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Original Article

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

Design and rationale for a pragmatic stepped-wedge trial of older patients with cancer

Running Title: The ACP-PEACE pragmatic stepped-wedge trial

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ABSTRACT

Introduction: Advance Care Planning (ACP) is associated with improved health outcomes for patients with cancer and its absence is associated with unfavorable outcomes for patients and their caregivers. However, older adults do not complete ACP at expected rates due to patient and clinician barriers. We present the original design, methods, and rationale for a trial aimed at improving ACP for older patients with advanced cancer and the modified protocol in response to changes brought by the COVID-19 pandemic.

Methods and Analysis: The Advance Care Planning: Promoting Effective and Aligned Communication in the Elderly study is a pragmatic, stepped-wedge cluster randomized trial examining a Comprehensive ACP Program. The Program combines two complementary evidence-based interventions: clinician communication skills training (VitalTalk) and patient video decision aids (ACP Decisions). We will implement the Program at 36 oncology clinics across three unique U.S. health systems. Our primary outcome is the proportion of eligible patients with ACP documentation completed in the Electronic Health Record. Our secondary outcomes include resuscitation preferences, palliative care consultations, death, hospice use, and final cancer-directed therapy. From a subset of our patient population, we will collect surveys and video-based declarations of goals and preferences. We estimate 11,000 patients from the three sites will be enrolled in the study.

Ethics and Dissemination: Regulatory aspects of this trial include Institutional Review Board (IRB) approval via single IRB of record mechanism, Data Use Agreements among partners, and a Data Safety and Monitoring Board. We plan to present findings at national meetings and publish the results.

ARTICLE SUMMARY: STRENGTHS AND LIMITATIONS

- The strengths of this study lie in its pragmatic design, allowing for "real world" evidence for two interventions that have been previously tested in more controlled settings.
- The stepped wedge design is practical and considered the design of choice when it is logistically impractical to simultaneously roll out the intervention to half of the clusters.
- The biggest limitation we are facing at this time has to do with the possible notable change in secular trends due to the Coronavirus Disease 2019 and the impact that has on ACP. To address this issue, we have adjusted our analysis plan to account for these changes.

INTRODUCTION

More than half of newly diagnosed malignancies occur in patients over the age of 65[1] and that same population accounts for over two-thirds of all adult U.S. cancer deaths.[2] In addition to high mortality, older adults with cancer suffer disproportionately from receiving medical interventions that do not reflect their values and preferences.[3-5] Advance care planning (ACP) seeks to align medical care with patients' values and preferences.[6, 7] ACP is consistently associated with better outcomes[8, 9] while a lack of ACP is associated with greater use of unwanted medical interventions, more terminal hospitalizations, lower hospice use, higher healthcare costs, and worse bereavement outcomes.[3, 10-14] Despite evidence supporting ACP, participation rates remain low among older adults with serious illness, such as cancer.[15]

Effective ACP requires that patients experience accurate and comprehensible communication early in their illness,[14, 16-18] a collaborative effort requiring education for both patients and clinicians. Unfortunately, studies suggest that traditional written ACP can be ineffective in sufficiently informing patients and often occurs late in the disease process,[19-24] with the risk that patients' understanding is clouded by pain, medication, or psychological distress.[10, 20, 25] The heightened emotional state associated with hearing bad news late in a disease course interferes with patients' cognitive processing, and this reaction may be exacerbated by clinician inattention to affect.[21, 26-29] Patients assign considerable importance to their physicians' statements regarding ACP and the quality of communication[30] and while 90% of patients say they want to talk to their doctors about their stress and concerns,[31, 32] physicians generally, and oncologists specifically, often do not communicate effectively regarding ACP and end of life.[30, 32-38] Therefore, an effective intervention should both prepare patients for shared decision making and improve clinicians' communication skills.

We have developed a Comprehensive ACP Program to drive improved communication and ACP for an aging U.S. cancer population using a combination of empirically proven patient video decision aids and clinician communication skills training. This program integrates video decision aids for patients (ACP Decisions) and a clinician communication training program (VitalTalk) into 12 disease-based oncology clinics each across three health systems with the aim of improving conversations and documentation of ACP. By providing both patients and clinicians with the necessary tools and training, we create an inclusive approach to optimize ACP before the toughest choices arise for patients.

Most trials targeting older patients with serious illness evaluate interventions under ideal conditions and involve few facilities.[39-42] Thus, we need research for this population using pragmatic trials.[43] We sought to test this intervention in a manner that allows for improvements in processes as we learn them.[44] Advance Care Planning: Promoting Effective and Aligned Communication in the Elderly (ACP-PEACE) is a pragmatic stepped-wedge cluster randomized trial (SW-CRT) that conducts a real-world test of the Comprehensive ACP Program in older patients with cancer. In this paper, we present the design, methodology, and rationale for the ACP-PEACE trial and discuss our adjustments for the novel coronavirus COVID 19 pandemic.

METHODS

Overview

We are studying the combination of clinician training and patient videos via a pragmatic SW-CRT and analyzing electronic health records (EHRs) for ACP outcomes for patients aged 65 and older. Utilizing small sub-samples of patients, we will also assess patient-centered outcomes using surveys and video declarations in which patients discuss their values and preferences in

their own words on video (Figure 1). We used the SPIRIT reporting guidelines for this manuscript.[45]

Study Timeline

The ACP-PEACE study has two phases, a characteristic of the funding mechanism. The UG3 phase (year 1) of the study focused on developing and refining the intervention and data acquisition. In this phase we established our organizational structure, developed the processes and infrastructure needed to conduct the trial, and pilot-tested the study intervention in three clinics, one from each participating health system. During the UH3 phase (years 2-5), we planned to introduce the intervention to the 36 remaining oncology clinics in six-month waves; two clinics per system for a total of six clinics every six months (Figure 2).

Sites and randomization

We will draw participants from disease-based oncology clinics from three unique systems - Duke Health (North Carolina), Mayo Clinic (Minnesota), and Northwell Health (New York). These sites are geographically, socioeconomically, and culturally distinct. Each participating clinic has more than one practicing oncologist and to be eligible for randomization, at least 30% of the patient population must be age 65 or older.

For the UH3 phase, we have identified a total of 36 oncology clinics (12 per site) as candidate clinics based on recent data from each system. The pilot clinics that participated in the UG3 phase tested the intervention process and will not be included in the final analysis. In the UH3 phase, we will utilize stepped-wedge cluster randomization with the clinic as the unit of randomization. With the clinic as the unit of randomization, we avoid the contamination that can

occur when randomizing individuals within each clinic. The sequence of randomization was generated prior to initiation of the trial via random number generator. Every six months after the baseline, two clinics from each system will be randomized to the intervention. (Figure 3a)

During the original Step 2, COVID-19 spread throughout the country interrupting the stepped-wedge design in two key respects: (1) The team was unable to conduct the in-person trainings for the Step 2 intervention clinics; and, (2) ACP activities are likely to increase during this period due to a response to the pandemic, irrespective of the study. Upon the recommendation of the NIH Collaboratory Statistics Core, we modified the original design to "restart" the trial for the remaining 30 clinics using the original Step 2 as the new baseline. The training of the remaining 30 control clinics will be over four steps to keep the trial completion on the same overall timeline (Figure 3b).

Population

We will evaluate the outcomes for patients aged 65 or older with advanced cancer across all 36 clinics. As the intervention will be implemented clinic-wide, rather than targeted to specific study patients, all intervention clinic patients can receive the intervention. We will analyze data for patients with advanced cancer aged 65 or older; patients' data will be counted towards control or intervention based on the allocation of each clinic at the end of each period of the stepped-wedge design. Therefore, a given patient could contribute data during more than one period and could contribute data to both control and intervention periods.

During the UH3 years, research assistants at each site will conduct in-person surveys with 450 randomly selected patients (150 per site) for our secondary exploratory patient-centered outcomes. Patients selected for surveys will be distributed evenly among clinics within each

system and will include an equal number of surveys of patients from clinics in the control and intervention phases. Patients will be surveyed only once as patients surveyed in the control phase will be excluded from completing the later intervention survey. Additionally, from among this group of 450 surveyed patients, a sub-group of 240 will be randomly selected and asked to conduct a video declaration activity. All patients selected for surveys or videos will be excluded from the primary study population to avoid bias rendered from additional contact with the study team.

Intervention design, implementation, and adherence monitoring

The Comprehensive ACP intervention combines VitalTalk and ACP Decisions, two evidence-based interventions previously used separately, to create an innovative dual approach to improving ACP. These interventions are complementary, as one targets improvement of clinicians' skills and the other prepares patients for shared decision making. VitalTalk is the most widely disseminated teaching method for effective communication skills training based on practice and feedback on one's own communication skills. Supported by numerous previous studies,[46-52] VitalTalk leverages didactics, demonstration, and small group sessions using role play with trained actors portraying patients through which clinicians learn effective delivery of serious news, prognosis discussion, early and late goals-of-care conversations. For this study, the VitalTalk course will be a half-day session that teaches a framework for late goals-of-care discussions, including skills around delivery of serious news, responding to emotion, assessing prognostic awareness, identifying what is most important to patients, and making recommendations.

The ACP Decisions program uses short video decision aids to address the most common issues facing older patients with serious illness. Videos in over 25 languages can be prescribed to patients and caregivers and are easily accessed in a mobile app or through a web-based platform. The ACP Decisions videos have been shown to increase knowledge, decision certainty, and the stability of preferences over time, and to better inform the way that patients choose health care interventions towards the end of life.[53-72] The video collection includes certified video decision aids,[73] regarding ACP, advance directives, health care agents, goals of care, cardiopulmonary resuscitation, and hospice, that have been studied in a statewide implementation showing greater patient-aligned medical care.[72]

We will provide in-person training every six months at each new clinic added to the intervention period of the trial. The Comprehensive ACP training program utilizes the VitalTalk methodology and infrastructure and the ACP Decisions Program tools to instruct clinicians and staff on how to (1) more effectively communicate with patients with cancer, (2) have ACP conversations with patients, (3) introduce the videos to patients and families, (4) use the videos as an adjunct to ACP counseling by clinicians, (5) select the appropriate video(s) according to patient needs, and (6) use the application or electronic platform for viewing videos. The combined program will involve a half-day face-to-face joint VitalTalk and ACP Decisions training. Any staff member affiliated with the selected facilities will be eligible to participate in training. As staff turnover among the sites is expected, training will be made available on an ongoing basis throughout the trial.

Immediately following the initial training at each site, we will deploy the remainder of the intervention infrastructure. The ACP Decisions videos will be programmed into desktop devices, tablets, and password-protected electronic platforms of each health system's intranet.

When clinics initiate the intervention, they will implement the videos with all patients with flexibility as to which providers (physician, nurse, social worker) introduce the videos and exactly which videos are utilized to meet their patients' clinical needs. Additionally, the in-person clinician training will be supplemented with emails, pocket cards, offers of coaching, and online educational videos. The study team will facilitate dissemination of implementation successes and challenges via a learning network by conducting one-hour webinars at each of the practices randomized to the intervention every other month to discuss quality improvement activities relating to the study. The intensity of the VitalTalk training implementation will be assessed as the proportion of eligible staff trained, including new staff joining the practice over the implementation period. The intensity of implementation of the ACP Decisions videos will be assessed as the ratio of the number of videos viewed using the site-specific access codes captured at the ACP Decisions website to the number of eligible patients at each site for each six-month intervention period. Fidelity to the video component of the intervention will be monitored by tracking of video use (which videos are used at each clinic, playthrough rate, and frequency). Feedback on video viewing will be shared with each site at the end of each six-month implementation phase. Last, we aim to evaluate the impact of the study with a novel video declaration process, allowing patients to state their values and preferences in their own terms, which is described in detail in the Appendix.[59]

Control condition

Clinics in the control phase will use whatever ACP procedures already exist in place at their respective system. Although current ACP-improvement initiatives may be present and vary

from clinic to clinic, this heterogeneity reflects the current dynamic state of "usual" care and is therefore appropriate in this pragmatic trial.[43]

Outcomes

The outcomes of the ACP-PEACE trial can be divided into three main categories: patient-level, clinician-level, and system-level. Our primary outcome is the proportion of eligible patients with ACP documentation completed in the EHR. Presence of completed ACP documentation will be defined via one or both of the following two means: 1) Structured EHR data: scanned forms including advance directives, living wills, or Physician's Orders for Life Sustaining Treatment (or state-specific equivalent) and code status orders indicating Do Not Resuscitate Status (or similar site-specific codes for limitations on treatments) and 2) Natural Language Processing (NLP) extraction (described below in detail): clinical documentation that will include goals-of-care discussion, ACP, hospice discussion, discussion of palliative care, or limitations on code status. From the EHR or the local tumor registry, we are also determining demographic covariates and baseline data. Secondary outcomes include resuscitation preferences, palliative care consultations, death, hospice use/utilization at the end of life, and final cancer-directed therapy.

We are deriving patient-centered outcomes from the patient survey and video declarations. The surveys measure our patient-centered secondary outcomes such as patient confidence that their future medical care will match their values, satisfaction with their clinicians' communication,[74, 75] satisfaction with their medical decision,[76] and regret about their medical decision (Appendix).[77, 78] Finally, for each of the 450 surveyed patients who die during the study period, we will extract data, via a chart abstraction tool, regarding ACP preferences and

care received in the final three months of life to explore whether patients receive goal-concordant care.

We are also collecting a small set of clinician data points. Participating clinicians provide information on demographics, clinical experience, prior communication training, and socioemotional orientation.[52] Table 1 lists each data element, with its purpose, proposed source, and the target population from whom we need the data for successful completion of the study. System-level data measurement will include measurement of the training and video use as described above as well as exploratory analysis of coaching calls and implementation activities.

Table 1. Data Elements and Outcomes

Data Element	Purpose	Source	Population
A. Patient-Level			
1. Demographics	Covariate (moderator)	EHR, Tumor Registry	Entire study population
2. ACP documents	1º outcome	EHR	Entire study population
3. Resuscitation Preference	2º outcome	EHR	Entire study population
4. Palliative care consults	2º outcome	EHR	Entire study population
5. Hospice use/ Utilization at the end of life	2º outcome	EHR, Tumor Registry, Other	Entire study population – for those patients who die
6. Final Cancer-Directed Therapy	2º outcome	EHR, Tumor Registry	Entire study population – for those patients who die
7. Death	Covariate	EHR, Tumor Registry, Other	Entire study population
8. Patient confidence	2º outcome	Survey	Subgroup of 450 patients
9. Communication satisfaction	2º outcome	Survey	Subgroup of 450 patients
10. Decisional satisfaction	2º outcome	Survey	Subgroup of 450 patients
11. Decisional regret	2º outcome	Survey	Subgroup of 450 patients
12. Family Communication	Exploratory	Survey	Subgroup of 450 patients
13. Goal-concordant care	Exploratory	EHR	Subgroup of 450 patients
14. Video declaration	Exploratory	Video App	Subgroup of 240 patients
B. Clinician-Level			
1. Demographic	Covariate (moderator)	Survey	All clinicians who participate
2. Experience	Covariate	Survey	All clinicians who participate
3. Communication training	Covariate	Survey	All clinicians who participate
4. Socioemotional Orientation	Covariate	Survey	All clinicians who participate
C. System-Level			
1. Practice variation	Exploratory	Audio Record	
2. Leadership/Teamwork	Exploratory	Audio Record	
3. Intervention/Video use	Monitoring fidelity	Video App	Entire study population

Data sources, data elements, and linkage

Baseline (i.e., pre-intervention) data for all randomized clinics will include a six-month period prior to date of intervention delivery. Patients will be identified as having advanced cancer from each site's tumor registry and/or from clinical ICD codes, which have been studied in some cancers and have demonstrated strong specificities.[79] While these methods have lower sensitivity, they capture enough patients with advanced cancer with high specificity for outcome assessment without systematic bias towards intervention or control periods. Demographic information and baseline characteristics relevant to general oncology will be collected from the EHR. Our primary and secondary outcomes will be abstracted from the local EHRs and tumor registries as detailed below in outcomes.

