METEOR: Think NIV Pilot Study

Maximizing Extubation Outcomes Through Educational and Organizational Research: Think NIV Pilot Study

NCT04052542

Timothy D Girard, MD, MSCI
Department of Critical Care Medicine
University of Pittsburgh School of Medicine

Statement of Compliance

This investigation will be conducted in compliance with the protocol, International Conference on Harmonization guideline E6: Good Clinical Practice (ICH E6): Consolidated Guideline, and the applicable regulatory requirements from United States (US) Code of Federal Regulations (CFR) (Title 45 CFR Parts 46 and Title 21 CFR including Parts 50 and 56) concerning informed consent and Institutional Review Board (IRB) regulations.

Contact Details

Primary Investigator	Timothy D Girard, MD, MSCI	
	Phone	(412) 383-0582
	E-mail	timothy.girard@pitt.edu
Project Manager	Kelsey Linstrum, MS	
	Phone	(412) 383-0464
	E-mail	kml168@pitt.edu

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PART I: PROTOCOL SUMMARY

Title: METEOR: Think NIV Pilot Study

Objective: Pilot test three strategies designed to speed implementation of preventive post-extubation noninvasive ventilation (NIV): one control strategy (traditional online continuing medical education) and two novel strategies (interprofessional education and just-in-time education)

Study Design: Three parallel interrupted time series studies

Inclusion Criteria: Two study populations will be included. **Learners** will include [1] frontline care providers, including physicians, advanced practice providers, nurses, and respiratory therapists, [2] working in one of three participating UPMC ICUs: UPMC Presbyterian MICU, UPMC Mercy MSICU, and UPMC Passavant MSICU. **Patients** will include all mechanically ventilated patients treated in the participating UPMC ICUs and surviving to extubation.

Exclusion Criteria: Frontline care providers will be excluded if they:

[1] Have not worked in their current UPMC ICU for more than one month prior to the current study

[2] Have not directly cared for a mechanically ventilated patient in a UPMC ICU during the three months preceding the current study

Educational Strategies:

[1] Traditional online continuing education

[2] Interprofessional education

[3] Just-in-time education

Study Procedures: During a one-month intervention period, we will pilot test the educational strategies in three participating UPMC ICUs. Prior to receiving education, participants will be invited to complete a short online survey. Participants in the control group will be invited to complete a 30-minute online continuing education module, which will conclude with a survey. Participants in the interprofessional education group will be invited to attend a 90-minute, in-person, interprofessional education session that will occur in or near the participating ICU. A trained advance practice provider will provide participants in the just-in-time education group with 5-10 minutes of education in the ICU when the ICU team is rounding on a patient who is identified to be high risk for extubation failure. The just-in-time education may occur more than once per day, depending in the number of high-risk patients identified. All educational strategies will include content on the benefits of preventive post-extubation NIV, the indications and contraindications for preventive post-extubation NIV, and the value of working together as an interprofessional ICU team when implementing preventive post-extubation NIV. Each educational intervention will include a survey designed to determine the feasibility, acceptability, and preliminary impact of the educational strategies. We will also directly observe instances of interprofessional and just-in-time education and conduct in-person interviews to assess these factors in a qualitative manner. Lastly, during the intervention period and the 6 months before and after the intervention period, we will collect data from the electronic health record and analyze changes in percent of high-risk patients who receive preventive post-extubation NIV, reintubation rate, duration of mechanical ventilation, ventilator-associated pneumonia, and in-hospital mortality.

PART II: STUDY DESCRIPTION

1.0 Background

1.1 Acute Respiratory Failure

Acute respiratory failure requiring invasive mechanical ventilation affects nearly 800,000 patients in the United States each year.[1] Approximately half of these patients are >65 years old,[1] a vulnerable group at high risk for poor short- and long-term outcomes. Even among younger patients, mortality among mechanically ventilated ICU patients is extremely high, with in-hospital mortality averaging 35% for all patients and approaching 50% for syndromes like ARDS.[1-3] Costs for these patients are also high, with an estimated $27 billion spent annually on their acute hospital care alone.[1]

1.2 Post-Extubation Outcomes for High-Risk Patients

Recent improvements in the management of sepsis, ARDS, and other causes of respiratory failure have led to better clinical outcomes, such that 70%-80% of mechanically ventilated ICU patients recover to the point of extubation.[2,4] The current evidence-based management of these patients is to extubate once the patient passes a spontaneous breathing trial (SBT) and is alert with adequate cough and minimal secretions. This SBT-based strategy, especially when paired with sedation interruption, greatly improves outcomes,[5,6] but many patients remain at high risk for post-extubation respiratory failure. Multiple large cohort studies have found that 10% to 20% of patients recovering from acute respiratory failure require reintubation after planned extubation,[2,4] and reintubation is strongly associated with death,[7-10] increased costs,[11] prolonged hospital stays,[7,11] and long-term functional disability.[12] This risk is greatest in elderly patients[4,7,10] and patients with chronic pulmonary disease.[7,10] In one recent study, 24% of mechanically ventilated ICU patients were both >65 years old and had chronic cardiac or respiratory disease—these patients had a reintubation rate of 34% compared with 9% among other patients ($p<0.01$).[10]

