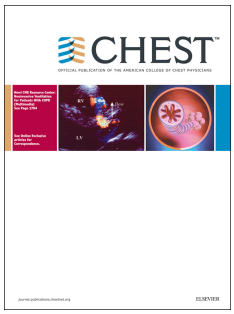
Accepted Manuscript



Liberation from Mechanical Ventilation: An Official American College of Chest Physicians/American Thoracic Society Clinical Practice Guideline

Daniel R. Ouellette, MD, FCCP, Sheena Patel, MPH, Timothy D. Girard, MD, Peter E. Morris, MD, FCCP, Gregory A. Schmidt, MD, FCCP, Jonathon D. Truwit, MD, FCCP, Waleed Al-Hazzani, MD, Suzanne M. Burns, RN, MSN, ACNP, RRT, Scott K. Epstein, MD, FCCP, Andres Esteban, MD, Eddy Fan, MD, Miguel Ferrer, MD, PhD, Gilles L. Fraser, PharmD, Michelle Gong, MD, Catherine L. Hough, MD, Sangeeta Mehta, MD, Rahul Nanchal, MD, FCCP, Amy J. Pawlik, DPT, William Schweickert, MD, Curtis N. Sessler, MD, FCCP, Thomas Strøm, MD, John P. Kress, MD, FCCP

PII: S0012-3692(16)60809-7

DOI: 10.1016/j.chest.2016.10.015

Reference: CHEST 758

To appear in: *CHEST*

Received Date: 28 July 2016

Revised Date: 27 September 2016

Accepted Date: 19 October 2016

Please cite this article as: Ouellette DR, Patel S, Girard TD, Morris PE, Schmidt GA, Truwit JD, Al-Hazzani W, Burns SM, Epstein SK, Esteban A, Fan E, Ferrer M, Fraser GL, Gong M, Hough CL, Mehta S, Nanchal R, Pawlik AJ, Schweickert W, Sessler CN, Strøm T, Kress JP, Liberation from Mechanical Ventilation: An Official American College of Chest Physicians/American Thoracic Society Clinical Practice Guideline, *CHEST* (2016), doi: 10.1016/j.chest.2016.10.015.

Liberation from Mechanical Ventilation: An Official American College of Chest Physicians/American Thoracic Society Clinical Practice Guideline

Inspiratory Pressure Augmentation during Spontaneous Breathing Trials, Protocols Minimizing Sedation, and Non-invasive Ventilation Immediately After Extubation

Daniel R. Ouellette, MD, FCCP; Sheena Patel, MPH; Timothy D. Girard, MD; Peter E. Morris, MD, FCCP; Gregory A. Schmidt, MD, FCCP; Jonathon D. Truwit, MD, FCCP; Waleed Al-Hazzani, MD; Suzanne M. Burns, RN, MSN, ACNP, RRT; Scott K. Epstein, MD, FCCP; Andres Esteban, MD; Eddy Fan, MD; Miguel Ferrer, MD, PhD; Gilles L. Fraser, PharmD; Michelle Gong, MD; Catherine L. Hough, MD; Sangeeta Mehta, MD; Rahul Nanchal, MD, FCCP; Amy J. Pawlik, DPT; William Schweickert, MD; Curtis N. Sessler, MD, FCCP; Thomas Strøm, MD; and John P. Kress, MD, FCCP

Affiliations: Henry Ford Health System (Dr Ouellette), Detroit, MI; CHEST (Ms Patel), Glenview, IL; University of Pittsburgh (Dr Girard), Pittsburgh, PA; University of Kentucky (Dr Morris), Lexington, KY; University of Iowa (Dr Schmidt), Iowa City, IA; Froedtert and Medical College of Wisconsin (Dr Trwuit), Milwaukee, WI; McMaster University (Dr Al-Hazzani), Hamilton, Canada; University of Virginia Health System (Ms Burns), Charlottesville, VA; Tufts University Medical Center (Dr Epstein), Boston, MA; Unidad de Cuidados Intensivos, University Hospital of Getafe, CIBER de Enfermedades Respiratorias (Dr Esteban), Madrid, Spain; University of Toronto (Dr Fan) Toronto, ON Canada; University of Barcelona (Dr Ferrer), Barcelona, Spain; Maine Medical Center (Dr Fraser), Portland, MA; Montefiore Medical Center (Dr Gong), Bronx, NY; University of Washington, Harborview Medical Center (Dr Hough), Seattle, WA; University of Toronto (Dr Mehta), Toronto, Canada; Medical College of Wisconsin (Dr Nanchal), Milwaukee, WI; University of Chicago Medical Center (Dr Pawlik), Chicago, IL; University of Pennsylvania (Dr Schweickert), Pennsylvania, PA; Virginia Commonwealth University (Dr Sessler), Richmond, VA; Odense University Hopsital (Dr Strøm), Odense, Denmark; University of Chicago (Dr Kress), Chicago, IL

Conflicts of Interest: KCW reports being employed by the ATS as the Chief of Documents and Medical Affairs; the ATS is a co-sponsor of the guideline. DRO is the principal investigator for a project involving patients with ventilator associated pneumonia funded by Cardeas Pharmaceuticals. All funds to institution. SP has no conflicts of interest. TDG has received support from the NIH (AG034257, AG035117), has received honoraria from Hospira, Inc., and has given presentations at international conferences related to the subject of the manuscript. PEM has no conflicts of interest. GAS reports receiving textbook royalties. JDT has no conflicts of interest. WA has no conflicts of interest. SMB is the inventor of the Burns Wean Assessment Program (BWAP) 1990. SKE has received royalties as an author or co-author of 7 chapters in UpToDate. AE has no conflicts of interest. EF has no conflicts of interest. MF has no conflicts of interest. GLF has no conflicts of interest. MG has no conflicts of interest. CLH has no conflicts of interest. SM has no conflicts of interest. RN has no conflicts of interest. AJP - 1-hour presentation to Dignity Health conference, "E of the ABCDE Bundle." APTA Combined Sections meeting, "When Early Mobility

is Not the Answer." Course Director, CE course, "Therapeutic Management of Patients with Respiratory Failure in the ICU." WS received in-kind benefits from Hill-Rom, the Society for Critical Care Medicine, and the American College of Physicians, received grant support from Hill-Rom and NIH (MIND-USA multicenter trial), lectured for Hill-Rom, and consulted for Hill-Rom, the Society for Critical Care Medicine, and the American College of Physicians. CNS has no conflicts of interest. TS has no conflicts of interest. JPK has no conflicts of interest.

Funding/Support: This study was funded in total by internal funds from the American College of Chest Physicians

Disclaimer: CHEST Guidelines are intended for general information only, are not medical advice, and do not replace professional medical care and physician advice, which always should be sought for any medical condition. The complete disclaimer for this guideline can be accessed at http://www.chestnet.org/Guidelines-and-Resources

Correspondence to: Daniel R. Ouellette, MD, Henry Ford Hospital Pulmonary and Critical Care Medicine, K-17; 2799 West Grand Boulevard Detroit, MI 48202

ABSTRACT

Background: An update of evidence-based guidelines concerning liberation from mechanical ventilation is needed as new evidence has become available. The American College of Chest Physicians (CHEST) and the American Thoracic Society (ATS) have collaborated to provide recommendations to clinicians concerning ventilator liberation.

Methods: Comprehensive evidence syntheses, including meta-analyses, were performed to summarize all available evidence relevant to the guideline panel's questions. The evidence was appraised using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach and the results were summarized in evidence profiles. The evidence syntheses were discussed and recommendations developed and approved by a multi-disciplinary committee of experts in mechanical ventilation.

Results: Recommendations for three PICO (population, intervention, comparator, outcome) questions concerning ventilator liberation are presented in this document. The guideline panel considered the balance of desirable (benefits) and undesirable consequences (burdens, adverse effects, costs), quality of evidence, feasibility, and acceptability of various interventions with

respect to the selected questions. Conditional (weak) recommendations were made to use inspiratory pressure augmentation in the initial spontaneous breathing trial (SBT), and to use protocols to minimize sedation, for patients ventilated for more than 24 hours. A strong recommendation was made to use preventative non-invasive ventilation (NIV) for high-risk patients ventilated for more than 24 hours immediately after extubation to improve selected outcomes. The recommendations were limited by the quality of the available evidence.

Conclusion: The guideline panel provided recommendations for inspiratory pressure augmentation during an initial SBT, protocols minimizing sedation, and preventative NIV, in relation to ventilator liberation.

SUMMARY OF RECOMMENDATIONS

1. **For acutely hospitalized patients ventilated more than 24 hours, we suggest that the initial SBT be conducted with inspiratory pressure augmentation (5-8 cm H_2O) rather than without (T-piece or CPAP).** (Conditional recommendation, Moderate quality evidence)
   Remarks: This recommendation relates to how to conduct the initial SBT, but does not inform how to ventilate prolonged weaning patients between SBTs.

2. **For acutely hospitalized patients ventilated for more than 24 hours, we suggest protocols attempting to minimize sedation.** (Conditional recommendation, Low quality of evidence)
   *Remarks***:** There is insufficient evidence to recommend any protocol over another.

3. **For patients at high risk for extubation failure who have been receiving mechanical ventilation for more than 24 hours, and who have passed an SBT, we recommend extubation to preventative NIV** (Strong recommendation, moderate quality of evidence).
   *Remarks***:** Patients at high risk for failure of extubation may include those patients with hypercapnia, COPD, CHF, or other serious co-morbidities. Physicians may choose to

avoid extubation to NIV in selected patients for patient-specific factors including but not limited to the inability to receive ventilation through a mask or similar interface. Physicians who choose to use NIV should apply such treatment immediately after extubation to realize the outcome benefits.

