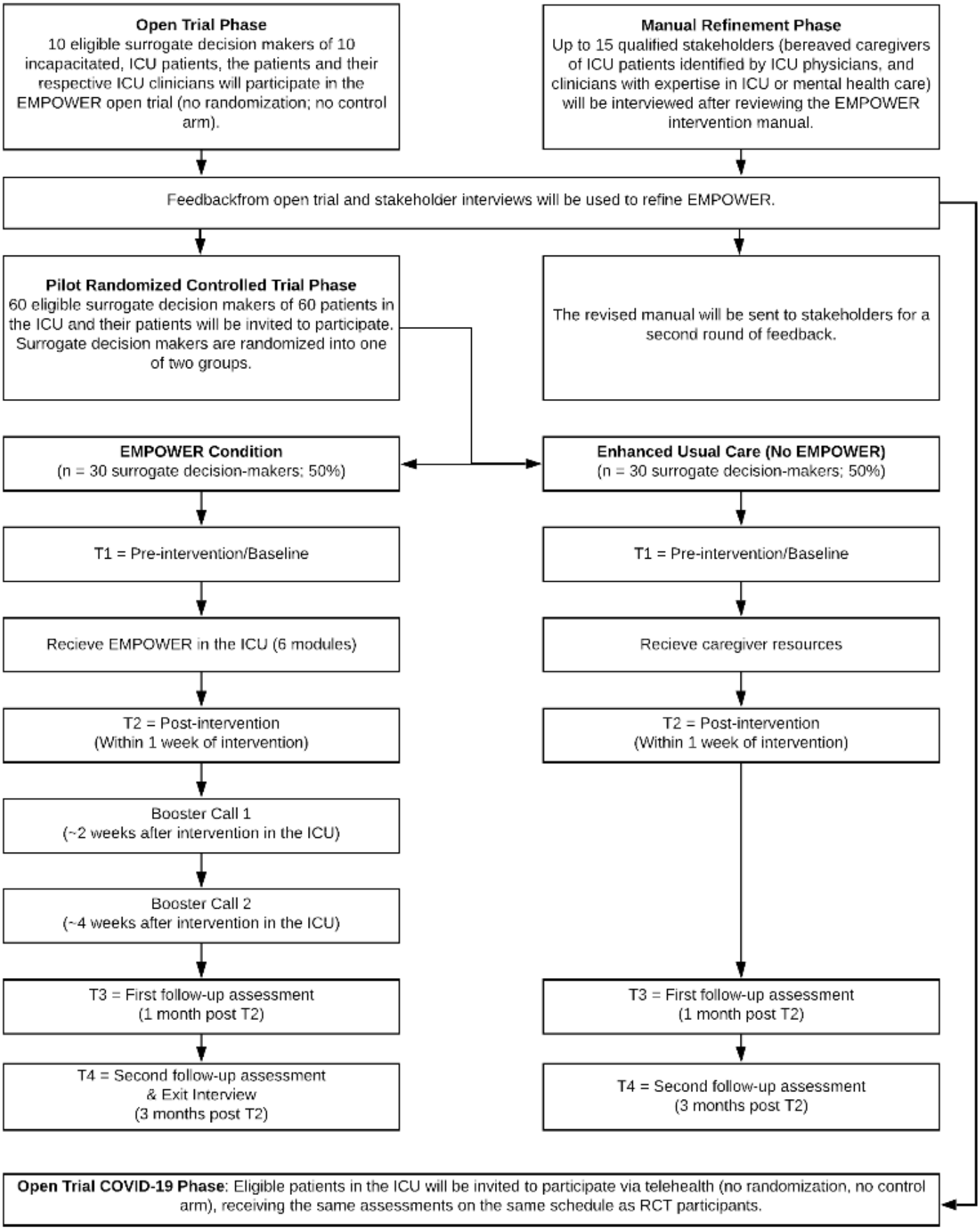
Enhancing & Mobilizing the Potential for Wellness & Emotional Resilience (EMPOWER) of Caregivers of ICU Patients

NCT: NCT03276559

Document Date: 12/14/2022

Section I: Protocol Schema for Open Trial, Pilot RCT, and COVID-19 Open Trial Phase



Section II: Body of Protocol

1.1 Introduction

Intensive Care Units (ICU) are stressful places where life-and-death medical decisions are made and patients and their informal caregivers or surrogate decision-makers are exposed to potentially traumatic experiences. Even within the ICU, we have found that as the number of life-prolonging procedures administered to the patient rises, the patient's quality of life falls.[1,2] Thus, interventions to improve the quality of life and care of ICU patients are needed.

Informal caregivers of patients (referred to further as "surrogate decision-makers") also suffer. Our pilot "Severity of Suffering" (SoS) study of patients who die in New York Presbyterian Hospital's (NYPH) ICU found that >60% of these patients had cancer. ICU nurses who reported on the patient's quality of life and care in their final week perceived that 53% of the cancer patients' informal caregiver experienced acute psychological distress, 43% had unrealistic expectations for the patient's recovery, and 41% insisted that the patient receive burdensome care (e.g., resuscitation). Over 85% of these patients were unable to communicate, leading to a situation in which a caregiver must make life-and-death decisions for a critically ill, incapacitated patient amid the challenges posed by peritraumatic stress and anticipatory grief. In turn, peritraumatic stress and grief would be expected to exacerbate **experiential avoidance**, defined as "the phenomenon that occurs when a person is unwilling to remain in contact with particular private experiences (e.g. bodily sensations, emotions, thoughts, memories, behavioral predispositions) and takes steps to alter the form or frequency of these events." [3,4] The confluence of peritraumatic stress, anticipatory grief, and experiential avoidance may additionally serve as a barrier to advance care planning (ACP). We have shown ACP leads to higher quality, less aggressive and more value- consistent end-of-life (EoL) care, as well as better patient quality of life,[5] both of which predict better bereavement adjustment.[6,7] We have also shown that informal caregivers of patients who die in the ICU are at elevated risk of posttraumatic stress disorder (PTSD) in the months that follow the potentially traumatic ICU "exposures".[8,9] ***These findings indicate a compelling need to address the peritraumatic stress and grief of surrogate decision-makers of patients in the ICU.***

Efforts targeting the plight of critically ill patients and their informal caregivers have produced mixed results for improving EoL care and informal caregiver mental health.[10-12] In a recent study of a palliative-care intervention in the ICU designed to reduce caregiver anxiety and depression, PTSD symptoms actually *increased* for those caregivers who received the intervention.[12] ***A primary limitation of these interventions is that they have targeted mental health outcomes but were not explicit mental health interventions.***

We propose here a proof-of-concept study to address this limitation. In response to requests by the directors of the NYPH Medical ICU (MICU), Dr. David Berlin and Dr. Lindsay Lief, to address the emotional distress of surrogate decision-makers, we have developed a mental health intervention for surrogate decision-makers of patients in the ICU. We aim to develop further and pilot test this brief mental health intervention called "Enhancing & Mobilizing the POtential for Wellness & Emotional Resilience among Surrogate Decision-Makers of ICU Patients" (EMPOWER) that can be delivered by a trained mental health provider to patient surrogate decision-makers in the ICU. EMPOWER is a cognitive-behavioral, acceptance-based intervention designed to reduce "experiential avoidance"[3,13] of unpleasant thoughts and feelings related to thinking about the patient's death. EMPOWER targets symptoms of peritraumatic stress and anticipatory grief to reduce experiential avoidance that interferes with optimal decision-making on the patient's behalf. It consists of discrete ~15-minute modules that can be delivered flexibly in a setting with multiple interruptions and unexpected crises. The intervention can be delivered in-person or via telehealth. By reducing surrogate decision-makers' experiential avoidance, EMPOWER removes a barrier to ACP, including the completion of advance directives, such as Do Not Resuscitate (DNR) orders. It also is expected to promote the receipt of EoL care consistent with patient values. In this way, EMPOWER should improve EoL care that enhances patient quality of life while also empowering surrogate decision-makers to cope with a loved one's impending death and adjust following the patient's ICU death or discharge. Specifically, we aim to:

#1: Develop EMPOWER for surrogate decision-makers of critically ill patients who are at risk of becoming incapacitated and/or who are currently unable to make medical decisions. *Key informants, including bereaved informal caregivers of ICU patients and clinicians, will be asked to evaluate the EMPOWER intervention manual to increase its potential tolerability, acceptability, and efficacy.*