1.3 Efficacy of Post-Extubation Noninvasive Ventilation (NIV)

When a mechanically ventilated patient with high risk characteristics passes an SBT, clinicians must decide whether to extubate. Continuing invasive mechanical ventilation exposes the patient to risk and undue burden, but extubating without providing support is also undesirable. Post-extubation noninvasive ventilation offers clinicians a third option. In a landmark randomized controlled trial, Ferrer et al.[13] studied high-risk mechanically ventilated ICU patients and found that extubation to immediate noninvasive ventilation (rather than conventional oxygen treatment) reduced both post-extubation respiratory failure (RR = 0.31, 95%CI: 0.15–0.62) and 90-day mortality (RR = 0.36: 95%CI: 0.15-0.85). A subsequent meta-analysis of five randomized controlled trials demonstrated that post-extubation noninvasive ventilation improves multiple outcomes, including post-extubation respiratory failure, ICU length of stay, and mortality.[13-17] Based on this evidence, recent clinical practice guidelines on liberation from mechanical ventilation sponsored by the American College of Chest Physicians (ACCP) and the American Thoracic Society (ATS) and co-chaired by Dr. Girard (PI of this

study), made a strong recommendation that high-risk patients who pass an SBT should be extubated to preventive noninvasive ventilation.[18-20] A similar recommendation was made in guidelines published by the European Respiratory Society (ERS) and ATS, which were co-authored by Dr. Hess (a consultant for this study).[21]

1.4 Implementation of Post-Extubation NIV

Despite compelling evidence of benefit, multiple international cohort studies show that post-extubation noninvasive ventilation is used infrequently in routine clinical practice.[2,22] One of the largest studies, for example, found that even though nearly 50% of invasively ventilated patients had a risk factor for failed extubation, less than 3% received preventative noninvasive ventilation after extubation.[22] Although no studies have specifically examined barriers to the use of post-extubation non-invasive ventilation, surveys about non-invasive ventilation in general,[23-26] including one led by our consultant Dr. Hess,[25] indicate that lack of familiarity with noninvasive ventilation, lack of awareness of the evidence, and concerns about the time required are key barriers to use. Due to these barriers, and likely others in the specific context of post-extubation use, many patients are not receiving an important evidenced-based practice. Based on epidemiologic data, we estimate that at least 200,000 mechanically ventilated patients/year in the United States are at high risk for extubation failure. If post-extubation noninvasive ventilation leads to a 9% absolute reduction in mortality for this vulnerable population, as estimated in a recent meta-analysis,[18-20] approximately 18,000 deaths per year in the United States alone could be prevented by implementation of post-extubation noninvasive ventilation.

1.5 Existing Implementation Strategies

Traditional strategies for knowledge transfer include education, guideline dissemination, audit and feedback of performance data, financial incentives, and automated reminders.[27] These strategies are extremely effort intensive yet often ineffective, typically resulting in either no significant improvements in performance or small improvements that are not sustained over time.[28,29] One reason for the failure of traditional knowledge transfer in the ICU is that these strategies do not fully account for the team-based nature of critical care.[30] Like non-invasive ventilation, most evidence-based practices in critical care are complex and multi-faceted, requiring ongoing coordination within a dynamic interprofessional care team.[31] Existing strategies for knowledge transfer fail to account for this complexity, instead generally focusing on static barriers on the part of individual providers.[32 33] Yet, targeting providers in isolation neglects the inherent role of coordination in evidence-based practice.[34,35] The ICU is a complex adaptive system in which actors have the freedom to act in unpredictable ways.[36] Absent a robust team, individual providers will find ways to circumvent even newer strategies like electronic prompts, making these interventions only modestly effective.[37] It is essential that the next generation of implementation strategies acknowledge and account for this complexity so that they empower interprofessional teams with the skills to overcome challenges to implementation of evidence-based practice as they dynamically arise as well as sustain improvement after the novelty of the new intervention has worn off.

1.6 Organizational Learning

Over the last three decades a rich body of research has evolved around the area of organizational learning, the process by which organizations create, retain and transfer knowledge.[38] Although individual learning underlies basic knowledge acquisition, for new knowledge to be useful to an organization it must embedded within a group repository that is accessible to other members so that it can be accessed and shared when needed. This is particularly true when, like in the ICU, performance is contingent upon coordination, since all members must be able to draw off the same knowledge repository for coordination to occur.[39] It is also particularly true when, like in the ICU, team membership is dynamic. Because ICU team members rotate in and out of the team, unembedded knowledge is easily lost. Current theory defines the system by which organizations acquire and apply specialized knowledge as a transactive memory system.[40] Colloquially, transactive memory systems are the knowledge of who knows what. When an organization has a robust transactive memory system, team members can rely each other to recall and apply key knowledge about important tasks. This "mutual confidence" frees up each individual team member to deepen their own expertise while at the same time ensuring that their knowledge remains accessible to others.[38] Extensive empirical data now indicate that transactive memory systems underlie organizational learning and are tightly linked to organizational performance in a variety of industries ranging from service to hospitality.[41] In this application, we posit that limitations of past implementation work can be addressed by two interventions designed to strengthen transactive memory systems in ICUs: interprofessional education and just-in-time education.

