A Randomized Trial of Behavioral Nudges to Improve Enrollment in Critical Care Trials

Study Protocol

Updated: April 2020

A randomized trial to assess the effect of a novel pre-consent survey comprised of nudges on critical care randomized controlled trial enrollment among surrogates of mechanically ventilated patients.

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1. Abstract

Difficulty recruiting patients is a widely recognized barrier to successful completion of randomized controlled trials (RCTs) and a significant contributor to the cost of conducting such studies. Difficulty recruiting patients is particularly problematic for critical care trials which often rely on surrogate decision makers (SDMs) for enrollment decisions. Evidence suggests that behavioral interventions, or nudges, may offer novel approaches to increase enrollment in RCTs by reframing decisions without restricting choice. We aim to determine the effectiveness of a scalable bundle of non-monetary nudges on increasing enrollment rates in a sham RCT among critically ill patients.

2. Background and Introduction

The joint problems of under-enrollment and selective enrollment in RCTs have long plagued efforts to evaluate new and existing medical interventions[1-4]. Under-enrollment occurs when too few research participants are enrolled to provide adequate statistical power to answer the study's primary research question, degrading the study's scientific value and hence, ethics[5-7]. Selective enrollment occurs when specific subgroups within the target population are enrolled in proportions greater or less than their representation in that population, limiting the generalizability of the trial's results and curtailing scientific value[8].

Forty percent of National Cancer Institute-sponsored trials are never completed, according to an Institute of Medicine report[9]. Studies often go unfinished due to enrollment difficulties[5,10-12]. Trials that fail to achieve target enrollment due to enrollment difficulties have been called the "ultimate inefficiency"[9]. Recruitment has been referred to as "the most difficult and challenging aspect of clinical trials[13]. Even when investigators enroll an adequate number of participants, they rarely do so on schedule[12,14], or in a manner that attracts the full range of available participants[8,15]. Further, participant recruitment represents one of the most substantial costs of conducting clinical trials, requiring an average of 13 hours and $500 per subject in cancer trials at academic medical centers[16]. Given the resources needed to successfully recruit patients to RCTs, and the gap between important research questions and available research funding, it is essential to find ways to enhance recruitment of patients to clinical trials[17]. Authorities have suggested that trialists should embed evaluations of recruitment strategies within their trials[18,19].

Behavioral economics is a relatively new discipline which merges psychology and economics to gain insights into how people make decisions. A key aspect of behavioral economics is the use of nudges. Nudges are behaviorally informed interventions which predictably influence behavior without limiting choices. Nudges have been proposed as a possible way to address difficulties in trial enrollment[20]. Financial incentives are one form of a nudge. However, many nudges are non-monetary. An example of a non-monetary nudge is providing information about norms. Injunctive norms involve the perception of what behavior is acceptable, while descriptive norms highlight what behaviors others are engaging in. Individuals are more likely to participate in an activity if they perceive it as acceptable and common. The duty of reciprocity is the sense that one should repeat pro-social behavior from which they have benefited. The mere-measurement effect is also known as the self-prophecy nudge. It reflects a tendency to perform actions after being asked about the action in a hypothetical setting. The foot-in-the-door nudge involves asking a participant to complete a small request which has a high consent rate followed by a larger request.

3. Objectives

3.1 Overall Objectives

The goal of this study is to test whether a novel pre-consent survey with incorporated nudges increases the enrollment rate into a sham RCT among critically ill patients. To accomplish this goal we will assess quantitatively how many surrogates assigned to each study arm enroll a patient into the sham RCT. We will also quantitatively assess for undue and unjust inducement.

3.2 Primary Outcome Variable(s)

This randomized trial has the single primary outcome of proportion of SDMs who enroll the patient into the sham RCT.

3.3 Secondary Outcome Variable(s)

Secondary outcomes included undue inducement, unjust inducement, patient and surrogate characteristics associated with enrollment. Undue inducement was defined as an interaction between intervention and risk perception on enrollment rate. Unjust inducement was defined as an interaction between intervention and highest level of education completed on enrollment rate.

4. Design

This is a single-blinded randomized controlled among surrogates of patients requiring mechanical ventilation admitted to one of ten ICUs across two University of Pennsylvania Health System (UPHS) hospitals.

5. Recruitment

5.1 Subjects

We will be recruiting 182 surrogate decision-makers of patients requiring mechanical ventilation admitted to one of ten ICUs across two UPHS hospitals. The research coordinator will review the electronic medical record of patients admitted to the ICUs to identify eligible participants. The coordinator will contact the attending physician for any identified patient to confirm eligibility and seek approval for the study team to approach the patient's family. The coordinator will approach approved families if they are present in the patient's room at the time of recruitment. The coordinator may defer approach if there is a procedure underway or if the family is in visible distress.

