NIH Collaboratory Rethinking Clinical Trials™
Health Care Systems Research Collaboratory

Regulatory/Ethics Consultation Call:

Advance Care Planning: Promoting Effective and Aligned Communication in the Elderly (ACP PEACE)

Monday, August 13, 2018
Meeting Participants

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AGENDA ITEMS	DISCUSSION	ACTION ITEMS
Review of Demonstration Project	• Study Co-Principal Investigator Angelo Volandes (Harvard) provided a summary of the ACP PEACE pragmatic clinical trial. The study tests the combination of 2 evidence-based, complementary advance care planning (ACP) interventions: communications skills training in serious illness for clinicians (VitalTalk) and advance care planning video decision aids for older patients with cancer (ACP Decisions). The goal is to evaluate the effects of the intervention on the rate of patients' completion of ACP documents, resuscitation preferences, palliative care consultations, and hospice use in the electronic health record (EHR). • **Collaborative network partners:** o Mayo Clinic o Duke Health o Northwell Health o Dana-Farber Cancer Institute o Boston Medical Center • **NIH Institute:** National Institute on Aging (NIA) • **Study design:** ACP PEACE is designed as a stepped-wedge, cluster-randomized trial evaluating a comprehensive ACP program among older oncology patients conducted in 3 large U.S. healthcare systems (Duke, Mayo, Northwell). In the UG3 phase, the study team will develop the organization, processes, and infrastructure of the ACP program and pilot the intervention in one oncology clinic in each of the partner systems. In the UH3 phase,	

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	the effects of the intervention will be tested using electronically collected EHR data from 4500 patients >65 years of age with advanced cancer across 36 randomized clinics. Other elements of the UH3 phase will involve in-person surveys, video ACP declarations, EHR chart reviews of a subgroup of patients, and implementation webinars with clinic staff and executive sponsors (see details in attached supplemental material). o **Primary outcome:** Rate of completion of ACP documents in the EHR from patients >65 years with advanced cancer, before and after the intervention. o **Secondary outcomes:** (1) Rate of completion of patient preferences for resuscitation, use of palliative care services, and hospice use and (2) evaluation of patient-centered outcomes (confidence, decisional satisfaction or regret) via in-person survey in a subset of 450 patients. • Since ACP PEACE is a stepped-wedge trial, there will be a control phase and an intervention phase for the 36 clinics in the UH3 implementation. The control phase consists of standard of care. • Clinician and other staff participation in communications skills training is voluntary. Those who do participate will receive an email survey after the intervention.	
Status of IRB approval	• The Dana-Farber Cancer Institute is serving as the central IRB, has approved the study, and all sites have ceded to this IRB.	
Risk classification	• The team anticipates the study to be minimal risk to participants. The intervention components (VitalTalk and ACP Decisions) are the standard of care in many healthcare systems. The intervention will be available to all patients with advanced cancer in the clinic, not only patients >65. • The IRB determined that ACP PEACE poses only minimal risk to participants.	
Consent	• Categories of participants related to requirement for informed consent: **Category 1:** 375 patients (UG3)/4500 patients (UH3) from whom data are collected via the EHR from a data repository. The study team seeks a waiver of consent for this category since no identifiable health data will be shared between systems. As an ethical matter, the study team will consider providing some type of general notification	Completed: The Collaboratory coordinating center sent the team the article, "Use of altered informed consent in pragmatic

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	to patients about the study and use of their health data. If an opt-out mechanism is provided, it would be important to track how and when this is actually used if feasible. **Category 2:** 15 patients (UG3)/450 patients (UH3) participate in a 5-minute in-person survey data collection. For a simple survey, this category meets criteria for waiving written consent in favor of oral consent. However, the study team will proceed with written consent for the UG3 phase but may consider a different plan for UH3 based on the expected number of patients involved and the nature of the activity. **Category 3:** Subset of 450 patients (UH3) who consent to giving a video ACP declaration via a tablet device. This category requires written opt-in consent; videos will be sent to Boston Medical Center for analysis. **Category 4:** 30 clinicians (UG3)/360 clinicians (UH3) who participated in the skills training who respond to an anonymous email survey. Survey contains language about the intent of the research and that survey completion is voluntary. Written consent is not required and consent is implied upon completing the survey. **Category 5:** 15 clinicians and administrators (UG3) interviewed by telephone about their experience with the intervention. Written consent is not required and an altered consent process is reasonable. The study team will seek email consent in advance and oral consent at the time of interview. No information about participants will be retained. **Category 6:** 72 clinic staff and executive sponsors who participate in webinars to discuss barriers and facilitators around implementation. These webinars do not occur until the intervention is turned on at their site. Because clinics will need to be prepared to share challenges and process experiences, the study team plans to seek oral consent in advance of the webinars. Regardless, it is unclear whether the informants here would be considered to be human subjects under federal regulations, so the team will consider this issue and discuss with the IRB.	clinical research" about different approaches to disclosure.
Privacy/HIPAA	• The method of harvesting patient data for Category 1 meets criteria for general HIPAA waiver. The other categories involving PHI (protected health information) currently have plans in place for obtaining consent where a HIPAA authorization could be obtained.	