INTRODUCTION

Mechanical ventilation is a life-saving intervention, but it is also associated with complications. Therefore, it is desirable to liberate patients from mechanical ventilation as soon as the underlying cause that led to the mechanical ventilation has sufficiently improved and the patient is able to sustain spontaneous breathing and adequate gas exchange. This clinical practice guideline provides evidence-based recommendations on 3 specific ventilator liberation techniques. The guidelines were a collaborative effort between the American Thoracic Society (ATS) and the American College of Chest Physicians (CHEST). Development of the guidelines followed systematic reviews of the literature and use of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework to develop recommendations. The guidelines address the following questions:

Question #1: In acutely hospitalized patients ventilated more than 24 hours, should the spontaneous breathing trial (SBT) be conducted with or without inspiratory pressure augmentation?

Question #2: In acutely hospitalized patients ventilated for more than 24 hours, do protocols attempting to minimize sedation compared to approaches that do not attempt to minimize sedation impact duration of ventilation, duration of ICU stay and short-term mortality (60 days)?

Question #3: In high-risk patients receiving mechanical ventilation for more than 24 hours who have passed an SBT, does extubation to preventative non-invasive ventilation (NIV) compared to no NIV have a favorable effect on duration of ventilation, ventilator-free days, extubation

success (liberation > 48 hours), duration of intensive care unit (ICU) stay, short-term mortality (60 days), or long-term mortality?

This guideline is the companion to another guideline that is being published separately and addresses questions related to physical rehabilitation protocols, ventilator liberation protocols, and cuff leak test.[1] Neither guideline is intended to impose a standard of care. They provide the basis for rational decisions in the liberation of patients from mechanical ventilation. Clinicians, patients, third-party payers, stakeholders, or the courts should not view the recommendations contained in these guidelines as dictates. Guidelines cannot take into account all of the often compelling unique individual clinical circumstances. Therefore, no one charged with evaluating clinicians' actions should attempt to apply the recommendations from these guidelines by rote or in a blanket fashion.

METHODS

Expert Panel Composition

CHEST's Professional Standards Committee (PSC), Guidelines Oversight Committee (GOC), and the ATS's Document Development and Implementation Committee (DDIC) selected and approved the co-chairs of the panel. Prospective panelists were selected by the co-chairs based on their expertise relative to the proposed guideline questions. The panelists were reviewed by representatives from both the American Thoracic Society and CHEST for possible conflicts of interest and credentials. The GOC then reviewed all panelists for final approval. The final panel consisted of the six co-chairs and fourteen panelists, who were then divided among 6 topic groups as content experts for their particular area of expertise.

Conflicts of Interest

All panel nominees were reviewed and vetted by a joint conflict of interest (COI) review committee composed of members from the ATS and CHEST. After review, nominees who were found to have no substantial COI were approved, while nominees with potential intellectual and financial conflicts of interest that were considered to be manageable were "approved with

management." Panelists who were approved with management were prohibited from participating in discussions or voting on recommendations in which they had substantial conflicts of interest. We created a grid associating panelists' COI with relevant PICO questions for use during voting. The COI grid can be found in the supplemental materials on the CHEST journal website [provide link].

The final panel consisted of the 6 co-chairs (TDG, JPK, PEM, DRO, GAS, and JDT), 7 pulmonary/critical care physicians, 4 critical care physicians, 1 critical care nurse, 1 physical therapist, and 1 critical care pharmacist. The panel worked with two methodologists (WA, SP), one of whom is also a critical care physician.

Formulation of Key Questions and Outcome Prioritization

The six co-chairs drafted a total of 6 key clinical questions in a PICO (Population, Intervention, Comparator, Outcome) format (Table 1). The co-chairs were asked to rate the outcomes to be used for all six questions numerically on a scale of 1-9, according to the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) Working Group's three categories of outcomes for decision-making (1-3 – not important; 4-6 – important; 7-9 – critical). We used the co-chairs' average score for each outcome to determine the outcome category, and we only assessed the outcomes rated as "critical" or "important".

Systematic Literature Searches

All panelists reviewed the PICO questions and with the help of the methodologist, finalized the search terms, inclusion and exclusion criteria, and databases that would be searched.

The methodologist performed a systematic search of the literature for relevant systematic reviews and individual studies in December 2014 using the following databases: MEDLINE via PubMed, the Cochrane Library, and CINAHL. Searches were conducted using a combination of the National Library of Medicine's Medical Subject Headings (MeSH) and other key words specific to each topic. Reference lists from relevant retrievals were also searched, and additional papers were manually added to the search results. To account for all of the literature pertaining to each topic, searches were not limited by language, study design, or publication date.

Additional details on literature searches and the selection of studies can be found in the supplemental materials on the CHEST website [provide link].

Study Selection and Data Extraction

Studies retrieved from the completed literature searches were then reviewed for relevance through two rounds of screening. Two reviewers excluded studies that did not meet the inclusion criteria based on title or abstract. We retrieved studies that met the inclusion criteria for full text review to determine their final inclusion. In both rounds of screening, studies were reviewed independently by two reviewers. Disagreements were resolved through discussion or by a third reviewer if required.

We extracted relevant data from each eligible study into structured data tables. One panelist performed the data extraction and another panelist independently reviewed the extracted data. Discrepancies were resolved by discussion. A discrepancy resolution plan employing a third reviewer was in place but never invoked.

Risk of Bias Assessment

The methodologist assessed the risk of bias of all included studies. We used the Cochrane Risk of Bias tool to assess risk of bias for randomized controlled trials (RCTs).[2] We used the Documentation and Appraisal Review Tool (DART) to assess the quality of systematic reviews when applicable.[3]

Meta-Analyses

When individual studies were available or a meta-analysis needed to be updated, we used the Cochrane Collaboration Review Manager, version 5.2[4] to pool the results across individual studies. We used a random-effects model and the method of DerSimonian and Laird to pool the individual estimates.[5] Relative risk (RR) was used to report the results for dichotomous outcomes and mean difference (MD) for continuous outcomes with accompanying 95% confidence intervals (CI). Statistical heterogeneity of the pooled results was assessed using the Higgins' I^2 and the Chi-square tests. A Higgins'I^2 value of $\geq$50% or Chi-square $p<0.05$ was considered to represent significant heterogeneity.

Assessing the Certainty of Evidence

We assessed the overall certainty of the evidence for each outcome of interest using the GRADE approach.[6] Evidence profiles were created using the Guideline Development Tool (GDT), which categorized the overall quality of the body of evidence into one of four levels: high, moderate, low, or very low. Each level represents the confidence in the estimated effects for a specific question (Table 2). Panel members in each group reviewed the evidence profiles and provided input and feedback.

Recommendations

The panel developed recommendations for each of the PICO questions based on the GRADE evidence profiles. We used the Evidence to Decision (EtD) framework to guide the discussions that ultimately led to the development of a recommendation. Panel members made decisions regarding the balance between benefits and harm, impact of patients' values and preferences, cost, health equity, feasibility, and acceptability of the intervention. Pertinent points were recorded during the discussion process. The advantage of using the EtD framework was to facilitate the discussion and to ensure that all important categories were discussed before formulating the recommendation.

Recommendations were graded using the GRADE approach.[7] The recommendations were either "strong" or "conditional" (weak) according to this approach. Strong recommendations use the wording "we recommend" and conditional recommendations are worded using "we suggest". The implications of the strength of recommendation are summarized in Table 3.

Consensus Development

The guideline panel met through online webinars multiple times to work through the EtD and develop recommendations for each PICO question. Because all panel members were not able to attend every webinar, all drafted recommendations were presented again to the full panel in an

online anonymous voting survey in order to reach consensus and gather feedback from those unable to participate. Panelists were requested to indicate their level of agreement on each recommendation based on a 5-point Likert scale derived from the GRADE grid.[8,9] Panelists were also invited to provide feedback on each recommendation with suggestions for rewording. Conflicted panelists (per the terms of management) were not permitted to vote on the related recommendation. No panelists had conflicts that required exclusion from voting. Approval of each recommendation required, by CHEST policy, a 75% voting participation rate and an 80% consensus. Any recommendation that did not meet these criteria was revised by the panel based on the feedback and a new survey that incorporated those revisions was completed.

Peer Review Process

Reviewers from the GOC, the CHEST Board of Regents (BOR) and the *CHEST* journal reviewed the content and methods, including consistency, accuracy and completeness. The manuscript was revised after consideration by the panel of the feedback received from the peer reviewers.

RESULTS

Question #1: In acutely hospitalized patients ventilated more than 24 hours, should the spontaneous breathing trial (SBT) be conducted with or without inspiratory pressure augmentation?

Background: Clinicians tend to underestimate the capacity of patients to breathe successfully when disconnected from the ventilator, as shown by two large weaning trials.[10,11] Moreover, weaning predictors such as maximal inspiratory pressure, static respiratory system compliance, and rapid-shallow breathing index, lack sufficient positive and negative predictive value to make them routinely useful for judging patients' ability to wean. Once patients meet several readiness

criteria, a preferred approach is to conduct a spontaneous breathing trial (SBT) involving little or no ventilator support. If the SBT provokes signs of respiratory failure, ventilation is resumed but, if it does not, the clinician may move towards extubation.

