Title: Implementation of Lung Protective Ventilation in

Patients with Acute Respiratory Failure

(IMPROVENT)

Location: All 11 Intermountain Healthcare hospitals that manage

mechanically ventilated patients

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Abbreviations, Acronyms and Symbols

ARDS	Acute Respiratory Distress Syndrome
ALI	Acute Lung Injury
PBW	Predicted Body Weight
ICU	Intensive Care Unit
ED	Emergency Department
STICU	Shock Trauma Intensive Care Unit
IMC	Intermountain Medical Center
POD	Persistent Organ Dysfunction
GLMM	Generalized Linear Mixed Model
EMR	Electronic Medical Records
VC	Volume Control
PRVC	Pressure Regulated Volume Control
MMV PRVC	Mandatory Minute Ventilation with Pressure Regulated Volume Control
SIMV/PS	Synchronized Intermittent Mandatory Ventilation Plus Pressure Support
VFD	Ventilator Free Days
ROSE	Reevaluation of Systemic Early Neuromuscular Blockade
PETAL	Prevention and Early Treatment of Acute Lung Injury
PEEP	Positive end Expiratory Pressure

Purpose of the Study and Hypotheses:

This is a quality improvement study with the purpose of observing and measuring the effects of implementation of a proven standardized lung protective ventilation protocol in the new electronic medical record system iCentra across all Intermountain Healthcare hospitals.

We hypothesize that implementation of a standardized computerized lung protective ventilation protocol across all Intermountain Healthcare hospitals will be feasible, will decrease initial tidal volumes to the target 6 ml/kg PBW, and will improve outcomes.

The objectives of this study are to:

- Determine if the implementation of lung protective ventilation (with a 6 ml/kg PBW tidal volume ventilation protocol on initiation of mechanical ventilation) improves outcomes in patients with acute respiratory failure requiring mechanical ventilation
- Determine if the implementation of lung protective ventilation (with a 6 ml/kg PBW tidal volume ventilation protocol on initiation of mechanical ventilation) improves outcomes in the sub-group of patients with the acute respiratory distress syndrome (ARDS)
- Measure compliance with the implementation of a computerized lung protective ventilation protocol at 11 Intermountain Healthcare hospitals

Specific Aim #1: Determine if the implementation of lung protective ventilation with a 6 ml/kg PBW tidal volume ventilation protocol on initiation of mechanical ventilation improves ventilator free days (VFDs) to day 28 (primary outcome), mortality, and secondary outcomes in **patients with acute respiratory failure requiring mechanical ventilation**.

- Process for Aim #1: Standardized management of mechanical ventilation and outcomes will be measured through electronic medical record data. A detailed plan on these metrics has been included (see research strategy for specific aims).
- **Hypothesis 1:** Deployment of the ventilation protocol will result in improvements in the number of VFDs to day 28, mortality, hospital discharge disposition, healthcare utilization and costs of care in patients with acute respiratory failure requiring mechanical ventilation.

Specific Aim #2: Determine if the implementation of lung protective ventilation with a 6 ml/kg PBW tidal volume ventilation protocol on initiation of mechanical ventilation improves VFDs to day 28, mortality, and secondary outcomes in **patients with <u>ARDS</u> requiring mechanical ventilation**.

- Process for Aim #2: Standardized management of mechanical ventilation for patients with ARDS and outcomes will be measured through electronic medical record data. A detailed plan on these metrics has been included (see research strategy for specific aims).
- Hypothesis 2: Deployment of the ventilation protocol in patients with ARDS will result in improvements in the number of VFDs to day 28, mortality, hospital discharge disposition, healthcare utilization and costs of care.

Specific Aim #3: Characterize protocol implementation of the high positive end expiratory pressure protocol (PEEP) and outcomes for mechanically ventilated patients with <u>moderate or severe hypoxemia</u> and <u>ARDS</u>.

- Process for Aim #3: Patients with ARDS will be analyzed based on hypoxemia conditions (as defined by their PaO₂ to FiO₂ ratio) using 3 classifications: mild (201-300), moderate (101-200), and severe (≤100). This subgroup analysis will evaluate protocol implementation of the high versus low positive end expiratory pressure (PEEP) protocol and assess relationship with patient outcomes. Data from Intermountain ICUs in 2014 have shown that approximately 500 patients meet the criteria for "severe" hypoxemia. Patients with moderate and severe hypoxemia will be identified to determine the frequency of high PEEP protocol usage (which is the recommendation in the protocol). Implementation of the high PEEP protocol will be based upon clinician discretion. We will assess outcomes in the 4 hypoxemia sub-groups noted above using a stratified Kaplan–Meier curve to determine differences in mortality using log rank statistics.
- Hypothesis 3: A high PEEP strategy in patients with moderate to severe hypoxemia and ARDS will improve outcomes.

Specific Aim #4: Measure compliance of the computerized lung protective ventilation protocol after implementation across Intermountain Healthcare's 11

hospitals that manage mechanically ventilated patients with acute respiratory failure.

- Process for Aim #4: Tool utilization and compliance will test the ability
 of a healthcare system to introduce this proven lung protective
 ventilation protocol in a new electronic medical record in a controlled
 clinical environment. To ensure that this is successful, Dr. Grissom will
 identify local champions to train and educate the healthcare providers.
- Hypothesis 4: Healthcare providers will utilize the computerized ventilation protocol and will comply with protocol instructions.

Study Design:

This is an observational quality improvement study comparing outcomes before, and after, implementation of a proven lung protective ventilation protocol in an electronic medical record system, iCentra, that will be implemented in phases across Intermountain Healthcare hospitals. A phased implementation with a twomonth washout period will be used to evaluate the primary outcome of interest, ventilator free days (VFDs) to 28 days. Secondary outcomes will include: use of the protocol by clinicians, compliance with protocol instructions, hospital discharge disposition, hospital, 30-day, and 90-day mortality, time to first ICU activity, hospital length of stay, ICU length of stay, heath care utilization, quality of life, and costs of care. As the iCentra electronic medical record is implemented at Intermountain Healthcare hospitals, clinicians will have the opportunity to use the computerized lung protective ventilation protocol, or to order mechanical ventilation settings independently. This is an observational study designed to measure how often the computerized lung protective ventilation protocol will be ordered, compliance with the instructions of the protocol, and clinical outcomes among patients who are managed with the protocol. Physicians may choose to use the protocol on intubated patients requiring mechanical ventilation or they may choose to order other specific mechanical ventilator settings.

A meta-analysis of mechanically ventilated patients without the acute respiratory distress syndrome (ARDS) reported that the cohort who received mechanical ventilation with initial tidal volumes between 6 and 10 ml/kg PBW had mean VFD of 21.9 (SD = 7.8). Using the distribution reported in the meta-analysis as the baseline for an a priori analysis, the current authors demonstrated that 3,900 patients would be sufficient to detect a 1.5-day increase in mean VFD with 80%

power (*ICC* = 0.10). The team anticipates this study will require a total of <u>16</u> months (two months of baseline during which the protocol will not have been implemented at any hospital, eight months of sequentially phasing in the protocol over two-month intervals across four sites along with a two-month washout period, and six months of follow-up once the protocol has been successfully implemented at every site) given that approximately 3,500 patients managed with volume control or pressure control ventilation are admitted each year to the 11 Intermountain hospitals included in this study and each site will not enroll during their two-month washout period, resulting in a total expected enrollment of about 4,000 over 16 months. This proposal will also follow each successive hospital that transitions to iCentra. Dr. Colin Grissom and his team will make certain that each site is prepared and has been provided the necessary educational materials. Dr. Grissom will be available for phone consultation from physicians and respiratory therapists for real-time assistance when utilizing the mechanical ventilation protocols.

Collaboration

This research will be conducted with committee identified above, in addition to Dr. Michael Lanspa, MD and Dr. Ithan Peltan, MD will provide medical oversight. Local site champions have been identified at the 11 hospitals where this protocol will be developed and these healthcare professionals will work closely with Dr. Grissom and his team.

Background and Significance:

Background

Mechanical ventilation with high tidal volumes may cause mechanical damage to the lung, trigger inflammation, and release cytokines into the systemic circulation. This process may cause fever, leukocytosis, new pulmonary infiltrates, prolong duration of mechanical ventilation, and increase mortality. Lung protective ventilation is an approach that limits tidal volume and distending pressure on the alveolus in order to prevent mechanical ventilation induced volutrauma (damage due to high tidal volume), barotrauma (damage due to high tidal volume).

Lung protective ventilation for patients with the acute respiratory distress syndrome (ARDS) improves outcomes. In a prospective randomized clinical trial

performed by the National Institutes of Health, National Heart Lung and Blood Institute (NIH/NHLBI) ARDS Network, ventilation with volume control using a tidal volume of 6 ml/kg as compared to 12 ml/kg predicted body weight (PBW) and targeting a plateau pressure of <30 cm H₂O as compared to <50 cm H₂O decreased mortality in patients with ARDS.² Among patients with ARDS, evidence supports that the timing of initiation of low tidal volume ventilation also influences mortality. A retrospective study of patients with ARDS showed that an increase in initial tidal volume of 1 ml/kg above 6 ml/kg PBW in patients with ARDS was associated with a 23% increase in intensive care unit (ICU) mortality risk.³ This finding suggests that initial tidal volume should be strictly set at 6 ml/kg PBW in patients with ARDS.

Mounting evidence also indicates that lung protective ventilation in intubated patients without ARDS may decrease the development of ARDS, pulmonary complications, and mortality. A meta-analysis of patients who were intubated and mechanically ventilated, but did not have ARDS, showed that ventilation with a mean tidal volume of 6.5 ml/kg as compared to 10.6 ml/kg PBW resulted in less development of acute lung injury or ARDS, less pulmonary infections, and lower mortality.4 Furthermore, of the 20 studies included in that meta-analysis, 15 set initial tidal volume in the intervention group to ≤6 ml/kg PBW—thereby demonstrating the trend that is occurring in medical practice. One of these studies even showed that tidal volume size was an independent predictor for development of acute lung injury (ALI) in patients who did not have ARDS at onset of mechanical ventilation. The odds ratio for developing ALI/ARDS was 1.3 for each millimeter of tidal volume more than 6 mL/kg PBW.5 Further evidence of benefit from tidal volume limitation has been supported by a recent patient level data analysis that showed a lower incidence of ARDS and fewer pulmonary complications in patients without ARDS treated with a tidal volume of <7 ml/kg PBW.⁶ A randomized controlled trial of intraoperative lung protective ventilation using 6-8 ml/kg versus 10-12 ml/kg PBW tidal volume in patients undergoing high-risk abdominal surgery resulted in significantly less pulmonary and nonpulmonary complications. Taken together, these studies indicate that patients with acute respiratory failure requiring mechanical ventilation, but without ARDS, should be supported with volume control ventilation using a tidal volume of no more than 8 ml/kg PBW upon initiation of mechanical ventilation, and may have the best outcomes using an initial tidal volume of ≤6 ml/kg PBW.