- **Interprofessional education:** Traditional continuing education focuses on individuals and occurs in professional silos—physicians learning from physicians, nurses learning from nurses, etc. As a result, the individual professions acquire different mental models and lack a shared understanding of the task at hand. Interprofessional education, in which members of different providers learn together, overcomes this problem by reinforcing not only shared mental models[42,43] but also cross-understanding, or the degree to which group members have accurate understandings of each other's' mental models.[44] Interprofessional education fosters the development of a shared language or common set of terms, which enables effective coordination. Interprofessional education also helps ensure that new knowledge occurs in a supportive context, enabling individuals to jointly practice coordinated actions in a team-based setting, promoting knowledge retention through the development of transactive memory systems.[45]
- **Just-in-time education:** Traditional continuing education occurs in classrooms or at home, separate from the "moment of need" and divorced from the practical context. Just-in-time education overcomes this problem by providing instruction at the bedside at the exact moment the knowledge is needed.[46] Because just-in-time education includes demonstrations and opportunities to observe effective practice, it enables the transfer of tacit, difficult-to-articulate knowledge.[47] Just-in-time education also strengthens transactive memory systems by tying knowledge acquisition directly to experience—instead of depending on subsequent experience to reinforce knowledge, knowledge acquisition and experience occur simultaneously.[48] In addition, just-in-time education ties knowledge acquisition to a specific case of immediate relevance,[49,50] reducing ambiguity in the learning process.

It also promotes coordination by directly providing individuals with the skills to perform their tasks within the context of a relational team.[51]

2.0 Objective and Hypothesis

2.1 Objective

During the METEOR: Think NIV Pilot Study, we seek to pilot test three strategies designed to speed implementation of post-extubation noninvasive ventilation: one control strategy (traditional online continuing medical education) and two novel strategies (interprofessional education and just-in-time education).

2.2 Hypothesis

We hypothesize that interprofessional education and just-in-time education are feasible and acceptable to members of the interdisciplinary ICU team; and that the pilot testing will yield important information that will enable us to both refine the interventions and perform power calculations for the subsequent clinical trial.

3.0 Study Population and Enrollment

3.1 Inclusion Criteria

Two study populations will be included.

- **Learners** will include [1] frontline care providers, including physicians, advanced practice providers, nurses, and respiratory therapists, [2] working in one of three participating UPMC ICUs: UPMC Presbyterian MICU, UPMC Mercy MSICU, and UPMC Passavant MSICU.
- **Patients** will include all mechanically ventilated patients treated in the participating UPMC ICUs and surviving to extubation.

3.2 Exclusion Criteria

Care providers will be excluded from the Learner population if they:

[1] Have not worked in their current UPMC ICU for more than one month
[2] Have not directly cared for a mechanically ventilated patient in a UPMC ICU during the three months preceding the current study

3.3 Enrollment

Study personnel will provide nursing and medical managers from each participating ICU with an introductory script that explain the study's methods and goals. Unit leadership will provide potential learners with the script, inviting them to participate and describing the study procedures and potential risks and benefits. Because exemptions 45 CFR 46.101(b)(1) and 45 CFR 46.101(b)(4) apply and it will not be practicable to obtain informed consent, we will request a waiver to document informed consent from learners (whose actions will indicate their consent to participate) and a waiver to request

informed consent from patients (for whom the only study procedure will be collected of existing data from the electronic health record).

3.4 Intervention Group Assignment

Given the nature of the interventions and the dynamics of interprofessional team care in the ICU, randomization at the level of the individual learner would likely result in significant cross contamination, thereby introducing bias in the trial. A better alternative in this case is to assign learners to interventions in groups. We will therefore assign all learners in a single ICU to the same intervention group. Given the pilot nature of this trial, we will assign one ICU to each group. For logistical reasons, learners in the UPMC Mercy MSICU will be assigned to traditional online continuing education, those in the UPMC Passavant MSICU will be assigned to interprofessional education, and those in the UPMC Presbyterian MICU will be assigned to just-in-time education.

4.0 Study Procedures

4.1 Pre-Education Survey

Prior to receiving the educational interventions, learners will be asked to complete a 10-minute survey designed to assess their baseline knowledge.

4.2 Educational Interventions

During a one-month study intervention period, the following three educational interventions will be piloted simultaneously.

- **Traditional online continuing education**. We will use an active control consisting of "best existing practice" for continuing education. Learners working in the ICU assigned to this arm will be offered a 30-minute, online, interactive, educational video describing the benefits of preventive post-extubation NIV, the indications and contraindications for preventive post-extubation NIV, and the value of working together as an interprofessional ICU team when implementing preventive post-extubation NIV. The video will be customized to each provider type (e.g., nurse, respiratory therapist, or physician). Learners will be offered provider-specific continuing education credits.
- **Interprofessional education**. Learners working in the ICU assigned to this arm will receive, a one-time, 90-120-minute, in-person, interprofessional educational workshop consisting of a 30-minute didactic session and a 60-90-minute small group session. The workshop is designed according to modern principles of adult learning and interprofessional education, including provider participation in development, fostering authenticity, reinforcing role identity, and relating content to life experience. Facilitators will be trained advance practice providers with content expertise who can speak to all targeted professions. Research staff will observe educational sessions.
- **Just-in-time education**. Learners working in the ICU assigned to this arm will receive, "just-in-time," point-of-care education. Trained advanced practice providers will be on-hand in the study ICU, where they will deliver the just-in-time education.