The eligibility criteria for participation are as follows:

Eligibility Criteria
ICU length of stay >24hrs
Mechanically ventilated via an endotracheal tube

Over 18 years of age
Anticipated to remain using an endotracheal tube at least 24 more hours
No limitations on life extending care
Surrogate fluent in English
Not enrolled in an active ICU trial
Patient unable to consent for self
ICU attending is not a study investigator
ICU attending identifies the patient's family as distrustful of the medical system
ICU attending declines approach for any reason (reason to be documented)
Surrogate present in patient's room

5.2 Informed Consent

A waiver of informed consent has been approved by the University of Pennsylvania Institutional Review Board. Once patients have been chart screened for eligibility, study personnel will approach potentially eligible surrogate. Study personnel will introduce themselves to the patient, inform the patient that they are part of a group conducting a research study, and ask permission to sit down and tell the patient more.

5.3 Accrual

We have received approval from the University of Pennsylvania IRB-approved protocol and obtained approval to conduct this study in all 6 ICUs located at the Hospital of the University of Pennsylvania and all 4 ICUs located at Presbyterian Hospital. Using an estimated baseline enrollment rate of 30% in the control group, a total of 182 participants achieves at least 80% power to detect a 20% absolute difference at alpha of 0.05. We will consecutively recruit all eligible surrogates from the ICU until we reach our target sample size. We will attempt visit each ICU session at least once a day. The research coordinator will approach eligible surrogates while they are present in the patient's room. For surrogates who initially defer a decision we will attempt to reengage the following day and each subsequent recruiting day until we either have a definitive decision or until the patient is ineligible. We anticipate that we can recruit at least 4 patients per week.

5.4 Key Inclusion Criteria

The eligibility criteria, all of which must be met, are:

1. Patient and surrogate must be 18 or older
2. ICU length of stay > 24 hours
3. Mechanically ventilated via an oral endotracheal tube
4. Patient is unable to consent for themselves

5.5 Key Exclusion Criteria

Patients will be excluded if one of the following criteria is met:

1. Limitations on life extending care
2. Anticipated extubation or tracheostomy placement in next 24 hours
3. Enrolled in another ICU trial
4. ICU attending is a study investigator

Surrogates will be excluded if one of the following criteria are met:

1. Not fluent in English
2. Identified by the ICU attending as having mistrust in the healthcare system

3. Not present in the patient's room at the time of recruitment

5.6 Remuneration

Subjects will not receive any compensation for participation.

6. Randomization

6.1 Groups

Surrogates who indicate they are willing to hear about a research study will be randomized to receive either a pre-consent nudge survey or standard informed consent procedures. The two groups only differ in the initial approach, whether they are asked to complete a survey before being informed of the sham trial or whether they are invited to consider the sham trial without a pre-consent survey. Both groups then fill out identical risk assessments and demographic surveys. After indicating their sham trial enrollment decision and completing risk assessments and demographic surveys, surrogates will be debriefed (see debriefing script).

6.2 Assignment

Group allocation will be determined by the REDCap randomization module with assignment probabilities of 50% to each group stratified by research coordinator.

7. Procedures

Study procedures are as following:

1. The research coordinator will review the electronic medical record of patients admitted to each of 10 ICUs to determine eligibility and documenting the results in the study screening database.
2. The research coordinator will contact the ICU attending of patients screened as eligible to confirm eligibility.
3. The research coordinator will visit each eligible patient's room to assess for the presence of visitors.
4. If visitors are present the research coordinator will enter patient information into the REDCap study module on the screening tablet.
5. The research coordinator will enter the room, identify themselves and confirm that the visitor is the patient's surrogate decision maker.
6. The research coordinator will ask the patient's identified surrogate decision maker if they are willing to hear about a research study.
7. Surrogate decision makers who indicate their wiliness to hear about a research study will then be randomized in the REDCap randomization module (as above).
8. If the participant is randomized to the intervention arm the research coordinator will follow the script (see below) introducing the survey. Following completion of the survey the research coordinator will then ask if they are willing to hear about a research trial.
9. If the participant is randomized to the control arm the research coordinator will follow the script (see below) introducing the sham mechanical ventilation weaning trial.

10. After the surrogate makes an enrollment decision (regardless of the decision) for the sham mechanical ventilation trial they will be asked to complete the risk perception assessment and demographic surveys.
11. If the surrogate askes for more time to make an enrollment decision the research coordinator will ask for a good time to return for a decision. Risk perception assessment and demographic survey data will be deferred until after a decision is made. The research coordinator will follow up the following day (or time set by surrogate) to seek an enrollment decision. Repeated attempts to obtain an enrollment decision will continue each recruitment day until a decision is made or until eligibility criteria is no longer met.
12. Immediately following the sham trial enrollment decision, risk assessment and demographic surveys the research coordinator will debrief the surrogate (see script below).
13. The research coordinator will update the screening database with the results of the recruitment attempt.
14. The research coordinator will document additional clinical data from the electronic medical record for participating patients into the REDCap study database.
15. We will continue subject recruitment until target enrollment is reached.