The SBT can be conducted using no inspiratory pressure augmentation (T-piece or CPAP) or with modest inspiratory pressure augmentation (pressure support, generally limited to 5-8 cm H_2O, or automatic tube compensation [ATC]). On the one hand, it could be argued that the patient demonstrating ability to breathe while receiving no inspiratory pressure augmentation has convincingly shown weaning readiness (i.e., this result may be very specific, but may not be sensitive). On the other hand, some patients failing an SBT without pressure augmentation might pass with pressure support, and some of these may be safely extubated (i.e., this result may be more sensitive, but less specific). There is no consensus as to how to conduct the SBT, leading to differing approaches across ICUs.

Summary of the evidence: We conducted a systematic review that identified four relevant trials and these formed the evidence base that served to guide the panel's recommendations.[12-15] All were prospective and randomized, and three were single-center trials. Three of the trials enrolled patients from mixed medical-surgical ICUs, whereas one trial enrolled from a medical ICU.[13] In all trials, patients had to be judged clinically stable and ready for weaning to be considered for study participation. For the spontaneous breathing trial (SBT), subjects were allocated to T-piece breathing (no pressure augmentation) or to a modest level of pressure support (pressure augmentation) for a period of 30 minutes to 2 hours. The amount of pressure support provided was 5, 7, or 8 cm H_2O or via automatic tube compensation (which provides inspiratory pressure support to overcome with work of breathing imposed by the artificial airway).

The SBT was terminated if the patient exhibited signs of poor tolerance; otherwise, the SBT was considered successful ("successful SBT"). When the SBT was successful, the patient was extubated at the end of the time period and provided supplemental oxygen. "Extubation success" was defined as not requiring reintubation or non-invasive ventilation in the next 48 hours.

Three trials provided information regarding the frequency of successful SBTs.[12-14] Extubation success could be assessed in all four trials whereas only two trials reported ICU mortality.[12-14] When the trials were pooled via meta-analysis, conducting the SBT with pressure augmentation was more likely to be successful (84.6% vs 76.7%; RR 1.11, 95% CI 1.02-1.18); produced a

higher rate of extubation success (75.4% vs 68.9%; RR 1.09, 95% CI 1.02-1.18); and was associated with a trend towards lower ICU mortality (8.6% vs 11.6%; RR 0.74, 95% CI 0.45-1.24) (Table 4).

There are several limitations to the studies used for analysis. The clinicians in the studies were unblinded to SBT technique. In addition, the total number of subjects in the trials was small and three of the four trials were performed in a single center. The mixed ICU populations from which study subjects were drawn limit our confidence when applying these results to individual patients. This is especially the case in subsets that accounted for only a small minority of all patients studied (e.g., those with respiratory failure due to neuromuscular disease). Finally, study patients were those undergoing their first SBT thus limiting generalizations to those who have failed one or more previous SBTs.

The evidence used to guide this recommendation was of moderate confidence for SBT and extubation success, but of low certainty for ICU mortality (Table 4). We considered but did not include for meta-analysis, one additional trial that conducted the SBT initially using T-piece and, if that failed, extended the duration using pressure support of 7 cm H_2O for 30 minutes.[16] If the SBT with pressure augmentation was successful, patients were extubated. Of all enrolled subjects (n=118), 31 failed the SBT without pressure augmentation but 21 of these were successful following pressure augmentation and were extubated. The rates of extubation success were similar in those who passed the SBT without pressure augmentation and those who failed initially but passed when pressure augmentation was added, further supporting our recommendation.

The panel judged that the desirable consequences of conducting the SBT with pressure augmentation outweighed any potential undesirable consequences. This judgment was based on the success of the SBT conducted with pressure augmentation as well as the high rate of extubation success associated with the intervention.

CHEST/ATS Recommendation: For acutely hospitalized patients ventilated more than 24 hours, we suggest that the initial SBT be conducted with inspiratory pressure augmentation (5-8 cm H_2O) rather than without (T-piece or CPAP). (Conditional recommendation, Moderate quality evidence).

Remarks: This recommendation relates to how to conduct the initial SBT, but does not inform how to ventilate prolonged weaning patients between SBTs.

Values and Preferences: This recommendation places a high value on reducing the duration of mechanical ventilation and maximizing the probability of extubation success.

Question #2: In acutely hospitalized patients ventilated for more than 24 hours, do protocols attempting to minimize sedation compared to approaches that do not attempt to minimize sedation impact duration of ventilation, duration of ICU stay, and short-term mortality (60 days)?

Background: Mechanically ventilated patients often receive sedative and analgesic drugs for a variety of reasons. These drugs have the potential to alter mental status and suppress respiratory drive. Accordingly, it is conceivable that these pharmacological effects may impede liberation from mechanical ventilation. Strategies to minimize the effects of these drugs (e.g. bedside nursing sedation algorithms, daily sedative interruption) have been used for several decades. We sought to review the published evidence evaluating the utility of sedation minimization strategies on duration of ventilation, duration of ICU stay and short-term mortality (60 days).

Summary of the evidence: We performed a systematic review that included six relevant trials.[17-22] These six trials formed the evidence base that was used to inform the guideline panel's judgment. All were unblinded, randomized trials that compared protocols that minimized sedation to cohorts of patients that were not managed with such protocols. Three studies used nursing sedation algorithms and three used protocols for daily sedative interruption. The studies included patients from both medical and surgical ICUs. For the outcomes of duration of ventilation and duration of ICU stay, all six trials had relevant data. For the outcome of short-term mortality, only three of the studies had relevant data.[17,19,20]

The outcome of duration of mechanical ventilation was assessed by the group to be of critical importance. Six trials were pooled via meta-analysis for the outcome of duration of mechanical ventilation (695 patients received protocolized sedation, 699 patients received no protocolized sedation). The six studies were judged to have serious risk of bias. The majority of studies did not blind patients, personnel or outcome assessors. Additionally, protocol adherence was not

measured or reported in the majority of studies. They were also noted to have serious levels of inconsistency and imprecision (i.e. wide confidence intervals around the absolute effect). Accordingly, the evidence was noted to be of very low quality.

Six trials were pooled via meta-analysis for the outcome of ICU length of stay (695 patients received protocolized sedation, 699 patients received no protocolized sedation). This outcome was noted by the group to be of critical importance. The six studies were noted to have serious risk of bias. They were also noted to have serious levels of inconsistency and imprecision. Accordingly, the evidence was noted to be of very low quality.

Six trials were pooled via meta-analysis for the outcome of short-term mortality (203/695 mortality with protocolized sedation, 217/699 mortality with no protocolized sedation). This outcome was noted by the group to be of critical importance. The six studies were noted to have serious risk of bias. In contrast to the previous two PICO outcome questions, the levels of inconsistency and imprecision were not noted to be serious. Accordingly, the evidence was noted to be of moderate quality.

The summary of the pooled evidence showed no significant difference in the duration of mechanical ventilation in the protocolized sedation group (mean difference 1.00 day shorter; 95% CI-2.14 to 0.14)(Table 5). The summary of the pooled evidence showed a shorter ICU length of stay in the protocolized sedation group (mean difference 1.78 days shorter; 95% confidence intervals -3.41 to -0.14). The summary of the pooled evidence showed no significant difference in short-term mortality in the protocolized sedation group (RR 0.93; 95% confidence intervals 0.77 to 1.11; p = 0.42).

An important limitation of the evidence subjected to meta-analysis was the wide variation in management of the control groups across the six studies. Those studies demonstrating no benefit of protocolized sedation strategies tended to have lighter levels of sedation in the control groups compared to those that did demonstrate a benefit.

Two studies that may inform practitioners concerning sedation strategies were not included in the analysis. One study that randomized 430 patients receiving mechanical ventilation to either a sedation protocol or to a sedation protocol plus daily sedation interruption demonstrated no difference in the duration of mechanical ventilation or in ICU length of stay.[23] In a different

approach, Strom and colleagues enrolled 140 patients receiving mechanical ventilation in a study that assigned patients to receive no sedation as the study intervention, compared with a sedation protocol with daily sedation interruption.[24] Of the patients who were alive and receiving mechanical ventilation after 48 hours, patients in the "no sedation" group had more ventilator free days, and a shorter ICU stay, than did those receiving daily sedation interruption. These studies were not included in the analysis because their intervention and comparator treatments did not match those stipulated by the PICO question.

Despite the limitations of the evidence, the panel judged the desirable effects of sedation protocols aimed at minimizing sedation (shorter duration of ICU stay and possible trend of reduced duration of ventilation) to outweigh the undesirable effects associated with not minimizing sedation in ventilated patients.

CHEST/ATS Recommendation: For acutely hospitalized patients ventilated for more than 24 hours, we suggest protocols attempting to minimize sedation. (Conditional recommendation, Low quality of evidence).

Remarks: There is insufficient evidence to recommend any protocol over another.

Values and Preferences: This recommendation places a high value on reducing mechanical ventilation duration and ICU length of stay, and views the burden of protocolized sedation as very low.

Question #3: In high-risk patients receiving mechanical ventilation for more than 24 hours who have passed an SBT, does extubation to preventative NIV compared to no NIV have a favorable effect on duration of ventilation, ventilator-free days, extubation success (liberation > 48 hours), duration of intensive care unit (ICU) stay, short-term mortality (60 days), or long-term mortality?