Compliance with lung protective ventilation in the emergency department (ED)^{8,9} and ICU¹⁰ is not optimal. In the International LUNG SAFE study that included more than 550 ICUs around the world, mean tidal volume in patients with ARDS was 7.5 to 8.0 ml/kg PBW,¹⁰ and tidal volumes in patients with severe acute respiratory failure and PaO2/FIO2 ratios <300 was over 8 ml/kg PBW. In Europe, a prospective clinical trial is underway to determine whether tidal volumes of 4 to 6 ml/kg PBW improves outcomes as compared to 8 to 10 ml/kg PBW in patients with acute respiratory failure and ARDS.¹¹ Interestingly, the senior investigator of that study has used electronic decision support since 2006 in his medical and surgical ICU to recommend a default tidal volume of 6 ml/kg PBW on all intubated patients regardless of diagnosis.^{12,13}

In the previous studies of electronic decision support to implement lung protective ventilation, ^{12,13} the instructions were only purposed to provide the tidal volume calculated from 6 ml/kg of PBW when physicians and nurses were reviewing mechanical ventilation parameters. The computerized protocol that we propose herein to implement across Intermountain Healthcare provides specific instructions on management of mechanical ventilation with adjustment of respiratory rate, tidal volume, fraction of inspired oxygen (FiO₂), and positive end expiratory pressure (PEEP) with lung protective targets of a tidal volume of 6 ml/kg PBW and an inspiratory plateau pressure of < 30 cm H₂O. We will also provide a computerized weaning protocol. This complete computerized lung protective mechanical ventilation protocol will allow standardization of care across Intermountain for all aspects of management of mechanical ventilation.

Significance

Data on initial set tidal volume in the ED and ICU across Intermountain Healthcare hospitals shows variability in compliance with lung protective ventilation—as represented by numbers of patients in different categories of initial set tidal volume measured in ml/kg PBW (**Figure 1, Table 1, and Figure 3** *in the Supporting Documents section*). These data include all patients who had initiation of mechanical ventilation in the ED or ICU with volume control ventilation and without a spontaneous breathing mode, such as pressure support or continuous positive airway pressure, at Intermountain Healthcare hospitals in 2014 (Intermountain Medical Center, McKay Dee Hospital, LDS Hospital, Utah Valley Regional Medical Center, Park City, American Fork, Riverton, Alta View, Logan, Valley View, and Dixie Regional Medical Center). Results from this

investigation demonstrated that only 20% of initial tidal volume settings in the ED and ICU were ≤6.0 ml/kg PBW (**Figure 1**), 50% of patients in the ED and 57% of patients in the ICU had initial tidal volume settings of ≤7.0 ml/kg PBW and 22% of ED patients and 18% of ICU patients had initial tidal volume settings >8 ml/kg PBW. This represents about one in five patients who were ventilated with high tidal volumes that may injure the lung. There was no initial determination of whether patients had ARDS in the data set.

Intermountain Healthcare will implement a computerized version of the ARDS Network 6 ml/kg PBW ventilation protocol in their new electronic medical record system from Cerner, called iCentra. This computerized ventilation, oxygenation, and weaning protocol will become the default mechanical ventilation protocol for use on all intubated patients at Intermountain Healthcare hospitals. Physicians will be free, however, to decline to use the computerized mechanical ventilation protocol and to provide instead alternative orders for mechanical ventilation. The computerized ventilation, oxygenation, and weaning protocols will be separated so that physicians may select any combination of the protocols for patient care. It is expected that most mechanically ventilated patients will be managed with the combination of ventilation, oxygenation, and weaning protocols. However, patients with elevated intracranial pressure may be excluded per the attending physician discretion from the 6 ml/kg PBW ventilation protocol. The oxygenation protocol will target a partial pressure of arterial oxygen (PaO₂) of 55 to 67 mm Hg with a normal PEEP protocol using the ARDS Network low PEEP table or alternatively, for patients with moderate to severe ARDS, a high PEEP protocol based on the ARDS Network high PEEP table (Table 2).14 There is also a high range oxygenation protocol targeting a PaO₂ of 68 to 80 mm Hg for patients with hypoxic brain injury or ischemia of other organs in which the physician may prefer a higher oxygen partial pressure.

Based on a meta-analysis of high versus low PEEP clinical trials, there is a mortality benefit using a high PEEP strategy in patients with moderate to severe ARDS.¹⁵ Uncertainty exists, however, in how to implement a high PEEP strategy¹⁶ and review of the application of PEEP to patients enrolled in the ARDS Network 2 studies after publication of the meta-analysis do not show widespread adoption of a high PEEP strategy (**Figure 2**). Completed clinical trials of patients with moderate to severe ARDS, however, have safely employed a high PEEP strategy with good clinical outcomes¹⁷, and the proposed trial "Reevaluation Of

Systemic Early neuromuscular blockade (ROSE)" from the NIH/NHLBI Prevention and Early Treatment of Acute Lung Injury (PETAL) Network will use a high PEEP strategy for moderate to severe ARDS based on the ARDS Network High PEEP protocol (**Table 2**). Intermountain Healthcare leads the Utah Clinical Center of the PETAL Network, and the high PEEP protocol that will be computerized in iCentra matches the PETAL Network high PEEP protocol for ROSE.

Based on current evidence, a lung protective ventilation strategy using the ARDS Network ventilation protocol with a target tidal volume of 6 ml/kg PBW is an accepted standard for all intubated patients at Intermountain Healthcare EDs and ICUs. Plans for implementation of the ARDS Network 6 ml/kg ventilation protocol into iCentra were made as an initiative to standardize care for mechanical ventilation across Intermountain Healthcare Hospitals. Lung protective ventilation has the potential to benefit patients who require mechanical ventilation for neurologic problems, surgery, drug overdose, or airway protection as well as hypoxemic respiratory failure.

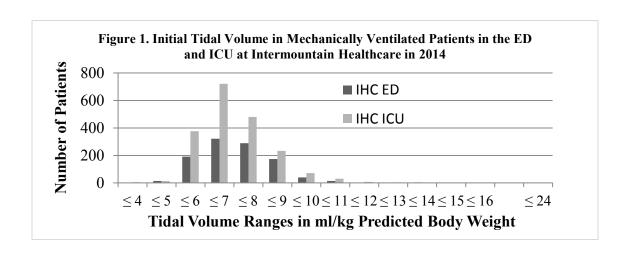


Table 1. Numbers of patients in initial tidal volume ranges in the ED and ICU

		>4	>5	>6	>7	>8	>9	>10	>11	>12	>13
		and	and	and	and	and	and	and	and	and	and ≤
	≤ 4	≤ 5	≤ 6	≤ 7	≤ 8	≤ 9	≤ 10	≤ 11	≤ 12	≤ 13	16
ED	3	14	191	322	289	174	40	14	0	2	4
ICU	5	13	377	721	480	233	71	31	7	4	2

Figure 2. Compliance with High PEEP Strategy in ARDS Network 2 Studies EDEN¹⁸, OMEGA¹⁹, and SAILS.²⁰

EDEN/OMEGA/SAILS enrollment values black line is high-PEEP (ROSE) compliant

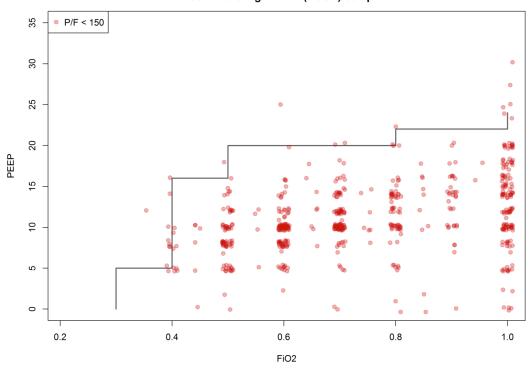


Table 2. Comparison of High and Low PEEP Strategies

	FIO2 0.3	FIO2 0.4	FIO2 0.5	FIO2 0.6	FIO2 0.7	FIO2 0.8	FIO2 0.9	FIO2 1.0
ROSE High PEEP	5	5-16	16-20	20	20	20-22	22	22-24
ALVEOLI High PEEP ¹⁴	5-14	14-16	16-20	20	20	20-22	22	22-24
ALVEOLI Low PEEP ¹⁴	5	5-8	8-10	10	10-14	14	14-18	18-24

Research Subjects:

Inclusion Criteria

- 1. Initiation of mechanical ventilation in the emergency department or intensive care unit at an Intermountain Healthcare hospital
- 2. Age ≥ 18 years

Exclusion Criteria

- Transition to comfort care in the emergency department or on the same day of admission to the ICU
- 2. Death on the same day of admission to the emergency department or ICU

Patient Selection

Those to be enrolled must have respiratory failure requiring intubation and initiation of mechanical ventilation. Patients will be divided into two different groups: those patients who are managed with the computerized lung protective ventilation protocol as ordered by the attending physician and those patients managed with physician specified mechanical ventilation settings.

Compensation

Subjects will not be compensated for participating in this study.

Sample Size

The minimum sufficient sample size to detect a significant change in VFD was computed across a range of effects and heterogeneity. We estimate about 3,900 subjects would be sufficient to detect a 1.5-day increase in mean VFD with 80% power (*ICC* = 0.10) from a baseline of 21.9 VFD (SD=7.8) with a one-tailed test (**Table 3**).