8. Consent

A waiver of informed consent has been approved by the University of Pennsylvania Institutional Review Board. Once patients have been chart screened for eligibility, study personnel will approach potentially eligible surrogate. Study personnel will introduce themselves to the patient, inform the patient that they are part of a group conducting a research study, and ask permission to sit down and tell the patient more. Following the study procedures and debriefing the participant will retain the debriefing handout which includes instructions on how to withdrawal from the study.

9. Analysis Plan

As we do not have any strong a priori evidence that any of the collected demographic will be strongly associated with the primary outcome, we will perform an unadjusted analysis as the primary analysis. The primary outcome will be an intention-to-treat analysis of the proportion of participants who enroll in the sham clinical trial. The intervention arm will be compared to the control arm using a chi-square test. In secondary analyses, we will test for undue inducement by assessing the interaction between the study group and risk perception on enrollment rate. We will test for unjust inducement by assessing the interaction between study group and level of education on enrollment rate. Stata v14 will be used for all analyses. Unless otherwise specified, a p-value <0.05 will be considered significant.

We will conduct a post-hoc exploratory analysis of patient and surrogate variables associated with sham trial enrollment. We will have a third party with critical care trial recruitment expertise, blinded to the data, review and rank the variables based on their mechanistic plausibility to impact enrollment decisions. The number of included variables in the final model will be determined by the number of events (enrollments into the sham trial) to not exceed a 1:10 covariate to event ratio.

10. Confidentiality of Subjects and Data

10.1 Data Management

Prudent steps will be taken to ensure that all information will be kept confidential and secure, including medical and survey data. All survey data will be collected on-site by trial research nurse/staff and entered into REDCap (Research Electronic Data Capture), hosted at the University of Pennsylvania. We will implement multiple, redundant protective measures to guarantee the security of participant data. All data for this project will be stored on UPHS secure/firewalled servers. These data servers are maintained in a guarded facility behind several locked doors, with very limited physical access rights. They are also cyber-protected by extensive firewalls and multiple layers of security comparable to what is used in commercial financial transactions. This multi-layer system of data security, identical to the system protecting the University of Pennsylvania Health Systems medical records, greatly minimizes privacy risks. Direct identifiers for patients and their surrogates will be omitted from all analytic files.

10.2 Subject Confidentiality

Only authorized project personnel will have access to the data. All study data will be stored behind firewalls on UPHS servers; none will be stored on stand-alone PCs or laptops. All study personnel who work with these data will have undergone required human subjects training. We will implement multiple, redundant protective measures to guarantee the privacy and security of the participant data. All data for this project will be stored on the secure/ firewalled servers of the UPHS in data files that will be protected by multiple password layers. These data servers are maintained in a guarded facility behind several locked doors, with very limited physical access rights. They are also cyber-protected by extensive firewalls and multiple layers of communication encryption. Electronic access rights are carefully controlled by Penn system managers.

10.3 Subject Privacy

We will approach surrogates in the patient's room. We will offer them the option to speak in the patient's room or in an alternative private location. Individual-level medical data for patients will be kept confidential and will only be stored on highly secure servers available for patient-level data. Only authorized project personnel will have access to the data and the data will be stored on servers only and not stand-alone PCs or laptops. All study personnel who work with this medical data will have undergone all of the required human subjects training.

11. Human Subjects Protection

11.1 Potential Risks

Potential risks include loss of confidentiality, disappointment in not being able to participate in the described simulated trial and negative impact on clinician-family trust with the use of deception. We protect the data in several ways as outline in the data protection section. We purposefully selected a simulated trial of prioritizing decreases in FiO2 vs PEEP in weaning of mechanical ventilation as a trial that would unlikely result in excessive optimism and therefor would yield minimal disappointment once it is disclosed that it is a simulated trial.

11.2 Potential Benefits

Participants will be instructed that this is research, and like all research, it is being conducted with the primary goal of producing generalizable knowledge. Thus, the primary benefits to be gained are those related to the knowledge to be gained. However, patients, as well as their families, may benefit directly from the opportunities to discuss their thoughts on research participation. In addition, the knowledge to be gained in this study may help develop a simple way to increase research participation.

11.3 Risk/Benefit Assessment

Participants will be offered enrollment in a sham randomized controlled trial comparing the effects of prioritizing decreases in FiO2 vs PEEP in weaning of mechanical ventilation. Thus, temporarily deceiving patients on the purpose of the study. Importantly, the risk is minimal because: (1) their participation in the main study and decision whether or not to participate in the sham RCT will not affect the treatment their loved one receives; (2) the proposed intervention in the sham RCT is within standard of care for mechanically ventilated patients and is minimally invasive, so discussion about this sham RCT and intervention is not expected to lead to additional distress for the participant; (3) the evidence to date suggests that the behavioral nudges employed in this study are without ethical concerns (4) we offer participants the opportunity to opt-out after a thorough debriefing procedure. Difficulty recruiting patients is a widely recognized barrier to successful completion of clinical trials and a significant contributor to the cost of conducting such studies. If a simple intervention such as the behavioral economic nudges we are testing are found to increase trial recruitment without blunting perception of risk it could have a dramatic effect on future critical care trials.