When a patient meets criteria for preventive post-extubation NIV, the educator will join the interprofessional ICU team at the bedside during rounds and will briefly review the evidence underlying risk assessment and proper use of preventive post-extubation NIV, providing instruction about how to provide preventive post-extubation NIV as well as how to anticipate potential barriers and pitfalls, while also fostering active collaboration. The just-in-time education is designed to cause minimal disruptions in workflow. Research staff will observe select educational sessions.

After each educational intervention, learners will be asked to complete a brief survey designed to determine the feasibility, acceptability, and preliminary impact of the educational strategies.

4.3 Follow-Up Interviews

Two to six weeks after the educational interventions, trained qualitative research coordinators will conduct learners to invite them to participant in in-person interviews that will qualitatively assess the feasibility, acceptability, and preliminary impact of the educational strategies using open-ended questions.

Lastly, during the intervention period and the 6 months before and after the intervention period, we will collect data from the electronic health record and analyze changes in percent of high-risk patients who receive preventive post-extubation NIV, reintubation rate, duration of mechanical ventilation, ventilator-associated pneumonia, and in-hospital mortality.

4.4 Statistical Considerations

We will use interrupted time series analysis to compare clinical outcomes measured during the six months before the implementation strategies with those measured during the six months after initiation of the strategies.[52] All analyses will be adjusted for baseline characteristics associated with the outcomes, including age, comorbid conditions, and severity of illness at admission. Additionally, interaction terms will be used to determine whether age and chronic cardiac and/or respiratory disease modified the effect of the implementation strategy on outcomes.

Due to the pilot nature of this study, we do not yet have preliminary data with which to perform power calculations or sample size analyses. The sample size will therefore be determined by feasibility (i.e., the number of learners who agree to participate and the number of eligible patients admitted to participating ICUs during the study period), and we will use the results of the current pilot study to determine the sample size of a subsequent cluster randomized trial.

4.5 Database and Case Report Forms

We will collect demographics from the ICU Team including, but not limited to, UPMC emails (for Wolff Center use to collect detailed information), education, background and training, and partial social security numbers to facilitate CME credits for physician team members, CUE credits for nursing staff members and comparative education method for respiratory therapists.

All qualitative data collection will be performed by trained qualitative research coordinators. We will audiotape and transcribe all recordings. Digital voice files and electronic files of transcribed sessions will be stored on a password-protected server. To maximize participation, we will provide appropriate compensation and schedule sessions for a time and place that is convenient for participants. No identifiers will be collected, and participants will be identified by profession and a number and not by name (e.g., Intensivist 1, Nurse 4, etc.). Interviews will be held in private locations.

De-identified patient data will be collected from the electronic health record and the ICU Registry. These data will include, but not be limited to, in-hospital mortality truncated at 60 days from the time of intubation, ICU and hospital length of stay, post-extubation respiratory failure, duration of mechanical ventilation, 28-day ventilator-free days, ventilator-associated pneumonia, and organ failure (tracked daily using the Sequential Organ Failure Assessment score).

5.0 Protection of Human Participants

5.1 Potential Risks

Since the interventions being studied are educational strategies applied to care providers rather than to patients, we anticipate that potential risk to patient participants will be limited to accidental disclosure of protected health information should there be a breach in our data security procedures. Potential risk to learner participants includes psychological discomfort associated with completing the surveys, which will address topics related to the ICU practice environment and working relationships with colleagues. Given that these topics are of a non-sensitive nature, we believe psychological discomfort will occur infrequently. An additional risk is accidental public disclosure of a participant's survey results. For this to occur, a survey must be accidentally misplaced and the unique key linking the participant's survey to the ICU identifiers must also be misplaced, and each must be recovered by the same person, a series of events that is extremely unlikely. A final risk is that learner participants could feel pressured to participate by their employer or a researcher and worry that their professional relationships will be jeopardized if they refuse. For our past work, the University of Pittsburgh Human Research Protection Office has considered similar studies to be "minimal risk" under the Department of Health and Human Services Code of Federal Regulations because it involved social research methods (e.g., surveys) and because the probability and magnitude of physical and psychological harm is similar to that normally encountered in daily life.

5.2 Protection Against Risks

We plan several steps to protect the rights of human subjects involved in this research. We will not record any personal information other than what is needed for a demographic description of the cohort (age, gender, job category, time in service); thus, interview participants will not be identifiable in any way. All voice recordings will be destroyed after transcription. All personal identifiers will be redacted by the transcriber, and all transcriptions will be triple-read to ensure that they contain no potential identifiers. We will contact all potential participants directly to give them the option of refusing confidentially in private and to assure them that we will not feedback

information regarding participation to their managers. This step will not only allow potential participants to refuse to participate without pressure or coercion from employers, but it will also ensure that information on whether or not they participated will not find its way back to their employer, preventing potential retaliation. We will take extensive precautions to guard against disclosure of protected health information and to maintain participant confidentially, as described in section 5.4.2.