We will also use NLP, a form of computer-assisted abstraction, to detect our primary and secondary outcomes. Our NLP software, ClinicalRegex, identifies predefined keywords or phrases within clinical notes, considering varieties in language and punctuation.[80-82] ClinicalRegex also allows for rapid semi-automated review that ensures that keywords have not been taken out of context. For each NLP process (i.e., goals-of-care discussion), we have built a keyword library that identifies relevant documentation within clinical notes. Each keyword library was refined and validated by manual review of clinical notes in local EHRs. With NLP, we will collect additional data on ACP documentation, goals-of-care discussions, limitation of life-sustaining treatment, palliative care consultation, and hospice assessment. Exploratory patient-centered outcomes and clinician outcomes will be derived from surveys collected through REDCap.[83, 84]

Data Use Agreements between all systems are on file and each site maintains and adheres to the process and procedures for the protection of human subjects and protected health

information (PHI) for their covered entities. Only the minimum amount of necessary PHI will be collected from participants. HIPAA compliant and password protected servers will be used to store all collected data. Individual password protected files will separate participant identifiers and a third password protected linking file will be maintained. This linking file has restricted access and utilizes a logging feature that identifies each user and instance of use. All data will be transmitted via secure methods approved by the respective institutions to the Dana-Farber Cancer Institute (DFCI) for data management and to Boston Medical Center for qualitative analysis and trial investigators will have access to the final data set and it will be made available upon reasonable request. The EHR data will undergo a review-adjudication process whereby DFCI data staff and key, unblinded investigators, review the raw data for each variable to identify out of range or unexpected values, a summary is sent to each site and conference calls are conducted with relevant investigators and programmers to adjudicate any issues. We will also validate a randomly selected subset of data, verifying key demographic characteristics and patient selection criteria against medical records. The EHR data is then uploaded to a REDCap database.

Masking

Blinding for this trial occurs at multiple levels. Research Co-Investigators at each site will be aware of the randomization order as well as which clinics receive the intervention and when. The investigators leading the trainings will likewise be aware of which clinics receive the intervention. Similarly, due to their roles in working with the data and generating video adherence reports for the intervention clinics, certain members of the implementation and data management teams will be unblinded to clinic assignments and outcomes. All other staff will remain blinded to randomization scheme and outcomes.

Statistical Analysis

Our primary analytical approach uses an intention to treat analysis, with no special allowance for noncompliance or nonadherence. With the stepped-wedge design, the outcomes during the intervention (exposed) periods will be compared to outcomes during the control (unexposed) periods. We will conduct two analyses based on the observations included in the analysis: (1) Open cohort with repeated measures design: individuals may leave and others may join during the study and the same individuals are allowed to appear in multiple periods, (2) Repeated cross-sectional design: subjects will only be included in the period when they first enter the study. Characteristics of the individuals and clusters will be summarized by exposure status.[85] We will use generalized linear mixed models to compare outcomes between intervention and control periods. The basic model is depicted in this equation:

$$g(Y_{ijk}) = \mu + \alpha_i + \beta_j + \gamma_k + X_{ij}\theta$$

where Y_{ijk} denotes the response from individual k at time j from cluster i. To account for clustering within each clinic, the model includes a random effect α_i for cluster i. Under the stepped wedge design, calendar time is associated with the exposure to the intervention. We will include a fixed effect β_j to adjust for potential confounding factors from calendar time. In the case that time effect might not be the same for all clusters, we will change the term from a fixed effect β_j to a random effect β_{ij}. To account for repeated measures from the same subject from the first analysis, we will include a random subject effect γ_k. The term X_{ij} represents the treatment indicator in cluster i at time j with θ representing the overall treatment effect. If there is evidence of treatment effect heterogeneity, we will either change the fixed effect θ to a random effect θ_i or change the fixed effect θ to $\theta_{(s)}$ which allows different treatment effects for different strata. We will also explore heterogeneity of intervention effect for different subgroups by adding an

interaction term between treatment status and subgroup to the models. These groups include site, sex as a biological variable, race/ethnicity (white vs. non-white), and different types of cancer diagnoses.

If necessary, we will include additional terms $\delta_1 Z_{ijk}$ and $\delta_2 W_{ij}$ to the model, where Z and W represent vectors of patient and cluster characteristics. The index j in the Z matrices allows us to include the time-varying covariates, which correspond to any patient characteristics that could change over time. We will use a logit link (g) for the binary outcomes which include our primary outcome of ACP documentation and our secondary outcomes of resuscitation preference and hospice use. Other outcomes such as number of palliative care consults and utilizations are considered as Poisson variables and modeled with a log link.

In adjustment for the COVID 19 pandemic, the analysis plan will remain the same for the data collected from the 30 clinics randomized to intervention after the original Step 2 (Figure 3b). The data collected from the 6 clinics that received intervention during Step 1 will allow us to examine the ACP Program intervention effect prior to COVID-19 by comparing the ACP rates prior to the intervention (original baseline) and after the intervention (original Step 1). Additionally, ACP rates from original baseline, Step 1 and Step 2 from the 30 clinics randomized to intervention after the original Step 2 will be used to estimate the "COVID-19 effect" on ACP.

We also have patient-centered secondary outcomes from survey results for analysis. Since patients will be surveyed in the step immediately before and after the intervention is initiated within each clinic, the number of intervention and control patients will be approximately equal at each time point. We will use linear mixed models that treat time (i.e., before or after intervention) as a fixed effect and clinic as a random effect to account for clustering of patients within clinics.

Finally, we will examine care delivery alignment with expressed goals from a subset of deceased patients of those 450 surveyed. Using a chart abstraction tool, two blinded expert investigators will judge whether patients received care concordant with their documented wishes. Coders will make determinations and discuss disagreements; final judgments will be determined by consensus. For qualitative coding evaluation, we will summarize the extent of agreement using kappa statistics and will compare results between those who died before and after receiving interventions.

Statistical power and sample size requirements

We used the Hooper et al.[86, 87] approach to conduct the power analysis. We originally estimated close to 5,000 patients from 36 oncology practices are eligible for the study at each time point and approximately 20% are new patients at each step. With 7 time points (baseline plus 6 steps), we anticipated a total of 11,000 unique patients will be included in the study. With the modified design, we estimate 4,160 patients from 30 oncology practices are eligible for the study at each time point and a total of 7,500 unique patients will be included in the stepped-wedge design analysis. With each clinic contributing an average of 139 patients at each step from the cohort design, the design effect due to clustering is 7.9 assuming an intra-cluster correlation of 0.05, and the design effect due to repeated assessment is 0.12 assuming the cluster autocorrelation coefficient is 0.7 and the individual autocorrelation coefficient is 0.9. These estimates correspond to an effective sample size (i.e., sample size required for individual randomization) of 4,405. For the repeated cross-sectional design, each clinic will contribute an average of 23 new patients at each step, and the effective sample size is 1,628 with the same assumptions on intra-cluster correlation and cluster autocorrelation. Preliminary estimates

indicate the rate for ACP documentation (the primary outcome) ranges from 15% to 30% for the control periods, which requires an effective sample size of 500 to 954 for detecting a 10% absolute increase in our primary outcome with a two-sided significance level of 0.05. Therefore, the study will have more than 90% power for either analysis using the open cohort with repeated measures design or the repeated cross-sectional design.

For the patient-centered survey outcomes, 225 patients will be surveyed during control periods and 225 will be surveyed during intervention periods. Assuming an ICC of 0.05 and an average cluster size of 12.5, the effective sample size is approximately 286. A sample of this size allows for 90% power to detect a small to moderate effect size (Cohen's *d*) of 0.39 and 99% power to detect a moderate effect size of 0.5 for outcomes such as patient confidence, decisional satisfaction and regret.

Regulatory considerations

Regulatory aspects of this trial include Institutional Review Board (IRB) approval, Data Use Agreements among partners, and an independent Data Safety and Monitoring Board. This study was approved via a single IRB of record mechanism as a multi-center trial with the DFCI as the lead site and registered on ClinicalTrials.gov (NCT03609177). Duke Health, Mayo Clinic, and Northwell Health are participatory sites and Boston Medical Center and Massachusetts General Hospital are non-participatory sites. Each site's own regulatory board established official "reliance agreements" to use the DFCI's Office of Human Research Subjects (OHRS) as their main regulatory agent. The three participating sites have formally designated via SMART IRB that the IRB of record is the DFCI IRB and agree to follow the rules and regulations set forth by the DFCI OHRS. All relevant parties are notified by email of any protocol

modifications. This study presents minimal risk to participants. Investigators will monitor and report any unforeseen adverse events to the IRB. We have proactively requested an audit to be conducted by DFCI's OHRS before the trial end. Committees consisting of the various investigators oversee overall project direction and administration, intervention implementation, data quality and monitoring, stakeholder engagement, and regulatory and ethical considerations. Data Use Agreements between all systems are on file and each site maintains and adheres to the process and procedures for the protection of human subjects and PHI for their covered entities. Patients will be notified of the study and their participation via broadcast notifications in the form of posters in each of the clinics and will have the option to opt out. A waiver of consent was approved for the EHR review of the primary study subjects who are not contacted by study staff unless a specific research declination is on file at that site. Waivers of consent were also approved for engaging participating clinicians and surveyed patients not completing the video declaration as their participation is confidential and voluntary giving implied consent and there is minimal risk with the study. Those surveyed patients who also elect to complete the video declaration first need to sign an approved written consent form obtained by RAs at each site.

RELEVANCE AND DISSEMINATION

The ACP-PEACE trial will be the first to study combining two evidence-based interventions in a pragmatic setting. The work combines clinician training in responding to emotion and handling difficult conversations with decision video aids for patients. The strengths of the study include the complementary nature of these approaches: targeting both clinicians and patients in a novel way. Additionally, the pragmatic nature of the trial allows us to collect evidence of the effect of these interventions in a "real-world" setting and provides rich

information on the implementation of ACP interventions. This study has the potential to add to a growing literature informing large systematic ways of improving ACP for older adults with cancer. We plan to publish the primary outcome related to ACP documentation and our secondary outcomes in a single paper. We will also perform further analyses of our NLP methods, exploratory outcomes, chart review, implementation outcomes, and video declarations and present these in publication and at national meetings.

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APPENDIX

VIDEO DECLARATION PROCEDURES

For the video declarations, the RA introduces the concept to patients with a standardized introduction that is piloted during the UG3 phase and modified as needed. The RA uses the camera on a tablet computer, ensuring that the tablet is situated in such a way that the patient cannot see themselves on screen while they are talking, and records the subject. The RA will then guide the subject to create a video declaration through a series of prompting questions. The subject answers each prompt, and at the end, the RA will merge all responses to create a continuous video, removing the RAs voice. The prompts include: 1) What's most important to you? 2) What concerns do you have about getting sick? 3) If you were very sick, are there any specific medical treatments that you do or do not want? Please think about things like having CPR if your heart stopped beating or having a breathing tube if you stopped breathing. 4) What spiritual beliefs do you have that might influence your medical decisions? In the UG3 phase, half of patients will be asked to answer question 3 without the second half of the prompt – specifically naming medical treatments with the aim of helping to inform our decisions about the usefulness of providing information on treatment decisions for the video declarations in the UH3 phase. After the recording is completed, the RA plays the video for the subject to ensure they feel it accurately represents their preferences. Patients may re-film their video declaration as many times as they want to ensure their preferences are accurately described. Once the patient approves the video, the RA discusses the process by which patients will share it with clinicians, family, or whomever else they wish to include. Patients have the option of receiving the video on a USB drive, through DropBox, or as an unlisted video on YouTube.

We will qualitatively analyze video declarations by first transcribing recordings verbatim and adding in any relevant non-verbal information, such as expressions of hesitation or sadness. We then draft a preliminary coding framework using an existing framework of cancer-specific palliative care.[88] We plan to include the following among our primary coding categories: 1) advance care planning; 2) acute issues; 3) psychosocial issues; 4) after death wishes; and 5) existential and spiritual issues. We begin by coding 15 videos (5 from each site) using this preliminary framework and then add further codes to include other emerging themes. Members from the entire research team review the revised coding structure and approve the final coding framework for coding the remaining transcripts, which is done independently by RAs at each site. Coders attend monthly phone meetings to review coding progress and resolve discrepancies until coding is complete. To enhance the trustworthiness of the analysis,[89] we will hold at least two peer debriefing meetings with the entire research team to show them the transcripts and the codes applied and ask for their feedback. Results from these meetings will be incorporated into the ongoing coding process. Finalized codes will be summarized into themes to be presented descriptively and accompanied by illustrative quotations highlighting the content. We are using NVIVO version 11 qualitative software to assist in data management. We anticipate that we will use the coding structure developed during the UG3 phase, but we will continue our plan of group-based coding with peer debriefing during the UH3 phase as well. Further analysis of the video declarations will examine the clarity and comprehensiveness with which the patients communicate their preferences (i.e., would a clinician watching the video understand how to enact this patient's advance directive) and will compare what is presented in the video declaration with preferences as codified in the patient's medical record documentation.

SURVEY INSTRUMENTS

Clinician Survey

1. **Age:**

2. **Gender:**
   - [1] ☐ Male
   - [2] ☐ Female
   - [3] ☐ Transgender
   - [4] ☐ I prefer not to answer

3. **What is your ethnic/race background:**
   - [1] ☐ American Indian or Alaska Native
   - [2] ☐ Asian
   - [3] ☐ Black or African American
   - [4] ☐ Native Hawaiian or other Pacific Islander
   - [5] ☐ White
   - [6] ☐ More than one race _____
   - [7] ☐ Other (specify)_____
   - [8] ☐ Unknown or not reported

4. **Do you consider yourself to be Hispanic or Latino?**
   - [1] ☐ Yes
   - [2] ☐ No

5. **What is your religion?**
   - [1] ☐ Christian
   - [2] ☐ Jewish
   - [3] ☐ Islamic/Muslim
   - [4] ☐ Buddhist/Hindu/Eastern
   - [5] ☐ No Affiliation
   - [6] ☐ Other (specify)_____

6. **On a scale of 0-100, (0 being not strong at all, 100 being very strong), how strong an influence do you consider your religious/spiritual beliefs and practices to be in your life?**

Not strong at all ---------- **Very Strong**

0 10 20 30 40 50 60 70 80 90 100

7. **How many years have you been in practice since completing your training?**
   - [1] ☐ 0-5
   - [2] ☐ 6-10
   - [3] ☐ 11-15
   - [4] ☐ 16-20
   - [5] ☐ 20+

8. **How many hours do you spend per week in direct patient care?**

1 ☐ 0-10
2 ☐ 11-20
3 ☐ 21-30
4 ☐ 31-40
5 ☐ > 40

9. **Prior to this study, and during any of the following stages of your career, have you participated in clinician-patient communication skills training? Please respond below for…** (We refer here to any kind of workshop, seminar, or interactive on-line training that specifically instructed you on effective ways or talking to your patients. We do not include attending single lectures without interactive or practice elements.)