Table 3. Minimum sample size for increase in mean VFD

ICC	1 day	1.5	2 day
		day	
0.01	6,800	3,200	2,300
0.10	8,500	3,900	2,300
0.20	8,300	4,000	2,400

The baseline VFD data for the power analysis was based on reported data from a meta-analysis of the association between tidal volume size and sedation needs

in patients without ARDS²⁵ among those who received initial tidal volumes between 6 and 10 ml/kg PBW – a demographic representative of our study population. The power analyses accounted for expected imbalance of patient enrollment (**Table 4**),^{26,27} heterogeneity among clusters,²⁸ and allowed for a variety of time effects (**Equation 1**).²⁹ This avoided artificial inflation of power at the study design stage.³⁰

The VFD y_{ikt} for each patient were simulated via a linear equation adapted from Hussy *et al.*³¹ with the addition of quadratic time effects:

$$y_{ikt} = \mu + \alpha_k + \beta_1 t + \beta_2 t^2 + \theta x_{ikt} + e_{ikt},$$
 (1)

where μ and e_{ikt} , were derived from the distribution of VFD reported in the metaanalysis by Serpa Neto *et al.*²⁵, θ varied from 1 to 2 per Grissom's instructions, α_k are the hospital-level random intercepts, $\beta = (\beta_1, \beta_2)$ is a vector of quadratic time effects, x_{ikt} is the initial tidal volume size for the *i*th subject in the *k*th cluster at time *t*.

	Volume	Proportion
McKay-Dee	542	0.1584
Utah Valley	608	0.1778
American Fork	68	0.0199
Dixie	479	0.14
Valley View	60	0.0175
IMC	1409	0.4119
LDS	206	0.0602
Riverton	49	0.0143

Table 4. Volume of mechanically ventilated patients in 2014

Methods/Procedures:

Research Strategy for Specific Aims 1 and 2

Lung protective ventilation management using the computerized ARDS Network 6 ml/kg PBW ventilation protocol will be phased in among 11 Intermountain Healthcare hospitals in the manner of a phased implementation design synchronized with the rollout of iCentra. This is a quality improvement initiative to introduce a best practices ventilation protocol across Intermountain Healthcare hospitals and we request waiver of informed consent from the Institutional

Review Board in order to measure the effect on clinical outcomes and change in practice associated with this implementation. With each successive hospital that transitions to iCentra, Dr. Grissom will provide educational presentations to the medical staff that manage mechanically ventilated patients. Dr. Grissom and Ms. Lori Carpenter, a respiratory therapist, will also educate the respiratory therapists at each hospital in the computerized ARDS Network ventilation protocol. Dr. Grissom will be available for phone consultation from physicians and respiratory therapists for real time assistance in utilizing the mechanical ventilation protocols.

The primary outcome is ventilator free days (VFDs) to day 28. We will use the same definition for liberation from mechanical ventilation as used in ARDS Network studies^{2,14} and in the proposed ROSE study from the NIH/NHLBI PETAL Network. Initiation of ventilator free days begins with two ventilator free days once unassisted breathing is present for 48 hours. Unassisted breathing is defined as²²:

- a. Extubated with face mask, nasal prong oxygen, or room air, OR
- b. T-tube breathing, OR
- c. Tracheostomy mask breathing, OR
- d. CPAP ≤ 5 without PS or IMV assistance
- e. Use of CPAP or BIPAP solely for sleep apnea management
- f. Use of a high flow oxygen system

Research Strategy for Specific Aim 3

Efficacy of a high PEEP strategy for patients requires identifying patients with moderate or severe ARDS, determining protocol compliance, and measuring outcomes. Determination of ARDS using the Berlin Definition²³ requires acute respiratory failure not fully explained by cardiac failure or fluid overload within one week of a known clinical insult, bilateral opacities on chest radiology imaging not fully explained by effusions, lobar/lung collapse, or nodules, and $PaO_2/FIO_2 \le 300$ mm Hg with PEEP or CPAP ≥ 5 cm H₂O. Applying these criteria to identify ARDS in a large pragmatic study with a target enrollment of approximately 3,500 patients is a significant challenge. We will focus on defining ARDS among those patients with mild, moderate, or severe hypoxemia as defined by a PaO_2 to FIO_2 ratio ≤ 300 and evaluate chest radiographs for bilateral infiltrates in that group. Then we will evaluate implementation of the high PEEP strategy and outcomes in the group of patients with ARDS who have a PaO_2 to FIO_2 ratio ≤ 200 . Even though a high PEEP strategy is recommended for moderate to severe ARDS as

defined by a PaO₂/FIO₂ ≤ 200, this is not strictly applied clinically based on our review of ARDS Network study data (**Figure 2**). Implementation of the high PEEP protocol for moderate to severe ARDS is left up to the clinician in the computerized mechanical ventilation protocol. By performing a sub-group analysis we will characterize the utilization of a high PEEP strategy in patients with moderate or severe ARDS at Intermountain Healthcare hospitals. Lastly, the benefit of segmenting the data into categories "mild", "moderate", and "severe" hypoxemia, is that it will allow our team to use a stratified Kaplan–Meier curve to assess differences in mortality using log rank statistics. This will directly show the relationship between hypoxemia, treatment and mortality. New findings from Specific Aim #3 may drastically influence the standard of care within Intermountain Healthcare and internationally.

Research Strategy for Specific Aim 4

Evaluation of compliance with the ARDS Network computerized protocol and association with clinical outcomes will be performed with extraction of data from the EMR. This will require specific data queries to collect information on initial set tidal volume, mode of ventilation, FIO₂, and PEEP as well as patient outcomes. Dr. Grissom along with Ms. Lydia Dong from the Intensive Medicine Clinical Program and Ms. Juhee Peterson from pulmonary and critical care research at Intermountain Medical Center have extensive experience with these types of queries of mechanical ventilation data from the Intermountain enterprise data warehouse (EDW). Transition to iCentra, however, will create challenges for extracting data from a new EMR system. Although this will require increased effort at creating new queries and mapping ventilator data, this will have long-term benefits for data extraction from iCentra for the Intensive Medicine Clinical Program, quality assurance initiatives, and pulmonary and critical care research at Intermountain Healthcare.

Study Duration

16 months, 1/1/2016 - 5/31/2017

Study Timeline

Approximately 3,500 patients managed with volume control or pressure control ventilation are admitted each year to the 11 Intermountain hospitals included in this study. The team anticipates this study will require a total of <u>16</u> months (two months during which the protocol will not have been implemented at any hospital,

eight months of sequentially phasing in the protocol over two-month intervals across four sites over, and six months of follow-up once the protocol has been successfully implemented at every site) given that approximately 3,500 patients managed with volume control or pressure control ventilation are admitted each year to the 11 Intermountain hospitals included in this study.

Note that although 11 hospitals will be included in the study (IMC, McKay-Dee, Utah Valley, American Fork, Dixie, Valley View, LDS, Riverton), only eight were included in the power analysis because three hospitals (Alta View, Park City, and Logan) were not featured in the baseline data set. The number of mechanically ventilated patients at Alta View, Park City, and Logan is very low, so their expected contribution to patient enrollment would not substantively change the results of the power analysis. These three hospitals will be included in the prospective implementation of a lung protective ventilation protocol for purposes of standardization of care. Critically ill patients with respiratory failure who are intubated at Alta View, Park City, and Logan may have initiation of lung protective mechanical ventilation for management in their ICU, or prior to transfer to an Intermountain tertiary hospital. With a two-month deployment period at each hospital – during which time data will not be collected – a sufficient number of patients could be enrolled in less than 16 months. This corresponds to two months of baseline data collection, eight months of phasing in the protocol, and six months of follow-up once the protocol has been successfully implemented at each of the sites. An example enrollment matrix simulated by a Poisson process is displayed in **Table 5**.

Table 5. 16-month enrollment matrix (n = 4,127)

	NOV	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	ОСТ	NOV	DEC	JAN	FEB
McKay-Dee	46	39			50	43	55	37	49	50	39	42	52	49	43	61
Utah Valley	52	60	57	57			54	45	72	38	57	54	46	60	48	49
American Fork	8	4	6	10			6	5	4	4	5	6	2	3	10	3
Dixie	45	43	37	34	31	52			33	38	41	43	37	36	47	52
Valley View	3	4	5	6	7	2			7	5	3	4	8	1	5	3
IMC	129	127	116	105	114	130	136	142			115	121	139	120	116	118
LDS	19	19	16	24	17	23	19	12			10	18	17	9	15	15
Riverton	3	3	5	3	1	5	4	5			2	6	7	5	4	1

Risks

The risk of this study is a potential loss of confidentiality, which will be managed as detailed below.

Benefits

This is a quality improvement study evaluating the benefits of a proven lung protective ventilation protocol across Intermountain Healthcare hospitals. Application of the protocol at the discretion of the attending physician to patients with acute respiratory failure requiring intubation and mechanical ventilation is expected to improve outcomes.

Waiver of Informed Consent

This study seeks a waiver of informed consent for these reasons:

- The risk of this study is a potential loss of confidentiality. The study involves no more than minimal risk to the subject, as the study is observational only and the study will not alter the care that enrolled subjects receive. The computerized lung protective mechanical ventilation protocol will be available to clinicians as an order in iCentra, but will not be required.
- The sample size required to detect a significant change in VFD is estimated to be about 3,900 subjects. Including only the data for which consent can be obtained would prevent accurate conclusions from being drawn.
 Consequently, the research could not practicably be carried out without a waiver of consent.

Waiver of Authorization

PHI will be collected as a part of this study. The PHI will be used only for study purposes and will not be reused or disclosed except as required by law. The information obtained from medical records will be kept separate from clinical records.

All digital study records will be kept within the Intermountain Healthcare firewall in a location that is only accessible to authorized members of the study team. All paper study records will be maintained on a floor with secure badge access that only the research team can access.

After the study is complete, study identifiers will be removed from the dataset.

The data to be collected is detailed below. In particular, the dates to be collected are important for evaluating the primary outcome of interest, VFDs to 28 days.