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	• Participants will be trained on using the tablets for the video declarations. Patients will set a password and use a USB, so no videos will reside on the tablets.	
Monitoring and oversight	• ACP PEACE plans to establish a Data and Safety Monitoring Board (DSMB) that will include a biostatistician and researchers from outside Dana-Farber and MGH with expertise in geriatrics, oncology, ACP, and cluster RCTs (details in supplemental material). • Per NIH policy, the overseeing institute, NIA, will identify 3 members to sit on the DSMB to review the protocol and identify any safety issues every 6 months. • It was suggested that the study team consider supplementing DSMB members with members who have expertise in EHR data and health data access since the timing of harvesting data in the trial may have an impact on when reviews are scheduled, ensuring the informatics are in place, etc. • Study team plans to have a data metric from each clinic at the end of each step.	
Issues beyond the study	• A certificate of confidentiality will be automatically provided per new NIH policy. This certificate adds provisions for future research uses and confidentiality obligations for future data sharing. • One goal of the NIH Collaboratory demonstration projects is to learn generalizable issues from pragmatic trials as distinct from traditional trials. For example, using a data monitoring committee (DMC) to ensure that the intervention is actually being delivered and ensuring the quality of the data. Need to be clear on instructions given to the DSMB or DMC. • A global question for the Collaboratory involves whether vulnerable subjects might be inadvertently enrolled in PCTs, and how that would be handled. • Consider discussing with PIs of the TiME and ICD Pieces demonstration projects how their studies approached opt-out and how/when it was actually used.	

2. Specific Aims: Too many Americans with serious illness die after receiving aggressive life-sustaining interventions that do not reflect their values, goals, and preferences.(1-4) Patients over age 65 and with cancer disproportionately experience this phenomenon and thereby suffer more.(5-7) Despite multiple calls for change from the Institute of Medicine, NIH, medical societies, and the public, many older patients with advanced cancer continue to die in acute care hospitals often tethered to technology that does not advance their goals.(2, 8, 9) Clinicians and health systems require evidence-based and disseminable approaches that promote high-quality, high-value, goal-concordant care that leaves patients feeling cared for and in control.

Advance care planning (ACP) empowers patients to express their values and goals for care before they become too ill to do so.(10-13) ACP also prepares patients, and their families, to make difficult decisions in real time when the moment arises.(14) Communication about the future remains one of the few interventions associated with enhanced patient-centered outcomes and higher satisfaction with care at the end of life.(15-18) Although ACP is fundamental to high-quality serious illness care, a crucial gap in the science of ACP persists: Can effective ACP interventions that improve patient knowledge and enhance clinician communication skills be disseminated and delivered to health systems in a manner that achieves sustainable and patient-centered benefits? The maximal public health impact of ACP will be achieved when these interventions are implemented effectively and efficiently on a large scale.

To address this gap, we have developed a **Comprehensive ACP Program** that implements ACP routinely into regular cancer care. The Comprehensive ACP Program combines two well-tested, evidence-based, and complementary interventions: clinician communication skills training and patient video decision aids. This inclusive ACP approach treats patients and clinicians as equal stakeholders providing both with the communication skills and tools needed to optimally make informed decisions before the toughest choices arise. We have shown the efficacy of the elements of the Comprehensive ACP intervention in several small randomized controlled trials (RCTs) for older patients with cancer.(19-23) Based on this evidence and the ease with which these interventions can be used, several large health care systems and the entire state of Hawaii have begun to adopt the component parts. However, these early initiatives were not designed to rigorously evaluate outcomes, an essential step prior to the widespread implementation of these tools in practice.

The **overall objective** of this application is to reduce the burden of cancer and its consequences for an aging US cancer population. To accomplish this, we propose to plan (UG3) and conduct (UH3) a pragmatic stepped wedge cluster randomized trial (SW-CRT) of a Comprehensive ACP Program among older oncology patients. We will recruit patients from organ-based oncology clinics served by three major health care systems: Duke Health (North Carolina), the Mayo Clinic (Minnesota), and Northwell Health (New York). *We hypothesize that a Comprehensive ACP Program of clinician serious illness communication skills training combined with video ACP interventions for patients will improve and sustain rates of ACP*. We will test our hypothesis and achieve our objective through the following **Specific Aims**:

Aim 1 (UG3): To establish the ***organization, processes, and infrastructure*** necessary to develop all aspects of a pragmatic SW-CRT of the intervention for 4,500 patients over 65 with advanced cancer in three health care systems, and to ***pilot test*** the intervention study protocol in one oncology clinic in each system.

