Enhancing & Mobilizing the POtential for Wellness & Emotional Resilience Among Surrogate Decision-Makers of ICU Patients (EMPOWER): Study protocol for a randomized controlled trial

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Study protocol

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Abstract

Background Critical illness increases the risk for poor mental health outcomes among both patients and their informal caregivers or surrogate decision-makers. Surrogates who must make life-and-death medical decisions on behalf of incapacitated patients may experience additional distress. EMPOWER (Enhancing & Mobilizing the POtential for Wellness & Emotional Resilience among Surrogate Decision-Makers of ICU Patients) is a novel cognitive-behavioral, acceptance-based intervention delivered in the intensive care unit (ICU) setting to surrogate decision-makers designed to improve both patients' quality of life and death and dying as well as surrogates' mental health. Methods Clinician stakeholder and surrogate participant feedback (n=15), as well as results from an open trial (n =10), will be used to refine the intervention, which will then be administered as a multisite randomized controlled trial (n = 60) to examine clinical superiority to usual care. Feasibility, tolerability, and acceptability of the intervention will be evaluated through self-report assessments. Hierarchical linear modeling will be used to adjust for clustering within interventionists to determine the effect of EMPOWER on surrogate differences in the primary outcome, peritraumatic stress. Secondary outcomes will include symptoms of posttraumatic stress disorder (PTSD), prolonged grief disorder (PGD) and experiential avoidance. Exploratory outcomes will include symptoms of anxiety, depression, and decision regret, all measured at one-month and three-months from baseline. Linear regression models will examine the effects of assignment to EMPOWER versus the enhanced usual care group on patient quality of life or quality of death and intensity of care the patient received during the indexed ICU stay assessed at the time of the post-intervention assessment on. Participant exit interviews will be conducted at the three-month assessment time point and will be analyzed using qualitative thematic data analysis methods. Discussion The EMPOWER study is unique in its application of evidence-based psychotherapy targeting peritraumatic stress to improve patient and caregiver outcomes in the setting of critical illness. The experimental intervention will be strengthened through the input of a variety of ICU stakeholders, including behavioral health clinicians, physicians, bereaved informal caregivers, and open trial participants. Results of the RCT will be submitted for publication in a peer-reviewed journal and serve as preliminary data for a larger, multisite RCT grant application. Trial registration: ClinicalTrials.gov Identifier NCT03276559 (Retrospectively registered September 8th, 2017)

Background

Critical illness increases the risk for poor mental health outcomes among both patients(1) and families(2). The burden of psychological distress may be especially great for surrogate decision-makers of patients in intensive care units (ICUs) who are unable to adequately communicate their treatment decisions due to factors including altered consciousness, requirement for invasive life support, or the severity of their underlying illness. In such situations, a surrogate decision-maker may need to make life-and-death decisions with limited knowledge of the patient's treatment preferences at a time when they may be personally experiencing significant psychological distress. Interventions are needed to support

the mental health of ICU surrogates and to provide tools for coping across the ICU period and immediate aftermath of either discharge or death.

Past efforts to address these challenges have so far produced disappointing results for improving end-of-life (EoL) care and surrogate mental health; moreover, some psychosocial interventions may carry risk. In a recent randomized controlled trial, posttraumatic stress disorder (PTSD) symptoms increased for surrogate decision-makers of ICU patients who received a family meeting intervention led by palliative care medical specialists that was designed to reduce surrogate anxiety and depression(3). Another intervention designed to improve mental health outcomes through sending handwritten condolence cards to relatives of patients who died in the ICU was shown to worsen depression and PTSD symptoms(4). A web-based, personalized decision aid for surrogates of ICU patients did not reduce surrogates' symptoms of depression, anxiety, or PTSD or change clinical outcomes compared to usual care(5). Finally, a multicomponent, nurse-led intervention designed to reduce depression, anxiety, and PTSD focused on the provision of emotional, communication, decisional, and anticipatory grief support for ICU family caregivers, but did not utilize targeted strategies to reduce clinical symptoms(6, 7). In fact, the investigative team specifically noted that the interventionists did not have advanced training in patient counseling(6), and similar to other trials, the results showed no significant effects on the primary mental health outcomes of anxiety or depression, or on secondary outcomes of PTSD(8).