5.3 Record Retention

Informed consent documents will be source documents kept in the study coordinator's locked files. Only key personnel will have access. All data will be kept for an indefinite amount of time at the University of Pittsburgh after the conclusion of the study.

5.4 Data and Safety Monitoring Plan (DSMP)

5.4.1 Adherence Statement

The DSMP outlined herein will adhere to the study protocol approved by the University of Pittsburgh IRB. The study will be conducted in compliance with the protocol, International Conference on Harmonization guideline E6: Good Clinical Practice (ICH E6): Consolidated Guideline, and the applicable regulatory requirements from United States (US) Code of Federal Regulations (CFR) (Title 45 CFR Parts 46 and Title 21 CFR including Parts 50 and 56) concerning informed consent and Institutional Review Board (IRB) regulations.

5.4.2 Data and Safety Monitoring Board (DSMB)

As described in detail in the METEOR: Think NIV Pilot Study DSMB Charter, a Data and Safety Monitoring Board (DSMB) will be created, consisting of three voting members with expertise in clinical research methodology and critical care medicine. DSMB responsibilities are to:

- protect the safety of the study participants;
- review the research protocol and plans for data and safety monitoring;
- evaluate the progress of the trial, including periodic assessments of data quality and timeliness, recruitment, accrual and retention, participant risk versus benefit, performance of the trial sites, and other factors that can affect study outcome;
- consider factors external to the study when relevant information becomes available, such as scientific or therapeutic developments that may have an impact on the safety of the participants or the ethics of the trial;
- make recommendations to the Principal Investigator concerning continuation, termination or other modifications of the trial based on the observed beneficial or adverse effects of the treatment under study; and
- ensure the confidentiality of the study data and the results of monitoring.

The DSMB will have one planned meeting before the intervention period. Additionally, the DSMB Chair, the Principal Investigator, or the NHLBI may call a meeting of the DSMB at any time. Though unexpected given the minimal risk nature of the study, any serious adverse events that are suspected by the Principal Investigator to be related to study participation—events referred to as Serious Unexpected Suspected Adverse Reactions (SUSARs)—as well as any other AE report that the Principal Investigator believes is appropriate for DSMB review will be reviewed by the DSMB Chair. The DSMB

Chair may distribute SUSAR reports to the other DSMB members for review. If a SUSAR occurs, the Principal Investigator will email a report to the DSMB Chair within 48 hours for review. The DSMB Chair will then indicate via email within 96 hours if additional information is required and whether additional action is recommended secondary to review of the SUSAR (e.g., DSMB teleconference).

5.4.3 Confidentiality

Protection of Participant Privacy: We will take extensive precautions to guard against disclosure of protected health information and maintain participant confidentially. All data management and analysis activities will take place on CRISMA's secure, HIPAA-compliant servers behind the UPMC firewall. Patient data will be obtained from the approved ICU Registry. Data in the registry is downloaded directly from the electronic health record (EHR) via secure FTP. No data containing any protected health information will ever leave the secure server. All investigators, programmers, and analysts working with the files will sign a confidentially agreement committing them to full privacy. We will also take several steps to protect the privacy of learner participants. Paper survey forms using during educational sessions will only include the participant's unique study ID and no other identifying information. Thus, if the survey form is lost, it will not be directly linkable to the participant without additional information. And, we will store the participant study ID linkage key on our secure, password-protected, HIPAA-compliant server, which is maintained according to strict federal security standards. This key will be destroyed after data collection is complete.

Database Protection: All data management and analysis activities will take place on CRISMA's secure, HIPAA-compliant servers behind the UPMC firewall. No data containing any protected health information will ever leave the secure server.

Confidentiality during Adverse Event (AE) Reporting: Adverse event reports and annual summaries to regulatory bodies will not include participant-or group-identifiable material. Each report will only include the identification code.

5.4.4 Adverse Event Information

Clinical Outcomes (Not Considered Adverse Events). In this study of critically ill patients who are at high risk for death or other adverse outcomes due to their underlying critical illness, clinical outcomes, including death and organ dysfunction, will be systematically tracked and will be included as part of the safety and effectiveness analyses for this study. For the purposes of reporting, death and organ dysfunction will not be recorded as adverse events (AEs) unless the investigator believes the event may have been related to study participation or is more severe or prolonged than expected given the underlying critical illness. This approach—considering death and organ dysfunction as outcomes rather than AEs and systemically tracking expected safety outcomes for analysis rather than solely recording individual AEs—is common during critical care trials because these outcomes/events occur frequently in the ICU, and this system mandates that data regarding death, organ dysfunction, and expected safety outcomes be tracked systematically for all patients and analyzed appropriately. Listed below are events that will be tracked as clinical outcomes and will not therefore be reported as AEs during this

study (unless believed to be study related and/or more severe or prolonged than expected given the underlying critical illness):