#2: Determine the feasibility, tolerability, acceptability, and preliminary effects of EMPOWER on surrogate mental health. *We hypothesize that revised EMPOWER will be feasible, tolerable, and acceptable. The intervention will also reduce peritraumatic distress post-intervention, and improve mental health outcomes at one-month and three-month follow up from post-intervention assessment compared to enhanced usual care.*

#3: Estimate the effects of EMPOWER on patient outcomes in the months following the baseline assessment. *Patients who receive EMPOWER are expected to have higher rates of engagement in advance care planning (e.g., a DNR order completed), better surrogate-reported quality of life/quality of death, and more value-concordant care (measured through comparing intensity of care at end-of-life to surrogate perception of patient treatment preferences) compared to patients whose surrogates receive enhanced usual care.*

This trial initially proposed to have 15 eligible stakeholders provide feedback about EMPOWER to inform improvements; to enroll 10 initial open trial cases and then to randomize 60 surrogate decision-makers of terminally, critically ill patients who are incapacitated or at risk of becoming incapacitated to EMPOWER or enhanced usual care. Beginning in April 2020, however, to meet the needs of family members in the COVID-19 pandemic, as well as to accommodate recruitment of human subjects with necessary social distancing practices, the RCT phase was paused to enter a new open trial phase (referred to hereafter as the COVID-19 open trial) that did not include randomization or a control arm. Upon approval of amendment #1610017622-13, we will return to the RCT phase. To adhere to recruitment strategies that were originally proposed, the number of participants enrolled in this study will not exceed the 60 participants initially projected, although due to the COVID-19 open trial, over 30 participants total may receive the EMPOWER intervention. Assessments will occur pre-intervention, immediately post-intervention, and then 1 month and 3 months from post-intervention assessment. Results will be used to seek NIH R01 funding for a larger-scale randomized controlled trial (RCT) intervention efficacy study of EMPOWER.

1.1 Overview

To obtain stakeholder input on EMPOWER and refine the intervention manual, we propose to enroll up to 10 bereaved caregivers of patients who were incapacitated and treated in the ICU and 10 clinicians with expertise in ICU and/ or mental health care to have them review the study protocol and intervention manual and to obtain structured feedback on EMPOWER. Interviews will be audio-recorded, transcribed verbatim by trained staff, and kept confidential. Participants will also have the option to respond to interview questions through written response. In addition, we will enroll family caregivers and ICU patients to pilot the EMPOWER intervention and examine its effects on both informal caregivers and patients in the ICUs at New York Presbyterian Hospital (NYPH)- Weill Cornell, New York Presbyterian Hospital-Queens, and Memorial Sloan Kettering Cancer Center (MSK), as well as among surrogate decision-makers from outside hospitals recruited online. Surrogate decision-makers will be screened for emotional dependency on the patient and feelings of emotional distress related to the patients' ICU admission. Eligible surrogate decision-makers will be enrolled. The first 10 surrogate decision-makers will be enrolled in an open trial. A pilot RCT will then begin, randomizing surrogate decision-makers to receive either EMPOWER or enhanced usual care using a block-randomization strategy to determine condition assignment., A second open trial phase, only assigning surrogates to the EMPOWER trial in response to the COVID-19 pandemic, began on April 2020, with a return to the RCT following approval of amendment #1610017622-13. 60 surrogate decision makers will be enrolled in the RCT and COVID-19 open trial phases combined. Surrogate decision-makers will be assessed at 4 time points (T1 = baseline, T2 = up to one week following intervention, T3 = one month from T2, and T4 = three months from T2). The EMPOWER intervention will be administered by trained interventionists either in-person or via telehealth. The intervention sessions will be audio-recorded for training purposes. If participants agree, the sessions will be video-recorded. Patients' medical chart information will be abstracted

following the death of the patient. If the patient is not deceased by the end of their surrogate decision-maker's participation in the study, medical chart information will be abstracted at T4.

1.2 Background and Rationale

ICU stays are established indicators of low quality EoL cancer care and oncologists have long recognized ICU stays as a marker of poor quality EoL cancer care. [14] Nevertheless, from 2007 to 2010, the percentage of US cancer patients admitted to the ICU during the last month of life increased from 24% to 29%.[15] Our recent research reveals that 60%-90% of the patients who die each week in the ICU at NYPH are cancer patients, and 85% of these cancer patients were sedated, on ventilators and unable to communicate. This leaves record numbers of surrogate decision-makers (family/friends) struggling to make life-and death decisions for a patient in the ICU with whom they cannot communicate. Given the ICU default position is to provide life-prolonging care, without advance care planning or surrogate decision-makers' agreement, more aggressive care would likely be given to patients to keep them alive. This exposes surrogate decision-makers to potentially traumatic experiences that further heighten their risk of PTSD.[8] One study reported 33% of family members were at serious risk of PTSD following the patients' ICU discharge or death, and rates rose to an alarming 82% in those who "shared in end-of-life decisions".[16]

Results from several NIH-funded studies of interventions in the ICU have not produced positive results for caregiver mental health[17]. Recent publications demonstrate worse, not better, mental health outcomes of caregivers.[10,12] Given that prior studies have focused on communication interventions with little attention to symptoms of peritraumatic stress or anticipatory grief, this is not surprising to mental health professionals.

The present study draws insights from international experts on peri and posttraumatic stress and grief to target specific symptoms of stress, trauma and grief among ICU patient surrogate decision-makers, thereby improving patient EoL outcomes. This EMPOWER study has been tailored for the fast-paced, often chaotic, ICU milieu with brief cognitive-behavioral therapy (CBT) interventions that have demonstrated evidence for significantly reducing PTSD symptoms in highly anxious hospitalized patients (multiple sessions that altogether will take around 90 minutes, can be completed within 2-3 days) while traditional CBT interventions are administered over weeks. EMPOWER will explore an exciting, albeit challenging, application of proven psychotherapeutic approaches to the realities of critical care medicine.

2.0 Objectives

Specific Aim #1:
Develop EMPOWER for surrogate decision-makers of critically ill ICU patients who are at risk of becoming incapacitated and/or who are currently unable to make medical decisions.
There are no hypotheses for this objective. Stakeholders, including bereaved ICU patient caregivers and clinicians, will be asked to evaluate the EMPOWER intervention manual to increase its potential tolerability, acceptability, and efficacy. Data from the open trial of 10 surrogate decision-makers will also identify tactical and measurement issues involved in the delivery and outcome measurements used in EMPOWER.

Specific Aim #2:
Determine feasibility, tolerability, acceptability, and preliminary effects of EMPOWER on surrogate decision-maker mental health.
Hypothesis #2:
Revised EMPOWER will be feasible, tolerable, acceptable. Those who are randomized to EMPOWER will have reduced peritraumatic distress at post-intervention assessment (T2). Those who are randomized to EMPOWER will have reduced symptoms of PTSD, prolonged grief disorder, anxiety, and depression, and less decisional regret and experiential avoidance at one-month and three-month follow up from baseline (T3 and T4).

Specific Aim #3:
Examine the effects of EMPOWER on patient outcomes, including intensity of care and quality of life/quality of

death, in the months following baseline assessment.

Hypothesis #3:

Patients whose surrogate decision-makers receive EMPOWER will have better quality of death (for patients who died), better quality of life (for patients who are still alive) and more value-concordant care compared to those whose surrogate decision-makers receive enhanced usual care at one-month (T3) and three-month (T4) follow up from post-intervention assessment.

3.0 Research Subject Selection

3.1 Eligibility Criteria

For stakeholders:

1. Bereaved family caregivers of patients treated in the ICU identified by referring clinicians and through support groups, clinics, and word of mouth
2. Clinicians with expertise in mental health care and/or critical care including but not limited to nurses, nurse practitioners, social workers, psychologists, psychiatrists, hospital chaplains, and physicians

For open trial participants:

1. Patients (>21 years) who cannot communicate and decide on treatments, who during the course of their current hospital stay were admitted to an ICU/step-down unit, and whose ICU physicians or fellows would not be surprised if the patient did not survive more than 3 months
2. Surrogate decision-makers whom ICU physicians or fellows indicate as the designated health care proxy or decision-making patient surrogates, or who are listed as such in the patient's medical charts
3. Surrogate decision-makers must speak English
4. Surrogate decision-makers must either meet the threshold for a high degree of emotional dependence (PDS [18] score >8) on the patient or on the McGill Quality of Life Scale[19] items (either anxiety item score>5).

