selected from those above the 75<sup>th</sup> and below the 25<sup>th</sup> percentile on scores on the Health Care Climate Questionnaire<sup>109</sup>), and bereavement outcomes (specifically, randomly selected from above the 75<sup>th</sup> and below the 25<sup>th</sup> percentiles on the PG-13<sup>68</sup> at the 2 month post-mortem visit. Two analytic teams, both dyads, will consider transcripts from one criterion separately, then compare with those analyzed by the other dyad. For example, one dyad will focus on thematic codes derived from transcripts of participants exposed to the intervention; the other will analyze transcripts of participants exposed to usual care. The two dyads will work independently. Based on our prior work, we expect that 80 interviews should result in reasonable saturation of concepts in order to refine the conceptual categories<sup>122</sup>. However, if saturation is not reached, we will continue to sample.

The coding team will subsequently convene to determine by group consensus whether particular themes distinguish the narratives of the two groups. We have used this method successfully in qualitative analyses of complex interventions<sup>123</sup>. Final coding will be done by the research assistant and post-doctoral fellow, under supervision of the PIs. Dr. Epstein will audit the results for consistency, clarity, and comprehensiveness.

### **Caregiver Aims Statistical Power Considerations**

VOICE is a cluster-randomized RCT with physicians (clusters) and patients per physician (cluster). Assuming that approximately 85% of patients will have caregivers, nearly all of whom (~ 95%) will be available for the 7-month post-loss assessment, the caregiver aims is a cluster-randomized RCT with 30 clusters, and 8 caregivers per cluster, divided equally between experimental and control conditions. Given the VOICE study's design, the power to test each specific aim (at =0.05) will depend primarily on the effect size associated with the intervention and the between-cluster variance in the outcome for each aim. We used Optimal Design<sup>125</sup>, software developed specifically to estimate power and effect size for longitudinal and multilevel research

including cluster-randomized RCTs, to evaluate statistical power for our proposed HLM analyses of the effects of the intervention on symptoms of prolonged grief disorder, as assessed by the PG-13 (Aim 1) and physical health, as assessed by the physical health summary score of the SF-12 (Aim 2). Given the assumptions noted in the prior paragraph, the sample size provides 80% power to detect minimum effect sizes of ~ 0.45 for the effects of the intervention on caregiver grief and functional disability post-loss, assuming a modest intra-class correlation of 0.05. Given similar assumptions, the design provides 73% and 62% power to detect minimum effect sizes of 0.40 and 0.35, respectively, for the effects of the intervention on these primary outcomes.

### **VOICE Data Safety and Monitoring Plan**

The proposed study is of minimal risk and will not require a Data Safety Monitoring Board (DSMB). Despite the low risk associated with this behavioral intervention, we have organized an internal data safety and monitoring plan, and will report directly to the URM Cancer Center and IRB.

The Principal Investigator, Dr. Epstein and the study clinical psychologist will comprise the internal data safety committee. The function of the internal committee will be to:

- a) Systematically review screening materials to ensure that screening is conducted appropriately.
- b) Systematically ensure that participants experiencing distress receive information on referrals.
- c) Conduct on-going preliminary data analyses on the Phase 2 to evaluate impact of educational interventions for oncologists, caregivers and patients on immediate and long term outcomes. In the unlikely event that the interventions decrease the likelihood of appropriate help seeking for participants or increase distress, the study protocol will be reexamined and modified appropriately.
- d) Monitor staff performance with regard to protection of privacy, confidentiality, maintenance of secure data bases, and study procedures designed to reduce the risk of distress.
- e) Ensure that the PI, sub-investigators, or a designated qualified individual, will be available by pager in case research staff needs to confer regarding participant symptoms.
- f) Review and report any adverse events associated with the study.

The internal review board will meet by conference call once monthly and confer on an as needed basis when adverse or difficult events occur. Additional oversight will be provided by the UCD IRB and the URM Cancer Center (see below).

**Investigators:** Will also conduct continuous review of data and patient safety. The review will include for each treatment condition: the number of patients, adverse reactions, and responses observed. The Principal Investigator will submit summaries of this data to the Cancer Center for review as required in the study's Cancer Center's review committee approval letter.