12. Study Instruments

12.1 Pre-consent Nudge Survey

Family Attitudes towards Participation in Advanced Illness Research Survey

This is a survey to help us understand the relationship between patient's behaviors and their family's feelings about participation in medical research. Answering these questions is voluntary. The care of your loved one will not be impacted by whether or not you participate. Responses will be anonymous and confidential.

1. Please answer the following to the best of your ability about your loved one:

	Yes	No
My loved one would give directions to someone they didn't know:	○	○
My loved one would delay an elevator and hold the door for someone they didn't know:	○	○
My loved one would give clothes or goods to a charity:	○	○
My loved one would give money to a charity:	○	○
My loved one would offer to help a handicapped or elderly person across the street:	○	○

2. Many treatments used today that improve survival for patients in the intensive care unit were discovered through many patients' participation in research studies.

	Yes	No
My loved one would participate in a research study if it was low risk to them and the information learned may help other patients in the future.	○	○

12.2 Sham Mechanical Ventilation Trial Consent Form

UNIVERSITY OF PENNSYLVANIA
RESEARCH SUBJECT
INFORMED CONSENT FORM

Protocol Title:	Randomized Trial of Reducing FiO2 vs PEEP in Weaning of Mechanical Ventilation
Principal Investigator:	Katherine R. Courtright, MD, MS
Emergency Contact:	Dustin Krutsinger, MD 319-400-4964 Dustin.Krutsinger@uphs.upenn.edu

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Why am I being asked to volunteer?

You are being invited to participate in a research study because you are currently hospitalized in the intensive care unit and on a mechanical ventilator. Your participation is voluntary which means you can choose whether or not you want to participate. If you choose not to participate, there will be no loss of benefits to which you are otherwise entitled. Before you can make your decision, you will need to know what the study is about, the possible risks and benefits of being in this study, and what you will have to do in this study. The research team is going to talk to you about the research study, and they will give you this consent form to read. You may also decide to discuss it with your family, friends, or family doctor. You may find some of the medical language difficult to understand. Please ask the investigator and/or the research team about this form. If you decide to participate, you will be asked to sign this form.

What is the purpose of this research study?

For a person on a breathing machine, two factors affect the oxygen level in the blood: the percentage of oxygen in the air delivered by the breathing machine and the pressure at which the air is delivered (PEEP). When a patient begins to improve and requires less support from the breathing machine, some doctors turn down the oxygen percentage first, and other doctors turn down the pressure first. It is not known which of these approaches best helps patients recover and get off the breathing machine. The purpose of this study is to compare the effects of two approaches to reduce the breathing machine support in improving patients on breathing machines.

How long will I be in the study?

If you consent to participate in this study by signing this consent form, your participation in the study will take place as long as you are on mechanical ventilation in the intensive care unit. You may remove yourself from the study at any point in time.

What am I being asked to do?

In this study, you would be randomly assigned to one of two approaches. The first approach would be to lower the oxygen percentage before lowering the pressure when you begin to recover. The other approach would lower the pressure before the oxygen percentage. If you decide to be in the study, no immediate changes would be made to the breathing machine. But when it was time for the support from the breathing machine to be reduced, the first changes would be determined by which approach you are assigned to by chance.

What are the possible risks or discomforts?

It is possible that either approach could cause organ damage or delay recovery, but doctors do not know which approach leads to better health outcomes such as improved survival and shorter time spent in ICU.

What if new information becomes available about the study?

During the course of this study, we may find more information that could be important to you. This includes information that, once learned, might cause you to change your mind about being in the study. We will notify you as soon as possible if such information becomes available.

What are the possible benefits of the study?

You are not expected to get any direct benefit from being in this research study. The knowledge to be gained in this study may benefit future mechanically ventilated patients.

What other choices do I have if I do not participate?

Your clinical care will not be changed if you decline to participate in this study.

Will I be paid for being in this study?

You will not be paid for participating in this study.

Will I have to pay for anything?

No charges or costs to you or your family will results from your participation in this study.

What happens if I am injured from being in the study?

We will offer you the care needed to treat injuries directly resulting from taking part in this research. We may bill your insurance company or other third parties, if appropriate, for the costs of the care you get for the injury, but you may also be responsible for some of them.

There are no plans for the University of Pennsylvania to pay you or give you other compensation for the injury. You do not give up your legal rights by signing this form.

If you think you have been injured as a result of taking part in this research study, tell the person in charge of the research study as soon as possible. The researcher's name and phone number are listed in the consent form.