- Death
- Respiratory failure, including need for mechanical ventilation (invasive or noninvasive) or episodes of hypoxemia
- Circulatory failure, including shock (whether requiring vasopressors or not) and cardiac arrhythmias, and hypertension
- Hepatic failure or injury leading to increased bilirubin, AST, or ALT
- Renal failure or injury leading to an increased creatinine or acute hemodialysis
- Coagulation derangements leading to elevated PT/INR or PTT, DIC, thrombocytopenia, or thrombocytosis
- Cognitive impairment that is believed to be newly acquired
- Alterations in vital signs (e.g., temperature, respiratory rate, oxygen saturation)
- Falls
- Pressure ulcers
- Thromboembolisms
- ICU readmissions
- Infections
- Self-removal of devices and invasive tubing and/or monitoring equipment
- Alterations in routine labs, including chemistries, complete blood counts, liver function tests, and creatine kinase

Adverse Event (AE) Classifications. We define an AE as any untoward medical occurrence for a study participant that is not tracked as a clinical outcome, regardless of whether the event is considered study related or not. All AEs will be assessed as to whether they are (1) related to study participation, (2) serious, and/or (3) unexpected according to the following definitions:

Related. AEs that an investigator suspects are related to study participation will be classified as Suspected Adverse Reactions (SARs). A high degree of certainty of relatedness is not required as long as a reasonable possibility exists that the AE is related to study participation.

Serious. AEs that result in any criteria below will be considered Serious Adverse Events (SAEs):

- Death
- A life-threatening episode requiring immediate intervention
- Inpatient hospitalization or prolongation of existing hospitalization
- Persistent or significant incapacitation or substantial disruption of the ability to conduct normal life functions
- A congenital anomaly/birth defect
- An episode that requires intervention to prevent the above and/or permanent impairment or damage

Unexpected. AEs, including SARs, that are more severe or prolonged than expected will be considered Unexpected.

All events that are related, unexpected, and serious will be reported as Serious Unexpected Suspected Adverse Reactions (SUSARs). Given that all known risks of participation in the proposed study qualify as minimal risks, we do not anticipate any

SUSARs. Nevertheless, we have established this system for monitoring and reporting should such as event occur.

Unanticipated Problems (UP). Per OHRP and NHLBI regulations and guidance, any incident, experience, or outcome that meets all of the following criteria will be reported as a UP: 1) unexpected, 2) related or possibly related to participation in the research, and 3) suggests that the research places subjects or others at a greater risk of harm than was previously known or recognized. Per this definition, all SUSARs will also be classified as UPs, but not all UPs will be classified as SUSARs.

Communication and Reporting of Adverse Events. All AEs will be reported to the University of Pittsburgh IRB per local policies. In addition, SUSARs and UPs will be reported as follows, in keeping with the NHLBI AE and UP reporting policies.

Event type	Timing of report	Reporter	Recipient
Fatal or life-threatening SUSAR	Within 7 days of initial receipt of information	PI	IRB, NHLBI
Non-fatal or non-life-threatening SUSAR	Within 15 days of initial receipt of information	PI	IRB, NHLBI
UP that is not an SAE	Within 14 days of PI becoming aware of UP	PI	IRB, NHLBI
All UPs	Within 30 days of the IRB's receipt of the report of the UP from the investigator	IRB	OHRP

5.4.5 Data Quality and Safety Review Plan and Monitoring

Description of Plan for Data Quality and Management. The PI or study staff will review all data collection forms on an ongoing basis for data completeness and accuracy as well as protocol compliance.

Frequency of Review. This will vary according to the data type, as follows:

Data Type	Frequency of review	Reviewer
Learner participant accrual (including compliance with protocol)	Weekly during the one-month pilot period	PI
Status of all enrolled participants (patients and learners)	1. End of pre-implementation period 2. End of pilot-period 3. End of post-implementation period	PI
Adherence data regarding evidence-based practice and implementation strategies	1. End of pre-implementation period 2. End of pilot-period 3. End of post-implementation period	PI

5.4.6 Informed Consent

When conducting interviews, surveys, educational sessions, and direct observation of the educational strategies in the ICU, we will obtain oral assent from all learner participants using an IRB-approved script. We will not obtain written consent for these activities because it is not feasible nor practicable given the sheer number and rapidity of these observations. Prior to each observation episode, research staff will introduce themselves, describe the project, and offer the opportunity for ICU staff to opt in or opt out. Staff wishing to opt out will be given a lapel pin to wear during the observation periods. Following periods of observation, we will once again give each participant the option to opt out if they feel uncomfortable being observed in our research. We will also allow any participant to later opt out after the period of observation, to the degree possible, thereby reducing the risk of pressure from superiors to participate in this research. We will seek a waiver of informed consent for inclusion of patients since the

research, which will be limited to collecting existing clinical data from the electronic health record months after the study period, involves no more than minimal risk and the research could not be practicably carried out without the waiver.

5.4.7 Reporting Changes in Study Status

Any action resulting in a temporary or permanent suspension of the study will be reported to the NHLBI Program Official responsible for the grant.