**Data Storage and Confidentiality:** Please see **Section IV: RISK/BENEFIT ASSESSMENT, Protection against risks, Privacy and Confidentiality.**

### **III. RISK/BENEFIT ASSESSMENT**

#### **Risk Category**

This is a Minimal Risk behavioral intervention study. The interventions are unlikely to pose harm or discomfort any greater than that ordinarily encountered in daily life or in obtaining routine medical care.

#### **Potential risks:**

*Oncologist risk.* Oncologist involvement in the study includes instruction in effective communication, survey completion and having office visits audio-recorded. There is a low potential that oncologists may experience some psychological discomfort when receiving instruction on ways to communicate more effectively with patients, particularly if these are new skills. Also, there is a low possibility that despite all protections, privacy and/or confidentiality may be breached. We believe the likelihood of such risks is low, that we have seriously

considered these risks, and that we have adequate protections in place. In addition, any psychological discomfort is likely to be reversible and short-lived.

***Patient risk.*** Patient involvement in the study includes instruction in effective communication, survey completion and having office visits audio-recorded. There is a low potential that patients may experience some psychological discomfort when receiving instruction on ways to communicate more effectively with their physicians or to be better advocates for their own treatment goals, particularly if these are new skills. Completing some of the survey measures about attitudes and quality of life may involve some psychological discomfort. Also, there is a low possibility that despite all protections, subject privacy and/or confidentiality may be breached. We believe the likelihood of such risks is low, that we have seriously considered these risks, and that we have adequate protections in place. In addition, any psychological discomfort is likely to be reversible and short-lived.

***Caregiver risk.*** Caregiver involvement in the study includes instruction in effective communication, survey completion and having office visits audio-recorded. There is a low potential that caregivers may experience some psychological discomfort when receiving instruction on ways to communicate more effectively with physicians or to be better advocates for their loved one's treatment goals, particularly if these are new skills. Completing some of the survey measures about attitudes and quality of life may involve some psychological discomfort. Also, there is a low possibility that despite all protections, subject privacy and/or confidentiality may be breached. We believe the likelihood of such risks is low, that we have seriously considered these risks, and that we have adequate protections in place. In addition, any psychological discomfort is likely to be reversible and short-lived.

## **Protection Against Risks**

***Privacy and confidentiality.*** Multiple procedures for protecting against and minimizing risks will be instituted. Staff will be trained regarding HIPAA and human subjects' protections regulations and procedures. Any data collected will be stripped of the following identifiers; names, initials, and any personal identifying information with the exception of dates, age, race, ethnicity, the last 3 digits of the zip code, and gender. A unique ID number will be generated for each subject and all data files. The linking file containing personal identifiers will not be stored in the central database repository. The data will be encrypted by applying a special scrambling code that makes the data unreadable to anyone who does not have a decryption key. Authorized personnel with access to this key can unscramble it. This file will be stored on a separate server and will only be accessible to database administrators with the appropriate permissions. URMCM-managed networks where data will be stored and maintained are protected by perimeter firewalls, supplemented by additional interior firewalls to protect particularly critical or vulnerable resources. All data transfers (including database, text and audio files) between sites and among investigators, data analysts and staff will be accomplished using a secure and encrypted data management program. No data will be stored on portable devices such as laptops, flash drives, smart phones and personal digital assistants.

During the period in which it is necessary to keep personal identifying information for follow-up purposes, all personal electronic data will be kept in a password protected file on a secure mainframe computer with firewall protection located behind locked doors, and paper data will be securely kept in a locked file cabinet. Subjects will be assigned identification numbers which will be used on all data; the link between name and ID number will also be kept in a separate password protected file. Participants will be advised as to the risks to confidentiality in the informed consent. Finally, no identifying information that associates names with voices will appear on transcripts of the recorded visits or on any portable electronic equipment. Although the professional transcriptionists will not receive any personal identifying information about the participants, they will still complete human subjects' protection certification prior to transcribing, and agree to maintain the confidentiality of the recorded materials. No identifying data will be used in any publications.