When is the Study over? Can I leave the Study before it ends?

This study is expected to end after a sufficient number of patients have participated, and all information has been collected. This study may also be stopped at any time by your physician, the study Sponsor, or the Food and Drug Administration (FDA) without your consent because:

- The Primary Investigator feels it is necessary for your health or safety. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision.
- The Sponsor, the study Principal Investigator, or the Food and Drug Administration (FDA) has decided to stop the study.

If you decide to participate, you are free to leave the study at anytime. Withdrawal will not interfere with your future care.

Who can see or use my information? How will my personal information be protected?

The investigator and staff involved with the study will keep your personal and medical information collected for the study strictly confidential. It will be kept in a secured file. The governing research body (Institutional Review Board) at the University of Pennsylvania may access the records upon request. All records will be stored in an encrypted and secured database with access restricted to study personnel.

Who can I call with questions, complaints or if I'm concerned about my rights as a research subject?

If you have questions, concerns or complaints regarding your participation in this research study or if you have any questions about your rights as a research subject, you should speak with the Principal Investigator listed on page one of this form. If a member of the research team cannot be reached or you want to talk to someone other than those working on the study, you may contact the Office of Regulatory Affairs with any question, concerns or complaints at the University of Pennsylvania by calling (215) 898-2614.

When you sign this form, you are agreeing to take part in this research study. This means that you have read the consent form, your questions have been answered, and you have decided to volunteer. Your signature also means that you are permitting the University of Pennsylvania to use your personal health information collected about you for research purposes within our institution.

Name of Subject (Please Print)	Signature of Subject	Date

Name of Person Obtaining Consent (Please Print)	Signature	Date

For subjects unable to give authorization, the authorization is given by the following authorized subject representative:

Authorized subject representative [Please Print]	Authorized subject representative Signature	Date

Provide a brief description of above person authority to serve as the subject's authorized representative.

A copy of this consent form will be given to you.

12.3 Risk Perception Assessment

Risk Assessment

1. On a scale of 1 to 7, how risky do you believe this study would be for participants?

Not Risky At All						Very Risky
1	2	3	4	5	6	7

2. Does the study seem...

	Yes	No
More risky than talking on the cell phone while driving?	○	○
More risky than receiving the flu vaccine?	○	○
More risky than flying on a plane?	○	○
More risky than driving 15 mph over the speed limit?	○	○
More risky than taking 3 times the recommended dose of a pain killer?	○	○
More risky than receiving stitches?	○	○
More risky than riding a motor cycle with no helmet?	○	○
More risky than getting a body piercing?	○	○
More risky than bungee jumping?	○	○

3. What factors influenced your decision to participate or not to participate in this trial?

_____

12.4 Surrogate Demographic Survey

Penn Medicine

Study ID_____

Demographic and Clinical information:

Please answer the following to the best of your ability about yourself (all will be kept confidential and secure and will not be shared):

1. Are you officially designated as the patient's durable power of attorney for health care?

- ☐ Yes
- ☐ No

2. Have you ever had a life-threatening illness or injury for which you needed life support to keep yourself alive? This type of care would usually mean that you were in an ICU, and being treated with a breathing machine or other machines or medicines necessary to keep you alive.

☐ Yes ☐ No

3. Have you ever participated in a medical research trial? This would usually mean being asked for consent before taking an experimental medication or other intervention and being monitored for a response.

☐ Yes ☐ No

4. Has anyone you known ever participated in a medical research trial? This would usually mean being asked for consent before taking an experimental medication or other intervention and being monitored for a response.

☐ Yes ☐ No

5. What is your gender?

- ☐ Male
- ☐ Female

6. What is your age? _____

7. What is ~~the~~ your marital status?

- ☐ Widowed
- ☐ Married/Partnered
- ☐ Never married
- ☐ Divorced
- ☐ Separated

8. Please specify your ethnicity:

- ☐ Hispanic or Latino
- ☐ Not Hispanic or Latino

9. Please specify your race:

- ☐ American Indian or Alaskan Native
- ☐ Asian
- ☐ Native Hawaiian or Other Pacific Islander
- ☐ Black or African-American
- ☐ White or Caucasian
- ☐ Other

10. What is your highest level of completed education?

- ☐ Less than High School
- ☐ High School/GED
- ☐ Some College
- ☐ College Degree
- ☐ Post-College Degree (MA, Professional degree, PhD)

11. What is your relationship to the patient?

- ☐ Spouse
- ☐ Adult child
- ☐ Parent
- ☐ Sibling
- ☐ Other blood relative
- ☐ Friend
- ☐ Other _____

12.5 Patient Demographic Survey

Penn Medicine

Study ID_____

Please answer the following to the best of your ability about your loved one (all will be kept confidential and secure and will not be shared):

1. In the past 3 months, approximately how long has the patient spent in a hospital or other health care facility?

- ☐ Less than 1 week
- ☐ 1 week to 1 month
- ☐ 1 month to 3 months
- ☐ Entire 3 month

2. Before the patient's current Intensive Care (ICU) stay, have they ever had a life-threatening illness or injury for which they needed life support to keep them alive? This type of care would usually mean that they were in an ICU, and being treated with a breathing machine or other machines or medicines necessary to keep them alive.