For adult pilot RCT participants:

1. Patients (>18 years) who during the course of their current hospital stay were admitted to an ICU/step-down unit
2. Surrogate decision-makers whom ICU physicians or fellows indicate as the designated health care proxy or decision-making patient surrogates, or who are listed as such in the patient's medical charts or by self-report of the surrogate
3. Surrogate decision-makers must speak English
4. Surrogate decision-makers must either meet the threshold for a high degree of emotional dependence (PDS [18] score >8) on the patient or on the McGill Quality of Life Scale [19] items (either anxiety item score>5).
5. Surrogate decision-makers who do not meet criterion #4 but are identified by clinical staff as distressed and whom clinical staff believe would benefit from the intervention.

For child pilot RCT/COVID-19 Open Trial participants:

1. Patients below the age of 18 who have spent at least 3 days in a pediatric intensive care unit
2. Surrogate decision-makers whom ICU physicians or fellows indicate as the designated health care proxy or decision-making patient surrogates, or who are listed as such in the patient's medical charts or by self-report of the surrogate, or are parents of the patient
3. Surrogate decision-makers must speak English

For adult open trial COVID-19 participants:

1. Patients (>18 years) who during the course of their current hospital stay were admitted to an ICU/step-down unit
2. Surrogate decision-makers whom a member of the patient's care team indicate as the designated health care proxy or decision-making patient surrogates, or who are listed as such in the patient's medical charts
3. Surrogate decision-makers must speak English
4. Surrogate decision-makers must either meet the threshold for a high degree of emotional dependence

(PDS 18 score >8) on the patient or on the McGill Quality of Life Scale items (either anxiety item score>5).

5. Surrogate decision-makers who do not meet criterion #4 but are identified by clinical staff as distressed and whom clinical staff believe would benefit from the intervention.

3.1 Exclusion Criteria

Patients and surrogate decision-makers who do not meet the eligibility criteria or surrogate decision-makers who endorse suicidal ideation in the past month based on responses to the Columbia Suicide Severity Rating Scale [20]

4.0 Informed Consent Process

Informed consent is a process, not a one-time event. During the informed consent process, the study staff obtaining consent will review the study in detail allowing for the participant (surrogate decision-maker, stakeholder, or patient) to interject with questions at any time during the discussion. It is extremely important that the participant has an opportunity to have his/her questions addressed as well as ample time to read the consent document and determine whether or not they would like to participate in the study. For consents occurring in-person, study staff and potential participants will review the consent form together. For consents occurring digitally, study staff will contact potential participants and provide them with a digital copy of the consent form in REDCap that they will able to simultaneously view virtually while speaking to the consenting professional. Attending physicians and fellows who are trained, IRB-approved members of the research team, such as but not limited to those working in the pediatric intensive care unit, may also obtain consent from surrogates and patients, including those under their care, using the procedures outlined in this section. Any reference to study personnel/staff in regard to recruitment/consenting procedures includes these physicians.

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

The study staff will explain in explicit detail what will be asked of participant if he/she agrees to participate in the study and estimate the potential time commitment involved. The participant will know what his/her responsibilities will entail, what risks or benefits may be involved, and what potential costs could be incurred should they agree to participate. Study staff will underscore the importance placed upon maintaining participant confidentiality, as well as participant's rights while involved in the study, which includes the right to withdraw participation at any time during the research due to the fact that their participation is entirely voluntary in nature.

The informed consent form will provide contact information for both the Principal Investigators as well as the Office for the Protection of Research Subjects. All informed consent processes will adhere to the policies set forth by the Institutional Review Board. All paper informed consent forms will be stored in a locked file cabinet in a locked office to maintain the privacy of all study participants. All digital consent forms will be stored in a password protected REDCap database accessible only to authorized study staff.

For adult patients recruited for the study who are uncommunicative, a waiver of informed consent is requested. For adult patients with capacity, the participating caregiver will be approached to ask if they believe the patient would be interested in consenting to release the medical records for the chart review, and if so, the best way and time to contact them. Research Assistants will then consent the patient using the previously-approved adult patient consent form, making any necessary accommodations for patients who may still be in the hospital or discharged (i.e., consenting in person with paper form, mailing consents, or consenting over the phone with REDCap consent). This approach will occur at any point following T2 at the discretion of the research team in order to minimize burden on the surrogate and patient and allow for the most logistically efficient scenario (i.e., waiting until the patient has been discharged). For all patients below the age of 18, regardless of communicative

status, surrogate decision-maker consent to access previously collected medical record data will be obtained. All surrogate decision-makers recruited for the study will be consented by a trained research assistant or trained member of the care team as outlined above, either in person or over a phone or video meeting when necessary. The consent form will be signed with the participant's full understanding of the study process.

For consented surrogates whose indexed patients are communicative and capable of consenting, but are considered high-risk or the consenting process is unable to be reasonably facilitated by the care team, these surrogates will be able to participate in the study without consent of the patient. In these cases, the patient's medical information will not be recorded.

Trained research assistants will go over informed consent with providers and stakeholders either in-person or through a phone call. If the consenting is done in-person, a research assistant will schedule a mutually convenient time when stakeholder's location or business schedule allows for in-person consent. The consent form will be signed with the provider's/stakeholder's full understanding of the study process. If the consenting is done over the phone, a trained research assistant will schedule a mutually convenient time for a phone call to conduct verbal informed consent of stakeholders. The trained research assistant will use the verbal consent script to review the main points of the written consent form with the stakeholder. The written informed consent form will be sent to the stakeholder by mail or email, depending on the stakeholder's preference, prior to the phone call. The written informed consent will be signed with the stakeholder's full understanding of the study process and sent back by mail or email, depending on the stakeholder's preference. Stakeholders who prefer to receive and return the informed consent form by mail will be provided with a self-addressed and stamped envelope. The interview will not take place until the signed written informed consent document is received and documented in the study record.

5.1 Study Design and Methods

5.2 Study Design

There are two phases in this study. The manual refinement phase involves obtaining feedback from stakeholders (bereaved caregivers and clinicians) about the EMPOWER intervention manual using qualitative analysis followed by a modified Delphi method. The second phase involves piloting EMPOWER to obtain information on its feasibility, tolerability, acceptability, and preliminary effect size estimates in order to plan a larger, efficacy RCT. We will conduct an open trial of the intervention followed by a parallel-arm RCT comparing EMPOWER to enhanced usual care. In order to supplement RCT recruitment, adapt to restrictions in ICU visitation and meet the needs of family caregivers impacted by the COVID-19 pandemic, a secondary open trial occurred beginning April 2020, with a return to RCT procedures following approval of amendment #1610017622-13.

Manual Refinement:

Up to 15 stakeholders who are bereaved caregivers and expert clinicians from Memorial Sloan Kettering Cancer Center (MSK), Weill Cornell Medicine (WCM) and the community will be enrolled to review the intervention manual to assess feasibility and to provide professional expertise. Participants will be provided a copy of the intervention manual to review by mail, email, or in-person delivery. They may also be provided with the questions they will be asked during the subsequent interview to help them prepare. Within 4 to 6 weeks, the research team will conduct an in-person, telephone, or videoconference interview of approximately 60 to 90 minutes to collect feedback on the manual. Interviews will be audio recorded. As an alternative or in addition to this interview, participants will be given the option to provide feedback in writing and through making notes and edits on the manual. Edited copies can be returned via mail, email, fax, or hand delivery. Received materials will be de-identified. Feedback from the stakeholders will be coded using qualitative data analytic approaches. We will transcribe the stakeholder key informant interviews and content-analyze the transcribed interviews and any additional written materials following Morses' guidelines[21]. The coding team will independently review the feedback materials and will synthesize and interpret participants' input about the content of the EMPOWER manual until consensus on a final set of thematic findings to tailor the manual is reached. The manual will then be refined applying these findings. A modified Delphi approach will be used by providing the stakeholders with a summary describing substantive changes to the manual by email or mail. They will be given the revised manual and asked to provide any comments or additional feedback they may have. This feedback will be requested through a self-report REDCap survey. Participants will be asked to respond to the survey within 4 weeks, at which point a reminder will be sent out if all responses have not been received. Survey results will be used to further refine the EMPOWER manual.