Aim 2 (UH3): To test the combined effects of a Comprehensive ACP Program on rates of ascertainable quality measures of end-of-life care. We will conduct a SW-CRT across all oncology practices in the three systems and evaluate the effectiveness of the intervention by comparing the following outcomes among ***4,500 patients over 65 with advanced cancer***:

Advance care plans completion; Medical orders for resuscitation preferences in the electronic health record; Palliative care consultations; and Hospice use. ***Hypothesis****: A higher proportion of patients in the intervention phase (vs. control) will: complete advance care plans* ***(primary trial outcome),*** *have documented electronic health record orders for resuscitation preferences, be seen in palliative care consultation, and enroll in hospice.*

Aim 3 (UH3): To characterize detailed patient-centered outcomes, including confidence in future care, communication and decisional satisfaction, and decisional regret in a subgroup of 450 patients over 65 with advanced cancer, as well as analyses of video declarations from 240 of these patients about their wishes. ***Hypothesis****: Patients in the intervention phase (vs. control) will have improved outcomes.*

IMPACT: Clinician communication training along with video decision support is a practical, evidence-based, and innovative approach to uniformly provide robust ACP. This work has the potential to improve the quality of care provided to millions of older Americans with cancer. Helping oncologists better serve the most frail and vulnerable older patients by delivering more patient-centered, goal-concordant care could dramatically improve the care of older patients with cancer in health systems.

THE DETAILED METHODS FOR THE <u>UG3 PHASE</u> OF THE PROJECT ARE DESCRIBED BELOW.

3.C.ii. (UG3) Overview of Aim 1: In the UG3 year, we will develop and refine the detailed plans for all aspects of the proposed pragmatic stepped wedge cluster randomized trial (SW-CRT). Specifically, we will: 1. Establish the organizational structure of the project; 2. Develop all the processes and infrastructure needed to conduct the trial; and, 3. Pilot test the study intervention protocol in one oncology clinic at each of the three health care system sites (Duke, Mayo, and Northwell). ***Details of the actual study methods are described in the UH3 phase.***

DETAILED METHODS FOR THE <u>UH3 PHASE</u> OF THE PROJECT ARE DESCRIBED BELOW.

3.C.iii.a. (UH3): Overview: In the 4-year UH3 phase we will conduct a pragmatic SW-CRT of a Comprehensive ACP Program in 36 organ-based oncology clinics at three world-class health care systems: Duke Health, the Mayo Clinic, and Northwell Health. Some of the proposed methods may be refined based on our pilot work conducted in the UG3 phase. Based on the finalized randomization scheme for the 36 clinics completed during the UG3 year, we will roll out the Comprehensive ACP Program at two oncology clinics in each of our health care systems every six months. Our intervention training team will travel to each system to deliver a communication training session, and to supply tablets on which patients, caregivers and clinicians can view the video decision aids, and instruction in their use. Every six months, two additional oncology clinics at each site will be trained in communication skills and have access to the videos until the beginning of the final UH3 year (total of six waves of trainings or "steps"; total of 12 clinics at each site; a total of 36 oncology clinics during the course of the UH3 phase). The data needed to assess the outcomes will be derived from the health care systems' EHRs; a small subgroup of patients will also be surveyed to assess patient-centered outcomes. Obtaining, merging, and cleaning data will occur throughout the UH3 phase to ensure adequate follow-up time and will end six months into the final UH3 year. Data analyses, manuscript preparation, and dissemination of the findings will occur during the final six months.

The Comprehensive ACP Program combines two well-tested, evidence-based, and complementary interventions: communication skills training and patient video decision aids. The videos are intended to reinforce, not replace, clinician counseling. There will be flexibility with regards to which clinicians (e.g., doctor, nurse, social worker) will introduce the videos to

patients and/or caregivers, what triggers/reminders will be implemented to help clinicians initiate ACP conversations during clinic visits with patients, and which videos among the entire suite will be used for individual patients. This is a SW-CRT in which the unit of random assignment is the clinic but the unit of analysis is the patient. While the intervention will be implemented clinic-wide, we will measure outcomes in our targeted sub-population for whom the opportunity and need to improve ACP is greatest: patients over 65 with advanced cancer (Aim 2). Outcomes will include: advance care plans, medical orders in the EHR for resuscitation preferences, palliative care consultations, and hospice use. Additional patient-centered outcomes (Aim 3) will richly characterize the experience of ACP for patients as well. The primary outcome for this pragmatic trial is advance care plans in older patients with advanced cancer. ***We hypothesize that a Comprehensive ACP Intervention of clinician communication skills training tailored toward goals-of-care conversations combined with video ACP interventions for patients will improve and sustain rates of ACP*.**

3.C.iii.g. Data Collection, Sources and Management
3.C.iii.g.1. Data Collection Protocol:

Patients: Baseline data collection of the 36 randomized clinics will begin by month 9 of the UG3 phase. Data Collection will continue and occur throughout the UH3 phase of the trial. Our primary (advance care plans) and secondary (preferences for resuscitation, palliative care consults, hospice use) outcomes will be abstracted from the EHR and the local tumor registry. Thus, no additional data collection will be done by the research team since these data are obtained as part of usual clinical care. For our exploratory patient-centered outcomes (confidence, video declaration, etc.), data collection will occur with an in-person survey conducted by a trained RA at each clinic site.

A subgroup of older patients with advanced cancer (N=450) will have an in-person survey over the course of the first 36 months of recruitment (≈13 patients per month at all three health care systems; ≈4 patients per month at each site). Surveys will be evenly distributed among the three health care systems (i.e., 150 patients from each system), and will include an even number of surveys of patients randomly chosen to clinics in the control phase (i.e., 75 patients surveyed in control phase) and in the intervention phase (i.e., 75 patients surveyed in intervention phase). From among this group of 450 participants, we aim to conduct the video declaration of preferences activity with 240 patients.