   A) Professional school (PA, nursing, medical school, etc.)? Y/N
   B) Residency (if applicable)? Y/N
   C) Fellowship (if applicable)? Y/N
   D) Post-training clinical practice? Y/N

10. **Have you ever attended a VitalTalk course? Y/N**

Health care providers commonly try to balance all aspects of patient care, including the social and emotional aspects of patient care and the technological and scientific aspects. Virtually no one is exactly equal on these two aspects.

11. **Do you think you are more inclined toward social and emotional aspects of patient care or more inclined toward the technological and scientific aspects?**
    ☐ Social & emotional
    ☐ Technological & scientific

12. **Are you a little more inclined to the aspects you chose in the last question or a lot more inclined?**
    ☐ A little more inclined
    ☐ A lot more inclined

Thank you again for your time. The survey is complete.

Patient Survey

Verbally Administered by Research Assistant

1. How confident are you that you will get the type of medical care you want if you become seriously ill and could no longer communicate your preferences?
   1 ☐ Not at all confident
   2 ☐ Slightly confident
   3 ☐ Somewhat confident
   4 ☐ Fairly confident
   5 ☐ Very confident

When answering the following questions, please think about the primary provider who has been treating your cancer.

2. Who do you consider to be your primary cancer provider?
   1 ☐ Oncologist
   2 ☐ Oncology Nurse Practitioner
   3 ☐ Oncology Physician Assistant
   4 ☐ Other (What is the role of that provider: _____)

3. In general, how often does this provider explain things in a way that is easy to understand?
   1 ☐ Never
   2 ☐ Sometimes
   3 ☐ Usually
   4 ☐ Always

4. In general, how often does this provider listen carefully to you?
   1 ☐ Never
   2 ☐ Sometimes
   3 ☐ Usually
   4 ☐ Always

5. In general, how often does this provider seem to know the important information about your medical history?
   1 ☐ Never
   2 ☐ Sometimes
   3 ☐ Usually
   4 ☐ Always

6. In general, how often does this provider show respect for what you have to say?
   1 ☐ Never
   2 ☐ Sometimes
   3 ☐ Usually
   4 ☐ Always

7. In general, how often does this provider spend enough time with you?
   1 ☐ Never
   2 ☐ Sometimes
   3 ☐ Usually
   4 ☐ Always

8. Using any number from 0 to 10, where 0 is the worst provider possible and 10 is the best provider possible, what number would you use to rate this provider?
   - ☐ 0 Worst provider possible
   - ☐ 1
   - ☐ 2
   - ☐ 3
   - ☐ 4
   - ☐ 5
   - ☐ 6
   - ☐ 7
   - ☐ 8
   - ☐ 9
   - ☐ 10 Best provider possible

9. Has your oncology team discussed with you what to expect with your illness in the future?
   - [1] ☐ Yes, definitely
   - [2] ☐ Yes, somewhat
   - [3] ☐ No

10. Has your oncology team ever asked what's most important to you?
   - [1] ☐ Yes, definitely
   - [2] ☐ Yes, somewhat
   - [3] ☐ No

11. Has your oncology team talked about how the treatment plan should match what is most important to you?
   - [1] ☐ Yes, definitely
   - [2] ☐ Yes, somewhat
   - [3] ☐ No

When answering the following questions, please think about the last decision about your cancer treatment you made together with a health care provider.

12. I am satisfied that I was adequately informed about the issues important to my decision.
   - [1] ☐ Strongly disagree
   - [2] ☐ Disagree
   - [3] ☐ Neither agree nor disagree
   - [4] ☐ Agree

5 ☐ Strongly agree

13. The decision I made was the best decision possible for me personally.
1 ☐ Strongly disagree
2 ☐ Disagree
3 ☐ Neither agree nor disagree
4 ☐ Agree
5 ☐ Strongly agree

14. I am satisfied that my decision was consistent with my personal values.
1 ☐ Strongly disagree
2 ☐ Disagree
3 ☐ Neither agree nor disagree
4 ☐ Agree
5 ☐ Strongly agree

15. I expect to successfully carry out (or continue to carry out) the decision I made.
1 ☐ Strongly disagree
2 ☐ Disagree
3 ☐ Neither agree nor disagree
4 ☐ Agree
5 ☐ Strongly agree

16. I am satisfied that this was my decision to make.
1 ☐ Strongly disagree
2 ☐ Disagree
3 ☐ Neither agree nor disagree
4 ☐ Agree
5 ☐ Strongly agree

17. I am satisfied with my decision.
1 ☐ Strongly disagree
2 ☐ Disagree
3 ☐ Neither agree nor disagree
4 ☐ Agree
5 ☐ Strongly agree

When answering the following questions, please think about the last decision about your cancer treatment you made together with a health care provider.

18. It was the right decision.

[1] ☐ Strongly disagree
[2] ☐ Disagree
[3] ☐ Neither agree nor disagree
[4] ☐ Agree
[5] ☐ Strongly agree

19. I regret the choice that was made.
[1] ☐ Strongly disagree
[2] ☐ Disagree
[3] ☐ Neither agree nor disagree
[4] ☐ Agree
[5] ☐ Strongly agree

20. I would go for the same choice if I had to do it over again.
[1] ☐ Strongly disagree
[2] ☐ Disagree
[3] ☐ Neither agree nor disagree
[4] ☐ Agree
[5] ☐ Strongly agree

21. The choice did me a lot of harm.
[1] ☐ Strongly disagree
[2] ☐ Disagree
[3] ☐ Neither agree nor disagree
[4] ☐ Agree
[5] ☐ Strongly agree

22. The decision was a wise one.
[1] ☐ Strongly disagree
[2] ☐ Disagree
[3] ☐ Neither agree nor disagree
[4] ☐ Agree
[5] ☐ Strongly agree

23. Have you talked with a family member or close friend about the types of medical care you want or don't want if you become seriously ill in the future and could no longer communicate your preferences?

[1] ☐ No
[2] ☐ Yes

20a. Of those listed below, who was that person/those people? (Select all that apply)

[1] ☐ Spouse/partner
[2] ☐ Daughter
[3] ☐ Son
[4] ☐ Daughter-in-law
[5] ☐ Son-in-law
[6] ☐ Stepdaughter
[7] ☐ Stepson
[8] ☐ Sister
[9] ☐ Brother
[10] ☐ Sister-in-law
[11] ☐ Brother-in-law
[12] ☐ Mother
[13] ☐ Stepmother
[14] ☐ Mother-in-law
[15] ☐ Father
[16] ☐ Father-in-law
[17] ☐ Granddaughter
[18] ☐ Grandson
[19] ☐ Niece
[20] ☐ Nephew
[21] ☐ Aunt
[22] ☐ Cousin
[23] ☐ Stepdaughter's son/daughter
[24] ☐ Stepson's son/daughter
[25] ☐ Daughter-in-law's son/daughter
[26] ☐ Son-in-law's son/daughter
[27] ☐ Boarder/renter
[28] ☐ Paid aide/Housekeeper/Employee
[29] ☐ Roommate
[30] ☐ Ex-wife/Ex-husband
[31] ☐ Boyfriend/girlfriend
[32] ☐ Neighbor
[33] ☐ Friend
[34] ☐ Service/Someone from the place you live
[35] ☐ Co-worker
[36] ☐ Minister, Priest, or other Clergy
[37] ☐ Psychiatrist, Psychologist, Counselor, or Therapist

38 ☐ Other Relative
39 ☐ Other Non-Relative

Research Consent Form for Non-Clinical Research
Dana-Farber/ Harvard Cancer Center
BIDMC/BCH/BWH/DFCI/MGH/Partners Network Affiliates OHRS 10.02.2017

Protocol Title: Advance Care Planning: Promoting Effective and Aligned Communication in the Elderly

DF/HCC Principal Research Investigator / Institution: James Tulsky, MD/DFCI

DF/HCC Site-Responsible Research Investigator(s) / Institution(s):

James Tulsky, MD/DFCI

Angelo Volandes, MD/MGH

A. INTRODUCTION

We are inviting you to take part in a research study. Research is a way of gaining new knowledge. A person who participates in a research study is called a "participant." In this research study, we are working to help oncologists better serve patients by delivering more patient-centered medical care that is consistent with what patients want and their underlying goals and values.

The goal of this study is to test an intervention that seeks to increase the likelihood that older patients' values and goals are incorporated into cancer care decision-making.

It is expected that about 12,000 people will take part in this research study. An institution that is supporting a research study either by giving money or supplying something that is important for the research is called the "sponsor." The sponsor of this protocol is the National Institutes of Health (NIH) and the study will run for 5 years. This research consent form explains why this research study is being done, what is involved in participating in the research study, the possible risks and benefits of participation, alternatives to participation, and your rights as a research participant. The decision to participate is yours. If you decide to participate, please sign and date at the end of the form. We will give you a copy so that you can refer to it while you are involved in this research study.

You have been chosen to participate in this study, based on your doctor's recommendation and because you are an older adult with advanced cancer.

Your doctor felt that you might be willing to talk about your goals and wishes related to your medical care so your doctors and family can understand what is most important for you. You have been chosen to participate in this study, based on your doctor's recommendation. (Some de-identified information was provided to us through your medical records).

We encourage you to take some time to think this over and to discuss it with other people and to ask questions now and at any time in the future.

Dr. Angelo Volandes, a Massachusetts General Hospital (MGH) Investigator on this study, and his spouse are co-founders of and receive income from ACP Decisions Nous, a nonprofit organization developing the advanced care planning video decision support tools being evaluated in this study. Dr. Volandes' financial interests have been reviewed and are managed by Massachusetts General Hospital and Partners HealthCare in accordance with their conflict of interest policies. MGH will only be receiving de-identified data.

B. WHY IS THIS RESEARCH STUDY BEING DONE?

The purpose of this study is to improve the quality of care provided to older Americans with cancer. We are working to help oncologists better serve patients by delivering more patient-centered medical care that is consistent with what patients want.

C. WHAT OTHER OPTIONS ARE THERE?

Taking part in this research study is voluntary. You may choose not to be in the study, or, if you agree to be in the study, you may withdraw from the study at any time. If you withdraw from the study, no new data about you will be collected for study purposes.

If you participate, we will also ask if you wish to create a video of yourself describing what is important to you, any worries you have, and your preferences for medical care. We call these "video declarations."

- A Research Assistant will also ask you to complete a written video declaration.

- If you agree, we will record that declaration.
- We will ask you to talk about your Advance Care Planning preferences, for medical care so your doctors and family can understand what is most important for you.
- We will show your video to you when you are done.
- If you aren't happy with the video, you can record it again.
- When the recording is complete, the RA will play the video for you to see if you feel it accurately represents your preferences.
- There might be occasions when we would like to publicly share the information that we have learned through this research for demonstration purposes and at similar venues. We will provide you with an option to let us know if you are willing to publicly share your video via in-person or online webinar/lecture.

This visit will involve the following:

- **Recording a personal video declaration that includes both video and audio recording**

D. HOW LONG WILL I BE IN THIS RESEARCH STUDY?

You will be in this research study for the length of time that your scheduled appointment will take. After you complete the interview and video recording, investigators will continue to have access to your medical record and video for the purpose of analyzing the study outcomes.

You may be taken off the research study for reasons such as:

- It is considered to be in your best interest
- There is any problem with following study procedures
- There are any problems with research funding
- Or for any other reason

If you are removed from the research study, the research Investigator will explain to you why you were removed.

In addition, you can stop participating in the research study at any time.

E. WHAT ARE THE RISKS OR DISCOMFORTS OF THE RESEARCH STUDY?

There are risks to taking part in any research study, but the risks in this study are small and non-medical. The main risk is loss of confidentiality. You might become a little uncomfortable, sad, or even distressed as you contemplate serious illness with your provider, and there will be clinicians trained to help you with any discomfort you might feel.
During the research study, you will be provided with any new information that may affect your health or willingness to participate. You may be asked to sign a new consent form that shows that you have been informed of new information relating to this research study.

F. WHAT ARE THE BENEFITS OF THE RESEARCH STUDY?

Taking part in this research study may or may not benefit you. We hope the information learned from this research study will help you and your doctors in the clinics to benefit from the study by having your treatments better aligned with your preferences. There is the potential for the results learned from the study to help us to improve the Advance Care Planning of the overall outpatient clinic population, and particularly those with advanced cancer. There is the potential to validate an intervention that could ensure that treatments are better aligned with patients' preferences.

G. CAN I STOP BEING IN THE RESEARCH STUDY AND WHAT ARE MY RIGHTS?

You have the right to choose not to sign this form. If you decide not to sign this form, you cannot participate in this research study.

You can stop being in the research study at any time. Tell the research doctor if you are thinking about stopping or decide to stop. Leaving the research study will not affect your medical care. You can still get your medical care from your hospital or Investigator.

If you choose to not participate, or if you are not eligible to participate, or if you withdraw from this research study, this will not affect your present or future care and will not cause any penalty or loss of benefits to which you are otherwise entitled.

H. WHAT ARE THE COSTS?

There is no cost to you for participating in this study.

I. WHAT ABOUT CONFIDENTIALITY?

We will take measures to protect the privacy and security of all your personal information, but we cannot guarantee complete confidentiality of study data. All staff with access to information will be trained in privacy protection rules. Any personal information will be kept on a single central protected server with 24/7 security monitoring.

Applications will be designed with data security as the first goal and will be carefully reviewed for security prior to usage in the study. Participating oncologists will also be instructed on strict procedures to ensure the privacy and security of the video recordings at all levels of the data collection and storage process. The only people who will see this information will be study staff, investigators, other investigators who have been authorized by the research team to conduct analyses, and also those who have a contractual relationship with us in service of the research.

The results of this research study may be published. You will not be identified in publications without your permission.

This trial may be registered on https://www.clinicaltrials.gov, a publicly available registry of clinical trials. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

J. WHOM DO I CONTACT IF I HAVE QUESTIONS ABOUT THE RESEARCH STUDY?

If you have questions about the study, please contact your local research investigator or study staff as listed below:

DFCI

• Dr. James Tulsky, PI [Contact Information]
• Julie Goldman, Study Staff [Contact Information]

MGH

• Dr. Angelo Volandes, [Contact Information]

For questions about your rights as a research participant, please contact a representative of the Office for Human Research Studies at [Insert site name and phone number here] This can include questions about your participation in the study, concerns about the study, a research related injury, or if you feel/felt under pressure to enroll in this research study or to continue to participate in this research study.

K. PRIVACY OF PROTECTED HEALTH INFORMATION

Federal law requires Dana-Farber/Harvard Cancer Center (DF/HCC) and its affiliated research doctors, health care providers, and physician network to protect the privacy of information that identifies you and relates to your past, present, and future physical and mental health conditions ("protected health information"). If you enroll in this research study, your "protected health information" will be used and shared with others as explained below.