Background: Patients intubated for acute respiratory failure are at increased risk for complications including infection and multi-system organ failure.[25] The risk for complications and mortality rises with increasing duration of mechanical ventilation, as do the associated health care costs.[26] Delaying endotracheal tube removal in patients who otherwise appear ready for extubation adversely affects outcome by increasing the risk for pneumonia and the length of ICU and hospital stay when compared to patients extubated in a timely manner.[27] Conversely, studies

have found that patients requiring re-intubation (extubation failure) after satisfactorily tolerating an SBT have increased risk for complications, prolonged hospital stay and significantly increased mortality.[28]

NIV improves outcomes in patients with acute respiratory failure. Application of NIV to patients suffering from respiratory failure due to acute exacerbations of chronic obstructive pulmonary disease (COPD) reduces the need for intubation, the frequency of complications, the hospital length of stay, and the mortality rate compared to standard therapy.[29] Patients with acute cardiogenic pulmonary edema and respiratory failure have a more rapid improvement in respiratory distress, hypercapnia, metabolic acidosis, and reduction in intubation rate when NIV is employed compared with oxygen therapy alone.[30] The use of NIV in immunocompromised hosts with diffuse pulmonary infiltrates reduces the intubation rate as well as ICU and hospital mortality.[31]

While there has been considerable support for the use of NIV in selected groups of patients presenting with respiratory failure, the results have been less well defined for the application of NIV to patients following extubation. In one randomized trial in 221 patients who developed respiratory failure a mean of 9 hours after extubation, NIV was not effective in reducing the need for re-intubation and was associated with a higher ICU mortality rate in comparison with standard medical therapy (including supplemental oxygen and bronchodilators) in at-risk patients who had been extubated following a successful spontaneous breathing trial but subsequently developed respiratory failure.[32] In contrast, other trials show that NIV applied immediately after extubation may reduce re-intubation rates in critically ill patients, with meta-analyses of these studies indicating that duration of MV, ventilator-associated pneumonia, ICU length of stay, hospital length of stay, and mortality may also be improved.[33,34] We examined available data on the use of NIV immediately after extubation for ventilated patients who had passed an SBT and were at high risk of extubation failure to determine the effect of this treatment on the need for re-intubation, ICU length of stay, and short- and long-term mortality.

Summary of the evidence: Five randomized, controlled trials (RCT) met criteria for our assessment of the data. Nava and colleagues randomized 97 high-risk patients who were extubated following successful SBT to receive either NIV or standard care one hour after extubation.[35] High-risk patients were those who failed more than one SBT, had a $PaCO_2$>45 mm

Hg after extubation, more than one co-morbid condition, a weak cough, or upper airway stridor that did not require immediate re-intubation. The NIV group had a reduced need for re-intubation (4/48 v 12/49, p=0.027) and a reduction in ICU mortality (3/48 v 9/49, p<0.01).

Ferrer and colleagues randomized 162 patients to non-invasive ventilation or standard care after extubation.[36] Patients were selected following a successful SBT if they had risk factors for re-intubation defined as: age>65 years, cardiac failure as a cause for respiratory failure, or an APACHE II score greater than 12 on the day of extubation. Patients receiving NIV had reduced re-intubation rates (13/79 v 27/83, p=0.029) and ICU mortality (2/79 v 12/83, p=0.015), but not ICU length of stay or long-term mortality. Of interest, those patients who were hypercapnic during the SBT had reduced ICU mortality if they received NIV compared with standard care post-extubation (0/27 v 4/22, p=0.035). In follow-up, Ferrer and colleagues randomized 106 mechanically ventilated patients who had hypercapnia with a PaCO2>45 mm Hg during a successful SBT to post-extubation NIV or conventional oxygen treatment.[37] Respiratory failure defined by predetermined criteria was more frequent in the conventional oxygen group than in the NIV group (25/52 v 8/54, p<0.0001). Re-intubation rates, ICU length of stay, and ICU mortality rates were not statistically different between the groups, which was attributed to the fact that NIV was used as a "rescue strategy" in those patients developing respiratory failure. Mortality at 90 days, a secondary endpoint for this study, was lower in the patients receiving NIV than in the patients receiving conventional oxygen treatment (6/54 v 16/52, p=0.0244).

Khilnani et al. studied 40 patients with an acute exacerbation of COPD requiring mechanical ventilation.[38] After passing a weaning assessment, patients were randomized to receive NIV immediately following extubation versus conventional therapy, with no significant difference found between groups in terms of re-intubation or ICI length of stay. Mohamed and Abdalla examined outcomes in 120 patients randomized to NIV or an oxygen mask.[39] They found that patients treated with NIV had reduced ICU mortality (6.6% v16.6%, p<0.035) and re-intubation rates (15% v 25%, p=0.04) when compared with controls.

In assessing the aggregate data, all 5 studies noted above addressed extubation success. NIV was favored over standard care in high-risk patients following extubation (RR=1.14; 95% CI: 1.05-1.23) (Table 6). Four studies[35-37,39] examined the outcomes of ICU length of stay and short-term mortality, with the finding that NIV was significantly better than conventional therapy for each

outcome (ICU LOS: mean difference -2.48 days, 95% CI -4.03 to -0.93; short-term mortality: RR=0.37, 95% CI 0.19-0.70). Two studies[36,37] demonstrated significantly lower long-term mortality with NIV as compared with standard care in high-risk patients following extubation (RR=0.58, 95% CI 0.27-1.22). There was heterogeneity between studies in defining the high risk patient. Risk factors included a variety of co-morbidities to include COPD, CHF, hypercapnia, older age, and a higher severity of illness. Patients under 65 years of age, who pass their first SBT, have a normal pCO_2, have no significant respiratory or cardiac co-morbidities, and can protect their airway, would be considered to be at low risk for re-intubation in all of the included studies.

Two studies suggest that high-flow nasal cannula may improve patient outcomes after extubation in patients receiving mechanical ventilation. Maggiore and colleagues assigned 105 patients mechanically ventilated for more than 24 hours to either a Venturi mask or nasal high-flow therapy after extubation.[40] Patients receiving high-flow nasal therapy were less likely to be re-intubated than those patients receiving treatment by Venturi mask (4% v 21%, p=0.01). Hernandez and colleagues treated 264 patients receiving mechanical ventilation at low risk for re-intubation after extubation with a high-flow nasal cannula, and compared this group with 263 patients receiving conventional oxygen therapy.[41] Patients receiving high-flow nasal cannula treatment had less respiratory failure (22/264 v 38/263, p=0.03) and a lower rate of re-intubation at 72 hours (13/264 v 32/263, p=0.004). These studies became available after the literature search was conducted, but may inform clinicians about post-extubation strategies similar to preventative NIV.

The panel judged the desirable consequences of extubation to preventative NIV to clearly outweigh the undesirable consequences. The desirable consequences considered by the panel included improved extubation success as well as a 2-day reduction of ICU length of stay. The panel noted that potential undesirable consequences of NIV include nasal bridge damage, conjunctivitis, and nasal ulceration. However, the desirable consequences outweigh these potential harms.

CHEST/ATS Recommendation: For patients at high risk for extubation failure who have been receiving mechanical ventilation for more than 24 hours, and who have passed a spontaneous

breathing trial, we recommend extubation to preventative NIV (Strong recommendation, moderate grade of evidence).

Remarks: Patients at high risk for failure of extubation may include those patients with hypercapnia, COPD, CHF, or other serious co-morbidities. Physicians may choose to avoid extubation to NIV in selected patients for patient-specific factors including but not limited to the inability to receive ventilation through a mask or similar interface. Physicians who choose to use NIV should apply such treatment immediately after extubation to realize the outcome benefits.

Values and Preferences: This recommendation places a high value on early extubation which will lead to substantial benefits including a reduction in ventilator-related and ICU-related complications, and to reductions in health care costs accruing from reduction in ICU stay.

SUMMARY

These clinical practice guidelines include a strong recommendation that patients who are at high risk for extubation failure and who have passed a spontaneous breathing trial be extubated to preventative NIV. Moderate quality evidence exists that clinically important outcomes are improved by this strategy. Conditional recommendations are to use inspiratory pressure augmentation during the initial SBT, and to employ protocols to minimize sedation, in patients ventilated for more than 24 hours. The latter two recommendations are limited by the quality of the available evidence. As further research becomes available, these recommendations will be readdressed and updated.

REFERENCES

1. Girard TD, Al-Hazzani W, Kress JP, et al. Liberation from Mechanical Ventilation: An Official American Thoracic Society / American College of Chest Physicians Clinical Practice Guideline. Cuff Leak Test, Physical Therapy Protocols, and Ventilator

Liberation Protocols. *American Journal ofRrespiratory and Critical Care Medicine.* 2016;in press.