The primary limitation of the above interventions is that although they targeted longer-term (e.g., three- and six-months post-intervention) mental health outcomes, they were not explicitly designed using empirically-supported psychological treatments to address clinically significant mental health symptoms nor to provide coping skills that could be applied beyond the ICU stay. Furthermore, they were not delivered by trained mental health providers. In fact, White et al. concluded in response to the study findings, that a brief, "psychologically focused intervention" should be developed and tested(9).

To address this important scientific gap, we propose to target surrogate decision-maker mental health as a way to both improve surrogates' capacity to cope with the stress of the patient's ICU stay, but also improve decision-making on the patient's behalf. We propose to develop, refine, and evaluate EMPOWER (Enhancing & Mobilizing the POtential for Wellness & Emotional Resilience of Surrogate Decision-Makers of ICU Patients), a mental health intervention for surrogate decision-makers of ICU patients who are unable to communicate their EoL care preferences. Delivered by a trained mental health professional in the ICU setting, EMPOWER is theoretically grounded in cognitive-behavioral and acceptance-based therapies. EMPOWER aims to improve surrogate mental health outcomes, increase rates of advance care planning (e.g., rates of Do Not Resuscitate order or advanced directive completion), promote value-concordant care through clarifying surrogate perceptions of incapacitated patients' treatment

preferences, improve patient quality of life/death as perceived by the surrogate, and reduce surrogate decisional regret about the patient's ICU care.

Methods

Overview:

The methods for the EMPOWER study were developed in accordance with the SPIRIT guidelines(10). Any prospective amendments to the protocol, eligibility, or outcomes will first be approved by the institutional review boards of the study sites.

Key study objectives:

1. Develop EMPOWER for surrogate decision-makers of critically ill ICU patients who are 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 primary outcome will be symptoms of peritraumatic distress measured following the intervention compared to enhanced usual care. Additional outcomes at one-month and three-month follow-up from baseline will be compared to enhanced usual care as well.
3. Estimate the effects of EMPOWER on patient outcomes in the months following the baseline assessment. Patients who receive EMPOWER are hypothesized 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.

Trial design:
The EMPOWER study is comprised of two phases conducted simultaneously in preparation for the subsequent RCT. Phase 1 will first involve both an open trial will enroll 10 surrogate decision-makers to receive the EMPOWER intervention to obtain feedback about administration of EMPOWER from active surrogates. The concurrent manual refinement activities will involve obtaining feedback on the EMPOWER intervention manual itself from 15 stakeholders (bereaved informal caregivers and ICU clinicians or mental health providers). Feedback from both the open trial and stakeholder interviews will then be used to refine the EMPOWER intervention.

Phase 2 will involve a multicenter, open label, parallel group, exploratory randomized controlled trial, which will aim to enroll up to 60 eligible surrogates of 60 incapacitated patients in the ICU and up to 20 ICU clinicians. This sample size 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). Surrogates will be block-randomized to either the EMPOWER intervention or enhanced usual care and will complete self-report measures (n = 30 in each group). Approximately 20 ICU clinicians who are working with the patients and surrogates will also be surveyed in semi-structured interviews about their perceptions of the effects of EMPOWER. A usual care comparator will be enhanced with a packet providing general information and recommendations on serving as an informal caregiver from the National Alliance for Caregiving (http://www.caregiving.org/pdf/resources/CFC.pdf) as well a handout documenting site-specific resources for caregivers at each hospital. We will document the availability and use of social support services provided within each of the three participating ICU sites (please see below) to control for inter-institutional variability on the provision of supportive services as usual care.

Location and participants:

The study will take place at NewYork-Presbyterian Hospital/Weill Cornell Medical Center, NewYork-Presbyterian Queens, and Memorial Sloan Kettering Cancer Center in New York City. ICU physicians will refer potential patient and informal caregiver dyads to research assistants who will screen and consent them as research participants. This study will involve ICU clinicians, patients, and patients' surrogates as participants as well as stakeholders. Feedback from patients and informal caregivers are integrated into several stages of the EMPOWER trial. Bereaved informal caregivers of ICU patients and ICU clinicians will be consulted to improve the EMPOWER intervention. Additionally, participants in the open trial will be consulted through exit interviews to share their suggestions in improving the intervention, assessments, and recruitment procedures of the trial. All research participants will be compensated to promote retention and complete follow-up. Participating stakeholders will receive compensation of a $50 gift card after reviewing the manual and providing feedback. Participating surrogates in the open trial and RCT will receive $25 follow the completion of each assessment and exit interview. Participating ICU clinicians (non-stakeholder) during the RCT will receive compensation of $25 each time they complete a survey.