1. What protected health information about me will be used or shared with others during this research?

- Existing medical records, including mental health records.
- New health information created from study-related tests, procedures, visits, and/or questionnaires

2. Why will protected information about me be used or shared with others?

The main reasons include the following:

- To conduct and oversee the research described earlier in this form;
- To ensure the research meets legal, institutional, and accreditation requirements;

- To conduct public health activities (including reporting of adverse events or situations where you or others may be at risk of harm); and
- To provide the study sponsor with information arising from an adverse event or other event that relates to the safety or toxicity of the drug(s) used in the study and for the purpose of this or other research relating the study drug and its use in cancer; and,
- To better understand the diseases being studies and to improve the design of future studies; and,
- Other reasons may include for treatment, payment, or health care operations. For example, some medical information produced by this research study may become part of your hospital medical record because the information may be necessary for your medical care. (You will also be given a notice for use and sharing of protected health information.)

3. Who will use or share protected health information about me?

- DF/HCC and its affiliated research doctors and entities participating in the research will use and share your protected health information. In addition, other DF/HCC offices that deal with research oversight, billing or quality assurance will be able to use and share your protected health information.

4. With whom outside of DF/HCC may my protected health information be shared?

While all reasonable efforts will be made to protect the confidentiality of your protected health information, it may also be shared with the following entities:

- Outside individuals or entities that have a need to access this information to perform functions relating to the conduct of this research such as analysis by outside laboratories on behalf of DF/HCC and its affiliates (for example, data storage companies, insurers, or legal advisors).
- The sponsor(s) of the study, its subcontractors, representatives, business partners, and its agent(s): NIH
- Other research doctors and medical centers participating in this research, if applicable
- Federal and state agencies (for example, the Department of Health and Human Services, the Food and Drug Administration, the National

Institutes of Health, and/or the Office for Human Research Protections), or other domestic or foreign government bodies if required by law and/or necessary for oversight purposes.
- Hospital accrediting agencies
- A data safety monitoring board organized to oversee this research, if applicable

Some who may receive your protected health information may not have to satisfy the privacy rules and requirements. They, in fact, may share your information with others without your permission.

5. For how long will protected health information about me be used or shared with others?

- There is no scheduled date at which your protected health information that is being used or shared for this research will be destroyed, because research is an ongoing process.

6. Statement of privacy rights:

- You have the right to withdraw your permission for the research doctors and participating DF/HCC entities to use or share your protected health information. We will not be able to withdraw all the information that already has been used or shared with others to carry out related activities such as oversight, or that is needed to ensure quality of the study. To withdraw your permission, you must do so in writing by contacting the researcher listed above in the section: “Whom do I contact if I have questions about the research study?”
- You have the right to request access to your protected health information that is used or shared during this research and that is related to your treatment or payment for your treatment, but you may access this information only after the study is completed. To request this information, please contact the researcher listed above in the section: “Whom do I contact if I have questions about the research study?”

L. CONSENT TO OPTIONAL RESEARCH STUDIES:

You are being asked to participate in some optional studies. If you decide not to participate in any of the optional studies, you can still participate in the main research study. Please take your time to make your decision and discuss it with others and your primary care physician.

Your participation in these optional research studies is voluntary, and you will not be penalized or lose any benefits if you refuse to participate or decide to stop.

Optional Study #1:

We can share your declaration video with you if you wish to have a copy of it. There are multiple ways we can share your declaration video with you. The options available to you are dependent on the site where you receive your medical care. The safest and most secure way to share the video is either through an encrypted flash drive or through a tool called Dropbox for Business.

- Option 1: We can put your declaration video on an encrypted flash drive which is password protected and provide the flash drive to you; or

- Option 2: We can post your declaration video on a website called Dropbox for Business. You would be provided web link to view your video online. Dana-Farber has more privacy control over this site and can remove your video at any time. Dropbox for Business would require you to follow multiple steps to view your video.

If you prefer to not use Dropbox for Business or receive through an encrypted flash drive, we can still share your declaration video with you.

- Option 3: We can put your declaration video on an unencrypted flash drive which is not password protected and provide the flash drive to you; or

- Option 4: We can post your declaration video on a YouTube unlisted video setting under the study's YouTube account and provide the web link to you. An unlisted video can only be seen and shared by a web link. The

unlisted video should not be available on YouTube's search results or for people who do not have access to the web link. YouTube is user friendly, and would not require multiple steps to view your video

Please note, for Option 3 and Option 4, we cannot guarantee the confidentiality of your information. For example:

a. If you lose the unencrypted flash drive it may be recovered and accessible by someone else; or

b. If the YouTube web link is shared with another person, it may be possible for that person to post your unlisted video to a public playlist or to re-disclose the web link which would then be accessible by others.

I understand if my health information is disclosed to the media or the general public pursuant to this authorization, it is no longer protected by federal or state privacy regulations and may be re-disclosed by the recipient. I further understand that once such materials are in the possession of media or members of the general public, Dana-Farber will have no control over their use.

Please indicate whether or not you want to take part in this optional research study. If you would like to participate in this optional study and receive a copy of your video declaration, please indicate below and also check off the method above which you would like to receive it by.

☐ Not applicable

☐ Yes _____Initials _____Date

☐ No _____Initials _____Date

Research Consent Form for Non-Clinical Research

Optional Study #2:

There are times when the research team would like to share patients' videos with their colleagues, in scientific presentations or to train study staff. Would you be comfortable in sharing your video publicly for purposes like this? The risk is that the video could be widely shared, depending on the venue, and we will not have any control over this. We will not be analyzing anything so there will be no results.

I understand if my health information is disclosed to the media or the general public pursuant to this authorization, it is no longer protected by federal or state privacy regulations and may be re-disclosed by the recipient. I further understand that once such materials are in the possession of media or members of the general public, Dana-Farber will have no control over their use.

Please indicate whether or not you want to take part in this optional research study.

☐ Not applicable

☐ Yes _____Initials _____Date

☐ No _____Initials _____Date

N. Documentation of Consent

My signature below indicates:

- I have had enough time to read the consent and think about participating in this study;
- I have had all of my questions answered to my satisfaction;
- I am willing to participate in this study;
- I have been told that my participation is voluntary and I can withdraw at any time

_____ _____

Signature of Participant Date
or Legally Authorized Representative

_____

Relationship of Legally Authorized Representative to Participant

Research Consent Form for Non-Clinical Research
Dana-Farber/ Harvard Cancer Center
BIDMC/BCH/BWH/DFCI/MGH/Partners Network Affiliates OHRS 10.02.2017

Adult Participants

To be completed by person obtaining consent:

The consent discussion was initiated on_____(date).

Signature of individual obtaining consent: _____

Printed name of above: _____

Date: _____

☐ A copy of this signed consent form will be given to the participant or legally authorized representative, or, where the participant is a minor, the participant's parent or legal guardian.

For Adult Participants

☐ 1) The participant is an adult and provided consent to participate.

☐ 1a) Participant (or legally authorized representative) is a non-English speaker and signed the translated Short Form in lieu of English consent document:

As someone who understands both English and the language spoken by the participant, I interpreted and/or witnessed, in the participant's language, the researcher's presentation of the English consent form. The participant was given the opportunity to ask questions.

Signature of Interpreter/Witness: _____

Printed Name of Interpreter/Witness: _____

Date: _____

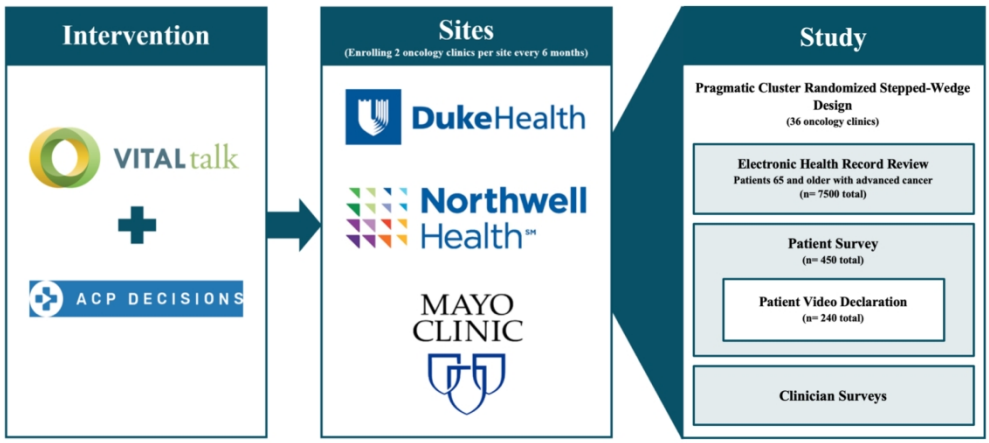
☐ 1b) Participant is physically unable to sign the consent form because:

☐ The participant is illiterate.
☐ The participant has a physical disability.
☐ Other (please describe): _____

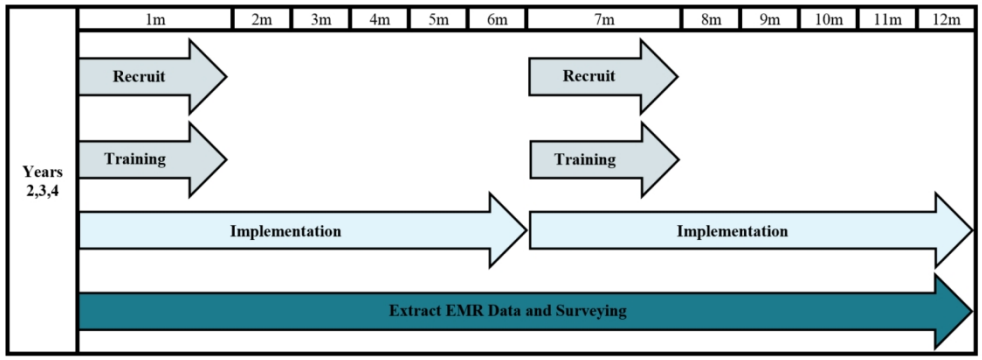
The consent form was read to the participant who was given the opportunity to ask questions and who communicated agreement to participate in the research.
Signature of Witness: _____

Printed Name of Witness: _____

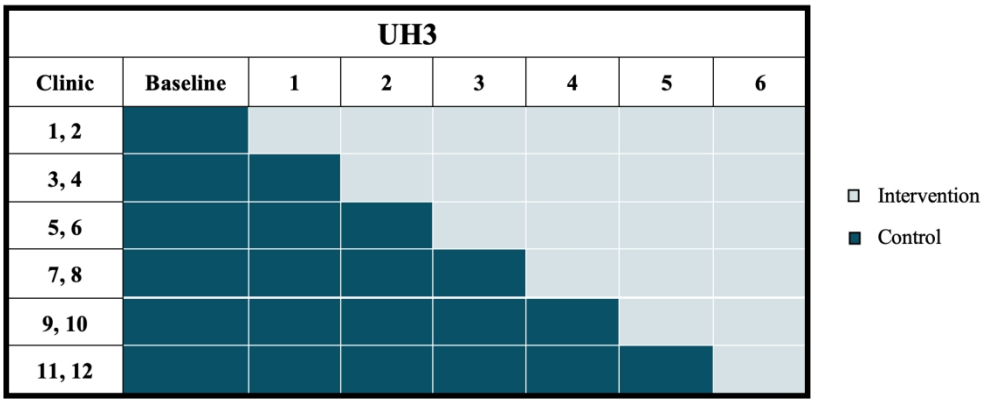
Date: _____



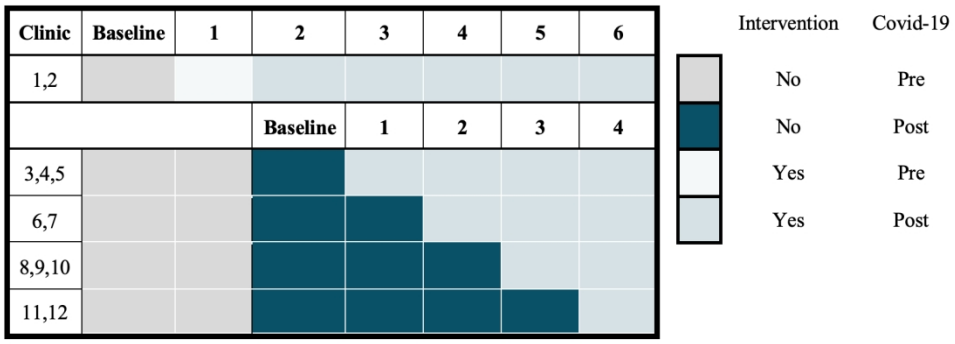
ACP Peace Model



Stepped-Wedge Recruitment and Implementation Yearly Timeline (repeated each year)



Original Stepped-wedge Cluster Randomization Scheme within Each Health Care System



Modified Stepped-wedge Cluster Randomization Scheme within Each Health Care System

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRITreporting guidelines, and cite them as:

Chan A-W, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, Hróbjartsson A, Mann H, Dickersin K, Berlin J, Doré C, Parulekar W, Summerskill W, Groves T, Schulz K, Sox H, Rockhold FW, Rennie D, Moher D. SPIRIT 2013 Statement: Defining standard protocol items for clinical trials. Ann Intern Med. 2013;158(3):200-207

		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	*1*
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	*19*
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	*1, 19*
Protocol version	#3	Date and version identifier	2
Funding	#4	Sources and types of financial, material, and other support	*2*

Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	*1, 22-23*
Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	*1*
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	*2*
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	*20*
Introduction			
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	*5-6*
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	*6-8*
Objectives	#7	Specific objectives or hypotheses	*6*
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	*6*

Methods: Participants, interventions, and outcomes			
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	*7-8*
Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	*8-9*
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	*7, 9-11*
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	*9-11*
Interventions: adherence	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	*9-11*
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	*N/A: Patients are receiving the standard of care, non-controlled trial.*
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each	*12-13*

		outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	*7-8, See Figure 3a,b*
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	*18-19*
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	*N/A: In this pragmatic trial, all individuals who meet criteria and do not opt out are included in the analysis rather than individual patient recruitment. We have included the description of our population on page 8.*
Methods: Assignment of interventions (for controlled trials)			
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	*7-8*

Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	*7-8*
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	*7-9*
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	*15*
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	*15*
Methods: Data collection, management, and analysis			
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	*8-9, 12-15*
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	*N/A; The unit of randomization is the clinic and all eligible individuals who do not choose to opt out are included and are not followed up over time.*

Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	*8, 13-15*
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	*15-18*
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	*15-18*
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	15-18
Methods: Monitoring			
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	*15, 19-20*
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	*14*
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously	*19*

		reported adverse events and other unintended effects of trial interventions or trial conduct	
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	*19-20*
Ethics and dissemination			
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	*19-20*
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	*19-20*
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	*20*
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	*N/A*
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	*14-15, 19-20*
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	*22*
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	15

Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	*N/A*
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	*20-21*
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	*22-23*
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	*N/A*
Appendices			
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	*Appendix*
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	*N/A*

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Advance Care Planning: Promoting Effective and Aligned Communication in the Elderly (ACP-PEACE) The study protocol for a pragmatic stepped-wedge trial of older patients with cancer

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Original Article

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

The study protocol for a pragmatic stepped-wedge trial of older patients with cancer

Running Title: Protocol for the ACP-PEACE pragmatic stepped-wedge trial

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Patient and Public Involvement Statement: Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

ABSTRACT

Introduction: Advance Care Planning (ACP) is associated with improved health outcomes for patients with cancer and its absence is associated with unfavorable outcomes for patients and their caregivers. However, older adults do not complete ACP at expected rates due to patient and clinician barriers. We present the original design, methods, and rationale for a trial aimed at improving ACP for older patients with advanced cancer and the modified protocol in response to changes brought by the COVID-19 pandemic.