Data Collection:

Data Elements Extracted from the EDW for the Mechanical Ventilation Study

- Region
- Hospital
- Facility ID
- Account Number
- EMPI
- Admit Date
- Discharge Date
- Admit Year
- Age
- Gender
- ICD Diagnosis code
- ICD Diagnosis description
- ICD Diagnosis long description
- ICU Stay
- Length of Stay(Days)
- Mortality Indicator
- Patient Type(inpatient(I) vs outpatient(O))
- Patient Type(Detailed code)
- Patient Type Description
- Death Location
- Discharge Disposition Description
- Discharge Reason(same as above)
- ED Admit Date
- ED Discharge Date
- Total Cost
- Ventilator Location(First Vent Check Location)
- First Date of Ventilator Check
- Ventilator Mode
- First Date of Ventilator Check
- Intubation Date
- Intubation Location(Same as Ventilator Location)
- Room Trace(It is more detailed than the ones above)
- In Hospital Mortality

- Ventilator Mode
- Machine Corrected Volume
- Set Tidal Volume
- Spontaneous Volume
- Height
- Predicted Body Weight
- Tidal Volume per Predicted Body Weight
- Measured Volume per Predicted Body Weight
- Difference between Tidal Volume per PBW and Measured Volume per PBW
- Difference between admission date and death date
- 30 Day Mortality
- 60 Day Mortality
- 90 Day Mortality
- Initial Arterial Blood Gas recorded during hospital stay
- PaO2 (measured)
- PaO2 (corrected)
- FiO2
- PaO2 / FiO2

Data Analysis:

Primary Outcomes

The primary outcome will be VFD to day 28. Patients who experience death within 28 days of ICU admission will be counted as having zero VFD.

Secondary outcomes will include: hospital discharge disposition; hospital, 30-day, and 90-day mortality; time to first ICU activity; hospital, ICU length of stay; protocol compliance; implementation of a high PEEP strategy in patients with PaO_2/FIO_2 ratios \leq 200; heath care utilization; quality of life (SF-36 or similar); and costs of care.

Data Analysis

Descriptive analyses will include Fisher's exact test and Pearson's chi-square test for comparing pairs of binomially distributed variables with and without sparse cells, respectively. Wilcoxon rank sum test, a nonparametric analogue of Student's *t* test, will be used to compare non-Gaussian, continuous distributions. Bootstrapped Kolmogorov-Smirnov (K-S) test will compare distributions of

ordinal, discrete data. The bootstrapped K-S test is able to handle instances in which many ties are present between distributions.²⁴

Generalized linear mixed models (GLMM) with hospital-level random intercepts and an identify link function will be used to measure the effect of initial tidal volume size on VFD. It is proposed to measure the treatment as a continuous variable (rather than as a dichotomous indicator of whether the mechanically ventilated patient was cared for at a post-intervention site) in order to account for the variable "usual care" practices of tidal volume size. The protocol will be phased sequentially in a non-randomized phased implementation manner. Since it is hypothesized that the bundle will improve care and, resultantly, decrease duration of time on ventilator, statistical significance will be determined by a one-tailed, 5% significance test. Heterogeneity among clusters will also be measured and accounted for random intercepts. Potential secular trends will be adjusted for by inclusion of quadratic time effects, which would capture a variety of time effects – from linear to bell-shaped. Patient-specific confounders will be controlled for by additive inclusion of a matrix of patient-level covariates.

Mitigation Plans and Interim Analysis

We plan an interim analysis for futility and efficacy at the end of the third step, following the successful phasing in of the second cluster. If the mean VFD following implementation of the bundle is equivalent to the mean VFD prior to implementation (according to the two one-sided test procedure with 99% confidence having an equivalence margin of four hours) then futility will be declared and further data collection will cease. Conversely, if the mean VFD following implementation has increased by more than 2 days (according to a one-sided hypothesis test with 99% confidence), efficacy will have been established and further data collection will also cease.

Data Sharing:

Development of the ventilation protocol in iCentra for mechanical ventilation will likely increase the number of VFDs, decrease healthcare utilization and decrease cost. To ensure that the proposal deliverables are met, we have designed the following dissemination plan:

Internal Strategic Planning

The investigators have identified local site champions to educate and train the Intermountain Healthcare providers. The principal investigator intends to go on a "road show" to explain the utility of the ventilation strategy and will provide electronic media (PowerPoints, PDFs), etc. To reach a more general audience the team may also present at an Intermountain Research event (colloquium or summit) to showcase this Type 1 research.

External Strategic Planning

The study investigators will consult with Dr. Raj Srivastava, the Assistant Vice President for Research at Intermountain Healthcare, the Office of Research, and the internal communications team (via Craig Kartchner and Susan Gagnier) to reach the general community. Specific examples may include (but are not limited to): Twitter, Facebook post, institutional blog posts, hosting conferences, emailing network and insurance providers, etc.

Conference Proceedings and Peer-Reviewed Publications

The Office of Research will support this application by helping to write/edit/submit manuscripts, provide graphic design assistance, and grant full access to the statistical data department to ensure that data is analyzed using various parametric and non-parametric statistical tests.

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Figure 3. Initial Tidal Volume on Initiation of Mechanical Ventilation at Intermountain Healthcare Hospitals (Intermountain Medical Center = IMC, Utah Valley = UV, McKay Dee = MK, Dixie = DX, and LD = LDS Hospital).

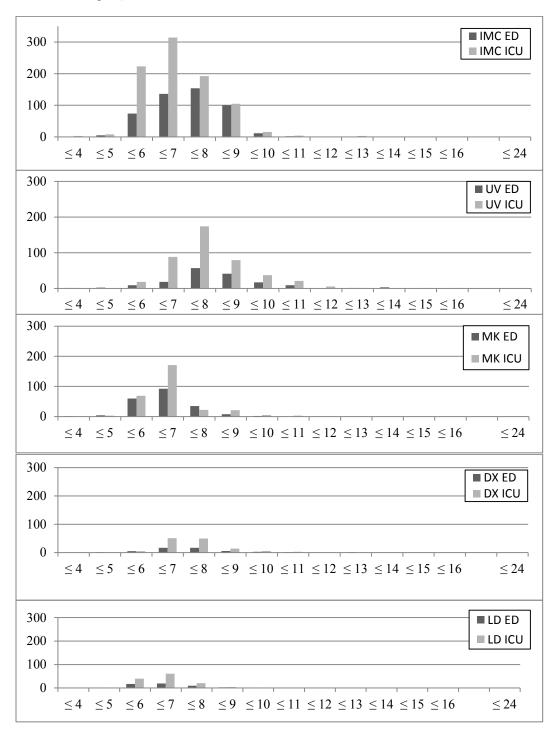


Figure 4: An example of the weaning protocol that will be used in this study.

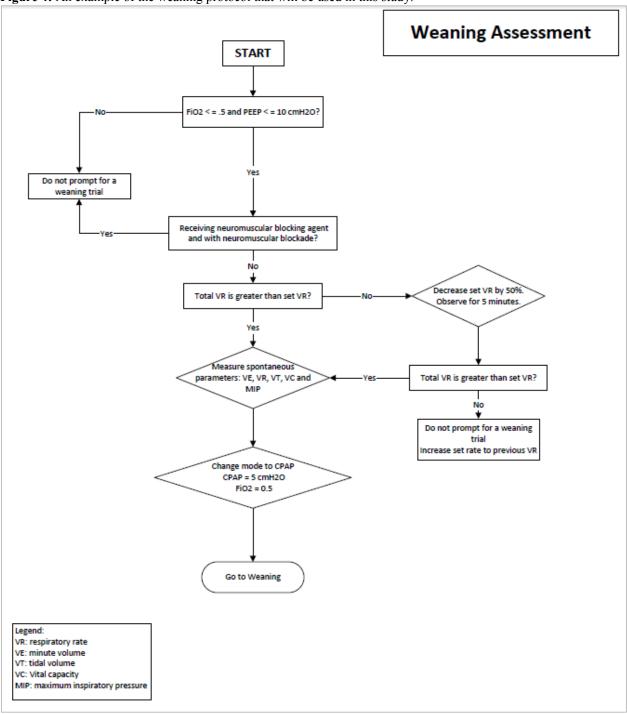
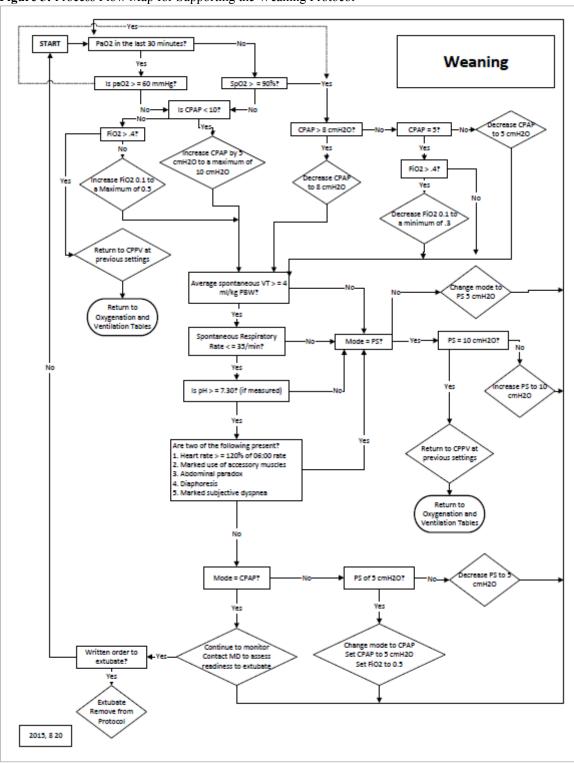


Figure 5: Process Flow Map for Supporting the Weaning Protocol



Rules for I Centra Ventilator Protocol

efi.			