2. Higgins J, Altman D, Sterne J, (editors). Chapter 8: Assessing risk of bias in included studies. In: Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from http://www.cochrane-handbook.org. 2011.
3. Diekember RL, Ireland BK, Merz LR. Development of the Documentation and Appraisal Review Tool for systematic reviews. *World J Meta-Anal.* 2015;3(3):142-150.
4. *Review Mangaer (RevMan)* [computer program]. Version 5.2. Copenhagen: The Nordic Cochrane Center, The Cochrane Collaboration; 2014.
5. Higgins J, Altman D, Sterne J, (editors). Chapter 9: Analysing data and undertaking meta-analyses. In: Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from http://www.cochrane-handbook.org. 2011.
6. Balshem H, Helfand M, Schünemann HJ, et al. GRADE guidelines: 3. Rating the quality of evidence. *Journal of Clinical Epidemiology.*64(4):401-406.
7. Andrews J, Guyatt G, Oxman AD, et al. GRADE guidelines: 14. Going from evidence to recommendations: the significance and presentation of recommendations. *Journal of Clinical Epidemiology.*66(7):719-725.
8. Jaeschke R, The GRADE Working Group. Use of GRADE grid to reach decisions on clinical practice guidelines when consensus is elusive. *BMJ.* 2008;337:327-330.
9. Lewis SZ, Diekemper R, Ornelas J, Casey KR. Methodologies for the development of CHEST guidelines and expert panel reports. *Chest.* 2014;146(1):182-192.
10. Brochard L, Rauss A, Benito S, et al. Comparison of three methods of gradual withdrawal from ventilatory support during weaning from mechanical ventilation. *American journal of respiratory and critical care medicine.* 1994;150(4):896-903. http://www.atsjournals.org/doi/abs/10.1164/ajrccm.150.4.7921460?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%3dpubmed.
11. Esteban A, Frutos F, Tobin MJ, et al. A comparison of four methods of weaning patients from mechanical ventilation. Spanish Lung Failure Collaborative Group. *The New England Journal of Medicine.* 1995;332(6):345-350.
12. Esteban A, Alia I, Gordo F, et al. Extubation outcome after spontaneous breathing trials with T-tube or pressure support ventilation. The Spanish Lung Failure Collaborative Group. *Am J Respir Crit Care Med.* 1997;156(2 Pt 1):459-465.
13. Haberthur C, Mols G, Elsasser S, Bingisser R, Stocker R, Guttmann J. Extubation after breathing trials with automatic tube compensation, T-tube, or pressure support ventilation. *Acta Anaesthesiologica Scandinavica.* 2002;46(8):973-979.
14. Matić I, Majerić-Kogler V. Comparison of pressure support and T-tube weaning from mechanical ventilation: randomized prospective study. *Croatian Medical Journal.* 2004;45(2):162-166. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/802/CN-00467802/frame.html.
15. Zhang B, Qin YZ. Comparison of pressure support ventilation and T-piece in determining rapid shallow breathing index in spontaneous breathing trials. *The American Journal of the Medical Sciences.* 2014;348(4):300-305.

16. Ezingeard E, Diconne E, Guyomarc'h S, et al. Weaning from mechanical ventilation with pressure support in patients failing a T-tube trial of spontaneous breathing. *Intensive Care Medicine.* 2006;32(1):165-169.
17. Anifantaki S, Prinianakis G, Vitsaksaki E, et al. Daily interruption of sedative infusions in an adult medical-surgical intensive care unit: randomized controlled trial. *Journal of Advanced Nursing.* 2009;65(5):1054-1060.
18. Brook AD, Ahrens TS, Schaiff R, et al. Effect of a nursing-implemented sedation protocol on the duration of mechanical ventilation. *Critical Care Medicine.* 1999;27(12):2609-2615.
19. Bucknall TK, Manias E, Presneill JJ. A randomized trial of protocol-directed sedation management for mechanical ventilation in an Australian intensive care unit. *Critical Care Medicine.* 2008;36(5):1444-1450.
20. 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. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/227/CN-00622227/frame.html http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(08)60105-1/abstract.
21. Kress JP, Pohlman AS, O'Connor MF, Hall JB. Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. *New England journal of medicine.* 2000;342(20):1471-1477. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/747/CN-00277747/frame.html http://www.nejm.org/doi/pdf/10.1056/NEJM200005183422002.
22. Mansouri P, Javadpour S, Zand F, et al. Implementation of a protocol for integrated management of pain, agitation, and delirium can improve clinical outcomes in the intensive care unit: a randomized clinical trial. *Journal of Critical Care.* 2013;28(6):918-922.
23. Mehta S, Burry L, Cook D, et al. Daily sedation interruption in mechanically ventilated critically ill patients cared for with a sedation protocol: a randomized controlled trial. *Jama.* 2012;308(19):1985-1992.
24. Strom T, Martinussen T, Toft P. A protocol of no sedation for critically ill patients receiving mechanical ventilation: a randomised trial. *Lancet.* 2010;375(9713):475-480.
25. Esteban A, Anzueto A, Frutos F, et al. Characteristics and outcomes in adult patients receiving mechanical ventilation: a 28-day international study. *Jama.* 2002;287(3):345-355.
26. Dasta JF, McLaughlin TP, Mody SH, Piech CT. Daily cost of an intensive care unit day: the contribution of mechanical ventilation. *Critical Care Medicine.* 2005;33(6):1266-1271.
27. Coplin WM, Pierson DJ, Cooley KD, Newell DW, Rubenfeld GD. Implications of extubation delay in brain-injured patients meeting standard weaning criteria. *Am J Respir Crit Care Med.* 2000;161(5):1530-1536.
28. Epstein SK, Ciubotaru RL, Wong JB. Effect of failed extubation on the outcome of mechanical ventilation. *Chest.* 1997;112(1):186-192.

29. Brochard L, Mancebo J, Wysocki M, et al. Noninvasive ventilation for acute exacerbations of chronic obstructive pulmonary disease. *The New England Journal of Medicine.* 1995;333(13):817-822.
30. Gray A, Goodacre S, Newby DE, Masson M, Sampson F, Nicholl J. Noninvasive ventilation in acute cardiogenic pulmonary edema. *The New England Journal of Medicine.* 2008;359(2):142-151.
31. Hilbert G, Gruson D, Vargas F, et al. Noninvasive ventilation in immunosuppressed patients with pulmonary infiltrates, fever, and acute respiratory failure. *The New England Journal of Medicine.* 2001;344(7):481-487.
32. Esteban A, Frutos-Vivar F, Ferguson ND, et al. Noninvasive positive-pressure ventilation for respiratory failure after extubation. *The New England Journal of Medicine.* 2004;350(24):2452-2460.
33. Burns KE, Adhikari NK, Keenan SP, Meade M. Use of non-invasive ventilation to wean critically ill adults off invasive ventilation: meta-analysis and systematic review. *BMJ.* 2009;338:b1574.
34. Burns KE, Adhikari NK, Meade MO. A meta-analysis of noninvasive weaning to facilitate liberation from mechanical ventilation. *Canadian journal of anaesthesia = Journal Canadien d'Anesthesie.* 2006;53(3):305-315.
35. Nava S, Gregoretti C, Fanfulla F, et al. Noninvasive ventilation to prevent respiratory failure after extubation in high-risk patients. *Critical Care Medicine.* 2005;33(11):2465-2470.
36. 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.
37. 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.
38. Khilnani GC, Galle AD, Hadda V, Sharma SK. Non-invasive ventilation after extubation in patients with chronic obstructive pulmonary disease: a randomized controlled trial. *Anaesth Intensive Care.* 2011;39:217-223.
39. Mohamed KAE, Abdalla MH. Role of non invasive ventilation in limiting re-intubation after planned extubation. *Egyptian Journal of Chest Diseases and Tuberculosis.* 2013;62(4):669-674.
http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/210/CN-00961210/frame.html
http://ac.els-cdn.com/S0422763813001866/1-s2.0-S0422763813001866-main.pdf?_tid=a51837fe-950e-11e4-8808-00000aab0f26&acdnat=1420485266_dc58e2dc6c19f2b4279d6ee300abd2ac.
40. Maggiore SM, Idone FA, Vaschetto R, et al. Nasal high-flow versus Venturi mask oxygen therapy after extubation. Effects on oxygenation, comfort, and clinical outcome. *Am J Respir Crit Care Med.* 2014;190(3):282-288.
41. Hernandez G, Vaquero C, Gonzalez P, et al. Effect of Postextubation High-Flow Nasal Cannula vs Conventional Oxygen Therapy on Reintubation in Low-Risk Patients: A Randomized Clinical Trial. *JAMA.* 2016;315(13):1354-1361.

Table 1. PICO Questions

Study Characteristic	Inclusion Criteria	Exclusion Criteria
KQ 1: Spontaneous Breathing Trial		
Populations	• Acutely hospitalized patients ventilated for >24 hours	Patients who didn't pass first SBT
Interventions	• SBT conducted with inspiratory pressure augmentation (i.e. pressure support ventilation, automatic tube compensation)	None
Comparators	• SBT conducted without inspiratory pressure augmentation	None
Outcomes	• Duration of ventilation • Ventilator-free days • Extubation Success • Successful SBT • Duration of ICU stay • Short-term mortality (<60 days) • Long-term mortality	None
Study Design	• Systematic Reviews, RCT, Observational	None
KQ 2: Sedation Protocols		
Populations	• Acutely hospitalized patients ventilated for >24 hours	None
Interventions	• Protocolized attempts to seek minimum sedation required	None
Comparators	• An approach that does not seek to minimize sedation	None
Outcomes	• Duration of ventilation • Ventilator-free days • Extubation Success • Duration of ICU stay • Short-term mortality (<60 days) • Long-term mortality	None
Study Design	• Systematic Reviews, RCT	None
KQ 3: Extubation to non-invasive ventilation		
Populations	• Patients ventilated for >24 hours, who have passed an SBT, but are at high risk for extubation failure	None
Interventions	• Extubation to preventative non-invasive ventilation	None
Comparators	• Extubation without preventative non-invasive ventilation	None
Outcomes	• Duration of ventilation • Ventilator-free days • Extubation Success • Duration of ICU stay • Short-term mortality (<60 days) • Long-term mortality	None
Study Design	• Systematic Reviews, RCT, Observational	None

Table 2. Quality of Evidence Grades

Grade	Definition
High	We are very confident that the true effect lies close to that of the estimate of the effect
Moderate	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very Low	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Table 3. Implications of strong and weak (conditional) recommendations for different users of guidelines

	Strong Recommendation	**Weak (conditional) Recommendation**
For patients	Most individuals in this situation would want the recommended course of action and only a small proportion would not.	The majority of individuals in this situation would want the suggested course of action, but many would not.
For clinicians	Most individuals should receive the recommended course of action. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.	Recognize that different choices will be appropriate for different patients, and that you must help each patient arrive at a management decision consistent with her or his values and preferences. Decision aids may well be useful helping individuals making decisions consistent with their values and preferences. Clinicians should expect to spend more time with patients when working towards a decision.
For policy makers	The recommendation can be adapted as policy in most situations including for the use as performance indicators.	Policy making will require substantial debates and involvement of many stakeholders. Policies are also more likely to vary between regions. Performance indicators would have to focus on the fact that adequate deliberation about the management options has taken place.