Methods and Analysis: The Advance Care Planning: Promoting Effective and Aligned Communication in the Elderly study is a pragmatic, stepped-wedge cluster randomized trial examining a Comprehensive ACP Program. The Program combines two complementary evidence-based interventions: clinician communication skills training (VitalTalk) and patient video decision aids (ACP Decisions). We will implement the Program at 36 oncology clinics across three unique U.S. health systems. Our primary outcome is the proportion of eligible patients with ACP documentation completed in the Electronic Health Record. Our secondary outcomes include resuscitation preferences, palliative care consultations, death, hospice use, and final cancer-directed therapy. From a subset of our patient population, we will collect surveys and video-based declarations of goals and preferences. We estimate 11,000 patients from the three sites will be enrolled in the study.

Ethics and Dissemination: Regulatory and ethical aspects of this trial include Institutional Review Board (IRB) approval via single IRB of record mechanism at Dana-Farber Cancer Institute, Data Use Agreements among partners, and a Data Safety and Monitoring Board. We plan to present findings at national meetings and publish the results. Trial registered at ClinicalTrials.gov (NCT03609177).

ARTICLE SUMMARY: STRENGTHS AND LIMITATIONS

- The strengths of this study lie in its pragmatic design, allowing for "real world" evidence for two interventions that have been previously tested in more controlled settings.
- The stepped wedge design is practical and considered the design of choice when it is logistically impractical to simultaneously roll out the intervention to half of the clusters.
- The biggest limitation we are currently facing has to do with the possible notable change in secular trends due to the Coronavirus Disease 2019 and the impact that has on Advance Care Planning. To address this issue, we have adjusted our analysis plan to account for these changes.
- We are limited by the quality of structured and present variables in the electronic health records of each site, especially for Advance Care Planning, however our use of Natural Language Processing helps to rectify for lack in accuracy.
- In addition to the above change in secular trends due to COVID, this trial design can be affected by ongoing innovation in cancer care delivery, such as the continuing growth of immunotherapy changing prognosis for some of these advanced cancers in significant ways, thus affecting our results.

INTRODUCTION

More than half of newly diagnosed malignancies occur in patients over the age of 65[1] and that same population accounts for over two-thirds of all adult U.S. cancer deaths.[2] In addition to high mortality, older adults with cancer suffer disproportionately from receiving medical interventions that do not reflect their values and preferences.[3-5] Advance care planning (ACP) seeks to align medical care with patients' values and preferences.[6 7] ACP is consistently associated with better outcomes[8 9] while a lack of ACP is associated with greater use of unwanted medical interventions, more terminal hospitalizations, lower hospice use, higher healthcare costs, and worse bereavement outcomes.[3 10-14] Despite evidence supporting ACP, participation rates remain low among older adults with serious illness, such as cancer.[15]

Effective ACP requires that patients experience accurate and comprehensible communication early in their illness,[14 16-18] a collaborative effort requiring education for both patients and clinicians. Unfortunately, studies suggest that traditional written ACP can be ineffective in sufficiently informing patients and often occurs late in the disease process,[19-24] with the risk that patients' understanding is clouded by pain, medication, or psychological distress.[10 20 25] The heightened emotional state associated with hearing bad news late in a disease course interferes with patients' cognitive processing, and this reaction may be exacerbated by clinician inattention to affect.[21 26-29] Patients assign considerable importance to their physicians' statements regarding ACP and the quality of communication[30] and while 90% of patients say they want to talk to their doctors about their stress and concerns,[31 32] physicians generally, and oncologists specifically, often do not communicate effectively regarding ACP and end of life.[30 32-38] Therefore, an effective intervention should both prepare patients for shared decision making and improve clinicians' communication skills.

We have developed a Comprehensive ACP Program to drive improved communication and ACP for an aging U.S. cancer population using a combination of empirically proven patient video decision aids and clinician communication skills training. This program integrates video decision aids for patients (ACP Decisions) and a clinician communication training program (VitalTalk) into 12 disease-based oncology clinics each across three health systems with the aim of improving conversations and documentation of ACP. By providing both patients and clinicians with the necessary tools and training, we create an inclusive approach to optimize ACP before the toughest choices arise for patients.

Most trials targeting older patients with serious illness evaluate interventions under ideal conditions and involve few facilities.[39-42] Thus, we need research for this population using pragmatic trials.[43] We sought to test this intervention in a manner that allows for improvements in processes as we learn them.[44] Advance Care Planning: Promoting Effective and Aligned Communication in the Elderly (ACP-PEACE) is a pragmatic stepped-wedge cluster randomized trial (SW-CRT) that conducts a real-world test of the Comprehensive ACP Program in older patients with cancer. In this paper, we present the design, methodology, and rationale for the ACP-PEACE trial and discuss our adjustments for the novel coronavirus COVID 19 pandemic.

METHODS

Overview

We are studying the combination of clinician training and patient videos via a pragmatic SW-CRT and analyzing electronic health records (EHRs) for ACP outcomes for patients aged 65 and older. Utilizing small sub-samples of patients, we will also assess patient-centered outcomes using surveys and video declarations in which patients discuss their values and preferences in

their own words on video (Figure 1). We used the SPIRIT reporting guidelines for this manuscript.[45]

Study Timeline

The ACP-PEACE study has two phases, a characteristic of the funding mechanism. The UG3 phase (year 1) of the study focused on developing and refining the intervention and data acquisition. In this phase we established our organizational structure, developed the processes and infrastructure needed to conduct the trial, and pilot-tested the study intervention in three clinics, one from each participating health system. During the UH3 phase (years 2-5), we planned to introduce the intervention to the 36 remaining oncology clinics in six-month waves; two clinics per system for a total of six clinics every six months (Figure 2).

Sites and randomization

We will draw participants from disease-based oncology clinics from three unique systems - Duke Health (North Carolina), Mayo Clinic (Minnesota), and Northwell Health (New York). These sites are geographically, socioeconomically, and culturally distinct. Each participating clinic has more than one practicing oncologist and to be eligible for randomization, at least 30% of the patient population must be age 65 or older.

For the UH3 phase, we have identified a total of 36 oncology clinics (12 per site) as candidate clinics based on recent data from each system. The pilot clinics that participated in the UG3 phase tested the intervention process and will not be included in the final analysis. In the UH3 phase, we will utilize stepped-wedge cluster randomization with the clinic as the unit of randomization. With the clinic as the unit of randomization, we avoid the contamination that can

occur when randomizing individuals within each clinic. The sequence of randomization was generated prior to initiation of the trial via random number generator. Every six months after the baseline, two clinics from each system will be randomized to the intervention. (Figure 3a)

During the original Step 2, COVID-19 spread throughout the country interrupting the stepped-wedge design in two key respects: 1. The team was unable to conduct the in-person trainings for the Step 2 intervention clinics; and, 2. ACP activities are likely to increase during this period due to a response to the pandemic, irrespective of the study. Upon the recommendation of the NIH Collaboratory Statistics Core, we modified the original design to "restart" the trial for the remaining 30 clinics using the original Step 2 as the new baseline. The training of the remaining 30 control clinics will be over four steps to keep the trial completion on the same overall timeline (Figure 3b).

Population

We will evaluate the outcomes for patients aged 65 or older with advanced cancer across all 36 clinics. As the intervention will be implemented clinic-wide, rather than targeted to specific study patients, all intervention clinic patients can receive the intervention. We will analyze data for patients with advanced cancer aged 65 or older; patients' data will be counted towards control or intervention based on the allocation of each clinic at the end of each period of the stepped-wedge design. Therefore, a given patient could contribute data during more than one period and could contribute data to both control and intervention periods.

During the UH3 years, research assistants at each site will conduct in-person surveys with 450 randomly selected patients (150 per site) for our secondary exploratory patient-centered outcomes. Patients selected for surveys will be distributed evenly among clinics within each

system and will include an equal number of surveys of patients from clinics in the control and intervention phases. Patients will be surveyed only once as patients surveyed in the control phase will be excluded from completing the later intervention survey. Additionally, from among this group of 450 surveyed patients, a sub-group of 240 will be randomly selected and asked to conduct a video declaration activity. All patients selected for surveys or videos will be excluded from the primary study population to avoid bias rendered from additional contact with the study team.

Intervention design, implementation, and adherence monitoring

The Comprehensive ACP intervention combines VitalTalk and ACP Decisions, two evidence-based interventions previously used separately, to create an innovative dual approach to improving ACP. These interventions are complementary, as one targets improvement of clinicians' skills and the other prepares patients for shared decision making. VitalTalk is the most widely disseminated teaching method for effective communication skills training based on practice and feedback on one's own communication skills. Supported by numerous previous studies,[46-52] VitalTalk leverages didactics, demonstration, and small group sessions using role play with trained actors portraying patients through which clinicians learn effective delivery of serious news, prognosis discussion, early and late goals-of-care conversations. For this study, the VitalTalk course will be a half-day session that teaches a framework for late goals-of-care discussions, including skills around delivery of serious news, responding to emotion, assessing prognostic awareness, identifying what is most important to patients, and making recommendations.

The ACP Decisions program uses short video decision aids to address the most common issues facing older patients with serious illness. Videos in over 25 languages can be prescribed to patients and caregivers and are easily accessed in a mobile app or through a web-based platform. The ACP Decisions videos have been shown to increase knowledge, decision certainty, and the stability of preferences over time, and to better inform the way that patients choose health care interventions towards the end of life.[53-72] The video collection includes certified video decision aids,[73] regarding ACP, advance directives, health care agents, goals of care, cardiopulmonary resuscitation, and hospice, that have been studied in a statewide implementation showing greater patient-aligned medical care.[72]

We will provide in-person training every six months at each new clinic added to the intervention period of the trial. The Comprehensive ACP training program utilizes the VitalTalk methodology and infrastructure and the ACP Decisions Program tools to instruct clinicians and staff on how to (1) more effectively communicate with patients with cancer, (2) have ACP conversations with patients, (3) introduce the videos to patients and families, (4) use the videos as an adjunct to ACP counseling by clinicians, (5) select the appropriate video(s) according to patient needs, and (6) use the application or electronic platform for viewing videos. The combined program will involve a half-day face-to-face joint VitalTalk and ACP Decisions training. Any staff member affiliated with the selected facilities will be eligible to participate in training. As staff turnover among the sites is expected, training will be made available on an ongoing basis throughout the trial.

Immediately following the initial training at each site, we will deploy the remainder of the intervention infrastructure. The ACP Decisions videos will be programmed into desktop devices, tablets, and password-protected electronic platforms of each health system's intranet.

When clinics initiate the intervention, they will implement the videos with all patients with flexibility as to which providers (physician, nurse, social worker) introduce the videos and exactly which videos are utilized to meet their patients' clinical needs. Additionally, the in-person clinician training will be supplemented with emails, pocket cards, offers of coaching, and online educational videos. The study team will facilitate dissemination of implementation successes and challenges via a learning network by conducting one-hour webinars at each of the practices randomized to the intervention every other month to discuss quality improvement activities relating to the study. The intensity of the VitalTalk training implementation will be assessed as the proportion of eligible staff trained, including new staff joining the practice over the implementation period. The intensity of implementation of the ACP Decisions videos will be assessed as the ratio of the number of videos viewed using the site-specific access codes captured at the ACP Decisions website to the number of eligible patients at each site for each six-month intervention period. Fidelity to the video component of the intervention will be monitored by tracking of video use (which videos are used at each clinic, playthrough rate, and frequency). Feedback on video viewing will be shared with each site at the end of each six-month implementation phase. Last, we aim to evaluate the impact of the study with a novel video declaration process, allowing patients to state their values and preferences in their own terms, which is described in detail in the Appendix.[59]

Control condition

Clinics in the control phase will use whatever ACP procedures already exist in place at their respective system. Although current ACP-improvement initiatives may be present and vary

from clinic to clinic, this heterogeneity reflects the current dynamic state of "usual" care and is therefore appropriate in this pragmatic trial.[43]

Outcomes

The outcomes of the ACP-PEACE trial can be divided into three main categories: patient-level, clinician-level, and system-level. Our primary outcome is the proportion of eligible patients with ACP documentation completed in the EHR. Presence of completed ACP documentation will be defined via one or both of the following two means: 1) Structured EHR data: scanned forms including advance directives, living wills, or Physician's Orders for Life Sustaining Treatment (or state-specific equivalent) and code status orders indicating Do Not Resuscitate Status (or similar site-specific codes for limitations on treatments) and 2) Natural Language Processing (NLP) extraction (described below in detail): clinical documentation that will include goals-of-care discussion, ACP, hospice discussion, discussion of palliative care, or limitations on code status. From the EHR or the local tumor registry, we are also determining demographic covariates and baseline data. Secondary outcomes include resuscitation preferences, palliative care consultations, death, hospice use/utilization at the end of life, and final cancer-directed therapy.

We are deriving patient-centered outcomes from the patient survey and video declarations. The surveys measure our patient-centered secondary outcomes such as patient confidence that their future medical care will match their values, satisfaction with their clinicians' communication,[74 75] satisfaction with their medical decision,[76] and regret about their medical decision (Appendix).[77 78] Finally, for each of the 450 surveyed patients who die during the study period, we will extract data, via a chart abstraction tool, regarding ACP preferences and

care received in the final three months of life to explore whether patients receive goal-concordant care.

We are also collecting a small set of clinician data points. Participating clinicians provide information on demographics, clinical experience, prior communication training, and socioemotional orientation.[52] Table 1 lists each data element, with its purpose, proposed source, and the target population from whom we need the data for successful completion of the study. System-level data measurement will include measurement of the training and video use as described above as well as exploratory analysis of coaching calls and implementation activities.