During the control and intervention phases of the trial respectively, an RA will use the EHR to identify potential participants with advanced cancer being seen in the clinic. The RA will review a list of scheduled patients two weeks prior to their clinic visit. Only returning patients (i.e., not new consults) who speak English and are known to the clinicians will be considered. Using the EHR and the International Classification of Diseases and Related Health Problems (ICD-10) code system, the RA will initially identify potential participants over age 65 with advanced cancer. The RA will use a broad selection of ICD-10 codes for advanced cancer in order to be as inclusive as possible in the screening process. The RA will then review the EHR to verify that the patient meets eligibility criteria. To conduct this screening procedure, a waiver of individual authorization for disclosure of personal health information (HIPAA) will be obtained from each site.

For those patients meeting all the criteria for advanced cancer, the RA will randomize the order of scheduled patients and then start at the top of this list and go down until fulfilling the enrollment target. The RA will then contact the patient's primary oncologist by email to solicit his/her opinion as to whether the patient is otherwise appropriate to approach for participation based on the clinician's more intimate knowledge of the patient's clinical status, psychological disposition, and decision making capacity. Once a potential subject is identified, a letter outlining the project will be mailed to the patient prior to the clinic visit.

On the day of his/her clinic visit, the patient will be approached at the conclusion of the scheduled clinic appointment to further explain the study and obtain written informed consent. The RA will verify the ability of the subject to provide consent by explaining the nature of the study and having the subject repeat (teach-back) the aims and risks of the study. Only those participants who can understand the aims of the project, what their involvement entails, that participation is voluntary, and the risks and benefits of participation will be eligible for the study.

Based on our prior studies *(See Section 3.C.i.b.),* data collection is estimated to take no longer than 30 minutes per patient (15 minutes for survey questions, 15 minutes for video declaration) and will be conducted after the scheduled clinic visit. The relatively brief interviewing time (30 minutes) in which the survey is conducted should assure completion of the interview without burdening participants who have advanced cancer. We do not foresee the additional time to complete the survey to be a barrier to successful recruitment and completion of the protocol.

All survey interviews will be conducted by a RA using a structured script. Participants will be provided written copies of the questions to follow along during the in-person interviews. For the subgroup of patients who complete the inpatient surveys, the RA will also ask participants to complete a video declaration. For those participants that agree to the video declaration, they will proceed with recording of their video declarations.

To assist participants in creating a video of themselves describing their ACP preferences, the RA will begin by reading a standardized introduction to the subject: *"Imagine you weren't able to talk to your doctors or family because you were very sick. We would like you to make a video about your preferences for medical care so your doctors and family can understand what's most important for you. Please try to be specific. For example, if you could not eat by mouth would you want doctors to insert a feeding tube? Or if you could no longer breathe on your own, would you want the doctors to place you on a breathing machine – a mechanical respirator? I'll show your video to you when you are done. If you aren't happy with it, you can record it again. Do you have any questions for me before we get started?"* The introduction will be pilot tested during the UG3 phase and modified as needed. The RA then uses the camera on the tablet (e.g., iPad) as a video device to record the subject. The tablet will be situated so that the subject is not viewing themselves on screen while they are talking, to lessen feelings of self-consciousness while recording. The RA will provide prompts as needed, such as if the person is exhibiting extreme hesitation in not knowing what to say, or if the person does not address their wishes regarding CPR or intubation. In these cases, the RA will ask some questions to facilitate the video process. When the recording is complete, the RA will play the video for the subject to see if they feel it accurately represents their preferences and if they would like to re-film their video declaration. (In our preliminary study, one out of 15 patients wished to re-record their video. However, we feel it is important to allow participants this flexibility when needed. Patients are able to re-film as many times as they want.) The patient will be given an online link to access the video, and will be asked if the patient would like the video to be sent to family, friends or the oncologist.

The RA will monitor the EHR and local tumor registry to see if any of the participants from the in-person survey die over the course of the trial. For those participants that die, the last three months of their EHR will be reviewed to assess their preferences, interventions received, and place of death and this will be compared to recorded wishes, either in video or ACP note format. ***Thus, in-person surveys, video declarations, and EHR chart reviews of a small subgroup of older patients with advanced cancer will be conducted throughout the UH3 phase of the study.***

Clinical Staff Survey: All clinicians that participate in the VitalTalk training (N=10 clinicians per oncology clinic; 36 clinics * 10 clinicians = 360) will receive an online survey (less than three

minutes) regarding demographics, experience with taking care of patients, communication training history, and socioemotional orientation (97) *(See Section 3.C.iii.h.1.iv. Clinician Outcomes)*.

3.C.iii.g.2. Data Sources:

3.C.iii.g.2.a. Electronic Health Record (EHR): All 3 sites have established EHR systems from which we will obtain our primary and secondary outcomes: Duke and Mayo use the Epic EHR, and Northwell uses Allscript. Each EHR has been in use at each site for clinical and data capabilities.

3.C.iii.g.2.b. Local Tumor Registry: Each of the 3 sites has a functioning tumor registry used for both clinical and research capabilities and each will provide the data necessary for capturing and extracting the necessary cancer diagnosis characteristics for the study.