☐ Yes ☐ No ☐ I don't know

3. Has the patient ever participated in a medical research trial? This would usually mean being asked for consent before taking an experimental medication or other intervention and being monitored for a response.

☐ Yes ☐ No ☐ I don't know

4. Based on the information that has been shared with you about your loved one's condition, do you feel that he or she is:

- ☐ Stable
- ☐ Improving
- ☐ Worsening

5. What is the patient's gender?

- ☐ Male
- ☐ Female

6. What is the patient's age? _____

7. What is the patient's marital status?

- ☐ Widowed
- ☐ Married/Partnered
- ☐ Never married
- ☐ Divorced
- ☐ Separated

8. Please specify the patient's ethnicity:

- ☐ Hispanic or Latino
- ☐ Not Hispanic or Latino

9. Please specify the patient's race:

- ☐ American Indian or Alaskan Native
- ☐ Asian
- ☐ Native Hawaiian or Other Pacific Islander
- ☐ Black or African-American
- ☐ White or Caucasian
- ☐ Other

10. What is the highest level of education the patient has completed?

- ☐ Less than High School
- ☐ High School/GED
- ☐ Some College
- ☐ College Degree
- ☐ Post-College Degree (MA, Professional degree, PhD)

12.6 Debriefing Form

Dear Sir or Madam,

Thank you for talking with us. We know having a loved one in the intensive care unit can be difficult. It means a lot to us that you talked to us during this time. We wanted to take a minute to better explain why we met.

Today's surveys and consent were actually part of a study to understand patients' loved ones' feelings about research and how researchers should talk to families in the ICU about research.

The study about different ways to reduce breathing machine support was a simulation, not a real study. If you said "yes", your loved one will not actually be in a breathing machine study.

Your loved one will not lose out on any of their current benefits or treatments. The medical team will continue to change the breathing machine in the best way they see fit.

A big challenge for ICU studies is enrolling enough people. The information you shared will help researchers' talk to families about research, improve future research studies, and speed up discoveries in advanced illnesses. We could not tell you the reason for our study earlier because you may have answered our questions differently.

Before I go on, do you have any questions?

Thank you for your time. We would like to use today's information to better understand patients' loved ones' decisions about research. While the reason for this study was not initially shared, details in the consent form about how we keep your information private are still true. As a reminder, your participation in this study is voluntary. You can withdraw at any time. If you withdraw, we only keep the medical record number so we do not approach you again.

Lastly, please do not tell anyone outside your immediate family about this study. If too many people know about our study it will make it hard to do our study and learn about patients' loved ones' attitudes about research.

We know we have shared a lot of information. It is important to us that all your questions are answered and that you understand the purpose of our study. Do you have any more questions for me?

Thank you, again, very much for your time today. If you have any more questions, be in touch by email or phone with the contacts below.

Sincerely,
The Research Team

Contact information for any questions:
Dustin Krutsinger, M.D.
Dustin.Krutsinger@uphs.upenn.edu
University of Pennsylvania Institutional Review Board: 215-573-2540

12.7 Script

Introduction (same across all arms)

- *"Hello my name is _____, I work as a research coordinator here at Penn. May I have a few minutes of your time to discuss a study?"*
  - YES
    - *"Great. Thank you for being willing to talk with us. Before I get started I just want to make sure we don't waste any of your time. Are you at least 18 years old and the primary decision maker for Mr/Ms_____?"* (Assess for English proficiency)
      - NO
        - *"I am sorry, we have to discuss this study with someone who is at least 18 years old and a primary decision maker for _____."*
        - Inquire about name, location and in person availability. Once the health decision maker is available RANDOMIZE and proceed to the appropriate arm in the script.
      - YES
        - *"Great. Give me one second to pull up some materials."*
        - RANDOMIZE and proceed to the appropriate arm in the script.
  - MAYBE/TELL ME MORE ABOUT STUDY
    - *"I can definitely tell you more about this study, I just need to pull up some materials. Before I do that, I want to make sure I don't waste your time. Are you at least 18 years old and the primary decision maker for Mr/Ms_____?*
      - NO
        - *"I am sorry, we have to discuss this study with someone who is at least 18 years old and a primary decision maker for _____."*
        - Inquire about name, location and in person availability. Once the health decision maker is available RANDOMIZE and proceed to the appropriate arm in the script.
      - YES
        - *"Great. Give me one second to pull up those materials."*
        - RANDOMIZE and proceed to the appropriate arm in the script.
  - NO
    - *"May I come back at another time that may work better for you?"*
      - NO
        - *"Thank you for your time. Take care."*
      - YES
        - Inquire about name, location and in person availability. Start at beginning of script if surrogate is available upon a return.
- **Patient randomized to Arm 1 start script on page 2, section A**
- **Patient randomized to Arm 2 start script on page 4, section B**