Ultimately, feedback will be used to inform modifications to the EMPOWER manual, as will review of results of the open trial experience and data described below. Additionally, we may use entirely anonymous quotes from participants' feedback in the final versions of the manual. When working with highly distressed populations, it can be particularly valuable and potentially powerful to include direct statements from other individuals who have been in a similar position to help explain relevant therapeutic concepts and the experience of surrogate decision-makers and to demonstrate that expert input was used in the intervention development process. As such, we think that including participants' quotes in the manual when applicable would strengthen the EMPOWER intervention by giving the approach additional credibility and potency.

Pilot Trials:

This is a clinical intervention study that will enroll 70 surrogate decision-makers (10 in the open trial + 60 in the RCT/COVID-19 open trial) who are the surrogates of 70 current patients from Weill Cornell Medicine/New York Presbyterian Hospital (NYPH), NewYork Presbyterian Queens' and MSK's ICUs including, but not limited to the MICU, CCU, SICU, and their step-down units. Research staff will obtain permission to approach surrogates from any member of the patient's care team (such as, but not limited to physicians or nurses) in order to reduce burden on critical care staff. If during the course of recruitment, potential participants suggest that another surrogate for the patient

not listed in the medical record would be better suited for participation in this study, research staff will confirm with the care team that the referred individual is involved in medical decision-making for the patient, thus satisfying criteria #2 of the inclusion criteria, and we will reach out to the referred individual as appropriate. Additional background information on candidates (normal visiting times, family dynamics) will be ascertained from allied health professionals such as, but not limited to, nurses or care coordinators. WCM's Institutional Review Board (IRB) has approved a HIPAA full waiver for the patient's medical information.

Surrogates from outside hospitals will also be recruited via publicization of the study in outside palliative/intensive care services and online resources, such as, but not limited to, Mettle Health. In these cases, participants will reach out to the study team using information provided in fliers by outside clinicians. General patient health (i.e. whether the patient has died during study course, reason for admission) and demographic data of the patient will be reported by the surrogate.

Surrogate decision-makers will be consented and screened. Surrogate decision-makers of adult patients who have greater than "5" on a 0-10 scale on the McGill Quality of Life Scale[19] measure items on anxiety, or who score greater than "8" on the first two items of the Bereavement Dependency Scale (PDS)[18] will be enrolled. Additionally, participants of adult patients who do not meet these criteria but are reported by an ICU clinician (such as, but not limited to, the patient's nurse) to be distressed and likely to benefit from the EMPOWER intervention may be enrolled. Participants who endorse suicidal ideation in the past month on the Columbia Suicide Severity Rating Scale[20] items will be excluded. Open trial participants will receive the intervention through an open trial with no comparison arm. RCT participants will be randomized using a block-randomization strategy[22] to receive EMPOWER or enhanced usual care.

The enhanced usual care arm will involve regular ICU care and provide information about ICU surrogate decision-maker resources specific to each site location. It is intended to serve as a control condition. Enhanced usual care participants will receive information about resources available to all ICU surrogate decision-makers (eg. ICU Caregiver support group information; ICU/Palliative care social worker's information) as well as an informative packet about caregiving. Pediatric patient surrogates and adult patient surrogates will receive separate information packets and resource lists tailored to their respective patient populations. EUC resources and information packets can be delivered to participants as hard or digital copies, delivered in-person, via mail, or as a pdf document accordingly. Participants recruited from outside hospitals will receive a list of nationally-available resources.

Surrogate decision-makers will be assessed pre-intervention/baseline (Time point 1, T1), post-intervention (within a week of the surrogate decision-maker's completion of the baseline assessment) (Time point 2, T2), 1-months after post-intervention assessment (Time point 3, T3), and 3-months after post-intervention assessment with an additional exit interview with the research staff that will take about 40 minutes to complete for those receiving EMPOWER only (Time point 4, T4). Assessments will be completed using paper-and-pencil assessments, over the phone with research staff, or online (REDCap). The exit interview will be audio recorded and can be in person, over the phone, or over videoconference.

The EMPOWER arm includes 6 modules that are approximately 15-20 minutes each, all delivered by the same interventionist one-on-one in person or if needed, over the phone or video conference. The intervention can be completed in approximately 1.5 to 2 hours in a single sitting in the ICU, or modules can be completed in piecemeal if the surrogate decision-maker prefers or needs to stop because of, for example, the need to attend to the patient or speak with the medical team. If the intervention is completed in piecemeal, it is expected the intervention will occur over the course of 2-3 days, although scheduling will be flexible to not burden participants and be sensitive to needs such as bereavement and urgent medical situations. There are 2 booster sessions (approximately 1 hour each) that are conducted via telehealth medium such as phone or video call 2 and 4 weeks after the initial 6 modules are completed. If the patient dies before the 6 modules are completed, the interventionist will make a condolence call during which he/she will offer to continue the modules if the surrogate decision-maker is interested (during that call or at a separate time). If the surrogate decision-maker declines completion of the 6 modules, the interventionist will indicate that he/she will call again in 2 weeks to offer support and review what they have previously discussed. Due to the wide variety of

participant experiences and circumstances in the ICU, parts of the intervention may be omitted or amended at the discretion of the interventionist to meet the needs of the participant. The EMPOWER intervention is designed to be administered in the ICU, but to accommodate the varying needs of participants, may be administered in other private clinical settings on the campuses of the recruiting sites as well as via applications used for telehealth, such as but not limited to Webex or Zoom.

All participants who receive EMPOWER (both open trial and RCT cases) will be audio- and/or video-recorded for supervision and training purposes, with the participant's approval. They can opt out of video-recording and still participate, but audio-recording is mandatory.

EMPOWER is based on well-established cognitive-behavioral and acceptance-based techniques that aim to reduce maladaptive avoidance of distressing emotions. The EMPOWER interventionist will be compassionate and will attempt to provide validation of the surrogate decision-makers' experience; to teach tools for remaining present-focused; to explore the surrogate decision-maker's and the patient's wishes, values, and decision challenges; to increase their sense of acceptance and permission to experience challenging emotions; and to prepare them to cope with future distressing situations.

The primary outcome will be peritraumatic distress. We hypothesize that at post-intervention assessment, surrogate decision-makers who receive EMPOWER will have significantly lower symptoms of peritraumatic distress when compared to surrogate decision-makers who receive ICU enhanced usual care.

Secondary surrogate decision-maker outcomes will be surrogate decision-maker Prolonged Grief Disorder (PGD) symptom severity (either pre-loss/anticipatory or post-loss/bereavement grief) and experiential avoidance at one-month and three-month follow up. Exploratory surrogate decision-maker outcomes will be symptom severity of PTSD, depression, anxiety, and decision regret at one-month and three-month follow up. For both secondary and exploratory outcomes, we hypothesize that surrogate decision-makers who receive EMPOWER will have significantly lower symptoms compared to surrogate decision-makers who receive ICU enhanced usual care.

Patient outcomes will include ACP, intensity of care, and quality of life/death one-month post-baseline. We hypothesize that patients whose surrogate decision-makers receive EMPOWER will report better quality of life/quality of death with more value-concordant care compared to those whose surrogate decision-makers receive enhanced usual care.

In the event of patient death, the study team will mail either a handwritten or typed condolence card with a standardized message. This condolence card may not be mailed at the discretion of the principal investigators.

5.1 Measures Used

Measures may be completed using hard copies, online (REDCap), or by RA interview, depending on the respondent's preference and research restrictions due to COVID-19. During the COVID-19 open trial, any hard copies will be mailed, digital copies will be emailed and RA interviews will occur over the phone or other telehealth medium.

Sociodemographic Characteristics:

Demographics: Surrogate decision-makers' will be asked in a self-report assessment occurring either in clinic or over the telephone their own and the patient's age (years), gender, race, education, mental health history, income, marital status, religious/spiritual beliefs, ACP knowledge/understanding, treatment preferences, prognostic understanding, and relationship with patient. Stakeholders will report on their own demographics.