3.C.iii.g.2.c. Surveys: Patient surveys will be completed in-person at each site by a trained study RA. Data will be entered into the REDCap software suite, approved institutionally for storage of sensitive information. Clinician surveys will be completed by email.

3.C.iii.g.2.d. Video Declarations: Data sources include the digital video recording, a transcript of what was said by the subject during the recording, and any notes taken by the RA about the video declaration process (e.g., subject was upset, needed to record more than once, etc.).

3.C.iii.g.2.e. Implementation: Implementation assessments will be completed on transcripts of recordings of webinars and key-informant interviews.

3.C.iii.h. Data Elements (Table 4).
3.C.iii.h.1. Patient-level data:

3.C.iii.h.1.i. Identification of target population & other independent variables:
Demographic: We will obtain key baseline patient demographic information from each site's local EHR. This will include: From EHR: age, gender, race/ethnicity, education, 1^{o} language, marital status, and religion.
Diagnosis: We will obtain baseline information about cancer diagnosis from each local tumor registry and the EHR. This will include: Cancer type, stage, and most recent chemotherapy agent.

3.C.iii.h.1.ii. Pragmatic Outcomes:
ACP documents: We will obtain the presence and content of ACP documents from each site's EHR. These will include: Scanned and completed advance care plans (advance directives such as a living will or health care proxy; POLST form).
Resuscitation Preferences: We will obtain the presence and content of orders for resuscitation and treatment preferences from each site's EHR. These will include: Full code, Do-not-resuscitate (DNR), Do-not-intubate (DNI), Do-not-hospitalize (DNH), and documented preferences around feeding tubes, artificial hydration, and dialysis. We will obtain the last order and the history of orders for each patient during the study period.
Health services utilization: We will obtain the number, count, and timing of palliative care consultation from each site's EHR. We will obtain additional utilization measures from each site's local tumor registry. These will include: hospice use, final chemotherapy and/or biologic agent and timing of delivery of last dose.
Death: We will obtain death information from each site's local EHR and tumor registry. This will include: place of death, date of death, interventions in last three months of life.

Intervention implementation: We will obtain outcomes data about the use of the ACP Decisions Video App by monitoring the use of the videos remotely via the app that will be available on desktops or tablets.

3.C.iii.h.1.iii. Patient-Centered Outcomes:
Patient confidence: From in-person survey: We will ask patients how confident they are that they will get the type of medical care they want if they become seriously ill. This is a single question with Likert responses ranging from not at all to very confident.
Patient satisfaction with clinician communication: From in-person survey: We will administer the 10-item communication subscale from the Consumer Assessment of Health Plans (CAHPS®) and ask patients to focus on recent ACP communication.
Patient decisional satisfaction: From in-person survey: We will ask the Satisfaction with Decision Scale, a six-item scale that has excellent reliability (Cronbach's alpha = 0.86) and good discriminant validity. It includes items such as "The decision I made was the best decision possible for me personally" and "I am satisfied that my decision was consistent with my personal values."
Patient decisional regret: From in-person survey: We will ask the five-item Decision Regret Scale, which measures regret after a decision has been made with questions such as "I regret the choice that was made" and "I would go for the same choice if I had to do it over again." It has a Cronbach's alpha of 0.81-0.92 and correlates well with other measures of regret.
Video declaration: From the video declarations, data elements will include frequency of codes that categorize what was discussed in the video (ACP, existential and spiritual issues, etc.) and themes which summarize our codes to richly describe the patient's experience. In addition, we will measure the clarity with which the video declaration communicates a clear clinical plan and the extent to which it is concordant with documented wishes *(See Section 3.C.iv.c. for further details on the qualitative analysis plan).*

Table 4: Data Element and Sources						
Data Element	**Purpose**	**SOURCE**				
		EHR	**Tumor Registry**	**Survey**	**Video App**	**Audio Record**
Patient-Level						
Demographic	covariate (moderator)	X				
Cancer type & stage	target sub-population identification, covariate	X	X			
ACP documents	1º outcome	X				
Resuscitation Preference	2º outcome	X				
Palliative care consult	2º outcome	X				
Hospice use	2º outcome	X	X			
Death	covariate	X	X			
Goal-concordant care	Exploratory	X				
Intervention/Video use	monitoring fidelity				X	
Patient-Centered						
Patient confidence	2º outcome			X		
Communication satisfaction	2º outcome			X		
Decisional satisfaction	2º outcome			X		
Decisional regret	2º outcome			X		
Video declaration	Exploratory				X	
Clinician-Level						
Demographic	covariate (moderator)			X		
Experience	covariate			X		
Communication training	covariate			X		
Socioemotional Orientation	covariate			X		
Implementation						
Practice variation	Exploratory					X
Leadership/Teamwork	Exploratory					X

Protection of Human Subjects

The ***overall objective*** of this application is to reduce the burden of cancer and its consequences. To accomplish this, we propose to plan (UG3) and conduct (UH3) a pragmatic stepped wedge cluster randomized trial (SW-CRT) of a Comprehensive ACP Program among older oncology patients. We will recruit patients from organ-based oncology clinics served by three major health care systems: Duke Health, the Mayo Clinic, and Northwell Health. ***We hypothesize that a Comprehensive ACP Program of clinician serious illness communication skills training combined with video ACP interventions for patients will improve and sustain rates of ACP***. We will test our hypothesis and achieve our objective through the following **Specific Aims**:

Aim 1 (UG3): To establish the ***organization, processes, and infrastructure*** necessary to develop all aspects of a pragmatic SW-CRT in three health systems and to ***pilot test*** the intervention study protocol in one oncology clinic in each system.