Eligibility criteria:
Inclusion criteria for open trial and RCT participants:

1. Patients (>21 years) in the ICU/step-down units who cannot communicate treatment preferences, as determined by ICU physicians or fellows, and whose ICU physicians or fellows would not be surprised if the patient did not survive more than 3 months
2. Informal caregivers of ICU patients whom ICU physicians or fellows indicate as the decision-making surrogate for the patient, or who is listed as such in the patient's medical record

3. Surrogates must speak English
4. Surrogates must either meet the threshold for a high degree of dependence on the patient (determined by the summed score of the overall dependence and emotional dependence on the patient items of the Partner Dependency Scale(11) as greater than 8) or a high degree of anxiety (determined by scoring greater than 5 on either anxiety item from the McGill Quality of Life Scale(12))
5. ICU attendings whose patients are enrolled in the study

Exclusion criteria for open trial and RCT participants:

1. Patients and surrogates who do not meet the eligibility criteria or surrogates who endorse suicidal ideation in the past month based on responses to the Columbia Suicide Severity Rating Scale(13)

Inclusion 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, hospital chaplains, psychiatrists and other physicians

Exclusion criteria for stakeholders:

1. Bereaved informal caregivers or clinicians who do not meet the eligibility criteria

Interventions:

The EMPOWER intervention will be administered by trained mental health professionals such as psychologists or social workers. The EMPOWER intervention targets symptoms of peritraumatic stress and anticipatory grief that may interfere with optimal decision-making on the patient's behalf or lead to adverse health outcomes such as prolonged grief disorder or PTSD following the patient's death or discharge from the ICU. The EMPOWER intervention seeks to act on these symptoms through the reduction of "experiential avoidance" (14, 15) and teaching of coping skills, empirically-supported techniques from cognitive-behavioral therapy(16-18) and acceptance and commitment therapy(19-21) that can be applied during the ICU stay and in the immediate aftermath of the ICU stay. It consists of six discrete modules that take approximately 15 to 20 minutes each to complete and can be delivered flexibly to accommodate the numerous interruptions and unexpected crises typical in an ICU setting. The EMPOWER modules include empathetic listening and alliance building, breathing retraining, grounding exercises, guided mindfulness meditation, psychoeducation about cognitive-behavioral and acceptance-

based coping strategies, invoking of the patient's voice through an imaginal dialogue, and coping rehearsal to prepare for potentially distressing scenarios. The six modules can be delivered in the ICU in a single session or in multiple brief sessions based on the surrogate's preference. Following the initial EMPOWER session conducted in the ICU, two booster sessions will be delivered by phone two weeks and four weeks after the end of the intervention. Booster sessions will focus on issues relevant to the surrogate, such as bereavement, and reviewing the skills taught in the original session to coping with new challenges. Of note, the content and format of EMPOWER will be further developed through the input of surrogates in the open trial, bereaved informal caregivers who have had relevant experiences in the ICU, and clinicians with expertise in mental health and/or critical care.

EMPOWER will be delivered by at least Master's level mental health clinician interventionist who will receive intensive training prior to delivering the intervention and regular supervision after each session. The interventionists will communicate with the medical team as needed, but will provide a safe space separate from the ICU medical providers without any agenda about the patient's care. While a multidisciplinary approach in the ICU is invaluable, anecdotal evidence suggests that interpersonal dynamics between the surrogates and medical team sometimes complicate surrogates' ability to independently consider their and the patient's wishes (e.g., surrogates have reported feeling pressured by hospital staff to sign a DNR order while the patient is in the ICU and they feel conflicted and/or defensive about this request). Sessions will be audio- recorded (or video recorded if the surrogate provides permission) so that treatment fidelity can be regularly monitored and independently rated by trained research assistants.

Enhanced usual care will consist of the various interactions a surrogate may have with providers in the ICU, which may include social work and chaplaincy staff who serve as the psychosocial support providers. Additionally, a packet providing information about informal caregiving and resources will be provided to surrogates in the control group by research staff. Lastly, a referral list of site-specific resources such as caregiver support groups and hotlines will be provided. Use of the various components of enhanced usual care will be monitored and extensively tracked through review of notes in the patient's medical record and surrogate self-report. Enhanced usual

care was chosen as the comparator in this study in order to determine whether the EMPOWER intervention serves as an effective support for surrogates above and beyond standard practice. Having three sites, each with unique practices for supporting informal caregivers and surrogates, will allow the intervention to be compared to multiple smaller subsets of standard treatment, and at the same time reflect general psychosocial informal caregiver support as well.