Table 4. Evidence Profile for conducting the spontaneous breathing trial with or without inspiratory pressure augmentation

Bibliography: 1) Esteban A, Alia I, Gordo F, et al. Extubation outcome after spontaneous breathing trials with T-tube or pressure support ventilation. The Spanish Lung Failure Collaborative Group. Am J Respir Crit Care Med. 1997;156(2 Pt 1):459-465. 2) Haberthur C, Mols G, Elsasser S, Bingisser R, Stocker R, Guttmann J. Extubation after breathing trials with automatic tube compensation, T-tube, or pressure support ventilation. Acta anaesthesiologica Scandinavica. 2002;46(8):973-979. 3) Matić I, Majerić-Kogler V. Comparison of pressure support and T-tube weaning from mechanical ventilation: randomized prospective study. Croatian medical journal. 2004;45(2):162-166. 4) Zhang B, Qin YZ. Comparison of pressure support ventilation and T-piece in determining rapid shallow breathing index in spontaneous breathing trials. The American journal of the medical sciences. 2014;348(4):300-305.

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**SBT conducted with pressure augmentation**	**without pressure augmentation**	**Relative (95% CI)**	**Absolute (95% CI)**		
Extubation Success												
4	randomised trials	serious [1]	not serious	not serious	not serious	none	312/423 (73.8%)	303/452 (67.0%)	**RR 1.09** (1.02 to 1.18)	60 more per 1000 (from 13 more to 121 more)	MODERATE [1]	CRITICAL
Successful SBT												
3	randomised trials	serious [1]	not serious	not serious	not serious	none	388/488 (79.5%)	331/452 (73.2%)	**RR 1.11** (1.03 to 1.18)	81 more per 1000 (from 22 more to 132 more)	MODERATE [1]	IMPORTANT
Short term Mortality (assessed with: ICU Mortality)												
2	randomised trials	serious [1]	not serious	not serious	serious [2]	none	26/300 (8.7%)	36/307 (11.7%)	**RR 0.74** (0.45 to 1.24)	30 fewer per 1000 (from 28 more to 64 fewer)	LOW [1,2]	IMPORTANT
ICU LOS												

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	SBT conducted with pressure augmentation	without pressure augmentation	Relative (95% CI)	Absolute (95% CI)		
2	randomised trials	serious [3]	not serious	not serious	not serious	none	-/267	not pooled	ICU LOS was reported in 2 trials (Esteban 1997 and Matić 2004) Estimated effects were reported as median values: 270 (235-290) and 331 (292-396) hours observed in SBT with pressure and without pressure, respectively in Matić 2004; Esteban 1997 showed an estimated effect favoring the SBT without pressure (t-tube) with median values of 288 hours and 240 hours for SBT with pressure and t-tube		MODERATE [3]	IMPORTANT

CI: Confidence interval; **RR:** Risk ratio

1. One study with unclear randomization methods, one study with unclear allocation concealment methods, and two studies with unclear report on outcome assessment
2. Low number of events; 95% CI crosses line of no effect
3. Unclear randomization methods and unclear if outcome assessors were blinded in Matic 2004 study

Table 5. Evidence Profile for protocols attempting to minimize sedation compared to no attempt to minimize sedation

Bibliography: 1) Anifantaki S, Prinianakis G, Vitsaksaki E, et al. Daily interruption of sedative infusions in an adult medical-surgical intensive care unit: randomized controlled trial. Journal of advanced nursing. 2009;65(5):1054-1060. 2) Brook AD, Ahrens TS, Schaiff R, et al. Effect of a nursing-implemented sedation protocol on the duration of mechanical ventilation. Critical care medicine. 1999;27(12):2609-2615. 3) Bucknall TK, Manias E, Presneill JJ. A randomized trial of protocol-directed sedation management for mechanical ventilation in an Australian intensive care unit. Critical care medicine. 2008;36(5):1444-1450. 4) 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. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/227/CN-00622227/frame.html http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(08)60105-1/abstract. 5) Kress JP, Pohlman AS, O'Connor MF, Hall JB. Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. New England journal of medicine. 2000;342(20):1471-1477. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/747/CN-00277747/frame.html http://www.nejm.org/doi/pdf/10.1056/NEJM200005183422002. 6) Mansouri P, Javadpour S, Zand F, et al. Implementation of a protocol for integrated management of pain, agitation, and delirium can improve clinical outcomes in the intensive care unit: a randomized clinical trial. Journal of critical care. 2013;28(6):918-922.

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Protocolized sedation**	**no sedation minimization**	**Relative (95% CI)**	**Absolute (95% CI)**		
Duration of Ventilation (assessed with: days)												
6	randomised trials	serious [1]	serious [2]	not serious	serious [3]	none	528	531	-	MD **1 days lower** (2.14 lower to 0.14 higher)	VERY LOW	IMPORTANT
ICU Length of Stay												
6	randomised trials	serious [1]	serious [4]	not serious	serious [3]	none	695	699	-	MD **1.78 days fewer** (3.41 fewer to 0.14 fewer)	VERY LOW	IMPORTANT
Short-term Mortality												
6	randomised trials	serious [1]	not serious	not serious	not serious	none	203/695 (29.2%)	217/699 (31.0%)	**RR 0.93** (0.77 to 1.11)	**22 fewer per 1000** (from 34 more to 71 fewer)	MODERATE	IMPORTANT

CI: Confidence interval; **MD:** Mean difference; **RR:** Risk ratio

1. Majority of studies did not blind patients, personnel or outcome assessors. Additionally, compliance to protocol (intervention) was not reported or measured in a majority of studies, which could possibly effect reported differences between groups
2. I-squared value of 62%
3. Fairly wide confidence intervals around absolute effect
4. I-squared value of 71%

Table 6. Evidence Profile for extubation to non-invasive ventilation compared to extubation without non-invasive ventilation

Bibliography: 1) Nava S, Gregoretti C, Fanfulla F, et al. Noninvasive ventilation to prevent respiratory failure after extubation in high-risk patients. Critical care medicine. 2005;33(11):2465-2470. 2) 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. 3) 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. 4) Khilnani GC, Galle AD, Hadda V, Sharma SK. Non-invasive ventilation after extubation in patients with chronic obstructive pulmonary disease: a randomized controlled trial. Anaesth Intensive Care. 2011;39:217-223. 5) Mohamed KAE, Abdalla MH. Role of non invasive ventilation in limiting re-intubation after planned extubation. Egyptian Journal of Chest Diseases and Tuberculosis. 2013;62(4):669-674.

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Extubation to noninvasive ventilation**	**extubation without noninvasive ventilation**	**Relative (95% CI)**	**Absolute (95% CI)**		
Extubation Success												
5	randomised trials	serious [1]	not serious	not serious	not serious	none	230/261 (88.1%)	204/264 (77.3%)	**RR 1.14** (1.05 to 1.23)	**11 fewer per 100** (from 4 fewer to 18 fewer)	MODERATE	CRITICAL
ICU LOS												
4	randomised trials	serious [1]	not serious	not serious	not serious	none	241	244	-	MD **2.48 days fewer** (4.03 fewer to 0.93 fewer)	MODERATE	IMPORTANT
Short-term Mortality (ICU Mortality)												
4	randomised trials	serious [1]	not serious	not serious	serious [2]	none	12/241 (5.0%)	35/244 (14.3%)	**RR 0.37** (0.19 to 0.70)	**9 fewer per 100** (from 4 fewer to 12 fewer)	LOW	IMPORTANT
Long-term Mortality (follow up: 90 days)												
2	randomised trials	not serious	serious [3]	not serious	serious [4]	none	24/133 (18.0%)	40/135 (29.6%)	**RR 0.58** (0.27 to 1.22)	**12 fewer per 100** (from 7 more to 22 fewer)	LOW	IMPORTANT

CI: Confidence interval; **RR:** Risk ratio; **MD:** Mean difference

1. Unclear randomization methods and allocation concealment in studies. Many studies did not blind outcome assessors or research personnel
2. Low number of events
3. I-squared value of 57%

CHEST® Online Supplement

e-Table 1. COI Grid

Panelist's Name	PICO 1: In acutely hospitalized patients who have been ventilated >24 hours (P), should the spontaneous breathing trial (SBT) be conducted with inspiratory pressure augmentation (I) or no inspiratory pressure augmentation (C)?	PICO 2: Should acutely hospitalized patients who have been ventilated >24 hours (P) receive protocolized attempts to minimize sedation (I) or an approach that does not seek to minimize sedation (C)?	PICO 3: Should patients who have been ventilated >24 hours and passed an SBT, but are at high risk for extubation failure (P), be extubated with immediate non-invasive ventilation (I) or without immediate non-invasive ventilation (C)?	PICO 4: Should mechanically ventilated patients being considered for extubation (P) receive cuff leak test-based management (I) or not (C)?	PICO 5: Should acutely hospitalized patients who have been ventilated >24 hours (P) be managed with physical therapy protocols directed toward early mobilization (I) or be managed without protocolized attempts at early mobilization (C)?	PICO 6: Should acutely hospitalized patients who have been ventilated >24 hours (P) be managed with protocolized liberation (I) or non-protocolized liberation (C)?	All disclosures
Burns, Suzanne, RN, MSN, ACNP, RRT	Copyright for BWAP (Burns Wean Assessment Program);	Copyright for BWAP (Burns Wean Assessment Program);.	Copyright for BWAP (Burns Wean Assessment Program);	Copyright for BWAP (Burns Wean Assessment Program);.	Copyright for BWAP (Burns Wean Assessment Program);	Copyright for BWAP (Burns Wean Assessment Program);	Copyright for BWAP (Burns Wean Assessment Program)
Epstein, Scott, MD, FCCP	No relevant COIs	No relevant COIs	No relevant COIs	No relevant COIs	No relevant COIs	No relevant COIs	Royalties or In-kind Benefits – from the following: UpToDate, Kluwers, Author of several chapters