***Psychological or physical risk.*** We will institute several mechanisms to reduce the potential for arousal of psychological discomfort. Staff will receive training in techniques for approaching patients and caregivers and in sensitivity to communicating about prognosis in advanced cancer. Patients, caregivers and physicians will be informed they have the right to terminate coaching sessions or surveys, and to refuse surveys or leave survey questions blank if they are uncomfortable for any reason. Since the goal of the study is to examine whether educational interventions affect/improve clinical care, we believe it highly unlikely that the patients will receive worse than usual care based on the intervention. It is more likely that patients will receive improved

care due to improved communication with the oncologist. While it is possible to introduce tension in patient-physician relationships by coaching patients to be more assertive (e.g., ask questions, ask for clarification) who then encounter physicians who are unprepared for assertive patients, we will be avoiding this risk by providing parallel training for physicians that help them anticipate patients' concerns, and advise them that patients will have been coached to help them ask relevant questions. Participants in the control condition will receive usual care.

In the unlikely event of extreme psychological discomfort either during the intervention or follow-up, staff will be trained in procedures for ensuring necessary medical or professional intervention. All participants will be given the telephone number of the co-principal investigator and encouraged to notify him if they feel any distress or concerns because of the study questions or procedures. They will be referred for medical or psychological care as appropriate.

#### **Potential benefits of the proposed research to the subjects and others**

If the intervention is successful, there is potential benefit of the research to the patients and caregivers in the intervention arm; as a result of the intervention they may receive information and support that improve their understanding of their illness and their quality of life. Improved help-seeking may positively affect the clinical care provided by the oncologist, thereby improving outcomes. The intervention could also reduce the discomfort associated with participants' uncertainty about how to communicate with an oncologist about a life-limiting illness. For participants in the control group, the benefits would be indirect. Non-participant patients of intervention physicians may benefit from physicians' improved communication skills. The control assignment will not interfere with usual care provided to control patients.

We believe the potential risks to subjects are reasonable in relation to the value of this behavioral intervention on communication in advanced cancer, and that we have adequate safeguards to minimize risks inherent in research participation. Our study design improves the likelihood that we can adequately assess the effect of the educational intervention on clinical care and thereby contribute to future benefits for other patients and caregivers.

#### **IV. SUBJECT IDENTIFICATION, RECRUITMENT AND CONSENT/ASSENT**

The following three sections contain information relevant to oncologists, patients and caregivers.

##### ***Oncologists***

**Method of Subject Identification and Recruitment:** After obtaining IRB approval, oncologists from university-affiliated and community-based practices in the Rochester and surrounding regions will be solicited for participation through personal contacts with cancer center directors and presentations about the study in faculty, house staff meetings and grand rounds. Presentations will be given by Ronald Epstein, MD or Supriya Mohile, MD. An initial email will be sent by Dr. Mohile or Dr. Epstein mentioning the study name and indicating they will follow-up with a phone call within a week. The voluntary nature of potential enrollment will be stressed in all aspects of recruitment.

**Process of Consent:** Once oncologists indicate interest, they will meet with a study investigator who is a member of the Physician Recruitment & Data Collection Working Group to verify that clear understanding of all study components has been achieved. Prospective participants will then complete a written informed consent document that requests permission to a) guide recruitment efforts among their patients by determining eligibility, b) participate in an educational program to enhance their communication skills, c) audiotape one clinic encounter per enrolled patient, and d) complete brief baseline, post-visit and post-intervention surveys. Oncologists will be told that "the purpose of this study is to assess the impact of brief educational interventions on clinical care and outcomes of patients with cancer and their caregivers. Outcomes of interest include communication between patients, caregivers and physicians, as well as patient well-being and health services utilization." Further details about the aims of the study will not be disclosed to avoid biasing oncologists' interactions with patients and caregivers. Oncologists will be free to opt out of the study at any time.

**Subject Capacity:** All subjects will be professionally licensed oncologists.

**Subject/Representative Comprehension:** A study investigator with the Physician Recruitment and Data Collection Working group will ensure that each oncologist has a thorough understanding of the consent form before obtaining a signature.