Medical factors for Patients:

Patients' diagnoses (e.g., Stage IV pancreatic or NSCL cancer), reason for hospital/ICU admission, DNR/DNI order status, ACP items (including palliative care consultations), care plans obtained from the medical chart or ICU physicians and fellows, as well as clinically relevant symptoms related to patient incapacity, such as but not limited to, delirium. This information will be compiled as a medical chart abstraction and matched with surrogate-assessed patient treatment preferences assessed at T1 to create a measure of rates of value-concordant care. These medical factors, in addition to the CEQUEL [23], will serve to measure the outcomes specified in Aim #3.

Psychosocial factors for Surrogate decision-makers:

Screener: Consists of items from 4 items from McGill Quality of Life[19], two items from the Partner Dependency Scale [18], and two items from the Columbia Suicide Severity Rating Scale [20].

Adult Surrogate Pre-intervention/ Baseline Assessment (T1): Psychiatric History, Demographics, and Treatment Preferences; Prolonged Grief Disorder (PG-12) Caregiver Version; [24 25,26]; Fear of Losing Loved Ones Scale (FOLLOS); Peritraumatic Distress Inventory (PDI) [27]; Peritraumatic Dissociative Experiences Questionnaire (PDEQ) ICU Version[28]; Impact of ICU Events Scale-Revised (IES-R) [29]; Brief Experiential Avoidance Questionnaire (BEAQ); [30]State Trait Anxiety Inventory - State scale (STAI) [31]; Patient Health

Questionnaire (PHQ-9); [32] Distress Tolerance Scale (DTS) [33] revised version; Caregiver Self-Efficacy in the ICU Scale; Decision Regret Scale (DRS) – EMPOWER[34]; Regret Assessment.

Adult Surrogate Post-intervention Assessment (T2): PG-12 (if patient is alive); FOLLOS (if patient is alive); PG-13 (if patient is deceased); [24] [25,26] PDI; PDEQ; IES-R; BEAQ; STAI; DTS revised version; Caregiver Self-Efficacy in the ICU Scale; DRS - EMPOWER; Regret Assessment; Post-Intervention Satisfaction Questionnaire (PISQ).

Adult Surrogate 1 Month Post-T2 Assessment (T3): PG-12 (if patient is alive); FOLLOS (if patient is alive); PG-13 (if patient is deceased); PDI; IES-R; BEAQ; STAI; PHQ-9; DTS revised version; Critical Care Family Satisfaction Survey- EMPOWER; CEQUEL-R (if patient is alive); CEQUEL [23] (if patient is deceased); Quality of Life (if patient is alive); Quality of Death (if patient is deceased); DRS - EMPOWER; Regret Assessment; Medical Information Update

Adult Surrogate 3 Months Post-T2 Assessment (T4): PG-12 (if patient is alive); FOLLOS (if patient is alive); PG-13 (if patient is deceased); PDI; IES-R; BEAQ; STAI; PHQ-9; DTS revised version; CEQUEL-R (if patient is alive); CEQUEL (if patient is now deceased, but was alive at T3); Quality of Life (if patient is alive); Quality of Death (if patient is deceased); DRS - EMPOWER; Regret Assessment; Medical Information Update; Qualitative Exit Interview for (participants receiving EMPOWER intervention only).

Pediatric Surrogate Assessments: STAI, PDI, PG-12, IES-R, DRS-EMPOWER at all 4 timepoints, with brief demographics at T1, Post-Intervention Satisfaction Questionnaire at T2, and Qualitative Exit Interview at T4 (for participants receiving EMPOWER intervention only).

Measure Title	Time Points Used*	Description of Measure
McGill Quality of Life Scale	Screener	Items 5 through 8 are used to measure anxiety/depression.
Partner Dependency Scale (PDS)	Screener	Items 1 and 2 of the PDS are used to measure dependency. The language is altered to refer to the patient rather than a spouse.
Columbia Suicide Severity Rating Scale	Screener	Items 1 and 2 of the CSSRS are used to measure suicidal ideation.
Peritraumatic Distress Inventory (PDI) ICU Version	T1, T2, T3, T4	Measures peritraumatic distress.
Peritraumatic Dissociative Experiences Questionnaire (PDEQ) ICU Version	T1, T2	Measures experiences of dissociation that may occur in the ICU. Instructions are changed to prompt the participant to specifically answer the survey in reference to their experience in the ICU.
Impact of ICU Events Scale-Revised (IES-R)	T1, T2, T3, T4	Measures symptoms of PTSD.
Brief Experiential Avoidance Questionnaire (BEAQ)	T1, T2, T3, T4	Measures experiential avoidance.
State Trait Anxiety Inventory (STAI) - State	T1,.T2, T3, T4	Measures symptoms of generalized anxiety disorder.
Patient Health Questionnaire (PHQ-9)	T1, T3, T4	Measures symptoms of depression.
Distress Tolerance Scale (DTS)	T1, T2, T3, T4	Measures ability to tolerate distress. Items 1, 2, 9, and 13 are retained from the original.
Decision Regret Scale (DRS) – EMPOWER	T1, T2, T3, T4	Measures symptoms of decision regret. Modifies instructs of original instrument to include a specific indexed regret.
Regret Assessment	T1, T2, T3, T4	Measures distress or remorse after a health care decision made by the participant. Items were developed by clinicians and an expert in psychometrics to identify common difficulties faced by caregivers in the ICU setting.
Caregiver Self-Efficacy in the ICU Scale	T1, T2	Items were developed by clinicians and an expert in psychometrics to identify common difficulties faced by caregivers in the ICU setting.
Critical Care Family Satisfaction Survey - EMPOWER	T3	Measures caregiver's reported feelings towards the medical team and regarding medical decisions in the ICU. Items were developed by clinicians and an expert in psychometrics to tailor the instrument to the ICU setting based on a scale created by Wasser & Matchet[35].

Post-Intervention Satisfaction Questionnaire	T2	Measures satisfaction with EMPOWER intervention or usual care, as well as acceptability, feasibility, and tolerance. Items were developed by clinicians and an expert in psychometrics. Items measuring acceptability were developed based on an empirically- validated framework of healthcare intervention acceptability that measures constructs of participant affect, burden, intervention coherence, opportunity costs, perceived effectiveness, and self-
Enhanced Usual Care Tracker	T2 (for Enhanced Usual Care group only)	Measures utilization of Enhanced Usual Care resources.
Prolonged Grief Disorder (PG-12) Caregiver Version	T1, Status dependent @ T2, T3, T4	Measures anticipatory grief. Language is changed to reflect that the patient has not died yet, and does not contain the duration criterion of 6 months as in PG-13.
Prolonged Grief Disorder (PG-13)	Status dependent @ T2, T3, T4	Measures grief.
Fears of Losing Loved Ones Scale (FOLLOS)	T1, Status dependent @ T2, T3, T4	Measures attachment-related distress associated with anticipatory grief. Items were developed by clinicians and an expert in psychometrics.
Caregiver Evaluation of the Quality of End-of-Life Scale (CEQUEL)	Status dependent @ T3, T4	Measures caregiver's subjective evaluation of the patient's quality of death. If administered at T3 due to patient death, will not be administered at T4.
CEQUEL-Revised	Status dependent @ T3, T4	Administered to caregivers whose patients are still living. Retains items measuring caregiver satisfaction with medical care for the patient, but removes questions regarding patient's death.
CEQUEL-Revised	Status dependent @ T3, T4	Administered to caregivers whose patients are still living. Retains items measuring caregiver satisfaction with medical care for the patient, but removes questions regarding patient's death.
Quality of Life/Death	Status dependent @ T3, T4	Measures caregiver's perception of the patient's most recent week of life (either their most recent week, or most recent week before death). If Quality of Death is administered at T3, it will not be administered again at T4. Items have been previously published upon and validated[2].

*Refers to assessments for adult surrogate participants

Qualitative data:

All surrogate decision-makers will provide feedback on the intervention in a post-intervention satisfaction questionnaire at T2. Those assigned to the EMPOWER intervention will also participate in a qualitative exit interview at T4. Stakeholders will provide feedback on the intervention manual in self-report questionnaires, written form, and/or in-person interviews. Clinicians will provide information about the patient before recruitment occurs via the patient information form or discussion with research assistants.