Surrogate decision-makers will be permitted to continue to see any outside mental health professionals during the trial. Mental health treatment they receive from outside professionals will be documented and controlled during data analysis.

Assignment of Interventions:

Participants in the open trial will all be assigned to the EMPOWER intervention. Participants in the RCT will be randomized to either EMPOWER or the control group with a block randomization procedure in REDCap(22) using computer-generated random numbers generated in R Studio(23). Research assistants will randomize a participant using REDCap following the participant's completion of the consent, eligibility screener and baseline assessment. Because a co-principal investigator will be conducting supervision for the interventionists, and because different assessments will be administered depending on the intervention assignment, the only person completely blinded to group assignment will be the data analyst/statistician.

Outcomes:

1. The first goal of this study is to determine the feasibility and acceptability of the EMPOWER intervention. These outcomes will be measured quantitatively following the intervention (T2) through a post-intervention questionnaire and at the three–month follow up (T4) through a qualitative exit interview. More specifically, these assessments will measure participant-perceived helpfulness/satisfaction to determine acceptability. Tolerability will be measured in these assessments through participant reports of negative experiences, emotional difficulties, and perceived costs and benefits of participating in the intervention.

Targets will include completion of 4/6 modules for feasibility and for acceptability an average response score of at least 4 to items 1, 3, and 7 of the post-intervention satisfaction questionnaire among at least 60% of intervention recipients. Rates of recruitment, reasons for refusal, number of modules/booster calls completed, and study attrition will also be examined. Drop-out post-intervention will not be considered as a metric of tolerability due to the highly stressful and variable circumstances (e.g., bereavement) of ICU caregiving, unless participants drop out of the study and specifically express that they consider it to be too distressing.

2. The EMPOWER study also aims to improve surrogates' symptoms of psychological distress. This will be measured by comparing the EMPOWER group to the enhanced usual care group at multiple time points. The primary outcome will be in peritraumatic distress at post-intervention assessment (T2). Secondary outcomes will be differences in symptoms of PTSD, prolonged grief disorder, and experiential avoidance, and exploratory outcomes will be anxiety, depression, and decisional regret at one-month and three-month from baseline follow up (T3 and T4).
3. Additionally, the EMPOWER study aims to improve patient outcomes through promoting value-concordant care, quality of life, and quality of death. Rates of value-concordant care will be

measured through comparing surrogate perceptions of patient treatment preferences assessed at baseline (e.g., a preference to prioritize care focused on quality of life over quantity of life) with the intensity of care provided in the indexed ICU stay(e.g., indication of cardiopulmonary resuscitation, dialysis, mechanical ventilation, chemotherapy, or parenteral nutrition, and palliative care in the medical record). We will compare surrogate-assessed patient quality of death (for patients who died) using the CEQUEL (24) between groups, measured at either T3 or T4, depending on which time point first follows the patient's death. Surrogate-assessed patient quality of life will be assessed as relevant to the most recent week (or week alive) through Likert-type items previously published (25), as well as through a revised version of the CEQUEL, and will be measured at one-month follow up (T3), three-month follow up (T4), both, or neither, depending on patient status.

Measures

Demographics:

Surrogate decision-makers will be asked in a baseline 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, advance care planning knowledge/understanding, treatment preferences, prognostic understanding, and relationship with patient. Stakeholders will report on their own demographics.

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Medical factors for patients:

We will abstract the medical chart to record patients' primary hospital and ICU admitting diagnoses (e.g., Stage IV pancreatic or NSCL cancer), do not resuscitate/do not intubate order status, advance care planning items (e.g., Living Will, Health Care Proxy, Health Care Power of Attorney), palliative care consultations, care plans obtained from the medical chart or ICU physicians and fellows. 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(24), will serve to measure the outcomes specified in Objective #3.

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Psychosocial factors for surrogate decision-makers:
Screener: Consists of items from 4 items from McGill Quality of Life(12), two items from the Partner Dependency Scale(11), and three items from the Columbia Suicide Severity Rating Scale(13). We will also obtain the surrogate's physician/healthcare provider information at baseline should a medical or mental health emergency arise.