**Debriefing Procedures:** N/A

**Consent Forms:** There is a consent form for oncologists containing all the information required by the IRB guidelines.

**Documentation of Consent:** Written informed consent will be obtained from each subject and placed in a regulatory binder in a locked cabinet in the Family Medicine Research building at 1381 South Ave, Rochester, NY 14620. No personal identifying or confidential information will be stored on any laptops that may be used for data collection.

**Costs to the Subject:** There are no costs to the subject. Participation in the study does not require additional medical procedures. The only cost to the subject will be their time.

**Payment for Participation:** Oncologists will receive \$600 for completion of questionnaires and identifying eligible patients for the study.

### ***Patients***

**Method of Subject Identification and Recruitment:** All Phase 1 and Phase 2 patients will be identified by research assistants working closely with participating physicians and their clinic staff by reviewing the clinic roster in detail to ascertain that all potentially eligible patients are identified. Potentially eligible patients will receive a brochure that describes the study (see attached study brochure). Office staff will explain to the patient that a research assistant will be calling him/her in the next two weeks to find out if he/she might be interested in participating in the study. Patients who do NOT want to be contacted about the study will be asked to return an enclosed opt-out card to the study office within 4 days of receiving the study brochure. A research assistant will only call patients who have not returned the opt-out card within the stated time period.

**Process of Consent:** Patients will provide written consent (see patient consent forms). Patients will be given time to think about participation, and if desired be given a way to contact the research assistant at a later time. The screening and consent process will continue as long as needed until the person obtaining consent is comfortable that the prospective participant fully understands all aspects of study involvement. The research assistant will obtain written consent from those who voluntarily wish to enroll, using approved consent forms. All patients will be asked to allow audio-recording of one future visit with their oncologist, and for permission to collect baseline survey and demographic data. Patients who are unable to read any study-related materials but are able to speak and understand spoken English will have study materials read to them and explained by a research assistant.

**Phase 1 patients** will be told that their participation is limited to completing two sets of orally-administered surveys and allowing an office visit with an oncologist to be audio-recorded.

**Phase 2 patients** will be informed about the multiple phases of the study and that their actual total involvement will take about 60 minutes for the initial coaching, 50 minutes for the initial surveys and 10-30 minutes to complete the follow-up surveys in person or by phone. Phase 2 patients will be asked for written permission to a) audio-record one office visit with their oncologist, b) complete surveys at baseline, immediately after their office visit, 0-10 days after the office visit and every three months for up to four years, and c) for permission for research staff to access their medical records to ascertain their use of health services such as emergency department visits, hospital admissions, cancer treatments and community-based nursing services. The research assistant will review the consent form



with the patient. In addition, the patient will be advised that he/she may opt out of the study at any time without any future impact on treatment.

**Subject Capacity:** Patients deemed inappropriate or lacking in competency by their physicians will be excluded. We will not enroll subjects who are unable to consent for themselves. No person with decisional incapacity will be enrolled. Elderly persons (persons over age 65) with decisional capacity who meet other enrollment criteria will be included. No other vulnerable subjects will be targeted for inclusion in the study.

**Subject/Representative Comprehension:** Patients or their caregivers will be asked if the patient is able to understand consent forms in written in the English language, or are unable to do so due to health, sensory or cognitive impairment. The research assistant will review these forms in detail with the patient, and will ask questions to ensure the patient understands. The patient will be given repeated opportunities to ask questions, and these questions will be responded to until it is clear that the patient has full comprehension.

**Debriefing Procedures:** N/A

**Consent Forms:** There is a consent form for patients in the Phase 1, and a consent form for patients in the Phase 2. Both consent forms contain all the information required by the IRB guidelines.

**Documentation of Consent:** Written informed consent will be obtained from each subject and placed in a regulatory binder in a locked cabinet in the Family Medicine Research building at 1381 South Ave, Rochester, NY 14620. No personal identifying or confidential information will be stored on any laptops that may be used for data collection.

**Costs to the Subject:** There are no costs to the subject. Participation in the study does not require additional medical procedures. The only cost to the subject will be their time.