5.2 Data Collection (Please find the details on data to be collected in 5.2)

Note: All patient and surrogate decision-maker identifiable information will be kept in a password protected electronic database, REDCap. Self-report data will be entered into and stored on the WCM REDCap server. Audio and video recorded data collected at all study sites will be stored on WCM's secure server. Research study staff at MSK will be given access to the data. Collected data will only be identified via a study ID that will serve as a link to identifiable information. Hard copies of the collected data will be kept in a locked file cabinet within a locked office and will only be accessible to the study PI and relevant study staff.

Confidentiality will be ensured by removal of identifying information (name, age, gender, race/ethnicity,) of the patients and surrogate decision-makers and substituting their names with study participant numbers. As noted, all data will be de-identified. Nonetheless, we will maintain a file that links subject name with the study ID thereby enabling us to locate the study participant's research record upon request. This file will also be utilized by study staff in order to repeatedly interact with participants actively enrolled in the study. Data will be analyzed in aggregate only, and no identities will be revealed. For any qualitative data or vignettes presented at conferences, in publications, or incorporated into the EMPOWER manual or materials, pseudonyms will be created for participants.

Data collected will be obtained by trained research staff who have experience interviewing study participants. The data will be used specifically for the purposes outlined in this proposal and not for any other purpose. All study related documents will be stored in a secure location until the study has ended and all data analyses are complete. At that time, all study material will be placed in a secured long-term storage facility until it is deemed appropriate to destroy the study material.

To reduce missing data, following completion of all assessments, study staff will review the contents of the measures and scan them for missing information. If missing information is found, the staff member will contact the subject or review the medical chart to fill in missing data. In these circumstances, a research assistant will reach out by phone to the participant up to two times, and subjects may decline to provide any missing data.

Staff at WCM, MSK, and NYPQ have extensive experience interviewing health professionals in a hospital setting. All are seasoned interviewers and trainers with considerable experience interviewing diverse study subjects. Training consists of learning the instruments, practice sessions, and instruction in administration of the research interviews, including IRB approved procedures for approaching and consenting potential study participants.

5.3 Description of Study Process

5.3.1 Instrument Administration / Interviewing Procedures

Manual Refinement:

For the manual refinement phase of the study, bereaved surrogate decision-maker stakeholders will be referred by clinicians and word of mouth. Clinician stakeholders will be referred by study investigators and colleagues based on their expertise. Interviews with stakeholders will be conducted over the phone, through videoconferencing, or in a room at WCM/NYP or MSK that is quiet and private. Stakeholder participants who enroll will be provided with the EMPOWER intervention manual and will be asked to review it. Feedback will be

obtained via interview and will be audio-recorded. Stakeholders may alternately choose to provide their feedback as written comments. After the manual is revised based on stakeholder feedback, stakeholders will be provided with a summary of the changes made and a copy of the revised manual and will be asked if they have any additional comments or suggestions in a survey that also asks for background information. We will additionally make intervention refinements based on our experiences in the open trial. The only measures used in this phase of the study will be the Stakeholder Demographics form and the qualitative interview.

Open Trial and RCT:

Research assistants will screen charts and obtain permission to approach from a member of the patient's care team, such as, but not limited to physicians or nurses. Additionally, in service of determining optimal screening procedures for the purposes of planning a larger trial, clinical staff such as, but not limited to nurses, will be surveyed to identify surrogate decision-makers of patients that they consider to be distressed and would benefit from the EMPOWER intervention. Research staff will approach eligible surrogate decision-makers either in-person or over the phone and explain the study purpose, process, location, time, risks/ benefits, and compensation in detail, assuring them of their privacy and the protocol for addressing acute distress. For potential participants that are unable to be located during normal business hours in the ICU, a note will be left in the patient's room indicating that study staff will contact them via telephone. Staff will confirm comprehension and provide opportunities for questions and concerns. Surrogate decision-makers of adult patients will be screened for the extent to which they are dependent on the patient and anxious, in addition to screening for suicidal ideation, after providing study consent. If they are eligible, then the T1 assessment will take place or be scheduled. For those participants in open trials or randomized to the treatment condition, attempts to schedule an EMPOWER session will be made, with efforts made to accommodate the surrogate decision-makers' schedule.

This procedure is slightly modified for surrogate decision-makers of pediatric patients, who will be screened only for suicidal ideation as exclusion criteria. If eligible, these participants will either complete the PICU-specific brief T1 assessment administered via REDCap, paper, or RA interview, or the brief PICU-specific T1 assessment will be administered by the interventionist at the start of their initial meeting for the EMPOWER intervention or before receipt of EUC resources.

Research staff will assess surrogate decision-makers at T2, T3, and T4 in person, by phone or online. Phone outreach for scheduling assessments or scheduling delivery of either the EMPOWER or EUC interventions, as well as for coordination of other relevant study activities, may occur via texting participants after consent for texting has been obtained. Private/sensitive information outside of coordination of study activities will not be shared via text.

Depending on the status of the patient in the dyad, different measures will be administered as detailed in section 5.2. Expected time burden for the surrogate decision-maker to complete T1, T2, and T3 is approximately 20 minutes. T4, as it consists of a slightly larger battery and an exit interview, takes approximately one hour to complete for those assigned to the EMPOWER intervention. At WCM, $25 will be deposited on ClinCards, which are debit cards approved by WCM for payment of research participants, after each assessment. Other sites may use their preferred form of payment to compensate the research participants recruited at their respective sites. The research team will aim to administer all assessments in accordance with the time points outlined in this protocol, but due to the context of the ICU caregiving, flexibility will be allowed for participants experiencing major events such as emergent medical situations or bereavement. If patient status is unable to be obtained via the medical record (i.e. due to discharge or transfer to an outside hospital or rehab), participants will be contacted a week prior to the scheduled assessment time point to ensure that the correct questionnaires will be administered. Three attempts, each a week apart, will be made to contact the participant.

Additional data gathered for this study will be obtained from patients' medical charts.

5.3.2 Compensation

Participating stakeholders will receive compensation of a $50 gift card after reviewing the manual and providing feedback.

Participants in the open trial and RCT will receive compensation of $100 in ClinCards for completing the 4 assessments ($25 for each assessment). The ClinCard is a reloadable debit card approved by WCM; other study sites may compensate study participants for the same amount of money with their institution's preferred payment method.

5.4 Adverse Reactions and Their Management

No major adverse reactions are expected.

5.4.1 Reporting Adverse or Unanticipated Events

Potential adverse events (AEs) for this project are expected to be all non-medical in nature.

The Principal Investigators (PIs) will report unanticipated and serious adverse events to the IRB in a timely manner on an ongoing basis. For the purpose of this study, a Serious Adverse Event (SAE) is defined as an event that, as a direct result of the study, causes serious harm to the subject (e.g., that involvement in the study caused the death or serious injury to the subject). AEs are also reported as part of the progress reports in the non-competitive and competitive renewals for the NIH.

Monitoring Safety of Participants:

There are several ongoing mechanisms for monitoring the occurrence of AEs. The study staff will monitor day-to-day study activities. This monitoring is facilitated by: (1) the PIs' telephone numbers provided to participants upon entry into the study to report concerns related to study participation; (2) weekly meetings with project staff and investigators to discuss study progress, reactions to the conduct of the study, and any AEs; and (3) direct supervision of the study interviewers. To address participants' potential psychological distress, the PIs will have a referral list of phone numbers for local mental health service clinicians.

Plans for Assurance Compliance Regarding AE Reporting:

The PIs are required to report AEs to the IRB on an ongoing basis. In addition, yearly IRB renewal submissions require detailed AE reporting. AEs are also reported as part of the progress reports in the non-competitive and competitive renewals for the NIH.

5.4.2 Anticipated Reactions

Although there are no risks of physical injury, we anticipate that there may be questions in the interview that some study participants find upsetting. However, since study items and topics were chosen to reflect what are likely to be existing concerns, the present study is not expected to markedly increase participants' psychological distress above their routine concerns. Topics covered during the intervention sessions may be emotional, but related distress is expected to be transient and will be supported by a mental health provider. In addition, experienced personnel trained in interviewing medically ill individuals and their families will administer all instruments and will be supervised by the PIs.