- □ BWP: Body weight predicted (formula below)
 - \circ Males: PBW (kg) = 50 + 2.3[height (inches) -60]
 - \circ Females: PBW (kg = 45.5 + 2.3 [height (inches) -60]
- □ ABG: arterial blood gas
- □ VR: respiratory rate (breaths per minute)
- □ VT: tidal volume (milliliters)
- □ VE: minute volume (liters per minute)
- □ CMV: continuous mandatory ventilation
- □ VC: Volume Control
- □ PEEP: positive end expiratory pressure (cmH2O)
- ☐ Measured Pplat: actual measured plateau pressure

General:

- ☐ If the PBW does not appear or is too small or too large, check the height and gender in the computer they could be entered wrong or not at all.
- ☐ The protocol will not generate new instructions if it has been 2 or more hours since a complete ventilator assessment has been entered.
- □ Always do a ventilator assessment before drawing an ABG.
- ☐ Check for typos. The computer relies on accurate and timely charting.
- ☐ The protocol will run off arterial blood gas or oxygen saturation measured by the pulse oximeter.
- □ Protocol suspensions can be entered proactively or retroactively.
- □ Suspend the protocol when the patient will be receiving a procedure, traveling, going to surgery or hyperbaric.
- ☐ Unsuspend the protocol when back in the unit
- ☐ Enter at the previous settings
- ☐ Enter at the current settings charted (patient may have different needs after the procedure)
- The protocols are orders. Deviation from the protocol requires a physician order.

ABG Recommended For:

□ Change in Mode.

ABG Required For:

- □ 10% change in VT setting.
- □ Change in VR setting if patient is not assisting.
- Receive ventilation protocol instructions.

Ventilation:

- ☐ The low range for the set ventilatory rate is 6 breaths per minute for all protocols.
- □ Ventilation instructions are only given after an ABG.
- ☐ The protocol will set a back up VR if the patient is breathing over the set rate. Backup VR is based on a calculated VE goal.
- □ Set VT at 6ml/kg PWB
- □ VE goal = Current VE *(PaCO2/50 * HCO3-/24)

☐ Entry criteria for weaning:

□ Without neuromuscular blockade

□ Weaning assessment will be attempted every 4 hours.

 \Box Peep < = 10 cmH2O

 \Box Total VR > set VR

 \Box FiO2 < = .5

	Backup set $VR = VE$ goal / set VT
	Volume control ventilation will be required unless FiO2 <= 0.5 and PEEP <= 10cmH2O, then the
	patient can be evaluated for pressure support weaning.
	Tidal Volume (VT) Goal is 6 ml / kg / PBW
	Measure and record inspiratory plateau pressure (Pplat) with every ventilator assessment and after
	changes in VT and PEEP.
	If Pplat is > 30 cmH2O an ABG is recommended to determine if a VT reduction is indicated.
	If unable to measure a Pplat when in PRVC, change the mode to A/C for 2 to 3 minutes. Measure the
	Pplat. Return the patient to previous mode.
	Do not increase ventilator rate (VR) above 35 bpm.
	Do not decrease VT below 4 ml/kg
	If the patient is not over breathing the set rate do not decrease VT and VR at the same time.
Oxy	ygenation:
	The protocol will not decrease PEEP for 6 hours after it has been increased.
	If PEEP is > 10 cmH2O, do not decrease > 2cmH2O every 2 hours.
	If the SpO2 or PaO2 fall below the target ranges after a decrease in FiO2 and/or PEEP and it has been
	less than 30 minutes, the patient will be returned to the previous FiO2 and PEEP settings.
	Each subsequent repeat of therapy reduction followed by therapy increase will result in waiting periods
	(4, 8, and 24 hours).
Nig	tht time:
	Night rests on CMV will start at 22:00 and end at 06:00 when ordered.
We	aning:
	Weaning may occur 24 hours a day.
	Weaning may be initiated at any time.

Table B.1. Tidal Volumes from Predicted Body Weight from Height and Gender

HEIG	ΗΤ	PBW	4 mi	5 m i	6 m l	7 m l	8 mi
4' 0" (4	48)	17.9	72	90	107	125	143
4' 1" (4	49)	20.2	81	101	121	141	162
4' 2" (50)	22.5	90	113	135	158	180
4' 3" (51)	24.8	99	124	149	174	198
4' 4" (52)	27.1	108	136	163	190	217
	53)	29.4	118	147	176	206	235
4' 6" (54)	31.7	127	159	190	222	254
4' 7" (55)	34	136	170	204	238	272
4' 8" (56)	36.3	145	182	218	254	290
4' 9" (57)	38.6	154	193	232	270	309
4' 10" (58)	40.9	164	205	245	286	327
4' 11" (59)	43.2	173	216	259	302	346
	60)	45.5	182	228	273	319	364
5' 1" (0	61)	47.8	191	239	287	335	382
5' 2" (0	62)	50.1	200	251	301	351	401
5' 3" (63)	52.4	210	262	314	367	419
	64)	54.7	219	274	328	383	438
	65)	57	228	285	342	399	456
5' 6" (6	66)	59.3	237	297	356	415	474
5' 7" (67)	61.6	246	308	370	431	493
5' 8" (6	68)	63.9	256	320	383	447	511
5' 9" (69)	66.2	265	331	397	463	530
	70)	68.5	274	343	411	480	548
	71)	70.8	283	354	425	496	566
	72)	73.1	292	366	439	512	585
	73)	75.4	302	377	452	528	603
	74)	77.7	311	389	466	544	622
	75)	80	320	400	480	560	640
	76)	82.3	329	412	494	576	658
	77)	84.6	338	423	508	592	677
	78)	86.9	348	435	521	608	695
	79)	89.2	357	446	535	624	714
	80)	91.5	366	458	549	641	732
	81)	93.8	375	469	563	657	750
	82)	96.1	384	481	577	673	769
	83)	98.4	394	492	590	689	787
7' 0" (8	84)	100.7	403	504	604	705	806

HEIGHT	PBW	4 mi	5 ml	6 mi	7 ml	8 ml
4' 0" (48)	22.4	90	112	134	157	179
4' 1" (49)	24.7	99	124	148	173	198
4' 2" (50)	27	108	135	162	189	216
4' 3" (51)	29.3	117	147	176	205	234
4' 4" (52)	31.6	126	158	190	221	253
4' 5" (53)	33.9		170			
4' 6" (54)	36.2			217		
4' 7" (55)		104	193		270	
4' 8" (56)	40.8		204		286	
4' 9" (57)	43.1		216			
4' 10" (58)	45.4		227		318	
4' 11" (59)	47.7		239		334	
5' 0" (60)	50	200	250	300	350	400
5' 1" (61)	52.3	209	262	314	366	418
5' 2" (62)	54.6	218	273	328	382	437
5' 3" (63)	56.9	228	285	341	398	455
5' 4" (64)	59.2	237	296	355	414	474
5' 5" (65)	61.5	246	308	369	431	492
5' 6" (66)	63.8	255	319	383	447	510
5' 7" (67)	66.1		331			529
5' 8" (68)	68.4	274	342	410	479	547
5' 9" (69)		283	354			
5' 10" (70)	73	292	365	438	511	584
5' 11" (71)	75.3		377		527	
6' 0" (72)		310	388			621
6' 1" (73)		020		479		
6' 2" (74)		329				
6' 3" (75)		338		507	592	
6' 4" (76)		347			608	
6' 5" (77)		356	446			
6' 6" (78)	91.4		457		640	731
6' 7" (79)	93.7	375	469		656	750
6' 8" (80)	96	384	480	576	672	768
6' 9" (81)	98.3				688	786
6' 10" (82)	100.6	402	503	604	704	805
6' 11" (83)	102.9					823
7' 0" (84)	105.2	421	526	631	736	842

PBW and Tidal Volume for Females

PBW and Tidal Volume for Males

Table B.2.	1.	VT > 6 ml/	/kg	2.	VT = 6 ml/k	kg .	VT <u>≥</u> 4	ml/kg and < 6 ml/l	kg
рН	3. Pplat < 25 cm H2O	Pplat 25 – 30 cm H2O	4. Pplat > 30 cm H2O	5. Pplat < 25 cm H2O	Pplat 25 – 30 cm H2O	Pplat > 30 cm H2O	6. Pplat < 25 cm H2O	Pplat 25 – 30 cm H2O	Pplat > 30 cm H2O
> 7.45	1. ↓ VT by 1 ml/kg	2. ↓ VT by 1 ml/kg	3. ↓ VT by 1 ml/kg	4. ↓ VR by 20%	5. ↓ VR by 20%	6. ↓VT by 1 ml/kg	7. ↑ VT by 1 ml/kg ↓ VR by 20%	8. ↓ VR by 20%	9. ↓ VT by 1 ml/kg but do not ↓ < 4 ml/kg
7.30 – 7.45	10. ↓ VT by 1 ml/kg	11. ↓ VT by 1 ml/kg	12. ↓ VT by 1 ml/kg	13. No Change in Therapy	14. No Change in Therapy	15. ↓ VT by 1 ml/kg	16. ↑ VT by 1 ml/kg	17. No Change in Therapy	18. ↓ VT by 1 ml/kg but do not ↓ < 4 ml/kg
7.15 – 7.29 and VR < 35 bpm (measured rate)	19. ↑ VR by 20% increments ^a ↓ VT by 1 ml/kg	20. ↑ VR by 20% increments ^a ↓ VT by 1 ml/kg	21. ↑ VR by 20% increments ^a ↓ VT by 1 ml/kg	22. ↑ VR by 20% increments ^a	23. ↑ VR by 20% increments ^a	24. ↓ VT by 1 ml/kg ↑ VR by 20% increments ^a	25. ↑ VR by 20% increments ^a ↑ VT by 1 ml/kg	26. ↑ VR by 20% increments ^a	27. ↑ VR by 20% increments ^a
7.15 – 7.29 and VR = 35 bpm (measured rate)	28. ↓ VT by 1 ml/kg Check with MD to consider Bicarb	29. ↓ VT by 1 ml/kg Check with MD to consider Bicarb	30. ↓ VT by 1 ml/kg Check with MD to consider Bicarb	31. Check with MD to consider Bicarb	32. Check with MD to consider Bicarb	33. ↓ VT by 1 ml/kg Check with MD to consider Bicarb	34. ↑ VT by 1 ml/kg Check with MD to consider Bicarb	35. Check with MD to consider Bicarb	36. ↓ VT by 1 ml/kg but do not ↓ < 4 ml/kg Check with MD To consider Bicarb
< 7.15 and VR < 35 bpm (measured rate)	37. ↑ VR by 20% increments Check with MD to consider Bicarb	38. ↑ VR by 20% increments Check with MD to Consider Bicarb	39. ↑ VR by 20% increments Check with MD to Consider Bicarb	40. ↑ VR by 20% increments Check with MD to Consider Bicarb	41. ↑VR by 20% increments Check with MD to Consider Bicarb	42. ↓ VT by 1 ml/kg Check with MD to consider Bicarb	43. ↑ VR by 20% increments ^a ↑ VT by 1 ml/kg Check with MD to consider Bicarb	44. ↑ VR by 20% increments Check with MD to Consider Bicarb	45. ↑ VR by 20% increments Check with MD to Consider Bicarb
< 7.15 and VR = 35 bpm (measured rate)	46. Check with MD to consider Bicarb prior to ↑ VT by 1 ml/kg	47. Check with MD to consider Bicarb prior to ↑ VT by 1 ml/kg	48. Check with MD to consider Bicarb prior to ↑ VT by 1 ml/kg	49. Check with MD to consider Bicarb prior to ↑ VT by 1 ml/kg	50. Check with MD to consider Bicarb prior to ↑ VT by 1 ml/kg	51. Check with MD to consider Bicarb prior to ↑ VT by 1 ml/kg		53. Check with MD to consider Bicarb prior to ↑ VT by 1 ml/kg	54. Check with MD to consider Bicarb prior to ↑ VT by 1 ml/kg