CHEST® Online Supplement

Esteban, Andres, MD	No relevant COIs	No relevant COIs	No relevant COIs	No relevant COIs	No relevant COIs	No relevant COIs	No COI's to disclose
Fan, Eddy, MD	PSI Foundation Grant Mechanical Ventilation; Nihon Khoden Grant HFOV	No relevant COIs	No relevant COIs	No relevant COIs	CIHR Grant Early Rehabilitation to Institution	PSI Foundation Grant Mechanical Ventilation to Institution; Nihon Khoden Grant HFOV;	PSI Foundation Grant Mechanical Ventilation to Institution; PSI Foundation Grant ECMO to Institution; Nihon Khoden Grant HFOV to Institution; CIHR Grant Early Rehabilitation to Institution; Alung Technologies Inc Speaking Activity; ATS MV in ARDS Guideline Chair; SCCM Scientific Review Committee Chair
Ferrer, Miguel, MD, PhD	No relevant COIs	No relevant COIs	No relevant COIs	No relevant COIs	No relevant COIs	No relevant COIs	No COI's to disclose
Fraser, Giles, PharmD, MCCM	No relevant COIs	No relevant COIs	No relevant COIs	No relevant COIs	No relevant COIs	No relevant COIs	No COI's to disclose

CHEST® Online Supplement

Girard, Timothy, MD	No relevant COIs	Speaking Activity Hospira, Inc.; DSMB data and safety monitoring board; activites occurred within past 3 years but have ended	No relevant COIs	No relevant COIs	No relevant COIs	No relevant COIs	Speaking Activity Hospira, Inc.; DSMB data and safety monitoring board; activites occurred within past 3 years but have ended
Gong, Michelle, MD	NHLBI Grant Lung Injury Prevention; CMS Grant Electronic Interface for acute care; NHLBI Grant Low cost pragmatic trials to institution	NIA Grant Delirium; NHLBI Grant Lung Injury Prevention; CMS Grant Electronic Interface for acute care; NHLBI Grant Low cost pragmatic trials to institution	NHLBI Grant Lung Injury Prevention; CMS Grant Electronic Interface for acute care; NHLBI Grant Low cost pragmatic trials to institution	NHLBI Grant Lung Injury Prevention; CMS Grant Electronic Interface for acute care; NHLBI Grant Low cost pragmatic trials to institution	NHLBI Grant Lung Injury; CMS Grant Electronic Interface for acute care; NHLBI Grant Low cost pragmatic trials to institution	NHLBI Grant Lung Injury Prevention; CMS Grant Electronic Interface for acute care; NHLBI Grant Low cost pragmatic trials to institution	NHLBI Grant Lung Injury Prevention in salary support; CMS Grant Electronic Interface for acute care; NIA Grant Delirium; NHLBI Grant Low cost pragmatic trials to institution

Hough, Catherine, MD	NIH/NHLBI Grant Clinical Research Network for the Treatment of ALI and ARDS; NIH/NBLBI Improving decision making for patients with prolonged mechanical ventilation to institution; University of Washington Grant Insomnia and functional recovery after acute lung injury; PCORI Grant Improving psychological distress among critical illness survivors and their informal; NIH/INI Grant "The Mind USA Study"; NIH/NHLBI Grant "Identifying Effective Strategies to Disclose Prognosis in Patients with ARDS"	NIH/NHLBI Grant Clinical Research Network for the Treatment of ALI and ARDS; NIH/NBLBI Improving decision making for patients with prolonged mechanical ventilation to institution; University of Washington Grant Insomnia and functional recovery after acute lung injury; PCORI Grant Improving psychological distress among critical illness survivors and their informal; NIH/INI Grant "The Mind USA Study"; NIH/NHLBI Grant "Identifying Effective Strategies to Disclose Prognosis in Patients with ARDS"	NIH/NHLBI Grant Clinical Research Network for the Treatment of ALI and ARDS; NIH/NBLBI Improving decision making for patients with prolonged mechanical ventilation to institution; University of Washington Grant Insomnia and functional recovery after acute lung injury; PCORI Grant Improving psychological distress among critical illness survivors and their informal; NIH/INI Grant "The Mind USA Study"; NIH/NHLBI Grant "Identifying Effective Strategies to Disclose Prognosis in Patients with ARDS"	NIH/NHLBI Grant Clinical Research Network for the Treatment of ALI and ARDS; NIH/NBLBI Improving decision making for patients with prolonged mechanical ventilation to institution; University of Washington Grant Insomnia and functional recovery after acute lung injury; PCORI Grant Improving psychological distress among critical illness survivors and their informal; NIH/INI Grant "The Mind USA Study"; NIH/NHLBI Grant "Identifying Effective Strategies to Disclose Prognosis in Patients with ARDS"	NIH/NHLBI Grant Clinical Research Network for the Treatment of ALI and ARDS; NIH/NBLBI Improving decision making for patients with prolonged mechanical ventilation to institution; University of Washington Grant Insomnia and functional recovery after acute lung injury; PCORI Grant Improving psychological distress among critical illness survivors and their informal; NIH/INI Grant "The Mind USA Study"; NIH/NHLBI Grant "Identifying Effective Strategies to Disclose Prognosis in Patients with ARDS"	NIH/NHLBI Grant Clinical Research Network for the Treatment of ALI and ARDS; NIH/NBLBI Improving decision making for patients with prolonged mechanical ventilation to institution; University of Washington Grant Insomnia and functional recovery after acute lung injury; PCORI Grant Improving psychological distress among critical illness survivors and their informal; NIH/INI Grant "The Mind USA Study"; NIH/NHLBI Grant "Identifying Effective Strategies to Disclose Prognosis in Patients with ARDS"	NIH/NHLBI Grant Clinical Research Network for the Treatment of ALI and ARDS; NIH/NBLBI Improving decision making for patients with prolonged mechanical ventilation to institution; University of Washington Grant Insomnia and functional recovery after acute lung injury; PCORI Grant Improving psychological distress among critical illness survivors and their informal; NIH/INI Grant "The Mind USA Study"; NIH/NHLBI Grant "Identifying Effective Strategies to Disclose Prognosis in Patients with ARDS"
Kress, John, MD, FCCP	No relevant COIs	Speaking Activity Hospira	No relevant COIs	No relevant COIs	No relevant COIs	No relevant COIs	Speaking Activity Hospira

CHEST® Online Supplement

Mehta, Sangeeta, MD	No relevant COIs	No relevant COIs	No relevant COIs	No relevant COIs	No relevant COIs	No relevant COIs	No COIs to disclose
Morris, Peter, MD, FCCP	No relevant COIs	No relevant COIs	No relevant COIs	No relevant COIs	NIH Grant Early ICU Rehablilitation in Mechanically Ventilated; Department of Defense Grant Early ICU Rehabilitation of Burn Patients requiring mechanical ventilation	No relevant COIs	NIH Grant Early ICU Rehablilitation in Mechanically Ventilated Patients; NIH Grant ARDS network; Department of Defense Grant Early ICU Rehabilitation of Burn Patients requiring mechanical ventilation; involved in many industry studies that have contracts with Wake Forest. Committee membership - SCCM committee on the institution of ABC guidelines.
Nanchal, Rahul, MD, FCCP	Clinical and Translational Science Institute (CTSI) Grant Biomarkers of Aspiration and Risk of Ventilator Associated Events	Clinical and Translational Science Institute (CTSI) Grant Biomarkers of Aspiration and Risk of Ventilator Associated Events	Clinical and Translational Science Institute (CTSI) Grant Biomarkers of Aspiration and Risk of Ventilator Associated Events	Clinical and Translational Science Institute (CTSI) Grant Biomarkers of Aspiration and Risk of Ventilator Associated Events	No relevant COIs	Clinical and Translational Science Institute (CTSI) Grant Biomarkers of Aspiration and Risk of Ventilator Associated Events	Clinical and Translational Science Institute (CTSI) Grant Biomarkers of Aspiration and Risk of Ventilator Associated Events

CHEST® Online Supplement

Ouellette, Daniel, MD, FCCP	Cardeas Pharmaceutical Grant $32,000 per year for two years to institution. Ventilator Associated Pneumonia -	Cardeas Pharmaceutical Grant $32,000 per year for two years to institution. Ventilator Associated Pneumonia -	Cardeas Pharmaceutical Grant $32,000 per year for two years to institution. Ventilator Associated Pneumonia -	Cardeas Pharmaceutical Grant $32,000 per year for two years to institution. Ventilator Associated Pneumonia -	Cardeas Pharmaceutical Grant $32,000 per year for two years to institution. Ventilator Associated Pneumonia -	Cardeas Pharmaceutical Grant $32,000 per year for two years to institution. Ventilator Associated Pneumonia -	Cardeas Pharmaceutical Grant $32,000 per year for two years to institution. Ventilator Associated Pneumonia – Chair, Guideline Oversight Committee
Pawlik, Amy, DPT	No relevant COIs	No relevant COIs	No relevant COIs	No relevant COIs	No relevant COIs	No relevant COIs	No COI's to disclose