6.0 References

1. Wunsch H, Linde-Zwirble WT, Angus DC, Hartman ME, Milbrandt EB, Kahn JM. The epidemiology of mechanical ventilation use in the United States. *Crit Care Med.* 2010;38(10):1947-1953.
2. Esteban A, Frutos-Vivar F, Muriel A, et al. Evolution of mortality over time in patients receiving mechanical ventilation. *Am J Respir Crit Care Med.* 2013;188(2):220-230.
3. Rubenfeld GD, Caldwell E, Peabody E, et al. Incidence and outcomes of acute lung injury. *N Engl J Med.* 2005;353(16):1685-1693.
4. Miltiades AN, Gershengorn HB, Hua M, Kramer AA, Li G, Wunsch H. Cumulative probability and time to reintubation in U.S. ICUs. *Crit Care Med.* 2017;45(5):835-842.
5. Girard TD, Kress JP, Fuchs BD, et al. Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (Awakening and Breathing Controlled trial): a randomised controlled trial. *Lancet.* 2008;371(9607):126-134.
6. Ely EW, Baker AM, Dunagan DP, et al. Effect on the duration of mechanical ventilation of identifying patients capable of breathing spontaneously. *N Engl J Med.* 1996;335(25):1864-1869.
7. Epstein SK, Ciubotaru RL, Wong JB. Effect of failed extubation on the outcome of mechanical ventilation. *Chest.* 1997;112(1):186-192.
8. Epstein SK, Ciubotaru RL. Independent effects of etiology of failure and time to reintubation on outcome for patients failing extubation. *Am J Respir Crit Care Med.* 1998;158(2):489-493.
9. Frutos-Vivar F, Esteban A, Apezteguia C, et al. Outcome of reintubated patients after scheduled extubation. *J Crit Care.* 2011;26(5):502-509.
10. Thille AW, Harrois A, Schortgen F, Brun-Buisson C, Brochard L. Outcomes of extubation failure in medical intensive care unit patients. *Crit Care Med.* 2011;39(12):2612-2618.
11. Seymour CW, Martinez A, Christie JD, Fuchs BD. The outcome of extubation failure in a community hospital intensive care unit: a cohort study. *Crit Care.* 2004;8(5):R322-327.
12. Rishi MA, Kashyap R, Wilson G, Schenck L, Hocker S. Association of extubation failure and functional outcomes in patients with acute neurologic illness. *Neurocrit Care.* 2016;24(2):217-225.
13. Ferrer M, Sellares J, Valencia M, et al. Non-invasive ventilation after extubation in hypercapnic patients with chronic respiratory disorders: randomised controlled trial. *Lancet.* 2009;374(9695):1082-1088.

14. Nava S, Gregoretti C, Fanfulla F, et al. Noninvasive ventilation to prevent respiratory failure after extubation in high-risk patients. *Crit Care Med.* 2005;33(11):2465-2470.
15. Ferrer M, Valencia M, Nicolas JM, Bernadich O, Badia JR, Torres A. Early noninvasive ventilation averts extubation failure in patients at risk: a randomized trial. *Am J Respir Crit Care Med.* 2006;173(2):164-170.
16. Khilnani GC, Galle AD, Hadda V, Sharma SK. Non-invasive ventilation after extubation in patients with chronic obstructive airways disease: a randomised controlled trial. *Anaesth Intensive Care.* 2011;39(2):217-223.
17. Mohamed KAE, Abdalla MH. Role of noninvasive ventilation in limiting reintubation after planned extubation. *Egypt J Chest Dis Tuberc.* 2013;62(4):669-674.
18. Schmidt GA, Girard TD, Kress JP, et al. Official executive summary of an American Thoracic Society/American College of Chest Physicians clinical practice guideline: Liberation from mechanical ventilation in critically ill adults. *Am J Respir Crit Care Med.* 2017;195(1):115-119.
19. Ouellette DR, Patel S, Girard TD, et al. Liberation From mechanical ventilation in critically ill adults: An official American College of Chest Physicians/American Thoracic Society clinical practice guideline: Inspiratory pressure augmentation during spontaneous breathing trials, protocols minimizing sedation, and noninvasive ventilation immediately after extubation. *Chest.* 2017;151(1):166-180.
20. Girard TD, Alhazzani W, Kress JP, et al. An official American Thoracic Society/American College of Chest Physicians clinical practice guideline: Liberation from mechanical ventilation in critically ill adults. Rehabilitation protocols, ventilator liberation protocols, and cuff leak tests. *Am J Respir Crit Care Med.* 2017;195(1):120-133.
21. Rochwerg B, Brochard L, Elliott MW, et al. Official ERS/ATS clinical practice guidelines: noninvasive ventilation for acute respiratory failure. *Eur Respir J.* 2017;50(2):1602426.
22. Schnell D, Timsit JF, Darmon M, et al. Noninvasive mechanical ventilation in acute respiratory failure: trends in use and outcomes. *Intensive Care Med.* 2014;40(4):582-591.
23. Burns KE, Sinuff T, Adhikari NK, et al. Bilevel noninvasive positive pressure ventilation for acute respiratory failure: survey of Ontario practice. *Crit Care Med.* 2005;33(7):1477-1483.
24. Sinuff T, Kahnamoui K, Cook DJ, Giacomini M. Practice guidelines as multipurpose tools: a qualitative study of noninvasive ventilation. *Crit Care Med.* 2007;35(3):776-782.
25. Hess DR, Pang JM, Camargo CA, Jr. A survey of the use of noninvasive ventilation in academic emergency departments in the United States. *Respir Care.* 2009;54(10):1306-1312.
26. Fisher KA, Mazor KM, Goff S, et al. Successful use of noninvasive ventilation in chronic obstructive pulmonary disease. How do high-performing hospitals do it? *Ann Am Thorac Soc.* 2017;14(11):1674-1681.
27. Shojania KG, Grimshaw JM. Evidence-based quality improvement: the state of the science. *Health Aff (Millwood).* 2005;24(1):138-150.