Aim 2 (UH3): To test the combined effects of a Comprehensive ACP Program on rates of ascertainable end-of-life variables. We will conduct a SW-CRT across all oncology practices in the three systems and to evaluate the effectiveness of the intervention by comparing the following outcomes among ***4,500 patients over 65 with advanced cancer***: 1. Advance care plans completion, 2. Medical orders for resuscitation preferences in the electronic health record (EHR), 3. Palliative care consultations, and 4. Hospice use. **Hypothesis:** ***A higher proportion of patients in the intervention phase (vs. control) will: complete advance care plans (primary trial outcome), have documented electronic medical orders for resuscitation preferences, be seen in Palliative Care consultations, and enroll in hospice.***

Aim 3 (UH3): To characterize detailed patient-centered outcomes in a subgroup of 450 patients over 65 with advanced cancer (240 of which will also complete video declarations of their wishes). **Hypothesis:** ***Patients with advanced cancer in the intervention phase (vs. control) will have improved patient-centered outcomes.***

Accordingly, this Human Subjects Research meets the definition of a clinical trial.

1. Risks to Human Subjects

a. Human subjects involvement, characteristics, and design

We will enroll patients over the age of 65 with advanced cancer cared for in outpatient practices participating in our study. We anticipate that about half of the patients will be female and that the patients will be ethnically, socioeconomically, and culturally representative of the populations served in the three geographically distinct health care systems: Duke (South); Mayo (Mid-West); and, Northwell (Mid-Atlantic).

As specified in the RFA, the primary outcome needs to come from electronic records.

During the UG3 planning phase of the project there will be three classes of subjects: (1) 375 patients with data collected electronically from the clinical data repositories of the three health systems (§**3.C.ii.b.**); (2) 15 patients (5 each from the pilot clinic site from each health system) enrolled to participate in survey data collection (§**3.C.ii.b.5.)**; (3) 30 clinician email surveys for clinicians who participate in in-person training (§**3.C.ii.b.2.)**; and, (4) 15 clinicians and administrators interviewed by telephone about their experience with the intervention (§**3.C.ii.b.8)**.

During the UH3 phase of the project there will be six classes of subjects: (1) 4,500 patients with data collected electronically from the clinical data repositories of the three health systems (§**3.C.iii.d.3**); (2) 450 patients over the age of 65 with serious illness enrolled to participate in survey data collection (§**3.C.iv.c**); (3) a subset of 240 of these 450 surveyed patients who participate in the 'video declaration' activity (§**3.C.iii.g.2.d**); (4) 360 clinicians who participated in the training will be enrolled to do email surveys (§**3.C.iii.g.2.c**); and, (5) 72 clinic staff and executive sponsors who participate in implementation webinars(§**3.C.iii.g.1**).

Patients who participate in the survey will receive $20 compensation (in the form of gift card or equivalent) for their in-person survey. The short in-person survey will include questions regarding confidence, satisfaction with physician communication, patient decisional satisfaction and regret, and may or may not include a video declaration of preferences.

The video declaration of preferences will be conducted with a subset of consenting patients. The declaration will comprise a set of data sources including the digital video recording, a transcript of what was said by the subject during the recording, and any notes taken by the RA about the video declaration process (e.g., subject was upset, needed to record more than once, etc.).

We are not targeting any special vulnerable populations; however, we will not exclude pregnant women. Pregnancy status is irrelevant to participation in this study and will not be asked or assessed.

Sampling plan:

Our three health care systems are world class centers for cancer care and include a socioeconomically and culturally diverse group of people from three geographically distinct networks of oncology clinics: Duke (South), Mayo (Mid-West), and Northwell (Mid-Atlantic). Our three health care systems represent the geographic diversity of health care systems in the United States. All three health care systems' oncology clinics are organized based on organ/system (lung, brain, gastrointestinal, genitourinary, etc.), and each organ-based clinic will be treated as an individual clinic site. Oncology clinics will be eligible to participate if they include more than one practicing oncologist and serve a patient population that is at least 30% over the age of 65. Based on the three health care systems' most recent data, we have identified 39 candidate oncology clinics (13 from each system: 1 pilot clinic for the UG3 phase; 12 clinics for the UH3 phase).

Clinic-wide interventions:

As the Comprehensive ACP Program will be implemented facility-wide, all patients randomized to clinics receiving the intervention will be able to view the ACP videos and be cared for by clinicians who are trained in communication skills. The Comprehensive ACP Program combines two well-tested, evidence-based, and complementary interventions: communication skills training with the VitalTalk program and the ACP Decisions patient video decision aids. The suite of ACP Decisions video tools are designed to address common decisions confronting patients with advanced cancer and their families. As the intervention is rolled out, clinics will undergo a half-day face-to-face VitalTalk and ACP Decisions training.