**Payment for Participation:**

**Phase 1 patients** will receive \$15 after completion of each of two sets of surveys; one will be completed at enrollment and the other brief survey following the audio-recorded office visit. Maximum payment will be \$30.

**Phase 2 patients** will receive follow-up phone calls from coaches and research assistants, and \$15 for completion of each set of surveys. Surveys will occur at enrollment, right after the audio-recorded visit, approximately 1 week after the visit and then every three months up to four years post-enrollment. Maximum payment will be \$300.

### ***Caregivers***

**Method of Subject Identification and Recruitment:** All patients will also be asked by the research assistant (RA) to identify a caregiver, if they have one. Once identified, the RA will independently approach the Caregiver either in person or by telephone,

**Process of Consent:** The caregivers will be provided with a study brochure by the research assistants to ascertain willingness to participate, and their ability to provide written consent. The research assistant will review the consent form in detail with the patient, and the patient will be advised that he/she may opt out of the study at any time, without any future impact on treatment. Caregivers will be told the same details about the study as the patients, complete surveys at the same time intervals as the patients. Caregivers will be asked for permission to be contacted if the patient dies within four years of enrollment and to sit down with a member of the study team or speak on the telephone if preferred, to answer some pre-approved and structured questions within approximately one month after the death of the patient. Caregivers can refuse at any time.

**Subject Capacity:** We will not enroll caregivers who are unable to consent for themselves. No caregivers with decisional incapacity will be enrolled.

**Subject/Representative Comprehension:** The caregivers will be asked if they are able to understand consent forms in written in the English language, or are unable to do so due to health, sensory or cognitive impairment. Caregivers unable to understand the consent form due to cognitive, health, or sensory impairment will be excluded. The research assistant will review the consent forms in detail with the caregiver, and will ask questions to ensure the caregiver understands of the consent form. The caregiver will be given repeated opportunities to ask questions, and these questions will be responded to until it is clear that he/she has full comprehension.

**Debriefing Procedures:** N/A

**Consent Forms:** There is a consent form for Caregiver in the Phase 1 and a consent form for Caregiver in the Phase 2. Both forms contain all the information required by IRB guidelines.

**Documentation of Consent:** Written informed consent will be obtained from each subject and placed in a regulatory binder in a locked cabinet in the Family Medicine Research building at 1381 South Ave, Rochester, NY 14620. No personal identifying or confidential information will be stored on any laptops that may be used for data collection.

**Costs to the Subject:** There are no costs to the caregiver. Participation in the study does not require additional medical procedures. The only cost to the subject will be their time.

**Payment for Participation:**

**Phase 1 Caregivers** will receive \$15 for completion of each set of surveys. The first payment will occur after completion of the enrollment surveys and the next will occur once the surveys are completed right after the audio-recorded doctor's visit. Maximum payment will be \$30.

**Phase 2 Caregivers** will receive \$15 for completion of each set of surveys. The first payment will occur after completion of the enrollment survey, the next will occur once the surveys are completed right after the audio-recorded doctor's visit, then approximately three months later. In addition, if the patient dies within four years of enrollment, the caregiver will be asked to participate in an interview approximately 1, 2, and 7 months after the patient dies. He/she will be paid \$15 for each interview. Maximum payment for the study will be \$300.

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## Appendices:

### Appendix I: Survey Timing

<b>Survey or Encounter</b>	<b>Goal</b>	<b>Maximum</b>	<b>Rationale and Additional Guidance</b>
Index visit (Visit01)	Within 3 weeks of baseline survey	8 weeks after baseline survey (repeat single McGill QOL question if >4 weeks, repeat entire baseline surveys if >8 weeks)	Goal is to administer baseline survey as close as possible to the index visit so that recorded health status reflects health status at index visit.
Coach Satisfaction Survey	Within 1 week of index visit	Within 1 month of index visit	At UCD and UR, coaches will hand satisfaction instrument to patient after coaching session and request return by mail.
2-4 day f/u (Visit02)	2 days after index visit	10 days after index visit	
3 month f/u (Visit03)	3 months from index visit	5 months from index visit	Clock starts at index visit.
6 month f/u (Visit04)	6 months from index visit	8 months from index visit	
9 month f/u (Visit05)	9 months from index visit	11 months from index visit	
12 month f/u (Visit06)	12 months	14 months from index visit	
Additional f/u surveys q 3 months	15, 18, 21, 24 months	17, 20, 23, 26 months	
1 month caregiver postmortem	1 month	3 months	If not completed after 3 months, and caregiver still willing, possibly consider making a protocol exception with permission of the PI. Must be discussed.
2 month caregiver postmortem	2 months	4 months	If 1 month surveys have not been completed administer both 1 and 2 months together if possible. If not possible administer the 2months as soon after as possible.
7 month caregiver postmortem	7 months	9 months	