Pre-intervention/Baseline Assessment (T1): Psychiatric History, Demographics, and Treatment Preferences; Prolonged Grief Disorder (PG-12) Caregiver Version(26-28); Peritraumatic Distress Inventory (PDI)(29); Peritraumatic Dissociative Experiences Questionnaire (PDEQ)(30); Impact of Events Scale-Revised (IES-R)(31); Brief Experiential Avoidance Questionnaire (BEAQ)(32); State Trait Anxiety Questionnaire- Trait Scale (STAI-Y Trait)(33); Patient Health Questionnaire (PHQ-9)(34); Distress Tolerance Scale (DTS)(35) revised version; Caregiver Self-Efficacy in the ICU Scale; Decision Regret Scale (DRS) - EMPOWER(36).

Post-intervention Assessment (T2): PG-12 (if patient is alive); PG-13 (if patient is deceased)(26-28); PDI; PDEQ; IES-R; BEAQ; STAI-Y Trait; DTS revised version; Caregiver Self-Efficacy in the ICU Scale; DRS - EMPOWER; Post-Intervention Satisfaction Questionnaire (PISQ).

1 Month Post-Baseline Assessment (T3): PG-12 (if patient is alive); PG-13 (if patient is deceased); PDI; IES-R; BEAQ; STAI-Y Trait; PHQ-9; DTS revised version; Critical Care Family Satisfaction Survey-EMPOWER; CEQUEL-R (if patient is alive)(24); CEQUEL(24) (if patient is deceased); Quality of Life (if patient is alive)(37); Quality of Death (if patient is deceased)(37); DRS - EMPOWER; Medical Information Update

3 Months Post Baseline Assessment (T4): PG-12 (if patient is alive); PG-13 (if patient is deceased); PDI; IES-R; BEAQ; STAI-Y Trait; PHQ-9; DTS revised version; Critical Care Family Satisfaction Survey-EMPOWER; 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; Medical Information Update; Qualitative Exit Interview.

Qualitative data:

Surrogates will provide feedback on the intervention in a post-intervention satisfaction questionnaire at T2 and a one-on-one semi-structured exit interview at T4 conducted over the phone or in person. 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 through a patient information form and then will report on their beliefs about the effect of the intervention using the Provider Questionnaire.

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(38). 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.

Objective #1: *Refine EMPOWER for surrogate decision-makers of critically ill patients who are unable to communicate in the ICU.*

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(39) 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.

Objective #2: *Determine the feasibility, acceptability, tolerability, and preliminary effects of EMPOWER on surrogate 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. These will be used to determine whether the EMPOWER intervention meets the targets detailed in the above outcomes. 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 on peritraumatic stress at T2 in the RCT, we will use a hierarchical linear modeling (HLM) and an intent-to-treat approach. HLM is statistically appropriate because it corrects for clustering within interventionists and within surrogates by modeling them as random effects. This will also provide a treatment assignment model coefficient and effect size estimate for our future, larger study.

HLM modeling will determine differences between surrogates and patients assigned to EMPOWER vs. enhanced usual care to examine the primary, secondary, and exploratory outcomes described above. HLM models will include covariates, either as fixed-effect or time-varying (e.g., patient death), if those variables

are found to be significantly statistically associated with both intervention assignment and the outcome examined.

Objective #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).

Adverse reactions and events

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 study principal investigators (PIs).

Potential adverse events for this project are expected to be all non-physical in nature. The principal investigators 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 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). Adverse events are also reported as part of the progress reports in the non-competitive and competitive renewals for the National Institutes of Health.

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. Any subject participating in the study may decline to continue participation and may withdraw from the study at any time. Any participant who expresses a desire for more intensive psychosocial support for issues such as PTSD or bereavement following the intervention will receive a customized set of referrals from the principal investigators.

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(13). If research staff identify signs indicating a significant and acute risk of harm to self or 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.

Patient confidentiality will only be broken if information is collected either during the intervention or through an assessment that the participant poses a significant and acute risk of harm to self or others. Prior to inclusion in the study, 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 deemed to be at acute risk of self-harm or harm to others cannot be reached by the study team within 3 hours (after at least two telephone call attempts and an email requesting a call back), the participant's emergency contact(s) will be contacted. If an acutely distressed individual who has denied active suicidality or homicidality, but for whom the study team has significant concern, 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 for the participants.