All study staff involved in the research are educated on the protection of human research participants and the proposed research will comply with the regulations set forth in 45 CFR Part 46, Protection of Human Subjects. All personnel involved in the proposed protocol have been educated regarding HIPAA regulations and fully understand their responsibility to safeguard the personal health information of every participant involved in the research.

5.4.3 Reaction Management

Any subject participating in the study may decline to continue participation and may withdraw from the study at any time.

Interviewers will be instructed that, should a subject ask about the aims and procedures of the study, they are to describe the project as a study to learn more about supporting surrogate decision-makers of patients in the ICU.

We will collect participants' medical and mental health history, details about outside clinicians, and emergency contact information. Participants will be screened for suicidality based on our screening and management guidelines with the Columbia Suicide Severity Rating Scale embedded[20]. If research staff identify signs indicating a significant and acute risk of self-harm or harm to others, such information will immediately be shared with the PIs of the study, so that timely and appropriate assessment and care can be provided by a licensed/ board-certified mental health provider or local clinicians when geographically necessary.

Subjects will be assured that all responses will be kept confidential. All of the data collected during the interview process will be de-identified. To ensure confidentiality, data collected will be linked to the participant's personal information only by means of an assigned study identification number. Authorized study staff are the only individuals who have access to the participant's personal information. This information is stored in a password protected computer file for the pilot open trial and secure REDCap data base for RCT/Covid-19 open trial as well as in a locked file cabinet in a locked office. All necessary
precautions will be taken to ensure that there is no breach of confidentiality.

There will be only one exception to the strict patient confidentiality policy, described above, which pertains to information obtained during the research assessment or intervention sessions, which would indicate that the participant is seriously suicidal and may pose a significant and acute risk of self-harm or harm to others. Participants will be informed of this exception, and will also be informed that such information will be shared with the PIs of the study so that timely and appropriate psychiatric assessment and care can be provided. If a participant at acute risk of self-harm (endorses items 3 of the Columbia Suicide Severity Rating Scale) or harm to others cannot be reached by the study team within 3 hours (after at least two phone call attempts and an email requesting a call back), the participant's emergency contact(s) will be contacted. If a participant endorses passive but not acute suicidal ideation (i.e. endorses items 1 or 2 but not item 3 of the Columbia Suicide Severity Rating Scale) and is unable to be contacted by the research team in a timely manner, emergency contacts will be contacted at the discretion of the study mental health professionals based on their clinical judgment. If an acutely distressed individual who denies active suicidality or homicidality cannot be reached within 24 hours (after at least two phone call attempts and an email requesting a call back), the participant's emergency contact(s) will be contacted. These details are outlined in the informed consent.

6.1 Statistical Analysis

6.2 Data Management

Data will be entered into a secured REDCap database and stored on the WCM server. The PI and staff will review data entry regularly and within the first month, responses will be reviewed for distributions and to address concerns identified by respondents. Any necessary changes to ensure data quality or integrity will be submitted to the IRB as an amendment and modifications made to the REDCap database following IRB approval.

6.1 Data Analysis Plan

Below are descriptions of the statistical procedures performed to test each of the hypotheses. Participant data will be stored in a locked file cabinet and using a secured REDCap database. Missing data will be estimated using a multiple imputation procedure described by Schafer and Olsen[37]. There will not be a data monitoring committee due to the trial's relatively short duration and the minimal risks the intervention poses. Trial data will

not be independently audited. An interim analysis of the pilot data will occur to inform the conduct of the randomized control and edits to the EMPOWER manual. Data for participants who come bereaved before the administration of EMPOWER or EUC interventions will be treated as exploratory and analyzed separately.

Specific Aim #1: ***Develop EMPOWER for surrogate decision-makers of critically ill patients who at risk of becoming unable to communicate and/or are currently are unable to communicate in the ICU.***

There are no hypotheses for this aim. We will use thematic content analysis, a well-established, systematic qualitative analysis approach in health research, to identify themes from stakeholder participants' narratives and exit interviews. We will follow Morse's[21] guidelines for conducting rigorous qualitative research (e.g., audit trail, saturation) using Atlas.ti software. We will independently review each interview transcript as well as qualitative data gathered from manual edits and Delphi survey responses and will synthesize and interpret participants' feedback about the content of the EMPOWER manual.

Specific Aim #2: ***Determine the feasibility, tolerability, acceptability, and preliminary effects of EMPOWER on surrogate decision-maker mental health.***

We will compute descriptive statistics to characterize the feasibility and acceptability of EMPOWER by examining helpfulness/satisfaction ratings, rates of recruitment, reasons for refusal, and number of modules/booster calls completed. Targets will include completion of 4/6 modules for feasibility and tolerability. Target acceptability will be an average score greater than 3 on the acceptability items in the post-intervention satisfaction questionnaire among participants who received EMPOWER. Tolerability will also be measured by open ended-responses to qualitative questions asked at T4 regarding negative experiences, emotional difficulties, and perceived costs and benefits of participating in the intervention. Drop-out will not be considered as a metric of tolerability due to the highly stressful and variable circumstances of ICU caregiving, unless participants drop out of the study and specifically express that they consider it to be too distressing. Qualitative data analysis will be used to analyze data from open-ended questions to identify the most helpful components of EMPOWER.

To evaluate the preliminary effects of EMPOWER among participants in the combined RCT and COVID-19 open trial phases, we will use a hierarchical linear modeling (HLM) and an intent-to-treat approach. HLM is statistically appropriate because of the clustering within interventionists and within surrogate decision-makers. HLM will correct for this clustering by modeling interventionists and surrogate decision-makers as random effects, as has been done in prior trials [38] [39]. This will also provide a treatment assignment model coefficient and effect size estimate for our future, larger study.

HLM modeling will determine differences between surrogate decision-makers and patients assigned to EMPOWER vs. enhanced usual care. The primary outcome is post-intervention (T2) differences in PDI scores. Secondary outcomes are differences in scores on the PGD 12/13 and BEAQ at one-month (T3) and three-month (T4) follow up from T2. Exploratory outcomes are differences in scores on the IES-R, STAI, PHQ-9 and Decision Regret Scale at one-month (T3) and three-month (T4) follow up. HLM models will include covariates, either as fixed-effect or time-varying, if those variables are found to be significantly statistically associated with both intervention assignment and the outcome examined.

Specific Aim #3: ***Examine the effects of EMPOWER on patient outcomes in the month following the ICU admission.***

Logistic regression models will regress patient quality of life or quality of death (depending on whether the patient survives or dies in the observation period) for EMPOWER versus enhanced usual care condition. Logistic regression analyses will model the effects of EMPOWER on the odds of patients receipt of value-concordant care (i.e., surrogate baseline assessment of patient preferences regarding quality of life versus quantity of life matched with receipt of intensive life-prolonging procedures/palliative care).

6.1 Statistical power and sample size considerations

The pilot RCT will enroll 60 participants (30 EMPOWER, 30 enhanced usual care). This number of participants ensures stable estimates of treatment effects and confidence intervals, and, in case the effects of EMPOWER happen to be large, adequate (~80%) statistical power to detect a minimum treatment effect size (Cohen's d) of 0.75 (at alpha=0.05).

Of note, participants from the COVID-19 open trial will be considered in this N of 60. Accounting for these participants, the projected balance between groups will be 2:1, or 40 EMPOWER participants to 20 EUC. At 80% statistical power and alpha=0.05, this assignment ratio is still sufficient to detect a minimum treatment effect size (Cohen's d) of 0.75.

7.0 External Collaboration

Data is securely saved on a RedCap database which both MSK and WCM investigators on this protocol have access to. This study has been open and IRB approved at MSK since 2018.