Table 1. Data Elements and Outcomes

Data Element	Purpose	Source	Population
A. Patient-Level			
1. Demographics	Covariate (moderator)	EHR, Tumor Registry	Entire study population
2. ACP documents	1º outcome	EHR	Entire study population
3. Resuscitation Preference	2º outcome	EHR	Entire study population
4. Palliative care consults	2º outcome	EHR	Entire study population
5. Hospice use/ Utilization at the end of life	2º outcome	EHR, Tumor Registry, Other	Entire study population – for those patients who die
6. Final Cancer-Directed Therapy	2º outcome	EHR, Tumor Registry	Entire study population – for those patients who die
7. Death	Covariate	EHR, Tumor Registry, Other	Entire study population
8. Patient confidence	2º outcome	Survey	Subgroup of 450 patients
9. Communication satisfaction	2º outcome	Survey	Subgroup of 450 patients
10. Decisional satisfaction	2º outcome	Survey	Subgroup of 450 patients
11. Decisional regret	2º outcome	Survey	Subgroup of 450 patients
12. Family Communication	Exploratory	Survey	Subgroup of 450 patients
13. Goal-concordant care	Exploratory	EHR	Subgroup of 450 patients
14. Video declaration	Exploratory	Video App	Subgroup of 240 patients
B. Clinician-Level			
1. Demographic	Covariate (moderator)	Survey	All clinicians who participate
2. Experience	Covariate	Survey	All clinicians who participate
3. Communication training	Covariate	Survey	All clinicians who participate
4. Socioemotional Orientation	Covariate	Survey	All clinicians who participate
C. System-Level			
1. Practice variation	Exploratory	Audio Record	
2. Leadership/Teamwork	Exploratory	Audio Record	
3. Intervention/Video use	Monitoring fidelity	Video App	Entire study population

Data sources, data elements, and linkage

Baseline (i.e., pre-intervention) data for all randomized clinics will include a six-month period prior to date of intervention delivery. Patients will be identified as having advanced cancer from each site's tumor registry and/or from clinical ICD codes, which have been studied in some cancers and have demonstrated strong specificities.[79] While these methods have lower sensitivity, they capture enough patients with advanced cancer with high specificity for outcome assessment without systematic bias towards intervention or control periods. Demographic information and baseline characteristics relevant to general oncology will be collected from the EHR. Our primary and secondary outcomes will be abstracted from the local EHRs and tumor registries as detailed below in outcomes.

We will also use NLP, a form of computer-assisted abstraction, to detect our primary and secondary outcomes. Our NLP software, ClinicalRegex, identifies predefined keywords or phrases within clinical notes, considering varieties in language and punctuation.[80-82] ClinicalRegex also allows for rapid semi-automated review that ensures that keywords have not been taken out of context. For each NLP process (i.e., goals-of-care discussion), we have built a keyword library that identifies relevant documentation within clinical notes. Each keyword library was refined and validated by manual review of clinical notes in local EHRs. With NLP, we will collect additional data on ACP documentation, goals-of-care discussions, limitation of life-sustaining treatment, palliative care consultation, and hospice assessment. Exploratory patient-centered outcomes and clinician outcomes will be derived from surveys collected through REDCap.[83 84]

Data Use Agreements between all systems are on file and each site maintains and adheres to the process and procedures for the protection of human subjects and protected health

information (PHI) for their covered entities. Only the minimum amount of necessary PHI will be collected from participants. HIPAA compliant and password protected servers will be used to store all collected data. Individual password protected files will separate participant identifiers and a third password protected linking file will be maintained. This linking file has restricted access and utilizes a logging feature that identifies each user and instance of use. All data will be transmitted via secure methods approved by the respective institutions to the Dana-Farber Cancer Institute (DFCI) for data management and to Boston Medical Center for qualitative analysis and trial investigators will have access to the final data set and it will be made available upon reasonable request. The EHR data will undergo a review-adjudication process whereby DFCI data staff and key, unblinded investigators, review the raw data for each variable to identify out of range or unexpected values, a summary is sent to each site and conference calls are conducted with relevant investigators and programmers to adjudicate any issues. We will also validate a randomly selected subset of data, verifying key demographic characteristics and patient selection criteria against medical records. The EHR data is then uploaded to a REDCap database.

Masking

Blinding for this trial occurs at multiple levels. Research Co-Investigators at each site will be aware of the randomization order as well as which clinics receive the intervention and when. The investigators leading the trainings will likewise be aware of which clinics receive the intervention. Similarly, due to their roles in working with the data and generating video adherence reports for the intervention clinics, certain members of the implementation and data management teams will be unblinded to clinic assignments and outcomes. All other staff will remain blinded to randomization scheme and outcomes.

Statistical Analysis

Our primary analytical approach uses an intention to treat analysis, with no special allowance for noncompliance or nonadherence. With the stepped-wedge design, the outcomes during the intervention (exposed) periods will be compared to outcomes during the control (unexposed) periods. We will conduct two analyses based on the observations included in the analysis: (1) Open cohort with repeated measures design: individuals may leave and others may join during the study and the same individuals are allowed to appear in multiple periods, (2) Repeated cross-sectional design: subjects will only be included in the period when they first enter the study. Characteristics of the individuals and clusters will be summarized by exposure status.[85] We will use generalized linear mixed models to compare outcomes between intervention and control periods. The basic model is depicted in this equation:

$$g(Y_{ijk}) = \mu + \alpha_i + \beta_j + \gamma_k + X_{ij}\theta$$

where Y_{ijk} denotes the response from individual k at time j from cluster i. To account for clustering within each clinic, the model includes a random effect α_i for cluster i. Under the stepped wedge design, calendar time is associated with the exposure to the intervention. We will include a fixed effect β_j to adjust for potential confounding factors from calendar time. In the case that time effect might not be the same for all clusters, we will change the term from a fixed effect β_j to a random effect β_{ij}. To account for repeated measures from the same subject from the first analysis, we will include a random subject effect γ_k. The term X_{ij} represents the treatment indicator in cluster i at time j with θ representing the overall treatment effect. If there is evidence of treatment effect heterogeneity, we will either change the fixed effect θ to a random effect θ_i or change the fixed effect θ to $\theta_{(s)}$ which allows different treatment effects for different strata. We will also explore heterogeneity of intervention effect for different subgroups by adding an

interaction term between treatment status and subgroup to the models. These groups include site, sex as a biological variable, race/ethnicity (white vs. non-white), and different types of cancer diagnoses.

If necessary, we will include additional terms $\delta_1 Z_{ijk}$ and $\delta_2 W_{ij}$ to the model, where Z and W represent vectors of patient and cluster characteristics. The index j in the Z matrices allows us to include the time-varying covariates, which correspond to any patient characteristics that could change over time. We will use a logit link (g) for the binary outcomes which include our primary outcome of ACP documentation and our secondary outcomes of resuscitation preference and hospice use. Other outcomes such as number of palliative care consults and utilizations are considered as Poisson variables and modeled with a log link.

In adjustment for the COVID 19 pandemic, the analysis plan will remain the same for the data collected from the 30 clinics randomized to intervention after the original Step 2 (Figure 3b). The data collected from the 6 clinics that received intervention during Step 1 will allow us to examine the ACP Program intervention effect prior to COVID-19 by comparing the ACP rates prior to the intervention (original baseline) and after the intervention (original Step 1). Additionally, ACP rates from original baseline, Step 1 and Step 2 from the 30 clinics randomized to intervention after the original Step 2 will be used to estimate the "COVID-19 effect" on ACP.

We also have patient-centered secondary outcomes from survey results for analysis. Since patients will be surveyed in the step immediately before and after the intervention is initiated within each clinic, the number of intervention and control patients will be approximately equal at each time point. We will use linear mixed models that treat time (i.e., before or after intervention) as a fixed effect and clinic as a random effect to account for clustering of patients within clinics.

Finally, we will examine care delivery alignment with expressed goals from a subset of deceased patients of those 450 surveyed. Using a chart abstraction tool, two blinded expert investigators will judge whether patients received care concordant with their documented wishes. Coders will make determinations and discuss disagreements; final judgments will be determined by consensus. For qualitative coding evaluation, we will summarize the extent of agreement using kappa statistics and will compare results between those who died before and after receiving interventions.

Statistical power and sample size requirements

We used the Hooper et al.[86 87] approach to conduct the power analysis. We originally estimated close to 5,000 patients from 36 oncology practices are eligible for the study at each time point and approximately 20% are new patients at each step. With 7 time points (baseline plus 6 steps), we anticipated a total of 11,000 unique patients will be included in the study. With the modified design, we estimate 4,160 patients from 30 oncology practices are eligible for the study at each time point and a total of 7,500 unique patients will be included in the stepped-wedge design analysis. With each clinic contributing an average of 139 patients at each step from the cohort design, the design effect due to clustering is 7.9 assuming an intra-cluster correlation of 0.05, and the design effect due to repeated assessment is 0.12 assuming the cluster autocorrelation coefficient is 0.7 and the individual autocorrelation coefficient is 0.9. These estimates correspond to an effective sample size (i.e., sample size required for individual randomization) of 4,405. For the repeated cross-sectional design, each clinic will contribute an average of 23 new patients at each step, and the effective sample size is 1,628 with the same assumptions on intra-cluster correlation and cluster autocorrelation. Preliminary estimates

indicate the rate for ACP documentation (the primary outcome) ranges from 15% to 30% for the control periods, which requires an effective sample size of 500 to 954 for detecting a 10% absolute increase in our primary outcome with a two-sided significance level of 0.05. Therefore, the study will have more than 90% power for either analysis using the open cohort with repeated measures design or the repeated cross-sectional design.

For the patient-centered survey outcomes, 225 patients will be surveyed during control periods and 225 will be surveyed during intervention periods. Assuming an ICC of 0.05 and an average cluster size of 12.5, the effective sample size is approximately 286. A sample of this size allows for 90% power to detect a small to moderate effect size (Cohen's *d*) of 0.39 and 99% power to detect a moderate effect size of 0.5 for outcomes such as patient confidence, decisional satisfaction and regret.

ETHICS AND DISSEMINATION

Regulatory considerations

Regulatory aspects of this trial include Institutional Review Board (IRB) approval, Data Use Agreements among partners, and an independent Data Safety and Monitoring Board. This study was approved via a single IRB of record mechanism as a multi-center trial with the DFCI as the lead site and registered on ClinicalTrials.gov (NCT03609177). Duke Health, Mayo Clinic, and Northwell Health are participatory sites and Boston Medical Center and Massachusetts General Hospital are non-participatory sites. Each site's own regulatory board established official "reliance agreements" to use the DFCI's Office of Human Research Subjects (OHRS) as their main regulatory agent. The three participating sites have formally designated via SMART IRB that the IRB of record is the DFCI IRB and agree to follow the rules and regulations set

forth by the DFCI OHRS. All relevant parties are notified by email of any protocol modifications. This study presents minimal risk to participants. Investigators will monitor and report any unforeseen adverse events to the IRB. We have proactively requested an audit to be conducted by DFCI's OHRS before the trial end. Committees consisting of the various investigators oversee overall project direction and administration, intervention implementation, data quality and monitoring, stakeholder engagement, and regulatory and ethical considerations. Data Use Agreements between all systems are on file and each site maintains and adheres to the process and procedures for the protection of human subjects and PHI for their covered entities. Patients will be notified of the study and their participation via broadcast notifications in the form of posters in each of the clinics and will have the option to opt out. A waiver of consent was approved for the EHR review of the primary study subjects who are not contacted by study staff unless a specific research declination is on file at that site. Waivers of consent were also approved for engaging participating clinicians and surveyed patients not completing the video declaration as their participation is confidential and voluntary giving implied consent and there is minimal risk with the study. Those surveyed patients who also elect to complete the video declaration first need to sign an approved written consent form obtained by RAs at each site.

Relevance and dissemination

The ACP-PEACE trial will be the first to study combining two evidence-based interventions in a pragmatic setting. The work combines clinician training in responding to emotion and handling difficult conversations with decision video aids for patients. The strengths of the study include the complementary nature of these approaches: targeting both clinicians and patients in a novel way. Additionally, the pragmatic nature of the trial allows us to collect

evidence of the effect of these interventions in a "real-world" setting and provides rich information on the implementation of ACP interventions. This study has the potential to add to a growing literature informing large systematic ways of improving ACP for older adults with cancer. We plan to publish the primary outcome related to ACP documentation and our secondary outcomes in a single paper. We will also perform further analyses of our NLP methods, exploratory outcomes, chart review, implementation outcomes, and video declarations and present these in publication and at national meetings.

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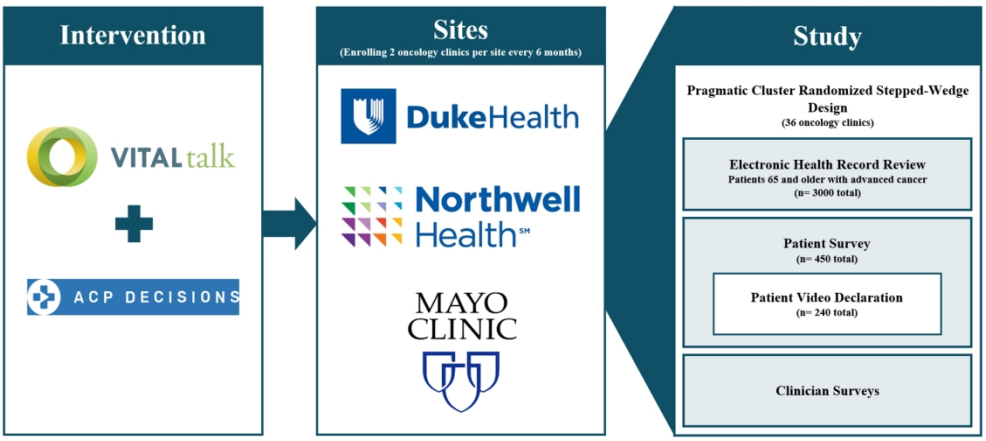

Figure 1. ACP-PEACE Model

157x70mm (300 x 300 DPI)

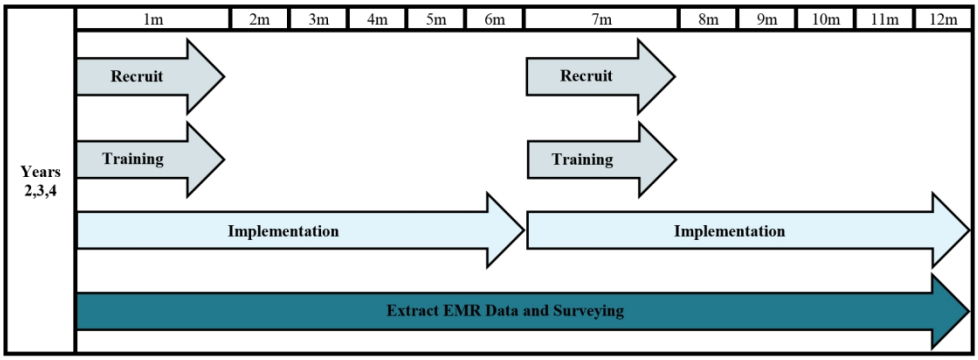

Figure 2. Stepped-Wedge Recruitment and Implementation Yearly Timeline (repeated each year)

144x53mm (300 x 300 DPI)