$PaO_2 < 50 \text{ or } SpO_2 < 85\%$

(Use PaO₂ if available, only use SpO₂ if PaO₂ not available)

When PaO_2 or SpO_2 are in this low range, repeated sequential adjustments may be made as guided by the cells in the table until adequate oxygenation with a $SpO_2 \ge 88\%$ is achieved

PEEP	FiO ₂ = .3	$FiO_2 = .4$	FiO ₂ = .5	$FiO_2 = .6$	$FiO_2 = .7$	$FiO_2 = .8$	FiO ₂ = .9	$FiO_2 = 1.0$
24	↑ FiO ₂ 0.3	↑ FiO ₂ 0.3	↑ FiO ₂ 0.3	↑ FiO ₂ 0.3	↑ FiO ₂ 0.3	↑ FiO ₂ 0.2	↑ FiO ₂ 0.1	PEEP ↑Trial
22	↑ FiO ₂ 0.3	↑ FiO ₂ 0.3	↑ FiO ₂ 0.3	↑ FiO ₂ 0.3	↑ FiO ₂ 0.3	↑ FiO ₂ 0.2 ↑PEEP 2		↑PEEP 2
20	↑ FiO ₂ 0.3	↑ FiO ₂ 0.3	↑ FiO ₂ 0.3	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.1 ↑PEEP 4	↑РЕЕР 4
18	$ \begin{array}{c} \uparrow \operatorname{FiO_2} \\ 0.2 \\ \uparrow \operatorname{PEEP} \\ 2 \end{array} $	↑ FiO ₂ 0.2 ↑PEEP 2		↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.1 ↑PEEP 4	↑ FiO ₂ 0.1 ↑PEEP 4	↑ FiO ₂ 0.1 ↑PEEP 4	↑PEEP 4
16		↑ FiO ₂ 0.1 ↑PEEP 4		↑ FiO ₂ 0.1 ↑PEEP 4	↑ FiO ₂ 0.1 ↑PEEP 4	↑ FiO ₂ 0.1 ↑PEEP 4		↑PEEP 4
14	$ \uparrow FiO_2 $ $ 0.2 $ $ \uparrow PEEP $ $ 4 $	↑ FiO ₂ 0.1 ↑PEEP 4		↑ FiO ₂ 0.1 ↑PEEP 4	↑ FiO ₂ 0.1 ↑PEEP 4	↑ FiO ₂ 0.1 ↑PEEP 4		↑PEEP 4
12		↑ FiO ₂ 0.1 ↑PEEP 4		↑ FiO ₂ 0.1 ↑PEEP 4	↑ FiO ₂ 0.1 ↑PEEP 4	↑ FiO ₂ 0.1 ↑PEEP 4		↑PEEP 4
10	↑ FiO ₂ 0.1 ↑PEEP 4	↑ FiO ₂ 0.1 ↑PEEP 4		↑ FiO ₂ 0.1 ↑PEEP 4	↑ FiO ₂ 0.1 ↑PEEP 4	↑ FiO ₂ 0.1 ↑PEEP 4	↑ FiO ₂ 0.1 ↑PEEP 4	↑PEEP 4
8		↑ FiO ₂ 0.1 ↑PEEP 4		↑ FiO ₂ 0.1 ↑PEEP 4	↑ FiO ₂ 0.1 ↑PEEP 4	↑ FiO ₂ 0.1 ↑PEEP 4		↑РЕЕР 4
5	↑ FiO ₂ 0.1 ↑PEEP 5	↑ FiO ₂ 0.1 ↑PEEP 5		↑ FiO ₂ 0.1 ↑PEEP 5	↑ FiO ₂ 0.1 ↑PEEP 5	↑ FiO ₂ 0.1 ↑PEEP 5		↑PEEP 5

PaO₂ 50 to 54 or SpO₂ 85 to 87%

(Use PaO₂ if available, only use SpO₂ if PaO₂ not available)

When PaO_2 or SpO_2 are in this low range, repeated sequential adjustments may be made as guided by the cells in the table until adequate oxygenation with a $SpO_2 \ge 88\%$ is achieved

PEEP	$FiO_2 = .3$	$FiO_2 = .4$	$FiO_2 = .5$	$FiO_2 = .6$	$FiO_2 = .7$	$FiO_2 = .8$	$FiO_2 = .9$	$FiO_2 = 1.0$
24	↑ FiO ₂ 0.1	Consider PEEP Increase Trial						
22	↑ FiO ₂ 0.1	↑ PEEP 2						
20	↑ FiO ₂ 0.1	↑ PEEP 2	↑ PEEP 2	↑ PEEP 2				
18	↑ FiO ₂ 0.1	↑ FiO ₂ 0.1	↑ PEEP 2	↑ PEEP 2				
16	↑ FiO ₂ 0.1	↑ FiO ₂ 0.1	↑ PEEP 2	↑ PEEP 2				
14	↑ FiO ₂ 0.1	↑ PEEP 2	↑ PEEP 2					
12	↑ FiO ₂ 0.1	↑ PEEP 2	↑ PEEP 2					
10	↑ FiO ₂ 0.1	↑ PEEP 2	↑ PEEP 2					
8	↑ FiO ₂ 0.1	↑ PEEP 2	↑ PEEP 2	↑ PEEP 2	↑ PEEP 2	↑ PEEP 2	↑ PEEP 2	↑ PEEP 2
5	↑ FiO ₂ 0.1	↑ PEEP	↑ PEEP 3	↑ PEEP 3	↑ PEEP 3	↑ PEEP 3	↑ PEEP	↑ PEEP 3

$PaO_2 = 55 - 67 \text{ or } SpO_2 88 - 93\%$

(Use PaO₂ if available, only use SpO₂ if PaO₂ not available)

PEEP	$FiO_2 = .3$	$FiO_2 = .4$	$FiO_2 = .5$	$FiO_2 = .6$	$FiO_2 = .7$	$FiO_2 = .8$	$FiO_2 = .9$	$FiO_2 = 1.0$
24	$ \uparrow FiO_2 $ 0.1 $ \downarrow PEEP 2 $	$ \uparrow FiO_2 $ 0.1 $ \downarrow PEEP 2 $			↑ FiO ₂ 0.1 ↓PEEP 2		↓PEEP 2	Maintain
22	$ \uparrow FiO_2 $ 0.1 $ \downarrow PEEP 2 $	$ \uparrow FiO_2 $ 0.1 $ \downarrow PEEP 2 $			↑ FiO ₂ 0.1 ↓PEEP 2	Maintain	Maintain	Maintain
20	$ \uparrow FiO_2 $ 0.1 $ \downarrow PEEP 2 $	$ \uparrow FiO_2 $ 0.1 $ \downarrow PEEP 2 $	Maintain	Maintain	Maintain	Maintain	↑ PEEP 2	$ \downarrow FiO_2 $ 0.1 $ \uparrow PEEP 2 $
18	$ \uparrow FiO_2 $ 0.1 $ \downarrow PEEP 2 $	$ \uparrow FiO_2 $ 0.1 $ \downarrow PEEP 2 $	Maintain	↑ PEEP 2	↑ PEEP 2	↑ PEEP 2	$ \downarrow FiO_2 \\ 0.1 \\ \uparrow PEEP 2 $	$ \downarrow FiO_2 \\ 0.1 \\ \uparrow PEEP 2 $
16	$ \uparrow FiO_2 $ 0.1 $ \downarrow PEEP 2 $	Maintain	Maintain	$ \downarrow FiO_2 $ $ 0.1 $ $ \uparrow PEEP 2 $	↓ FiO ₂ 0.1 ↑PEEP 2	$ \downarrow FiO_2 $ $ 0.1 $ $ \uparrow PEEP 2 $	$ \downarrow FiO_2 $ 0.1 $ \uparrow PEEP 2 $	$\begin{array}{c} \downarrow \text{FiO}_2 \\ 0.1 \\ \uparrow \text{PEEP 2} \end{array}$
14	$ \uparrow FiO_2 $ 0.1 $ \downarrow PEEP 2 $	Maintain	$ \downarrow FiO_2 $ 0.1 $ \uparrow PEEP 2 $	$ \downarrow FiO_2 $ 0.1 $ \uparrow PEEP 2 $	↓ FiO ₂ 0.1 ↑PEEP 2	$ \downarrow FiO_2 $ 0.1 $ \uparrow PEEP 2 $	$ \downarrow FiO_2 $ 0.1 $ \uparrow PEEP 2 $	$ \downarrow FiO_2 $ 0.1 $ \uparrow PEEP 2 $
12	↑ FiO ₂ 0.1 ↓PEEP 2	Maintain	$\begin{array}{c} \downarrow \text{FiO}_2 \\ 0.1 \\ \uparrow \text{PEEP 2} \end{array}$	↓ FiO ₂ 0.1 ↑PEEP 2	↓ FiO ₂ 0.1 ↑PEEP 2	$\begin{array}{c} \downarrow \text{FiO}_2 \\ 0.1 \\ \uparrow \text{PEEP 2} \end{array}$	↓ FiO ₂ 0.1 ↑PEEP 2	$\begin{array}{c} \downarrow \mathrm{FiO_2} \\ 0.1 \\ \uparrow \mathrm{PEEP} \\ 2 \end{array}$
10	↑ FiO ₂ 0.1 ↓PEEP 2	Maintain	$\begin{array}{c} \downarrow \text{FiO}_2 \\ 0.1 \\ \uparrow \text{PEEP 2} \end{array}$	↓ FiO ₂ 0.1 ↑PEEP 2	$\downarrow FiO_2 \ 0.1$ 1. $\uparrow PEEP$ 2	$ \downarrow FiO_2 \\ 0.1 \\ \uparrow PEEP 2 $	↓ FiO ₂ 0.1 ↑PEEP 2	↓ FiO ₂ 0.1 ↑PEEP 2
8	↑ FiO ₂ 0.1	Maintain	$ \downarrow FiO_2 \\ 0.1 \\ \uparrow PEEP 2 $	$ \downarrow FiO_2 \\ 0.1 \\ \uparrow PEEP 2 $	↓ FiO ₂ 0.1 ↑PEEP 2	↓ FiO ₂ 0.1 ↑PEEP 2	\downarrow FiO ₂ 0.1 \uparrow PEEP 2	$ \downarrow FiO_2 \\ 0.1 \\ \uparrow PEEP 2 $
5	Maintain	Maintain	↓ FiO ₂ 0.1 ↑PEEP 3	↓ FiO ₂ 0.1 ↑PEEP 3	↓ FiO ₂ 0.1 ↑PEEP 3	↓ FiO ₂ 0.1 ↑PEEP 3	↓ FiO ₂ 0.1 ↑PEEP 3	↓ FiO ₂ 0.1 ↑PEEP 3