**Eligibility, screen failures and withdrawals - patients**

**1) Definitions of study periods:**

- a) **Potential participants:** Patients who are eligible but have not yet consented
- b) **Screening period:** Time after the patient has signed a consent to participate but has not completed baseline surveys.
- c) **Enrolled in study:** Patient who remains eligible at time of baseline surveys (e.g. not in hospice, not hospitalized, no cognitively compromise so that communication is impossible) and has completed baseline surveys

**2) Declined to participate**

- a) Definition: Study is presented to a potential participant by nurse, physician, or RA and either a) patient refuses to speak to the RA about the study or b) RA presents the study and patient declines.

**3) Screen failure**

- a) Definition = Investigator-initiated exclusion of patients who have completed consent but are not enrolled because they are found to be ineligible prior to completion of baseline survey
- b) Examples – Patient who goes into hospice, dies or becomes permanently unable to complete surveys (e.g. due to stroke or brain metastasis) after consent but before completing baseline survey.
- c) Such a patient will be considered a **screen failure**, not withdrawal.
- d) Patients who are hospitalized after consent can be approached to complete baseline surveys after discharge if they survive.

**4) Patient-initiated withdrawal**

- a) Definition: A patient (not the physician or caregiver) who directly expresses unwillingness to continue participation in survey data collection.
  - a) We will obtain no survey data after withdrawal. We will obtain and analyze chart audit data unless the participant states they do not want their chart data obtained.
  - b) Any data collected prior to withdrawal **will** be considered in intention-to-treat analyses unless the patient explicitly requests that we delete all data collected to date.
- b) Non-withdrawals
  - i) Deaths will **not** be considered withdrawals.
  - ii) **Active enrolled participants with missing data** are those patients who have not withdrawn but are unable to participate in any future surveys.
  - iii) Only patients can withdraw themselves from the study; a caregiver or proxy cannot withdraw the patient from the study.
  - iv) Patients will not be withdrawn from the study if the caregivers withdraw from the study.
  - v) Withdrawal of consent – patient's who explicitly state they do not want any of their data used.
  - vi) Lost to Follow-up: Patients who do not respond to phone calls and mail after a reasonable attempts to contact them.
- c) Screening withdrawal – a patient who withdraws during the screening period.

**Eligibility, screen failures and withdrawals – caregiver**

**1) Definitions of study periods:**

- a) **Potential participants:** Caregivers who are eligible but have not yet consented
- b) **Screening period:** Time after the caregiver has signed a consent to participate but has not completed baseline surveys.
- c) **Enrolled in study:** Caregiver who remains eligible at time of baseline surveys (e.g. patient is still eligible) and has completed baseline surveys

## 2) Declined to participate

- a) Definition: Study is presented to a potential participant by nurse, physician, or RA and either a) caregiver refuses to speak to the RA about the study, or b) RA presents the study and caregiver declines.

## 3) Screen failure

- a) Definition = Investigator-initiated exclusion of caregivers who have completed consent but are not enrolled because they are found to be ineligible prior to completion of baseline survey
- b) Examples – Patient becomes ineligible after consent but before completing baseline survey.
- c) Such a caregiver will be considered a **screen failure**, not withdrawal.