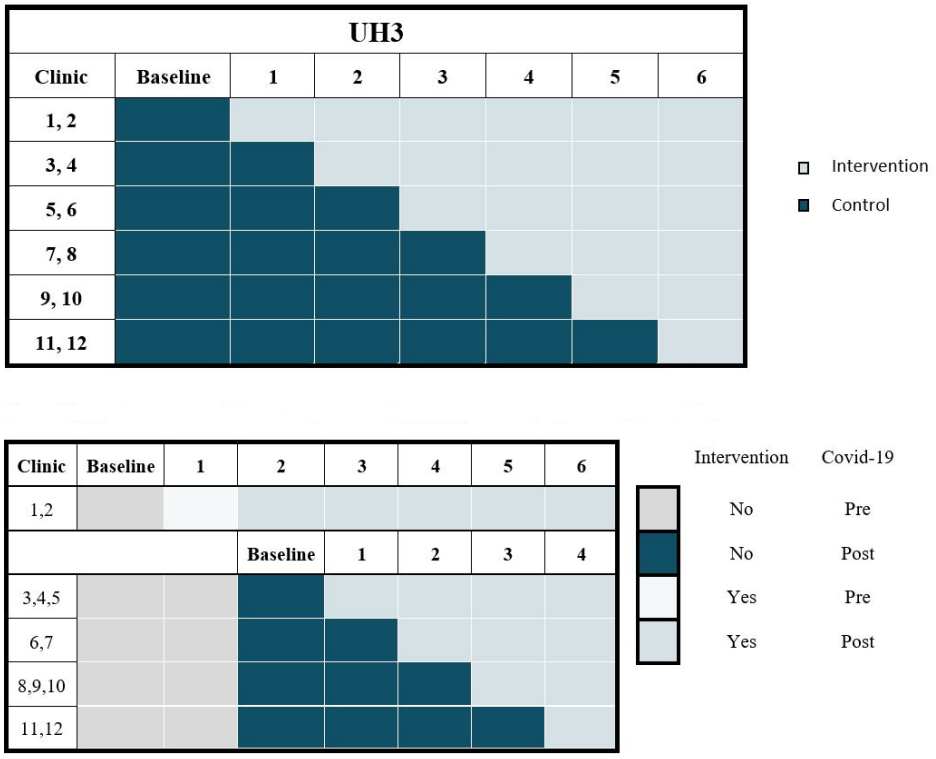

Figure 3a. Original Stepped-Wedge Cluster Randomization Scheme within Each Health Care System
Figure 3b. Modified Stepped-Wedge Cluster Randomization Scheme within Each Health Care System

291x242mm (96 x 96 DPI)

APPENDIX

VIDEO DECLARATION PROCEDURES

For the video declarations, the RA introduces the concept to patients with a standardized introduction that is piloted during the UG3 phase and modified as needed. The RA uses the camera on a tablet computer, ensuring that the tablet is situated in such a way that the patient cannot see themselves on screen while they are talking, and records the subject. The RA will then guide the subject to create a video declaration through a series of prompting questions. The subject answers each prompt, and at the end, the RA will merge all responses to create a continuous video, removing the RAs voice. The prompts include: 1) What's most important to you? 2) What concerns do you have about getting sick? 3) If you were very sick, are there any specific medical treatments that you do or do not want? Please think about things like having CPR if your heart stopped beating or having a breathing tube if you stopped breathing. 4) What spiritual beliefs do you have that might influence your medical decisions? In the UG3 phase, half of patients will be asked to answer question 3 without the second half of the prompt – specifically naming medical treatments with the aim of helping to inform our decisions about the usefulness of providing information on treatment decisions for the video declarations in the UH3 phase. After the recording is completed, the RA plays the video for the subject to ensure they feel it accurately represents their preferences. Patients may re-film their video declaration as many times as they want to ensure their preferences are accurately described. Once the patient approves the video, the RA discusses the process by which patients will share it with clinicians, family, or whomever else they wish to include. Patients have the option of receiving the video on a USB drive, through DropBox, or as an unlisted video on YouTube.

We will qualitatively analyze video declarations by first transcribing recordings verbatim and adding in any relevant non-verbal information, such as expressions of hesitation or sadness. We then draft a preliminary coding framework using an existing framework of cancer-specific palliative care.[88] We plan to include the following among our primary coding categories: 1) advance care planning; 2) acute issues; 3) psychosocial issues; 4) after death wishes; and 5) existential and spiritual issues. We begin by coding 15 videos (5 from each site) using this preliminary framework and then add further codes to include other emerging themes. Members from the entire research team review the revised coding structure and approve the final coding framework for coding the remaining transcripts, which is done independently by RAs at each site. Coders attend monthly phone meetings to review coding progress and resolve discrepancies until coding is complete. To enhance the trustworthiness of the analysis,[89] we will hold at least two peer debriefing meetings with the entire research team to show them the transcripts and the codes applied and ask for their feedback. Results from these meetings will be incorporated into the ongoing coding process. Finalized codes will be summarized into themes to be presented descriptively and accompanied by illustrative quotations highlighting the content. We are using NVIVO version 11 qualitative software to assist in data management. We anticipate that we will use the coding structure developed during the UG3 phase, but we will continue our plan of group-based coding with peer debriefing during the UH3 phase as well. Further analysis of the video declarations will examine the clarity and comprehensiveness with which the patients communicate their preferences (i.e., would a clinician watching the video understand how to enact this patient's advance directive) and will compare what is presented in the video declaration with preferences as codified in the patient's medical record documentation.

SURVEY INSTRUMENTS

Clinician Survey

1. **Age:**

2. **Gender:**
   - [1] ☐ Male
   - [2] ☐ Female
   - [3] ☐ Transgender
   - [4] ☐ I prefer not to answer

3. **What is your ethnic/race background:**
   - [1] ☐ American Indian or Alaska Native
   - [2] ☐ Asian
   - [3] ☐ Black or African American
   - [4] ☐ Native Hawaiian or other Pacific Islander
   - [5] ☐ White
   - [6] ☐ More than one race _____
   - [7] ☐ Other (specify)_____
   - [8] ☐ Unknown or not reported

4. **Do you consider yourself to be Hispanic or Latino?**
   - [1] ☐ Yes
   - [2] ☐ No

5. **What is your religion?**
   - [1] ☐ Christian
   - [2] ☐ Jewish
   - [3] ☐ Islamic/Muslim
   - [4] ☐ Buddhist/Hindu/Eastern
   - [5] ☐ No Affiliation
   - [6] ☐ Other (specify)_____

6. **On a scale of 0-100, (0 being not strong at all, 100 being very strong), how strong an influence do you consider your religious/spiritual beliefs and practices to be in your life?**

Not strong at all ---------- **Very Strong**

0 10 20 30 40 50 60 70 80 90 100

7. **How many years have you been in practice since completing your training?**
   - [1] ☐ 0-5
   - [2] ☐ 6-10
   - [3] ☐ 11-15
   - [4] ☐ 16-20
   - [5] ☐ 20+

8. **How many hours do you spend per week in direct patient care?**

[1] ☐ 0-10
[2] ☐ 11-20
[3] ☐ 21-30
[4] ☐ 31-40
[5] ☐ > 40

9. Prior to this study, and during any of the following stages of your career, have you participated in clinician-patient communication skills training? Please respond below for… (We refer here to any kind of workshop, seminar, or interactive on-line training that specifically instructed you on effective ways or talking to your patients. We do not include attending single lectures without interactive or practice elements.)

A) Professional school (PA, nursing, medical school, etc.)? Y/N
B) Residency (if applicable)? Y/N
C) Fellowship (if applicable)? Y/N
D) Post-training clinical practice? Y/N

10. Have you ever attended a VitalTalk course? Y/N

Health care providers commonly try to balance all aspects of patient care, including the social and emotional aspects of patient care and the technological and scientific aspects. Virtually no one is exactly equal on these two aspects.

11. Do you think you are more inclined toward social and emotional aspects of patient care or more inclined toward the technological and scientific aspects?
☐ Social & emotional
☐ Technological & scientific

12. Are you a little more inclined to the aspects you chose in the last question or a lot more inclined?
☐ A little more inclined
☐ A lot more inclined

Thank you again for your time. The survey is complete.

Patient Survey

Verbally Administered by Research Assistant

1. How confident are you that you will get the type of medical care you want if you become seriously ill and could no longer communicate your preferences?
   1☐ Not at all confident
   2☐ Slightly confident
   3☐ Somewhat confident
   4☐ Fairly confident
   5☐ Very confident

When answering the following questions, please think about the primary provider who has been treating your cancer.

2. Who do you consider to be your primary cancer provider?
   1☐ Oncologist
   2☐ Oncology Nurse Practitioner
   3☐ Oncology Physician Assistant
   4☐ Other (What is the role of that provider: _____)

3. In general, how often does this provider explain things in a way that is easy to understand?
   1☐ Never
   2☐ Sometimes
   3☐ Usually
   4☐ Always

4. In general, how often does this provider listen carefully to you?
   1☐ Never
   2☐ Sometimes
   3☐ Usually
   4☐ Always

5. In general, how often does this provider seem to know the important information about your medical history?
   1☐ Never
   2☐ Sometimes
   3☐ Usually
   4☐ Always

6. In general, how often does this provider show respect for what you have to say?

[1] ☐ Never
[2] ☐ Sometimes
[3] ☐ Usually
[4] ☐ Always

7. In general, how often does this provider spend enough time with you?
[1] ☐ Never
[2] ☐ Sometimes
[3] ☐ Usually
[4] ☐ Always

8. Using any number from 0 to 10, where 0 is the worst provider possible and 10 is the best provider possible, what number would you use to rate this provider?
☐ 0 Worst provider possible
☐ 1
☐ 2
☐ 3
☐ 4
☐ 5
☐ 6
☐ 7
☐ 8
☐ 9
☐ 10 Best provider possible

9. Has your oncology team discussed with you what to expect with your illness in the future?
[1] ☐ Yes, definitely
[2] ☐ Yes, somewhat
[3] ☐ No

10. Has your oncology team ever asked what's most important to you?
[1] ☐ Yes, definitely
[2] ☐ Yes, somewhat
[3] ☐ No

11. Has your oncology team talked about how the treatment plan should match what is most important to you?

1 Yes, definitely
2 Yes, somewhat
3 No

When answering the following questions, please think about the last decision about your cancer treatment you made together with a health care provider.

12. I am satisfied that I was adequately informed about the issues important to my decision.
1 Strongly disagree
2 Disagree
3 Neither agree nor disagree
4 Agree
5 Strongly agree

13. The decision I made was the best decision possible for me personally.
1 Strongly disagree
2 Disagree
3 Neither agree nor disagree
4 Agree
5 Strongly agree

14. I am satisfied that my decision was consistent with my personal values.
1 Strongly disagree
2 Disagree
3 Neither agree nor disagree
4 Agree
5 Strongly agree

15. I expect to successfully carry out (or continue to carry out) the decision I made.
1 Strongly disagree
2 Disagree
3 Neither agree nor disagree
4 Agree
5 Strongly agree

16. I am satisfied that this was my decision to make.
1 Strongly disagree
2 Disagree
3 Neither agree nor disagree
4 Agree

[5] ☐ Strongly agree

17. I am satisfied with my decision.
[1] ☐ Strongly disagree
[2] ☐ Disagree
[3] ☐ Neither agree nor disagree
[4] ☐ Agree
[5] ☐ Strongly agree

When answering the following questions, please think about the last decision about your cancer treatment you made together with a health care provider.

18. It was the right decision.
[1] ☐ Strongly disagree
[2] ☐ Disagree
[3] ☐ Neither agree nor disagree
[4] ☐ Agree
[5] ☐ Strongly agree

19. I regret the choice that was made.
[1] ☐ Strongly disagree
[2] ☐ Disagree
[3] ☐ Neither agree nor disagree
[4] ☐ Agree
[5] ☐ Strongly agree

20. I would go for the same choice if I had to do it over again.
[1] ☐ Strongly disagree
[2] ☐ Disagree
[3] ☐ Neither agree nor disagree
[4] ☐ Agree
[5] ☐ Strongly agree

21. The choice did me a lot of harm.
[1] ☐ Strongly disagree
[2] ☐ Disagree
[3] ☐ Neither agree nor disagree
[4] ☐ Agree
[5] ☐ Strongly agree

22. The decision was a wise one.

1 ☐ Strongly disagree
2 ☐ Disagree
3 ☐ Neither agree nor disagree
4 ☐ Agree
5 ☐ Strongly agree

23. Have you talked with a family member or close friend about the types of medical care you want or don't want if you become seriously ill in the future and could no longer communicate your preferences?
1 ☐ No
2 ☐ Yes

20a. Of those listed below, who was that person/those people? (Select all that apply)
1 ☐ Spouse/partner
2 ☐ Daughter
3 ☐ Son
4 ☐ Daughter-in-law
5 ☐ Son-in-law
6 ☐ Stepdaughter
7 ☐ Stepson
8 ☐ Sister
9 ☐ Brother
10 ☐ Sister-in-law
11 ☐ Brother-in-law
12 ☐ Mother
13 ☐ Stepmother
14 ☐ Mother-in-law
15 ☐ Father
16 ☐ Father-in-law
17 ☐ Granddaughter
18 ☐ Grandson
19 ☐ Niece
20 ☐ Nephew
21 ☐ Aunt
22 ☐ Cousin
23 ☐ Stepdaughter's son/daughter
24 ☐ Stepson's son/daughter
25 ☐ Daughter-in-law's son/daughter
26 ☐ Son-in-law's son/daughter
27 ☐ Boarder/renter
28 ☐ Paid aide/Housekeeper/Employee

☐ Roommate
☐ Ex-wife/Ex-husband
☐ Boyfriend/girlfriend
☐ Neighbor
☐ Friend
☐ Service/Someone from the place you live
☐ Co-worker
☐ Minister, Priest, or other Clergy
☐ Psychiatrist, Psychologist, Counselor, or Therapist
☐ Other Relative
☐ Other Non-Relative

Research Consent Form for Non-Clinical Research
Dana-Farber/ Harvard Cancer Center
BIDMC/BCH/BWH/DFCI/MGH/Partners Network Affiliates OHRS 10.02.2017

Protocol Title: Advance Care Planning: Promoting Effective and Aligned Communication in the Elderly

DF/HCC Principal Research Investigator / Institution: James Tulsky, MD/DFCI

DF/HCC Site-Responsible Research Investigator(s) / Institution(s):

James Tulsky, MD/DFCI

Angelo Volandes, MD/MGH

A. INTRODUCTION

We are inviting you to take part in a research study. Research is a way of gaining new knowledge. A person who participates in a research study is called a "participant." In this research study, we are working to help oncologists better serve patients by delivering more patient-centered medical care that is consistent with what patients want and their underlying goals and values.

The goal of this study is to test an intervention that seeks to increase the likelihood that older patients' values and goals are incorporated into cancer care decision-making.

It is expected that about 12,000 people will take part in this research study. An institution that is supporting a research study either by giving money or supplying something that is important for the research is called the "sponsor." The sponsor of this protocol is the National Institutes of Health (NIH) and the study will run for 5 years. This research consent form explains why this research study is being done, what is involved in participating in the research study, the possible risks and benefits of participation, alternatives to participation, and your rights as a research participant. The decision to participate is yours. If you decide to participate, please sign and date at the end of the form. We will give you a copy so that you can refer to it while you are involved in this research study.

You have been chosen to participate in this study, based on your doctor's recommendation and because you are an older adult with advanced cancer.

Your doctor felt that you might be willing to talk about your goals and wishes related to your medical care so your doctors and family can understand what is most important for you. You have been chosen to participate in this study, based on your doctor's recommendation. (Some de-identified information was provided to us through your medical records).

We encourage you to take some time to think this over and to discuss it with other people and to ask questions now and at any time in the future.

Dr. Angelo Volandes, a Massachusetts General Hospital (MGH) Investigator on this study, and his spouse are co-founders of and receive income from ACP Decisions Nous, a nonprofit organization developing the advanced care planning video decision support tools being evaluated in this study. Dr. Volandes' financial interests have been reviewed and are managed by Massachusetts General Hospital and Partners HealthCare in accordance with their conflict of interest policies. MGH will only be receiving de-identified data.