28. Bero LA, Grilli R, Grimshaw JM, Harvey E, Oxman AD, Thomson MA. Closing the gap between research and practice: an overview of systematic reviews of interventions to promote the implementation of research findings. The Cochrane Effective Practice and Organization of Care Review Group. *BMJ.* 1998;317(7156):465-468.
29. Sinuff T, Muscedere J, Adhikari NK, et al. Knowledge translation interventions for critically ill patients: a systematic review*. *Crit Care Med.* 2013;41(11):2627-2640.
30. Kahn JM, Rubenfeld GD. Translating evidence into practice in the intensive care unit: the need for a systems-based approach. *J Crit Care.* 2005;20(3):204-206.
31. Costa DK, Barg FK, Asch DA, Kahn JM. Facilitators of an interprofessional approach to care in medical and mixed medical/surgical ICUs: a multicenter qualitative study. *Res Nurs Health.* 2014;37(4):326-335.
32. Weiss CH, Wunderink RG. Prompting physicians to address a daily checklist for antibiotics: do we need a co-pilot in the ICU? *Curr Opin Crit Care.* 2013;19(5):448-452.
33. Cabana MD, Rand CS, Powe NR, et al. Why don't physicians follow clinical practice guidelines? A framework for improvement. *JAMA.* 1999;282(15):1458-1465.
34. Dietz AS, Pronovost PJ, Mendez-Tellez PA, et al. A systematic review of teamwork in the intensive care unit: what do we know about teamwork, team tasks, and improvement strategies? *J Crit Care.* 2014;29(6):908-914.
35. Kahn JM, Fuchs BD. Identifying and implementing quality improvement measures in the intensive care unit. *Curr Opin Crit Care.* 2007;13(6):709-713.
36. Alexanian JA, Kitto S, Rak KJ, Reeves S. Beyond the Team: Understanding Interprofessional Work in Two North American ICUs. *Crit Care Med.* 2015;43(9):1880-1886.
37. Semler MW, Weavind L, Hooper MH, et al. An electronic tool for the evaluation and treatment of sepsis in the ICU: A randomized controlled trial. *Crit Care Med.* 2015;43(8):1595-1602.
38. Argote L. *Organizational Learning: Creating, Retaining and Transferring Knowledge.* New York: Springer Science & Business Media; 2013.
39. Mathieu J, Maynard MT, Rapp T, Gilson L. Team effectiveness 1997-2007: A review of recent advancements and a glimpse into the future. *Journal of Management.* 2008;34(3):410-476.
40. Wegner DM. Transactive memory: A contemporary analysis of the group mind. In: Mullen B, Goethals GR, eds. *Theories of Group Behavior.* New York, NY: Springer New York; 1987:185-208.
41. Ren Y, Argote L. Transactive memory systems 1985–2010: An integrative framework of key dimensions, antecedents, and consequences. *The Academy of Management Annals.* 2011;5(1):189-229.
42. Ginsburg L, Tregunno D. New approaches to interprofessional education and collaborative practice: lessons from the organizational change literature. *J Interprof Care.* 2005;19 Suppl 1:177-187.
43. Mathieu JE, Heffner TS, Goodwin GF, Salas E, Cannon-Bowers JA. The influence of shared mental models on team process and performance. *J Appl Psychol.* 2000;85(2):273-283.

44. Huber GP, Lewis K. Cross-understanding: Implications for group cognition and performance. *Academy of Management Review.* 2010;35(1):6-26.
45. Hollingshead AB. Cognitive interdependence and convergent expectations in transactive memory. *J Pers Soc Psychol.* 2001;81(6):1080-1089.
46. Gottfredson C, Mosher B. *Innovative Performance Support: Strategies and Practices for Learning in the Workflow.* McGraw-Hill Education; 2011.
47. Nonaka I, von Krogh G. Tacit knowledge and knowledge conversion: Controversy and advancement in organizational knowledge creation theory. *Organization Science.* 2009;20(3):635-652.
48. Argote L, Miron-Spektor E. Organizational learning: From experience to knowledge. *Organization Science.* 2011;22(5):1123-1137.
49. Bohn RE. Noise and learning in semiconductor manufacturing. *Management Science.* 1995;41(1):31-42.
50. Szulanski G, Ringov D, Jensen RJ. Overcoming stickiness: How the timing of knowledge transfer methods affects transfer difficulty. *Organization Science.* 2016;27(2):304-322.
51. Faraj S, Sproull L. Coordinating expertise in software development teams. *Management Science.* 2000;46(12):1554-1568.
52. Kontopantelis E, Doran T, Springate DA, Buchan I, Reeves D. Regression based quasi-experimental approach when randomisation is not an option: interrupted time series analysis. *BMJ.* 2015;350:h2750.