A. Arm 1: Nudge Bundle Survey

1

- *"I have a survey to understand the relationship between patient's behaviors towards others and their family's attitudes towards participation in critical care research. The survey is voluntary and declining will not impact the care the patient will receive. Responses are confidential. Would you be willing to complete this survey?"*
  - NO
    - *"That's OK, I actually have a different study, a research trial that Mr/Ms_____ qualifies for. May I take a few minutes to tell you about it?*
      - No
        - "Thank you for your time. Take care"
      - Yes
        - "Great, let me pull up that information"
        - Continue in REDCap Trial information.
  - YES
    - *"Great, thank you for being willing to take a few minutes to fill out this survey. Please fill it out as best you can, note the questions are about your loved one."*
    - Continue in REDCap Survey and hand tablet to the surrogate.
    - *"Thank you very much for taking the time to fill out the survey. I actually do have a research trial that Mr/Ms _____ qualifies for. May I take a few minutes to tell you about it?*
      - NO
        - *"Thank you for your time.*
      - YES
        - *"Great. The overall purpose of our study is to determine the best protocol for a person who is improving and the medical team is beginning to turn down the amount of help the breathing machine is providing. I'll start by giving you a little background. When someone needs less help from the breathing machine, the clinical staff have two options that affect the oxygen level in the blood: the percentage of oxygen in the air delivered by the breathing machine and the pressure at which the air is delivered. When a patient begins to improve and requires less help from the breathing machine, some doctors turn down the oxygen percentage first, and other doctors turn down the pressure first. It is not known which of these approaches best helps patients recover and get off the breathing machine."*
        - *In this study, your loved one would be randomly assigned to one of two approaches. The first approach would be to lower the oxygen percentage before lowering the pressure when your loved one begins to recover. The other approach would lower the pressure before the oxygen percentage. If you decide to allow your loved one to be in this study, no immediate changes would be made to his/her breathing machine. When it was time for the support from the breathing machine to be reduced, the first changes would be determined by which approach your loved one was assigned to. It is possible that either approach could cause organ damage or delay recovery, but clinicians do not know which approach leads to improved survival and shorter time spent in the ICU. This study will help determine the best*

approach for using the breathing machines to help patients recover and leave the ICU.

- *Is this a study you would be willing or interested in having _____ participate in?*
  - No
    - *"Ok. I will not try to change your mind. We are asking people who say no to fill out a survey to help us understand why people say no. Would you be willing to fill that out quickly?"*
      - YES: Proceed to RISK ASSESSMENT SURVEY (PAGE 5)
  - Maybe, I would like more time to think about it
    - *"No problem, let me leave the consent form with you to discuss. When would be a good time for me to check back with you?*
  - Yes
    - Surrogate enrolls patient
      - *"Thank you for being willing to participate in this important study. I need to collect a little more information while I'm here; it will only take a few minutes."*
        - Continue on to risk assessment and demographic surveys. (Page 5)

B. Arm 2: Standard Consent

- *"Great. The overall purpose of our study is to determine the best protocol for a person who is improving and the medical team is beginning to turn down the amount of help the breathing machine is providing. I'll start by giving you a little background. When someone needs less help from the breathing machine, the clinical staff have two options that affect the oxygen level in the blood: the percentage of oxygen in the air delivered by the breathing machine and the pressure at which the air is delivered. When a patient begins to improve and requires less help from the breathing machine, some doctors turn down the oxygen percentage first, and other doctors turn down the pressure first. It is not known which of these approaches best helps patients recover and get off the breathing machine."*
- *In this study, your loved one would be randomly assigned to one of two approaches. The first approach would be to lower the oxygen percentage before lowering the pressure when your loved one begins to recover. The other approach would lower the pressure before the oxygen percentage. If you decide to allow your loved one to be in this study, no immediate changes would be made to his/her breathing machine. When it was time for the support from the breathing machine to be reduced, the first changes would be determined by which approach your loved one was assigned to. It is possible that either approach could cause organ damage or delay recovery, but clinicians do not know which approach leads to improved survival and shorter time spent in the ICU. This study will help determine the best approach for using the breathing machines to help patients recover and leave the ICU.*
- *Is this a study you would be willing or interested in having _____ participate in?*
    - No
        - *"Ok. I will not try to change your mind. We are asking people who say no to fill out a survey to help us understand why people say no. Would you be willing to fill that out quickly?"*
            - YES: Proceed to RISK ASSESSMENT SURVEY (PAGE 5)
    - Maybe, I would like more time to think about it
        - *"No problem, let me leave the consent form with you to discuss. When would be a good time for me to check back with you?*
    - Yes
        - Surrogate enrolls patient
            - *"Thank you for being willing to participate in this important study. I need to collect a little more information while I'm here; it will only take a few minutes."*
            - Continue on to risk assessment and demographic surveys. (Page 5)