B. WHY IS THIS RESEARCH STUDY BEING DONE?

The purpose of this study is to improve the quality of care provided to older Americans with cancer. We are working to help oncologists better serve patients by delivering more patient-centered medical care that is consistent with what patients want.

C. WHAT OTHER OPTIONS ARE THERE?

Taking part in this research study is voluntary. You may choose not to be in the study, or, if you agree to be in the study, you may withdraw from the study at any time. If you withdraw from the study, no new data about you will be collected for study purposes.

If you participate, we will also ask if you wish to create a video of yourself describing what is important to you, any worries you have, and your preferences for medical care. We call these "video declarations."

- A Research Assistant will also ask you to complete a written video declaration.

- If you agree, we will record that declaration.
- We will ask you to talk about your Advance Care Planning preferences, for medical care so your doctors and family can understand what is most important for you.
- We will show your video to you when you are done.
- If you aren't happy with the video, you can record it again.
- When the recording is complete, the RA will play the video for you to see if you feel it accurately represents your preferences.
- There might be occasions when we would like to publicly share the information that we have learned through this research for demonstration purposes and at similar venues. We will provide you with an option to let us know if you are willing to publicly share your video via in-person or online webinar/lecture.

This visit will involve the following:

- **Recording a personal video declaration that includes both video and audio recording**

D. HOW LONG WILL I BE IN THIS RESEARCH STUDY?

You will be in this research study for the length of time that your scheduled appointment will take. After you complete the interview and video recording, investigators will continue to have access to your medical record and video for the purpose of analyzing the study outcomes.

You may be taken off the research study for reasons such as:

- It is considered to be in your best interest
- There is any problem with following study procedures
- There are any problems with research funding
- Or for any other reason

If you are removed from the research study, the research Investigator will explain to you why you were removed.

In addition, you can stop participating in the research study at any time.

E. WHAT ARE THE RISKS OR DISCOMFORTS OF THE RESEARCH STUDY?

There are risks to taking part in any research study, but the risks in this study are small and non-medical. The main risk is loss of confidentiality. You might become a little uncomfortable, sad, or even distressed as you contemplate serious illness with your provider, and there will be clinicians trained to help you with any discomfort you might feel.
During the research study, you will be provided with any new information that may affect your health or willingness to participate. You may be asked to sign a new consent form that shows that you have been informed of new information relating to this research study.

F. WHAT ARE THE BENEFITS OF THE RESEARCH STUDY?

Taking part in this research study may or may not benefit you. We hope the information learned from this research study will help you and your doctors in the clinics to benefit from the study by having your treatments better aligned with your preferences. There is the potential for the results learned from the study to help us to improve the Advance Care Planning of the overall outpatient clinic population, and particularly those with advanced cancer. There is the potential to validate an intervention that could ensure that treatments are better aligned with patients' preferences.

G. CAN I STOP BEING IN THE RESEARCH STUDY AND WHAT ARE MY RIGHTS?

You have the right to choose not to sign this form. If you decide not to sign this form, you cannot participate in this research study.

You can stop being in the research study at any time. Tell the research doctor if you are thinking about stopping or decide to stop. Leaving the research study will not affect your medical care. You can still get your medical care from your hospital or Investigator.

If you choose to not participate, or if you are not eligible to participate, or if you withdraw from this research study, this will not affect your present or future care and will not cause any penalty or loss of benefits to which you are otherwise entitled.

H. WHAT ARE THE COSTS?

There is no cost to you for participating in this study.

I. WHAT ABOUT CONFIDENTIALITY?

We will take measures to protect the privacy and security of all your personal information, but we cannot guarantee complete confidentiality of study data. All staff with access to information will be trained in privacy protection rules. Any personal information will be kept on a single central protected server with 24/7 security monitoring.

Applications will be designed with data security as the first goal and will be carefully reviewed for security prior to usage in the study. Participating oncologists will also be instructed on strict procedures to ensure the privacy and security of the video recordings at all levels of the data collection and storage process. The only people who will see this information will be study staff, investigators, other investigators who have been authorized by the research team to conduct analyses, and also those who have a contractual relationship with us in service of the research.

The results of this research study may be published. You will not be identified in publications without your permission.

This trial may be registered on https://www.clinicaltrials.gov, a publicly available registry of clinical trials. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

J. WHOM DO I CONTACT IF I HAVE QUESTIONS ABOUT THE RESEARCH STUDY?

If you have questions about the study, please contact your local research investigator or study staff as listed below:

DFCI

• Dr. James Tulsky, PI [Contact Information]
• Julie Goldman, Study Staff [Contact Information]

MGH

• Dr. Angelo Volandes, [Contact Information]

For questions about your rights as a research participant, please contact a representative of the Office for Human Research Studies at [Insert site name and phone number here] This can include questions about your participation in the study, concerns about the study, a research related injury, or if you feel/felt under pressure to enroll in this research study or to continue to participate in this research study.

K. PRIVACY OF PROTECTED HEALTH INFORMATION

Federal law requires Dana-Farber/Harvard Cancer Center (DF/HCC) and its affiliated research doctors, health care providers, and physician network to protect the privacy of information that identifies you and relates to your past, present, and future physical and mental health conditions ("protected health information"). If you enroll in this research study, your "protected health information" will be used and shared with others as explained below.

1. What protected health information about me will be used or shared with others during this research?

- Existing medical records, including mental health records.
- New health information created from study-related tests, procedures, visits, and/or questionnaires

2. Why will protected information about me be used or shared with others?

The main reasons include the following:

- To conduct and oversee the research described earlier in this form;
- To ensure the research meets legal, institutional, and accreditation requirements;

- To conduct public health activities (including reporting of adverse events or situations where you or others may be at risk of harm); and
- To provide the study sponsor with information arising from an adverse event or other event that relates to the safety or toxicity of the drug(s) used in the study and for the purpose of this or other research relating the study drug and its use in cancer; and,
- To better understand the diseases being studies and to improve the design of future studies; and,
- Other reasons may include for treatment, payment, or health care operations. For example, some medical information produced by this research study may become part of your hospital medical record because the information may be necessary for your medical care. (You will also be given a notice for use and sharing of protected health information.)

3. Who will use or share protected health information about me?

- DF/HCC and its affiliated research doctors and entities participating in the research will use and share your protected health information. In addition, other DF/HCC offices that deal with research oversight, billing or quality assurance will be able to use and share your protected health information.

4. With whom outside of DF/HCC may my protected health information be shared?

While all reasonable efforts will be made to protect the confidentiality of your protected health information, it may also be shared with the following entities:

- Outside individuals or entities that have a need to access this information to perform functions relating to the conduct of this research such as analysis by outside laboratories on behalf of DF/HCC and its affiliates (for example, data storage companies, insurers, or legal advisors).
- The sponsor(s) of the study, its subcontractors, representatives, business partners, and its agent(s): NIH
- Other research doctors and medical centers participating in this research, if applicable
- Federal and state agencies (for example, the Department of Health and Human Services, the Food and Drug Administration, the National

Institutes of Health, and/or the Office for Human Research Protections), or other domestic or foreign government bodies if required by law and/or necessary for oversight purposes.
- Hospital accrediting agencies
- A data safety monitoring board organized to oversee this research, if applicable

Some who may receive your protected health information may not have to satisfy the privacy rules and requirements. They, in fact, may share your information with others without your permission.

5. For how long will protected health information about me be used or shared with others?

- There is no scheduled date at which your protected health information that is being used or shared for this research will be destroyed, because research is an ongoing process.

6. Statement of privacy rights:

- You have the right to withdraw your permission for the research doctors and participating DF/HCC entities to use or share your protected health information. We will not be able to withdraw all the information that already has been used or shared with others to carry out related activities such as oversight, or that is needed to ensure quality of the study. To withdraw your permission, you must do so in writing by contacting the researcher listed above in the section: “Whom do I contact if I have questions about the research study?”
- You have the right to request access to your protected health information that is used or shared during this research and that is related to your treatment or payment for your treatment, but you may access this information only after the study is completed. To request this information, please contact the researcher listed above in the section: “Whom do I contact if I have questions about the research study?”

L. CONSENT TO OPTIONAL RESEARCH STUDIES:

You are being asked to participate in some optional studies. If you decide not to participate in any of the optional studies, you can still participate in the main research study. Please take your time to make your decision and discuss it with others and your primary care physician.

Your participation in these optional research studies is voluntary, and you will not be penalized or lose any benefits if you refuse to participate or decide to stop.

Optional Study #1:

We can share your declaration video with you if you wish to have a copy of it. There are multiple ways we can share your declaration video with you. The options available to you are dependent on the site where you receive your medical care. The safest and most secure way to share the video is either through an encrypted flash drive or through a tool called Dropbox for Business.

- Option 1: We can put your declaration video on an encrypted flash drive which is password protected and provide the flash drive to you; or

- Option 2: We can post your declaration video on a website called Dropbox for Business. You would be provided web link to view your video online. Dana-Farber has more privacy control over this site and can remove your video at any time. Dropbox for Business would require you to follow multiple steps to view your video.

If you prefer to not use Dropbox for Business or receive through an encrypted flash drive, we can still share your declaration video with you.

- Option 3: We can put your declaration video on an unencrypted flash drive which is not password protected and provide the flash drive to you; or

- Option 4: We can post your declaration video on a YouTube unlisted video setting under the study's YouTube account and provide the web link to you. An unlisted video can only be seen and shared by a web link. The

unlisted video should not be available on YouTube's search results or for people who do not have access to the web link. YouTube is user friendly, and would not require multiple steps to view your video

Please note, for Option 3 and Option 4, we cannot guarantee the confidentiality of your information. For example:

a. If you lose the unencrypted flash drive it may be recovered and accessible by someone else; or

b. If the YouTube web link is shared with another person, it may be possible for that person to post your unlisted video to a public playlist or to re-disclose the web link which would then be accessible by others.

I understand if my health information is disclosed to the media or the general public pursuant to this authorization, it is no longer protected by federal or state privacy regulations and may be re-disclosed by the recipient. I further understand that once such materials are in the possession of media or members of the general public, Dana-Farber will have no control over their use.

Please indicate whether or not you want to take part in this optional research study. If you would like to participate in this optional study and receive a copy of your video declaration, please indicate below and also check off the method above which you would like to receive it by.

☐ Not applicable

☐ Yes _____ Initials _____ Date

☐ No _____ Initials _____ Date

Research Consent Form for Non-Clinical Research
Dana-Farber/ Harvard Cancer Center
BIDMC/BCH/BWH/DFCI/MGH/Partners Network Affiliates OHRS 10.02.2017

Optional Study #2:

There are times when the research team would like to share patients' videos with their colleagues, in scientific presentations or to train study staff. Would you be comfortable in sharing your video publicly for purposes like this? The risk is that the video could be widely shared, depending on the venue, and we will not have any control over this. We will not be analyzing anything so there will be no results.

I understand if my health information is disclosed to the media or the general public pursuant to this authorization, it is no longer protected by federal or state privacy regulations and may be re-disclosed by the recipient. I further understand that once such materials are in the possession of media or members of the general public, Dana-Farber will have no control over their use.

Please indicate whether or not you want to take part in this optional research study.

☐ Not applicable

☐ Yes _____ Initials _____ Date

☐ No _____ Initials _____ Date

N. Documentation of Consent

My signature below indicates:

- I have had enough time to read the consent and think about participating in this study;
- I have had all of my questions answered to my satisfaction;
- I am willing to participate in this study;
- I have been told that my participation is voluntary and I can withdraw at any time

_____ _____

Signature of Participant or Legally Authorized Representative — Date

_____

Relationship of Legally Authorized Representative to Participant

Research Consent Form for Non-Clinical Research
Dana-Farber/ Harvard Cancer Center
BIDMC/BCH/BWH/DFCI/MGH/Partners Network Affiliates OHRS 10.02.2017

Adult Participants

To be completed by person obtaining consent:

The consent discussion was initiated on_____(date).

Signature of individual obtaining consent: _____

Printed name of above: _____

Date: _____

☐ A copy of this signed consent form will be given to the participant or legally authorized representative, or, where the participant is a minor, the participant's parent or legal guardian.

For Adult Participants

☐ 1) The participant is an adult and provided consent to participate.

☐ 1a) Participant (or legally authorized representative) is a non-English speaker and signed the translated Short Form in lieu of English consent document:

As someone who understands both English and the language spoken by the participant, I interpreted and/or witnessed, in the participant's language, the researcher's presentation of the English consent form. The participant was given the opportunity to ask questions.

Signature of Interpreter/Witness: _____

Printed Name of Interpreter/Witness: _____

Date: _____

☐ 1b) Participant is physically unable to sign the consent form because:

☐ The participant is illiterate.
☐ The participant has a physical disability.
☐ Other (please describe): _____

The consent form was read to the participant who was given the opportunity to ask questions and who communicated agreement to participate in the research.
Signature of Witness: _____

Printed Name of Witness: _____

Date: _____

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRITreporting guidelines, and cite them as:

Chan A-W, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, Hróbjartsson A, Mann H, Dickersin K, Berlin J, Doré C, Parulekar W, Summerskill W, Groves T, Schulz K, Sox H, Rockhold FW, Rennie D, Moher D. SPIRIT 2013 Statement: Defining standard protocol items for clinical trials. Ann Intern Med. 2013;158(3):200-207

		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	*1*
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	*19*
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	*1, 19*
Protocol version	#3	Date and version identifier	2
Funding	#4	Sources and types of financial, material, and other support	*2*

Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	*1, 22-23*
Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	*1*
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	*2*
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	*20*
Introduction			
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	*5-6*
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	*6-8*
Objectives	#7	Specific objectives or hypotheses	*6*
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	*6*

Methods: Participants, interventions, and outcomes			
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	*7-8*
Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	*8-9*
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	*7, 9-11*
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	*9-11*
Interventions: adherence	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	*9-11*
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	*N/A: Patients are receiving the standard of care, non-controlled trial.*
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each	*12-13*

		outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	*7-8, See Figure 3a,b*
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	*18-19*
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	*N/A: In this pragmatic trial, all individuals who meet criteria and do not opt out are included in the analysis rather than individual patient recruitment. We have included the description of our population on page 8.*
Methods: Assignment of interventions (for controlled trials)			
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	*7-8*

Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	*7-8*
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	*7-9*
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	*15*
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	*15*
Methods: Data collection, management, and analysis			
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	*8-9, 12-15*
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	*N/A; The unit of randomization is the clinic and all eligible individuals who do not choose to opt out are included and are not followed up over time.*

Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	*8, 13-15*
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	*15-18*
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	*15-18*
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	15-18
Methods: Monitoring			
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	*15, 19-20*
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	*14*
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously	*19*

		reported adverse events and other unintended effects of trial interventions or trial conduct	
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	*19-20*
Ethics and dissemination			
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	*19-20*
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	*19-20*
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	*20*
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	*N/A*
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	*14-15, 19-20*
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	*22*
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	15

Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	*N/A*
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	*20-21*
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	*22-23*
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	*N/A*
Appendices			
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	*Appendix*
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	*N/A*