 $PaO_2 > 68 \text{ or } SpO_2 > 93\%$

(Use PaO₂ if available, only use SpO₂ if PaO₂ not available)

PEEP	$FiO_2 = .3$	$FiO_2 = .4$	$FiO_2 = .5$	$FiO_2 = .6$	$FiO_2 = .7$	$FiO_2 = .8$	$FiO_2 = .9$	$FiO_2 = 1.0$
24	↓ PEEP 2	↓ PEEP 2						
22	↓ PEEP 2	↓ PEEP 2	↓ FiO ₂ .1	↓ FiO ₂ .1				
20	↓ PEEP 2	↓ PEEP 2	↓ PEEP 2	↓ FiO ₂ .1				
18	↓ PEEP 2	↓ PEEP 2	↓ PEEP 2	↓ FiO ₂ .1				
16	↓ PEEP 2	↓ PEEP 2	↓ FiO ₂ .1					
14	↓ PEEP 2	↓ PEEP 2	↓ FiO ₂ .1					
12	↓ PEEP 2	↓ PEEP 2	↓ FiO ₂ .1					
10	↓ PEEP 2	↓ PEEP 2	↓ FiO ₂ .1					
8	↓ PEEP 3	↓ PEEP 3	↓ FiO ₂ .1					
5	Maintain	↓ FiO ₂ .1						

$PaO_2 < 50 \text{ or } SpO_2 < 85\%$

(Use PaO₂ if available, only use SpO₂ if PaO₂ not available)

When PaO_2 or SpO_2 are in this low range, repeated sequential adjustments may be made as guided by the cells in the table until adequate oxygenation with a $SpO_2 \ge 88\%$ is achieved

PEEP	FiO ₂ = .3	$FiO_2 = .4$	FiO ₂ = .5	$FiO_2 = .6$	$FiO_2 = .7$	$FiO_2 = .8$	FiO ₂ = .9	$FiO_2 = 1.0$
24	↑ FiO ₂ 0.3	↑ FiO ₂ 0.2	↑ FiO ₂ 0.2	↑ FiO ₂ 0.2	↑ FiO ₂ 0.2	↑ FiO ₂ 0.2	↑ FiO ₂ 0.1	PEEP ↑Trial
22	↑ FiO ₂ 0.3	↑ FiO ₂ 0.2 ↑PEEP 2		↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2		↑ PEEP 2
20	↑ FiO ₂ 0.3	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2		↑РЕЕР 4
18	↑ FiO ₂ 0.3	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.1 ↑PEEP 4	↑РЕЕР 4
16	↑ FiO ₂ 0.3	↑ FiO ₂ 0.2 ↑PEEP 2		↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.1 ↑PEEP 4	↑РЕЕР 4
14	↑ FiO ₂ 0.3	↑ FiO ₂ 0.2 ↑PEEP 2		↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.1 ↑PEEP 4	↑РЕЕР 4
12	$ \uparrow FiO_2 $ $ 0.2 $ $ \uparrow PEEP $ $ 2 $	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.1 ↑PEEP 4	↑PEEP 4
10		↑ FiO ₂ 0.2 ↑PEEP 2		↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.1 ↑PEEP 4	↑PEEP 4
8		↑ FiO ₂ 0.2 ↑PEEP 2		↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2		↑PEEP 4
5	↑ FiO ₂ 0.2 ↑PEEP 3	↑ FiO ₂ 0.2 ↑PEEP 3		↑ FiO ₂ 0.2 ↑PEEP 3	↑ FiO ₂ 0.2 ↑PEEP 3	↑ FiO ₂ 0.2 ↑PEEP 3		↑PEEP 5

PaO₂ 50 to 54 or SpO₂ 85 to 87%

(Use PaO₂ if available, only use SpO₂ if PaO₂ not available)

When PaO_2 or SpO_2 are in this low range, repeated sequential adjustments may be made as guided by the cells in the table until adequate oxygenation with a $SpO_2 \ge 88\%$ is achieved

PEEP	$FiO_2 = .3$	$FiO_2 = .4$	$FiO_2 = .5$	$FiO_2 = .6$	$FiO_2 = .7$	$FiO_2 = .8$	$FiO_2 = .9$	$FiO_2 = 1.0$
24	↑ FiO ₂ 0.1	Consider PEEP Increase Trial						
22	↑ FiO ₂	↑ PEEP						
	0.1	0.1	0.1	0.1	0.1	0.1	0.1	2
20	↑ FiO ₂	↑ PEEP						
	0.1	0.1	0.1	0.1	0.1	0.1	0.1	2
18	↑ FiO ₂	↑ PEEP						
	0.1	0.1	0.1	0.1	0.1	0.1	0.1	2
16	↑ FiO ₂	↑ PEEP	↑ PEEP					
	0.1	0.1	0.1	0.1	0.1	0.1	2	2
14	↑ FiO ₂	↑ PEEP	↑ PEEP					
	0.1	0.1	0.1	0.1	0.1	0.1	2	2
12	↑ FiO ₂	↑ FiO ₂	↑ FiO ₂	↑ FiO ₂	↑ PEEP	↑ PEEP	↑ PEEP	↑ PEEP
	0.1	0.1	0.1	0.1	2	2	2	2
10	↑ FiO ₂	↑ FiO ₂	↑ FiO ₂	↑ FiO ₂	↑ PEEP	↑ PEEP	↑ PEEP	↑ PEEP
	0.1	0.1	0.1	0.1	2	2	2	2
8	↑ FiO ₂	↑ FiO ₂	↑ PEEP					
	0.1	0.1	2	2	2	2	2	2
5	↑ FiO ₂ 0.1	↑ PEEP	↑ PEEP 3					

$PaO_2 = 55 - 68 \text{ or } SpO_2 88 - 93\%$

(Use PaO₂ if available, only use SpO₂ if PaO₂ not available)

PEEP	$FiO_2 = .3$	$FiO_2 = .4$	$FiO_2 = .5$	$FiO_2 = .6$	$FiO_2 = .7$	$FiO_2 = .8$	$FiO_2 = .9$	$FiO_2 = 1.0$
24	↑ FiO ₂ 0.1 ↓PEEP 2	↑ FiO ₂ 0.1 ↓PEEP 2	↑ FiO ₂ 0.1 ↓PEEP 2	↑ FiO ₂ 0.1 ↓PEEP 2	↑ FiO ₂ 0.1 ↓PEEP 2	↑ FiO ₂ 0.1 ↓PEEP 2	↑ FiO ₂ 0.1 ↓PEEP 2	Maintain
22	↑ FiO ₂ 0.1 ↓PEEP 2	↑ FiO ₂ 0.1 ↓PEEP 2	↑ FiO ₂ 0.1 ↓PEEP 2	↑ FiO ₂ 0.1 ↓PEEP 2	↑ FiO ₂ 0.1 ↓PEEP 2	↑ FiO ₂ 0.1 ↓PEEP 2	↑ FiO ₂ 0.1 ↓PEEP 2	Maintain
20	↑ FiO ₂ 0.1 ↓PEEP 2	↑ FiO ₂ 0.1 ↓PEEP 2	↑ FiO ₂ 0.1 ↓PEEP 2	↑ FiO ₂ 0.1 ↓PEEP 2	↑ FiO ₂ 0.1 ↓PEEP 2	↑ FiO ₂ 0.1 ↓PEEP 2	↑ FiO ₂ 0.1 ↓PEEP 2	Maintain
18	↑ FiO ₂ 0.1 ↓PEEP 2	↑ FiO ₂ 0.1 ↓PEEP 2	↑ FiO ₂ 0.1 ↓PEEP 2	↑ FiO ₂ 0.1 ↓PEEP 2	↑ FiO ₂ 0.1 ↓PEEP 2	↑ FiO ₂ 0.1 ↓PEEP 2	Maintain	Maintain
16	↑ FiO ₂ 0.1 ↓PEEP 2	↑ FiO ₂ 0.1 ↓PEEP 2	↑ FiO ₂ 0.1 ↓PEEP 2	↑ FiO ₂ 0.1 ↓PEEP 2	↑ FiO ₂ 0.1 ↓PEEP 2	↑ FiO ₂ 0.1 ↓PEEP 2	Maintain	↓ FiO ₂ 0.1 ↑PEEP 2
14	↑ FiO ₂ 0.1 ↓PEEP 2	↑ FiO ₂ 0.1 ↓PEEP 2	↑ FiO ₂ 0.1 ↓PEEP 2	↑ FiO ₂ 0.1 ↓PEEP 2	Maintain	Maintain	Maintain	↓ FiO ₂ 0.1 ↑PEEP 2
12	\uparrow FiO ₂ 0.1 \downarrow PEEP 2	$\uparrow \text{FiO}_2 \text{ 0.1}$ $\downarrow \text{PEEP 2}$	↑ FiO ₂ 0.1 ↓PEEP 2	↑ FiO ₂ 0.1 ↓PEEP 2	Maintain	↓ FiO ₂ 0.1 ↑PEEP 2	↓ FiO ₂ 0.1 ↑PEEP 2	↓ FiO ₂ 0.1 ↑ PEEP 2
10	\uparrow FiO ₂ 0.1 \downarrow PEEP 2	↑ FiO ₂ 0.1 ↓PEEP 2	Maintain	Maintain	Maintain	↓ FiO ₂ 0.1 ↑PEEP 2	↓ FiO ₂ 0.1 ↑PEEP 2	↓ FiO ₂ 0.1 ↑PEEP 2
8	↑ FiO ₂ 0.1 ↓PEEP 3	Maintain	Maintain	↓ FiO ₂ 0.1 ↑PEEP 2				
5	Maintain	Maintain	↓ FiO ₂ 0.1 ↑PEEP 3					