1. Name: Taylor Coats
Institution: Pacific University
Role: Co-Investigator/Sub-Investigator
Responsibilities: Obtaining informed consent from subjects, interacting with subjects, analyzing PHI/PII

2. Name: Carol Fadalla
Institution: Memorial Sloan Kettering Cancer Center
Role: Co-Investigator/Sub-Investigator
Responsibilities: Obtaining informed consent from subjects, interacting with subjects, analyzing PHI/PII

3. Natalia Halpern Lagos
Institution: Memorial Sloan Kettering Cancer Center
Role: Co-Investigator/Sub-Investigator
Responsibilities: Obtaining informed consent from subjects, interacting with subjects, analyzing PHI/PII

4. Name: Lauren Leffell
Institution: Memorial Sloan Kettering Cancer Center
Role: Co-Investigator/Sub-Investigator
Responsibilities: Interacting with subjects, analyzing PHI/PII

5. Name: Wendy G. Lichtenthal
Institution: Memorial Sloan Kettering Cancer Center
Role: Co-Investigator/Sub-Investigator
Responsibilities: Interacting with subjects, analyzing PHI/PII

6. Name: Kailey Roberts
Institution: Yeshiva University
Role: Co-Investigator/Sub-Investigator
Responsibilities: Interacting with subjects, analyzing PHI/PII

7. Name: Amanda Watsula
Institution: Memorial Sloan Kettering Cancer Center
Role: Co-Investigator/Sub-Investigator
Responsibilities: Obtaining informed consent from subjects, interacting with subjects, analyzing PHI/PII

8. Name: David Russell
Institution: Appalachian State University

Role: Co-Investigator/Sub-Investigator
Responsibilities: Analyzing PHI/PII

9. Name: Lilly Scherban
Institution: Yeshiva University
Responsibilities: analyzing PHI/PII

References

1. Wright AA, Zhang B, Ray A, et al: Associations between end-of-life discussions, patient mental health, medical care near death, and caregiver bereavement adjustment. Jama 300:1665-1673, 2008

2. Zhang B, Nilsson ME, Prigerson HG: Factors important to patients' quality of life at the end of life. Arch Intern Med 172:1133-42, 2012

3. Gamez W, Chmielewski M, Kotov R, et al: Development of a measure of experiential avoidance: the Multidimensional Experiential Avoidance Questionnaire. Psychol Assess 23:692-713, 2011

4. Hayes SC, Wilson KG, Gifford EV, et al: Experiential avoidance and behavioral disorders: A functional dimensional approach to diagnosis and treatment. Journal of consulting and clinical psychology 64:1152, 1996

5. Mack JW, Weeks JC, Wright AA, et al: End-of-life discussions, goal attainment, and distress at the end of life: predictors and outcomes of receipt of care consistent with preferences. J Clin Oncol 28:1203-8, 2010

6. Wright AA, Zhang B, Ray A, et al: Associations between end-of-life discussions, patient mental health, medical care near death, and caregiver bereavement adjustment. Jama 300:1665-73, 2008

7. Garrido MM, Prigerson HG: The end-of-life experience: modifiable predictors of caregivers' bereavement adjustment. Cancer 120:918-25, 2014

8. Wright AA, Keating NL, Balboni TA, et al: Place of death: correlations with quality of life of patients with cancer and predictors of bereaved caregivers' mental health. J Clin Oncol 28:4457-64, 2010

9. Siegel MD, Hayes E, Vanderwerker LC, et al: Psychiatric illness in the next of kin of patients who die in the intensive care unit. Crit Care Med 36:1722-8, 2008

10. Curtis JR, Back AL, Ford DW, et al: Effect of communication skills training for residents and nurse practitioners on quality of communication with patients with serious illness: a randomized trial. Jama 310:2271-81, 2013

11. Lautrette A, Darmon M, Megarbane B, et al: A communication strategy and brochure for relatives of patients dying in the ICU. N Engl J Med 356:469-78, 2007

12. Carson SS, Cox CE, Wallenstein S, et al: Effect of Palliative Care-Led Meetings for Families of Patients With Chronic Critical Illness: A Randomized Clinical Trial. Jama 316:51-62, 2016

13. Prigerson HG, Shear MK, Jacobs SC, et al: Consensus criteria for traumatic grief. A preliminary empirical test. Br J Psychiatry 174:67-73, 1999

14. Earle CC, Park ER, Lai B, et al: Identifying potential indicators of the quality of end-of-life cancer care from administrative data. J Clin Oncol 21:1133-8, 2003

15. Goodman DC, Morden NE, Chang C, et al: Trends in Cancer Care near the End of Life, in Bronner KK (ed): A Report of the Dartmouth Atlas Project, 2013

16. Azoulay E, Pochard F, Kentish-Barnes N, et al: Risk of post-traumatic stress symptoms in family members of intensive care unit patients. Am J Respir Crit Care Med 171:987-94, 2005

17. White DB, Angus DC, Shields AM, et al: A Randomized Trial of a Family-Support Intervention in Intensive Care Units. N Engl J Med, 2018

18. Johnson JG, Vanderwerker LC, Bornstein RF, et al: Development and validation of an instrument for the assessment of dependency among bereaved persons. Journal of Psychopathology and Behavioral Assessment 28:261-270, 2006

19. Cohen SR, Mount BM, Bruera E, et al: Validity of the McGill Quality of Life Questionnaire in the palliative care setting: a multi-centre Canadian study demonstrating the importance of the existential domain. Palliat Med 11:3-20, 1997

20. Posner K, Brown GK, Stanley B, et al: The Columbia–Suicide Severity Rating Scale: initial validity and internal consistency findings from three multisite studies with adolescents and adults. American Journal of Psychiatry 168:1266-1277, 2011

21. Denzin NK, Lincoln YS: Handbook of qualitative research, Sage publications, inc, 1994

22. Suresh K: An overview of randomization techniques: An unbiased assessment of outcome in clinical research. J Hum Reprod Sci 4:8-11, 2011

23. Higgins PC, Prigerson HG: Caregiver evaluation of the quality of end-of-life care (CEQUEL) scale: the caregiver's perception of patient care near death. PLoS One 8:e66066, 2013

24. Prigerson HG, Horowitz MJ, Jacobs SC, et al: Prolonged grief disorder: Psychometric validation of criteria proposed for DSM-V and ICD-11. PLoS Med 6:e1000121, 2009

25. Prigerson HG, Vanderwerker LC, Maciejewski PK: A case for inclusion of prolonged grief disorder in DSM-V, in Stroebe MS, Hansson RO, Schut H, et al (eds): Handbook of bereavement research and practice: Advances in theory and intervention. Washington, DC, US, American Psychological Association, 2008, pp 165-186

26. Zhang B, El-Jawahri A, Prigerson HG: Update on bereavement research: evidence-based guidelines for the diagnosis and treatment of complicated bereavement. J Palliat Med 9:1188-203, 2006

27. Brunet A, Weiss DS, Metzler TJ, et al: The Peritraumatic Distress Inventory: a proposed measure of PTSD criterion A2. Am J Psychiatry 158:1480-5, 2001

28. Marmar CR, Weiss DS, Metzler TJ: Peritraumatic dissociation and posttraumatic stress disorder. Trauma, memory, and dissociation:229-252, 1998

29. Weiss DS, Marmar CR: The impact of event scale- revised. , in Wilson JP, Keane TM (eds): Assessing psychological trauma and PTSD. New York, Guilford Press, 1997, pp 399-411.

30. Gamez W, Chmielewski M, Kotov R, et al: The brief experiential avoidance questionnaire: development and initial validation. Psychol Assess 26:35-45, 2014

31. Spielberger CD. State-Trait anxiety inventory. The Corsini encyclopedia of psychology. 2010 Jan 30:1-.

32. Kroenke K, Spitzer RL, Williams JB: The phq‐9. Journal of general internal medicine 16:606-613, 2001

33. Simons JS, Gaher RM: The Distress Tolerance Scale: Development and Validation of a Self-Report Measure. Motivation and Emotion 29:83-102, 2005

34. Brehaut JC, O'Connor AM, Wood TJ, et al: Validation of a Decision Regret Scale. Medical Decision Making 23:281-292, 2003

35. Wasser T, Matchett S: Final version of the critical care family satisfaction survey questionnaire. Critical care medicine 29:1654-1655, 2001

36. Sekhon M, Cartwright M, Francis JJ: Acceptability of healthcare interventions: an overview of reviews and development of a theoretical framework. BMC Health Services Research 17:88, 2017

37. Schafer JL, Olsen MK: Multiple imputation for multivariate missing-data problems: A data analyst's perspective. Multivariate behavioral research 33:545-571, 1998

38. Singer JD, Willett JB: Methodological issues in the design of longitudinal research: Principles and recommendations for a quantitative study of teachers' careers. Educational Evaluation and Policy Analysis 18:265-283, 1996

39. Raudenbush SW, Bryk AS: Hierarchical linear models: Applications and data analysis methods, Sage, 2002