## 4) Caregiver-initiated withdrawal

- a) Definition: A caregiver (not the physician or patient) who directly expresses unwillingness to continue participation in **any part of the study** after completion of the baseline survey.
- b) Data and analyses
  - i) We will obtain no caregiver data after withdrawal.
  - ii) Any data collected prior to withdrawal **will** be considered in intention-to-treat analyses unless the caregiver explicitly requests that we delete all data collected to date.
- c) Non-withdrawals
  - i) Patient or caregiver deaths will **not** be considered withdrawals
  - ii) Caregivers will be considered to be **active participants with missing data** if they a) have completed a baseline survey, b) are unable to participate in any future surveys or do not respond to phone calls and emails after reasonable attempts to contact them, and c) do not withdraw consent.
  - iii) Caregivers will not be withdrawn from the study if the patient withdraws from the study.
- d) Screening withdrawal – a caregiver who withdraws during the screening period.

## **Eligibility, screen failures and withdrawals – physician participants**

### 1) Definitions of study periods:

- a) **Potential participants:** Physicians who are eligible but have not yet consented
- b) **Screening period:** Time after the physician has signed a consent to participate but has not completed baseline surveys.
- c) **Enrolled in study:** Physician who remains eligible at time of baseline surveys and has completed baseline surveys

## 2) Declined to participate

- a) Definition: Study is presented to a potential participant and either a) refuses to be contacted, or b) declines.

## 3) Screen failure

- a) Definition = Investigator-initiated initiated exclusion of physicians who have completed consent but are not enrolled because they are found to be ineligible prior to completion of baseline survey .
- b) Examples – Physicians becomes ineligible after consent but before completing baseline survey.
- c) Such a physician will be considered a **screen failure**, not withdrawal.
- d) No patients or caregivers of that physician will have been recruited.

## 4) Physician-initiated withdrawal

- a) Definition: A physician who directly expresses unwillingness to continue participation in **any part of the study** after completion of the baseline survey.
- b) Example – physician moves out of town or leaves practice
- c) Data and analyses
  - i) We will obtain no physician data after withdrawal.
  - ii) We will continue to collect data from participating patients of that physician and their caregivers unless they withdraw.
  - iii) No patients of that physician will be recruited from that time forward.

- iv) Any physician data collected prior to withdrawal **will** be considered in intention-to-treat analyses unless the physician explicitly requests that we delete all data collected to date.
- d) Non-withdrawals
  - i) Physician deaths will **not** be considered withdrawals.
  - ii) Physicians will be considered to be **active participants with missing data** if they a) have completed a baseline survey, b) are unable to participate in any future surveys or do not return emails, phone calls and meeting invitations and c) do not withdraw consent.
- e) Screening withdrawal – a physician who withdraws during the screening period.

**VOICE papers author table**

	Citation	Status
1	Hoerger M; Epstein RM; Winters PC; Fiscella K; Duberstein PR; Gramling R; Butlow PN; Mohile SG; Kaesberg PR; Tang W; Plumb S; Walczak A; Back AL; Tancredi D; Venuti A; Cipri C; Escalera G; Ferro C; Gaudion D; Hoh B; Leatherwood B; Lewis L; Robinson M; Sullivan P; Kravitz RL. "Values and options in cancer care (VOICE): study design and rationale for a patient-centered communication and decision-making intervention for physicians, patients with advanced cancer, and their caregivers." <i>BMC Cancer</i> . 2013;13(1):188.	Published
2	Cameron RA; Mazer BL; DeLuca JM; Mohile SG; Epstein RM "In search of compassion: a new taxonomy of compassionate physician behaviours." <i>Health Expectations : An International Journal of Public Participation in Health Care and Health Policy</i> . 2013.	Published
3	Mazer BL; Cameron RA; DeLuca JM; Mohile SG; Epstein RM "'Speaking for' and 'speaking as': pseudo-surrogacy in physician-patient-companion medical encounters about advanced cancer." <i>Patient Education and Counseling</i> . 2014;96(1):36-42.	Published
4		
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**Presentations – submitted and presented**