- Risk Assessment Survey/Demographics
  - Individuals exposed to the simulation trial:
    - *"There will be three brief pages for you to fill out. "*
      - Hand tablet to surrogate to complete riskiness assessment. Provide appropriate guidance throughout the surveys particularly on how to use the slider bar for the first riskiness question.
    - *"The first page is a risk assessment survey. You will be asked questions to help us understand how risky you think this study is. There will also be a section for you to write in your specific thoughts regarding the risks of the study."*
    - *"The second page is a set of questions about you. Feel free to skip anything you are not comfortable answering"*
    - *"The third page is a set of questions about your loved one."*
      - Proceed to Debrief. (Page 6)
  - Individuals only exposed to nudge:
    - *"There will be two brief pages for you to fill out"*
    - *"The first page is a set of questions about you."*
    - *"The second page is a set of questions about your loved one."*
    - Provide appropriate guidance throughout the surveys.
    - "Thank you for your time today."

C. Debrief

- Was the oxygen concentration vs air pressure study discussed with the surrogate
  - NO
    - *"Thank you again for your time today. Take care."*
  - YES
    - *Dear Sir or Madam,*
    - *Thank you for taking the time to participate today. We realize having a loved one in the intensive care unit can be a stressful experience and your willingness to participate during this difficult time means a lot to us. We wanted to take a minute to clarify information regarding the purpose of our meeting today.*
    - *Today's procedures, which included the survey and consent process, were actually part of a study designed to better understand patients' loved ones' attitudes towards participation in research and how researchers should talk to patients and families in the ICU about research.*
    - *The trial discussed today involving different approaches to reducing ventilator support with oxygen concentration and air pressure was a simulation, not a real study. If you said "yes", your loved one has not actually been enrolled in a clinical trial.*
    - *Your loved one will not lose out on any benefits or treatment options to which they are already entitled. Your medical team will continue to adjust the ventilator in the best way they see fit.*
    - *A significant barrier for clinical trials in advanced illness is subject enrollment. The information you provided today will inform how researchers' approach families about research in the ICU, improve the quality of research findings in future clinical trials, and increase the rate of scientific progress in the management and treatment of advanced illnesses. We could not tell you beforehand that this was a simulation, as it would not result in a realistic experience, and the study results would not be valid.*
    - *Before I go on do you have any questions about what we have discussed?*
    - *We are very appreciative of your willingness to participate today and further medical research in this way. We would like to analyze the information you provided today, to better understand patients' loved ones' views of research and what goes into their decision processes. While the purpose of this study was not initially disclosed, details in the consent form regarding how we keep your information confidential or private, are still accurate. We have multiple layers of protection for the data we collect such as your identity and answers to our questions. However, we cannot guarantee total privacy. As a reminder, your participation in this study is voluntary and you have the right to withdraw from the study at any time. If you elect to withdraw from this study, we will only retain the medical record number in a screening list so that we do not approach you a second time.*
    - *Due to the nature of this study, please do not tell anyone outside your immediate family about the purpose of this study as it would reduce our ability to evaluate patients' loved ones' attitudes about participation in research.*
    - *We recognize we have covered a lot of information. It is important to us that all your questions are answered and you have an accurate understanding of our study and its purpose. Do you have any further questions for me at this time?*
    - *Thank you, again, very much for your time today. If you have any future questions do not hesitate to be in touch by email or phone with the contacts listed below.*
    - Provide debrief letter to participant

FAQs

- **General:**
  - Multiple surrogate decision makers.
    - *Can participate as a group, but ask that one person fill out the surrogate demographics information.*
  - *If the medical team wants to make a change that is not in agreement with the protocol, can they do that?*
    - *Yes, the clinical team can still make changes that they feel is in the best interest of the patient, even if that disagrees with the approach they were randomized to.*
- **Consent form:**
  - I would like to discuss with my (Doctor, Friend, Family, Patient when awake, etc) before deciding.
    - *That is fine, is there at time that I can come back later today or tomorrow?*
  - Multiple family members present are in disagreement over participation.
    - *"I understand that participating in research is not always an easy decision. It seems there is some uncertainty about participating. You could discuss it further amongst yourselves and I can come back at a later time if that would be helpful."*
  - What is mechanical ventilation?
    - *Mechanical ventilation is the breathing machine that delivers breaths to the patient through the breathing tube.*
- **Demographics**
  - Do I have to answer all these questions?
    - *No, you do not have to answer every question. Them more information you are able to give the more helpful it is.*
  - What is durable power of attorney for health care?
    - *It is a legal document that the patient would have filled out to officially designate you as the decision maker for health care decisions.*

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