Clinics in the control phase will use existing ACP procedures in place at their facilities until initiation of the intervention.

Procedures for assignment to a study group

Prior to randomization, the size of participant clinics will be determined based on the number of oncologists on staff (≤ 3 vs. >3). To balance the size of clinics between intervention and control phases of the trial, we will pair clinics of different sizes (one with ≤ 3 and one with >3) to receive the intervention at the same time. The step in which the pairs of oncology clinics within each health care system receive the intervention will be randomly assigned by the study statistician. The randomization scheme for the 36 participating clinics will be finalized during the UG3 year.

Based on the finalized randomization scheme for the 36 clinics completed during the UG3 year, two oncology clinics at each of our health care systems will have the Comprehensive ACP Program rolled out in the clinic every six months. Our intervention training team will travel to each system to deliver a large group forum communication training session, and tablets on which patients, caregivers and clinicians can view the video decision aids. Every six months, two additional oncology clinics at each site will be trained in communication skills and have access to the videos until the beginning of the final UH3 year (total of six waves of trainings or "steps"; total of 12 clinics at each site; a total of 36 oncology clinics during the course of the UH3 phase).

b. Sources of materials

The data needed to assess the primary outcomes will be derived from the health care systems' EHRs. Outcomes will include: advance care plans, medical orders in the EHR for resuscitation preferences, palliative care consultations and hospice use. We will also obtain information from local tumor registries for cancer diagnosis characteristics.

For a subset of patients, we will also have patient-centered outcomes from patient surveys and video declarations and we will have interviews and surveys from clinicians, clinic managers, and executive sponsors.

Data sources include in-person surveys with patient participants, email surveys with clinicians, transcripts of recordings of webinars and key-informant interviews, and the digital video recording and transcript of what was said by the subject during their video declaration and any notes taken by the RA about the video declaration process (e.g., participant has chosen to re-record their declaration). In addition, we will work with each health system to identify which of the 450 survey patient participants have died and will review medical records for the three months preceding death to compare the care received with documented preferences.

We will measure and monitor ACP video use by patients and clinicians using the app and electronic platform, which documents the date the patient and/or family were shown the video(s), which videos were viewed, and the playthrough rate (what percentage of the video was actually viewed).

Data Collection, Integrity and Storage: Each data collection site PI, Drs. Tilburt, Zafar, and D'Olimpio, will maintain and adhere to the process and procedures for the protection of human subjects and protected health information for their covered entities. All data collected by the RAs will be stored in password protected servers. Participant identifiers will be kept in separate password protected files and a third linking file will be maintained. The linking file will also be password protected, access will be minimized, and a logging feature will be used to identify each user and instance of use. Only the minimum amount of PHI necessary will be collected from study subjects. No linking files will ever leave a covered entity. Data from each of the

clinical sites will be transmitted via secure, institutionally approved methods to Dana-Farber for data management and MGH and BMC for analyses.

c. Potential risks

The interventions are low risk and are the standard of care in many health care systems. The interventions will be available to all patients in the clinic not only patients over the age of 65 with advanced cancer. The clinic is the unit of randomization to a minimal risk intervention.

We anticipate little risk to the subjects in this study. To be sure, such interactions may make some patients uncomfortable, sad, or even distressed as they contemplate death and dying with their provider. However, such interactions are explicitly part of the standard of care. Patients receiving the intervention will be asked to listen to and watch videos that contain verbal narratives and visual images related to ACP by clinicians (i.e., physicians, physician assistants, nurses, social workers) in their clinics trained in this practice. The videos describe three levels of care (life-prolonging care, limited care, and comfort care), and/or specific treatments (i.e., CPR, feeding tubes), and therefore may be distressing. Using similar video decision support tools in our prior studies that have included more than three thousand participants, including patients with advanced cancer, over 90% of subjects rated the videos as highly acceptable, helpful or extremely helpful, and would recommend or highly recommend them to others. In these prior studies, we have never had to stop an interview because of subject distress. However, as part of clinician training in this trial, clinicians will be instructed that should a patient or family member become distressed while watching a video and prefer not to continue, the video should be stopped.

In addition, there is a risk for loss of privacy, but we will have a series of mutually reinforcing measures to mitigate this risk.

2. Adequacy of Protection Against Risks

a. Recruitment and Consent Procedures:

There are special informed consent considerations in this pragmatic SW-CRT: the oncology clinic is the unit of randomization, the intervention is of low risk and will be implemented facility-wide, and data for our primary outcome is ascertained from existing sources. Thus for this aspect of our proposal, we will seek a waiver of individual informed consent and HIPAA authorization after careful review of the criteria to do so. The research involves no more than minimal risk to the subjects as described above. We do not believe the waiver will adversely affect the rights and welfare of the subjects. As a pragmatic trial of thousands of oncology patients and clinicians, this research could not practicably be carried out without the waiver nor without access to and use of PHI of patients. Finally, we have developed a plan to protect identifiers from improper use and disclosure.