$PaO_2 > 68 \text{ or } SpO_2 > 93\%$

(Use PaO₂ if available, only use SpO₂ if PaO₂ not available)

PEEP	$FiO_2 = .3$	$FiO_2 = .4$	$FiO_2 = .5$	$FiO_2 = .6$	$FiO_2 = .7$	$FiO_2 = .8$	$FiO_2 = .9$	$FiO_2 = 1.0$
24	↓ PEEP 2	↓ PEEP 2						
22	↓ PEEP 2	↓ PEEP 2						
20	↓ PEEP 2	↓ PEEP 2						
18	↓ PEEP 2	↓ PEEP 2	↓ FiO ₂ .1					
16	↓ PEEP 2	↓ PEEP 2	↓ FiO ₂ .1					
14	↓ PEEP 2	↓ PEEP 2	↓ PEEP 2	↓ PEEP 2	↓ PEEP 2	↓ FiO ₂ .1	↓ FiO ₂ .1	↓ FiO ₂ .1
12	↓ PEEP 2	↓ PEEP 2	↓ PEEP 2	↓ PEEP 2	↓ PEEP 2	↓ FiO ₂ .1	↓ FiO ₂ .1	↓ FiO ₂ .1
10	↓ PEEP 2	↓ PEEP 2	↓ PEEP 2	↓ FiO ₂ .1				
8	↓ PEEP 3	↓ PEEP 3	↓ FiO ₂ .1					
5	Maintain	↓ FiO ₂ .1						

$PaO_2 < 55 \text{ or } SpO_2 < 88\%$

(Use PaO₂ if available, only use SpO₂ if PaO₂ not available)

When PaO_2 or SpO_2 are in this low range, repeated sequential adjustments may be made as guided by the cells in the table until adequate oxygenation with a $SpO_2 \ge 92\%$ is achieved

PEEP	FiO ₂ = .3	$FiO_2 = .4$	FiO ₂ = .5	$FiO_2 = .6$	$FiO_2 = .7$	$FiO_2 = .8$	FiO ₂ = .9	$FiO_2 = 1.0$
24	↑ FiO ₂ 0.3	↑ FiO ₂ 0.2	↑ FiO ₂ 0.2	↑ FiO ₂ 0.2	↑ FiO ₂ 0.2	↑ FiO ₂ 0.2	↑ FiO ₂ 0.1	PEEP ↑Trial
22	↑ FiO ₂ 0.3	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2		↑ PEEP 2
20	↑ FiO ₂ 0.3	↑ FiO ₂ 0.2 ↑PEEP 2		↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.1 ↑PEEP 4	↑РЕЕР 4
18	↑ FiO ₂ 0.3	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.1 ↑PEEP 4	↑РЕЕР 4
16	↑ FiO ₂ 0.3	↑ FiO ₂ 0.2 ↑PEEP 2		↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.1 ↑PEEP 4	↑РЕЕР 4
14	↑ FiO ₂ 0.3	↑ FiO ₂ 0.2 ↑PEEP 2		↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.1 ↑PEEP 4	↑PEEP 4
12	$ \uparrow FiO_2 $ $ 0.2 $ $ \uparrow PEEP $ $ 2 $	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.1 ↑PEEP 4	↑РЕЕР 4
10		↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2		↑РЕЕР 4
8		↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.2 ↑PEEP 2	↑ FiO ₂ 0.1 ↑PEEP 4	↑РЕЕР 4
5	↑ FiO ₂ 0.2 ↑PEEP 3	↑ FiO ₂ 0.2 ↑PEEP 3		↑ FiO ₂ 0.2 ↑PEEP 3	↑ FiO ₂ 0.2 ↑PEEP 3	↑ FiO ₂ 0.2 ↑PEEP 3		↑РЕЕР 5

PaO₂ 55 to 67 or SpO₂ 88 to 92%

(Use PaO₂ if available, only use SpO₂ if PaO₂ not available)

When PaO_2 or SpO_2 are in this low range, repeated sequential adjustments may be made as guided by the cells in the table until adequate oxygenation with a $SpO_2 \ge 92\%$ is achieved

PEEP	$FiO_2 = .3$	$FiO_2 = .4$	$FiO_2 = .5$	$FiO_2 = .6$	$FiO_2 = .7$	$FiO_2 = .8$	$FiO_2 = .9$	$FiO_2 = 1.0$
24	↑ FiO ₂ 0.1	Consider PEEP Increase Trial						
22	↑ FiO ₂	↑ PEEP						
	0.1	0.1	0.1	0.1	0.1	0.1	0.1	2
20	↑ FiO ₂	↑ PEEP						
	0.1	0.1	0.1	0.1	0.1	0.1	0.1	2
18	↑ FiO ₂	↑ PEEP						
	0.1	0.1	0.1	0.1	0.1	0.1	0.1	2
16	↑ FiO ₂	↑ PEEP	↑ PEEP					
	0.1	0.1	0.1	0.1	0.1	0.1	2	2
14	↑ FiO ₂	↑ PEEP	↑ PEEP					
	0.1	0.1	0.1	0.1	0.1	0.1	2	2
12	↑ FiO ₂	↑ FiO ₂	↑ FiO ₂	↑ FiO ₂	↑ PEEP	↑ PEEP	↑ PEEP	↑ PEEP
	0.1	0.1	0.1	0.1	2	2	2	2
10	↑ FiO ₂	↑ FiO ₂	↑ FiO ₂	↑ FiO ₂	↑ PEEP	↑ PEEP	↑ PEEP	↑ PEEP
	0.1	0.1	0.1	0.1	2	2	2	2
8	↑ FiO ₂	↑ FiO ₂	↑ PEEP					
	0.1	0.1	2	2	2	2	2	2
5	↑ FiO ₂ 0.1	↑ PEEP	↑ PEEP 3					

$PaO_2 = 68 - 80 \text{ or } SpO_2 93 - 95\%$

(Use PaO₂ if available, only use SpO₂ if PaO₂ not available)

PEEP	$FiO_2 = .3$	$FiO_2 = .4$	$FiO_2 = .5$	$FiO_2 = .6$	$FiO_2 = .7$	$FiO_2 = .8$	$FiO_2 = .9$	$FiO_2 = 1.0$
24	↑ FiO ₂ 0.1 ↓PEEP 2	Maintain						
22	↑ FiO ₂ 0.1 ↓PEEP 2	Maintain						
20	↑ FiO ₂ 0.1 ↓PEEP 2	Maintain						
18	↑ FiO ₂ 0.1 ↓PEEP 2	Maintain	Maintain					
16	↑ FiO ₂ 0.1 ↓PEEP 2	Maintain	↓ FiO ₂ 0.1 ↑PEEP 2					
14	↑ FiO ₂ 0.1 ↓PEEP 2	Maintain	Maintain	Maintain	↓ FiO ₂ 0.1 ↑PEEP 2			
12	↑ FiO ₂ 0.1 ↓PEEP 2	Maintain	↓ FiO ₂ 0.1 ↑PEEP 2	↓ FiO ₂ 0.1 ↑PEEP 2	↓ FiO ₂ 0.1 ↑ PEEP 2			
10	↑ FiO ₂ 0.1 ↓PEEP 2	↑ FiO ₂ 0.1 ↓PEEP 2	Maintain	Maintain	Maintain	↓ FiO ₂ 0.1 ↑PEEP 2	↓ FiO ₂ 0.1 ↑PEEP 2	↓ FiO ₂ 0.1 ↑PEEP 2
8	↑ FiO ₂ 0.1 ↓PEEP 2	Maintain	Maintain	↓ FiO ₂ 0.1 ↑PEEP 2				
5	Maintain	Maintain	↓ FiO ₂ 0.1 ↑PEEP 3					

$PaO_2 > 80 \text{ or } SpO_2 > 95\%$

(Use PaO₂ if available, only use SpO₂ if PaO₂ not available)

PEEP	$FiO_2 = .3$	$FiO_2 = .4$	$FiO_2 = .5$	$FiO_2 = .6$	$FiO_2 = .7$	$FiO_2 = .8$	$FiO_2 = .9$	$FiO_2 = 1.0$
24	↓ PEEP 2	↓ PEEP 2						
22	↓ PEEP 2	↓ PEEP 2						
20	↓ PEEP 2	↓ PEEP 2						
18	↓ PEEP 2	↓ PEEP 2	↓ FiO ₂ .1					
16	↓ PEEP 2	↓ PEEP 2	↓ FiO ₂ .1					
14	↓ PEEP 2	↓ PEEP 2	↓ PEEP 2	↓ PEEP 2	↓ PEEP 2	↓ FiO ₂ .1	↓ FiO ₂ .1	↓ FiO ₂ .1
12	↓ PEEP 2	↓ PEEP 2	↓ PEEP 2	↓ PEEP 2	↓ PEEP 2	↓ FiO ₂ .1	↓ FiO ₂ .1	↓ FiO ₂ .1
10	↓ PEEP 2	↓ PEEP 2	↓ PEEP 2	↓ FiO ₂ .1				
8	↓ PEEP 3	↓ PEEP 3	↓ FiO ₂ .1					
5	Maintain	↓ FiO ₂ .1						