Discussion

This trial will evaluate the effects of a mental health intervention conducted in the ICU on surrogate decision-makers of incapacitated patients. Psychiatric symptoms of surrogates, patient quality of life and quality of death, and rates of nonbeneficial, burdensome care will be examined.

Previous trials led by ICU and palliative care clinicians have proven inefficacious in improving mental health outcomes in informal caregivers(3-9). This trial takes a different approach by examining a mental health solution for a mental health problem. Additionally, the EMPOWER intervention will be created and refined based on the input of a variety of ICU stakeholders, including behavioral health clinicians, physicians, and bereaved informal caregivers.

Due to the clinical and logistical aspects of the protocol, the EMPOWER trial will not be blinded. As well, this pilot RCT may be underpowered. Study participants, however, will be recruited from ICUs across three different hospitals to accelerate recruitment and maximize sample size and diversity. In addition, these data may be used in support of a large-scale, adequately powered study.

If efficacious, the EMPOWER intervention has the potential to improve both the mental health outcomes of informal caregivers and the quality of life at end-of-life for incapacitated patients receiving intensive care. Through stakeholder feedback, an initial open trial, and a RCT, this pilot study will extensively examine what may potentially serve as an efficient and flexible intervention for incapacitated patients and their surrogate-decision makers in the ICU.

Trial Status

Enrolment has been completed for both open trial and stakeholder feedback. Enrolment for the RCT portion of the EMPOWER trial will begin in January 2019.

Abbreviations

ICU: intensive care unit

PTSD: post-traumatic stress disorder

EoL: end-of-life

EMPOWER: Enhancing and Mobilizing the Potential Wellness and Emotional Resilience of Surrogate Decision-Makers of ICU Patients

RCT: randomized controlled trial

DNR/DNI: do not resuscitate/do not intubate

ACP: advanced care planning

HLM: hierarchical linear modeling

Declarations

Ethics approval and consent to participate
The EMPOWER study has been IRB-approved at NewYork Presbyterian Hospital- Weill Cornell Medicine, Memorial Sloan Kettering Cancer Center, and NewYork Presbyterian Hospital- Queens. This is protocol #1610017622A009, approved on January 25th, 2019.

Written informed consent of participants will be obtained by trained research assistants and will allow for permission to collect data from both the surrogate decision-maker and the incapacitated patient.

Recruitment for this study began on July 12th, 2017. Recruitment is expected to be completed by approximately June 28th, 2019.

Subjects will be assured that all responses will be kept confidential. All of the data collected during the interview process will be de-identified. 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 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. As mentioned previously, confidentiality will only be broken if information regarding homicidality or suicidality is obtained.

Consent for publication

Not applicable.

Availability of data and materials

Individual-level de-identified patient data will be made publicly available after the study-specific aims have be published. The statistical analyses will be available for those who request it based on published analyses. Authorship of the final report will be based on contribution to the trial as determined by the PIs.

Competing interests

The authors declare no financial disclosures or competing interests.

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Authors' contributions

HGP was involved in conception, trial design and drafting of the article and provided statistical expertise. WGL was involved in conception, trial design and drafting of the article. LL was involved in conception,

trial design and drafting of the article. DB was involved in conception, trial design, and drafting of the article. CB was involved in drafting of the article. CC was involved in drafting of the article. SV was involved in drafting of the article. JSG was involved in drafting of the article. CXP was involved in trial design and drafting of the article. DO was involved in trial design and drafting of the article. SR was involved in trial design and drafting of the article. MR was involved in trial design and drafting of the article. MV was involved in trial design and drafting of the article. JX provided statistical expertise.

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Authors' information

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Tables

Table 1 - The EMPOWER Intervention

EMPOWER Intervention			
In ICU	Delivered in single or multiple sessions	Module 1	Nurturance, Understanding, and Joining
		Module 2	Breathing Retraining, Grounding Exercises, and Mindfulness Meditation
		Module 3	Psychoeducation about Trauma, Grief, and the Cognitive-Behavioral Model
		Module 4	Increasing Acceptance and Sense of Permission to Experience Challenging Emotions
		Module 5	Connecting with the Patient’s Voice
		Module 6	Using the EMPOWER Toolbox and Coping Rehearsal
Phone	2 weeks post-Module 6	Booster Call 1	Check-in and review of psychoeducation and coping skills
Phone	4 weeks post-Module 6	Booster Call 2	Check-in and review of psychoeducation and coping skills