For the Mayo Clinic site, we will specifically exclude reviewing records of patients who have opted out of medical records research, as indicated in their Minnesota Research Authorization form.

For the subgroup of patients (N=450) being surveyed for patient-centered ***secondary outcomes***, individual written informed consent will be obtained. This will explicitly include permission to extract data from the EHR for the evaluation of the goal-concordant care assessment for those who die during the study period and for sharing data with Dana-Farber

and Boston Medical Center investigators for analyses. For the 240 of these 450 participants who create a video declaration of their wishes, consent will include permission to share identifiable images with investigators at Boston Medical Center for analytic purposes as we have done previously.

The main IRB submission will go through Dana-Farber Cancer Institute, the primary institution, with additional submissions to the Massachusetts General Hospital, Boston Medical Center, Duke, Mayo, and Northwell IRBs, which will likely cede primary review to Dana-Farber.

In addition, we will be asking for a HIPAA waiver for the review of patient data in preparation for this research (preparatory for research waiver). This will be needed to identify potential patient participants. It is our assessment that this study meets the regulatory requirements for the preparatory for research provisions of the HIPAA privacy rule (45 CFR 164.512(i)(1)(ii)) and will work with each institutional IRB and Privacy Officer to establish that this does meet the standards for the security of protected health information. In accordance with this provision, only researchers and staff who are a part of the "covered entity" will use the preparatory research provision to contact prospective research subjects and no identifiable PHI will leave any covered entity without consent and an approved procedure.

For all classes of professionals who will be subjects in this research we will have consent procedures in place in accordance with the mode of interactions (in person, by phone, or by email) with a waiver of documentation when needed.

b. Protections against risk

We will emphasize that participation in this research is voluntary.

Qualitative interviews with providers, staff, and management will be conducted by personnel who have no affiliation to these subjects' employer. It is quite important that providers, staff, and management are able to share openly, even if their feedback may be critical.

We will transmit no identifiable data back to the clinic sites to avoid any risk of retribution, retaliation, or adverse consequence to disclosures which may come about through this process. In addition, we will seek a Certificate of Confidentiality to protect providers, staff, and management from risk of disclosure.

3. Potential Benefits of the Proposed Research to Human Subjects and Others

There is the potential for patients and clinicians in the clinics to benefit from the study by having their treatments better aligned with their preferences. The minor risks for the subjects in this study may be considered counterbalanced by the potential direct benefits and knowledge gained. The results gleaned from the study are intended to improve the ACP of the overall outpatient clinic population, and particularly those with advanced cancer. Thus, the risk/benefit balance for this study appears favorable.

4. Importance of the Knowledge to be Gained

There is the potential to validate an intervention that could ensure that treatments are better aligned with patients' preferences. The minor risks for the subjects in this study may be considered counterbalanced by the potential direct benefits and knowledge gained. The results gleaned from the study are intended to improve the ACP of the overall outpatient clinic

population, and particularly those with advanced cancer. Thus, the risk/benefit balance for this study appears favorable.

Data and Safety Monitoring Plan

Oversight and Protocol Compliance: All research personnel will participate in human subjects training, an annual booster training, one-time data integrity and security training, and training on the protocol, which will include simulation and practice for all protocol procedures including obtaining informed consent and confirming comprehension. This will be supervised by Dr. Paasche-Orlow, who is a national expert in the informed consent process. We will have regular team meetings and regular surveying reliability checks to ensure protocol compliance. Patient surveyors will be supervised through monthly conference calls and one-on-one communication, as needed. The procedures described here address our efforts to minimize the risk of breach of confidentiality and to ensure that procedures remain in place for the protection of human subjects. All data management will be conducted at Dana-Farber Cancer Institute. The Center's researchers and staff have many years of experience working with similar data files.

Data Safety and Monitoring Board (DSMB): A DSMB will be set up for this large multi-site pragmatic trial. DSMB features will be written in a DSMB charter, including: membership (N=3-5), meeting schedule, format, and report form, and roles and responsibilities. DSMB members will include a biostatistician and researchers from outside Dana-Farber and MGH with expertise in geriatrics, oncology, ACP, and cluster RCTs. The roles and responsibilities will include, but are not limited to, defining and monitoring the following: adverse events, data quality and handling, recruitment, protocol modifications or deviations, and all other factors that might affect study outcome, participant safety, or ethics of the trial. The DSMB will be responsible for making recommendations regarding trial termination or modifications based on these activities and preset stopping rules. A mechanism for recording and reporting adverse events to the IRB(s) will be developed.

Adverse Event Reporting: This study presents minimal risk to participants. Nonetheless, the PIs will monitor and report Adverse Events to the Dana-Farber IRB.

Enrollment of Women and Minorities

We will be enrolling women and minorities in this project and have included specific planned analyses to evaluate the relevance of these characteristics at both the patient and provider level. We anticipate that the participant characteristics will directly reflect the distribution of gender, race and ethnicity at our clinical sites. Similarly, provider characteristics will reflect the distribution of gender, race and ethnicity at our clinical sites. These details are reflected in the enrollment tables provided.

Enrollment of Children

All participants in the study activities for this proposal are adults. As such, we will not be enrolling children.