	Presentation	Status
1	Duberstein, P.R. <i>Person-centered end-of-life care and bereavement outcomes: The VOICE Caregiver Study (2013-2017)</i> . University of Rochester CTSI Seminar, March 2013	Presented
2	Duberstein, P.R. <i>Person-centered end-of-life care and bereavement outcomes: The VOICE Caregiver Study (2013-2017)</i> . University of Rochester CTSI Seminar, March 2013	Presented
3	Duberstein, P.R., Prigerson, H.G., Kravitz, R.L., & Epstein, R.M. <i>Overtreatment fueled by over-optimism and terror management at the end-of-life: The crossroads of health services and psychology</i> . Preventing Overdiagnosis Conference, Dartmouth Institute for Health Policy and Clinical Practice, September 2013	Presented
4	Duberstein, P.R. <i>Person-centered end-of-life care: The VOICE studies (2011-2017)</i> . Seminar, Gothenburg University Neuroepidemiology Program, Gothenburg, Sweden, September 2014.	Presented

5	The VOICE Studies: A Person-Centered Approach to Suicide Prevention in Cancer Treatment Settings.symposium “Suicide prevention in older adults: New discoveries and innovative programs” (Number 91), has been accepted for presentation in a parallel plenary at the 28 <sup>th</sup> World Congress of the International Association for Suicide Prevention (IASP) to be held from June 16 <sup>th</sup> to 20 <sup>th</sup> , 2015, in Montreal.	Presented
6	Cameron R, Mazer B, Epstein RM. In search of compassion: a new taxonomy of compassionate physician behaviours Am Acad Comm in Healthcare Orlando 10-2014 -	Presented
7	Lowenstein L, Epstein RM, Yellamaty V, Plumb S, Conn K, Mohile S. Missed opportunities to discuss patient and caregiver aging concerns in oncology clinical encounters. Cancer and Aging SIG collaboration. Society of Behavioral Medicine 2014	Presented
8	Hoerger M, Tran Q, Kravitz RL, Duberstein PR, Winters P, Fiscella K, Epstein RM. Family-Centered Communication Skills are Associated with Oncologist-Patient-Caregiver Agreement in Quality-of-Life Forecasts for Patients with Advanced Cancer.Am Acad Hospice and Palliative Medicine (AAHPM) San Diego March 2014 (Poster)	Presented
9	Bartels J, Rodenbach R, Ciesinski K, Gramling R, Fiscella K, Epstein RM. Eloquent silence: a musical analysis when words fail. International Conference on Communication and Healthcare. New Orleans October 2015	Presented
10	Bartels J, Rodenbach R, Ciesinski K, Gramling R, Fiscella K, Dolan J, Street R, Epstein RM. Relationship between computer-associated conversational silences and expression of emotion in end-of-life oncology discussions between the doctor, patient, and computer. International Conference on Communication and Healthcare. New Orleans October 2015	Presented
11	Ronald M Epstein, MD1, Richard L Kravitz, MD, MSPH2, Joshua Fenton, MD, MPH2, Michael Hoerger, PhD3, Kevin Fiscella, MD, MPH1, Guibo Xing, PhD2, Daniel Tancredi, PhD2, Robert Gramling, MD1, Paul R Duberstein, PhD1. Patient-Caregiver Concordance in Advanced Cancer: Implications for Decision-Making and Quality of Care. International Conference on Communication and Healthcare. New Orleans October 2015	Presented
12	Epstein RM, Duberstein PR, Fiscella K, Gramling R, Mohile, S, Hoerger M, Tancredi D, Xing G, Kravitz RL. Talking about the hard stuff: Short-term outcomes of a multi-center RCT of oncologist, patient, and caregiver interventions to improve communication in advanced cancer. International Conference on Communication and Healthcare. New Orleans October 2015	Presented
13	Prognosis Discussion in End of Life Care: The Role of Physician Burnout, Relational Attachment and Gender	Accepted
14	Hoerger M et al. Cleveland G. Shields, PhD2, Kevin Fiscella, MD, MPH3, Joshua J. Fenton, MD, MPH4, Paul R. Duberstein, PhD3, Ronald M. Epstein, MD3. Oncologists’ Skills in Communication about End-of-Life Care: Impact on Patients with Advanced Cancer and their Caregivers	Accepted