Table 2 - List of Assessments

Measure Title	Time Points Used	Description of Measure
McGill Quality of Life Scale(12)	Screener	Items 5 through 8 are used to measure anxiety/depression
Partner Dependency Scale (PDS) (11)	Screener	Items 1 and 2 of the BDS are used to measure dependency. The language is altered to refer to the patient rather than a spouse.
Columbia Suicide Severity Rating Scale(13)	Screener	Items 1-3 of the CSSRS are used to measure suicidal ideation.
Peritraumatic Distress Inventory (PDI) ICU Version(29)	T1, T2, T3, T4	Measures peritraumatic distress. Instructions are altered to specify that participants complete the measure with a time frame of the past two days, using the patient's ICU stay as the specific traumatic event. Items are altered to use the present perfect tense rather than the past tense.
Impact of Events Scale-Revised (IES-R)(31)	T1, T2, T3, T4	Measures symptoms of PTSD. Instructions are altered to specify that participants complete the measure using the patient's ICU stay as the reference event.
Brief Experiential Avoidance Questionnaire (BEAQ)(14)	T1, T2, T3, T4	Measures experiential avoidance.
State Trait Anxiety Questionnaire-Trait Scale (STAI-Y Trait) (33)	T1,T2, T3, T4	Measures symptoms of state anxiety. Only utilizes the state scale of this measure.
Patient Health Questionnaire (PHQ-9)(34)	T1, T3, T4	Measures symptoms of depression.
Distress Tolerance Scale (DTS) (35)	T1, T2, T3, T4	Measures ability to tolerate distress. Items 1, 2, 9, and 13 are retained from the original. Instructions are altered to specify that participants complete the measure in regards to the patient's ICU stay.
Decision Regret Scale (DRS) – EMPOWER(36)	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 surrogate decision-makers 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 surrogate decision-makers in the ICU setting.
Peritraumatic Dissociative Experiences Questionnaire (PDEQ)(30)	T1, T2	Measures symptoms of dissociation. Instructions are altered to specify that participants complete the measure with a time frame of the past two days, using the patient's ICU stay as the specific traumatic event.
Critical Care Family Satisfaction Survey – EMPOWER	T3	Measures surrogate'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(40).

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-efficacy(41).
Prolonged Grief Disorder (PG-12) Caregiver Version(26-28)	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)(26-28)	Status dependent @ T2, T3, T4	Measures grief.
Caregiver Evaluation of the Quality of End-of-Life Scale (CEQUEL)(24)	Status dependent @ T3, T4	Measures surrogate'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(24)	Status dependent @ T3, T4	Administered to surrogate decision-makers whose patients are still living. Retains items measuring surrogate satisfaction with medical care for the patient, but removes questions regarding patient's death.
Quality of Life/Death	Status dependent @ T3, T4	Measures surrogate'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(37).
Survey of ICU Clinicians	Within one week of administration of control or EMPOWER intervention	Measures clinician perceptions of the EMPOWER intervention and comfort in approaching the surrogate for discussions regarding end of life care.

Figures

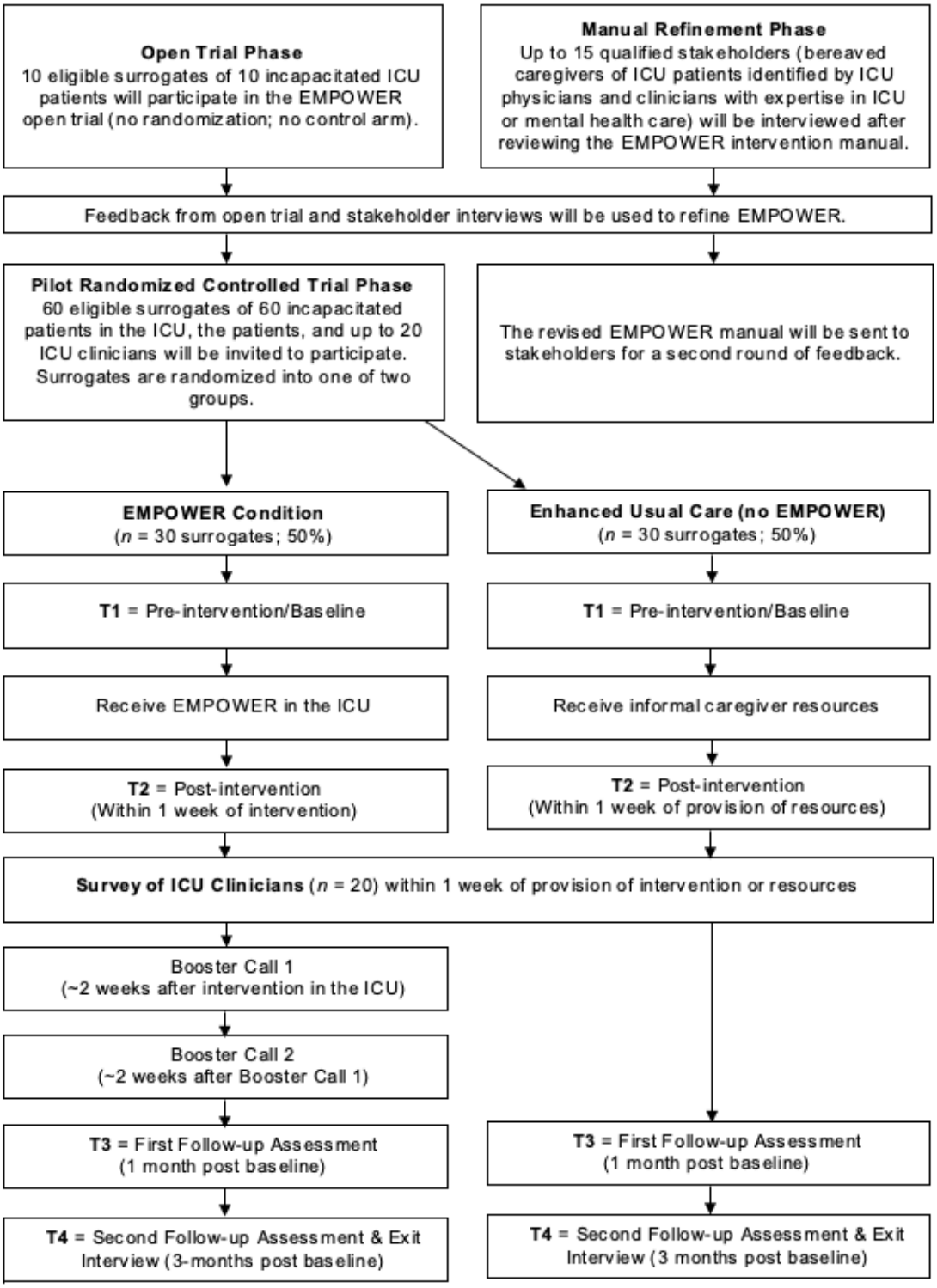

Figure 1

EMPOWER Timeline.

SPIRIT Figure for Randomized Controlled Trial Portion of EMPOWER Trial							
	Enrollment	Assessment					Close-out
TIMEPOINT	$-T_1$	*Baseline (T1)*	*Following Completion of Baseline Assessment*	*Within One Week of Completion of Intervention (T2)*	*One Month from Baseline (T3)*	*Three Months from Baseline (T4)*	*Chart Review*
SURROGATE ENROLLMENT:							
Eligibility screen	X						
Informed consent	X						
Allocation			X				
PHYSICIAN ENROLLMENT:							
Eligibility screen				X			
Informed consent				X			
INTERVENTIONS:							
EMPOWER			●	—	●		
Enhanced Usual Care[a]	●	—	—	—	—	●	
ASSESSMENTS:							
Demographics		X					
PG-12/13		X		X	X^s	X^s	
STAI		X		X	X	X	
PHQ-9		X			X	X	
BEAQ		X		X	X^s	X^s	
IES-R		X		X	X^s	X^s	
Distress Tolerance Scale		X		X	X	X	
PDI		X^p		X^p	X	X	
Decision Regret Scale		X		X	X	X	
PDEQ		X		X			
Caregiver Self-Efficacy in the ICU Scale		X		X			
EMPOWER/EUC Satisfaction Questionnaire				X			
Physician Questionnaire				X			
CEQUEL/CEQUEL-R					X	X	
Quality of Life/Quality of Death					X	X	
Critical Care Family Satisfaction Survey					X		
Medical Information Update					X	X	
Exit Interview[b]						X	
Medical Chart Review							X

[a] Exposure dependent on patient length of stay
[b] For participants assigned EMPOWER only
[p] Primary outcome
[s] Secondary outcomes

Figure 2

SPIRIT Figure.

Supplementary Files

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- supplement1.doc