CHEST® Online Supplement

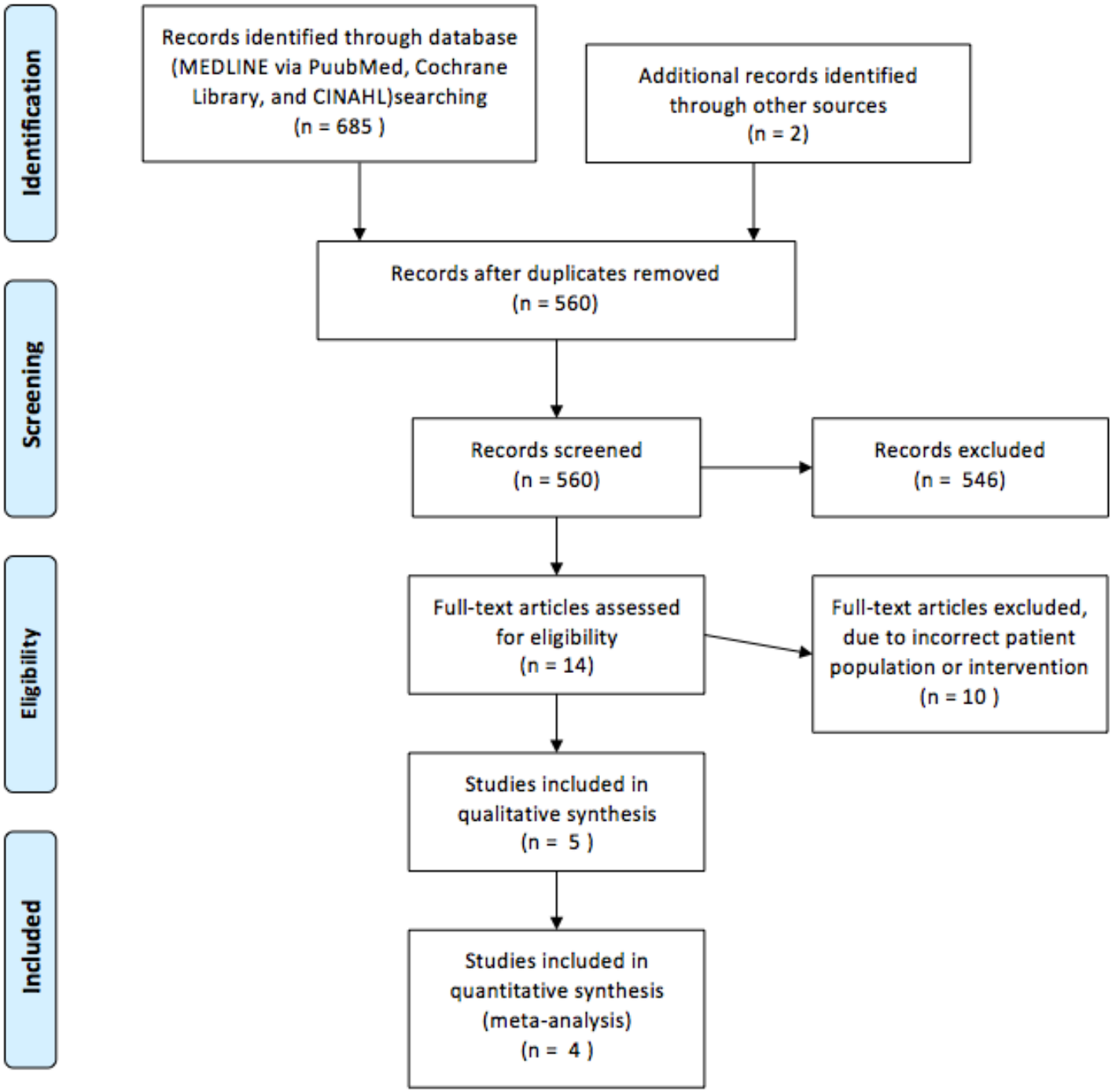
Schmidt, Gregory, MD, FCCP	No relevant COIs	NIH Grant ICU delrium	No relevant COIs	No relevant COIs	No relevant COIs	No relevant COIs	NIH Grant ICU delrium; Spectral Diagnositics Grant Septic shock; Author Royalty UpToDate 9/10/2013
Schweickert, William, MD	No relevant COIs	No relevant COIs	No relevant COIs	No relevant COIs	Hill Rom Grant Epidemiology of Early Mobilization	No relevant COIs	Hill Rom Grant Epidemiology of Early Mobilization
Sessler, Curtis, MD, FCCP	No relevant COIs	Speaking Activity Hospira payment from AACN	No relevant COIs	No relevant COIs	No relevant COIs	No relevant COIs	Speaking Activity Hospira payment from AACN Copywrite holder for RASS is Virginia Commonwealth University: Sessler, C.N., Grap, M.J., Brophy, G., Elswick, R.K. "Richmond Agitation-Sedation Scale (RASS)". Copyright. Registration number TX 7-616-498.

CHEST® Online Supplement

Stroem, Thomas, MD	No relevant COIs	No relevant COIs	No relevant COIs	No relevant COIs	No relevant COIs	No relevant COIs	Danish Strategic Research Council Grant Intensive Care to Professor Palle Toft - no salary support
Truwit, Jonathon, MD, FCCP	No relevant COIs	No relevant COIs	No relevant COIs	No relevant COIs	No relevant COIs	No relevant COIs	Research Support Astra Zeneca - Ticagrelor for Community Acquired Pneumonia; Advisory Board Spiration Data and Safety monitoring Advisory Board

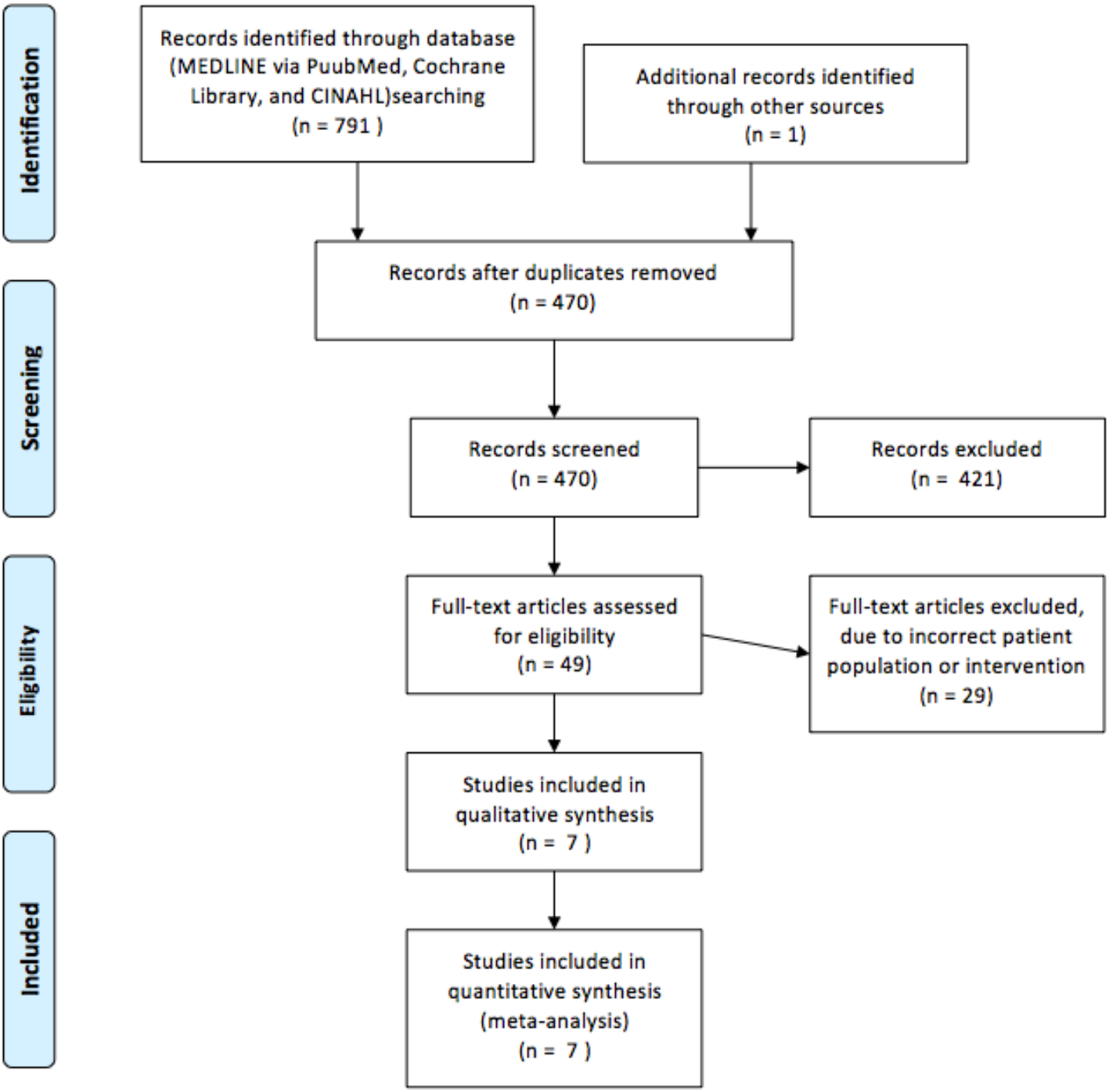
CHEST® Online Supplement

e-Figure 1 – PRISMA Flow Diagram for PICO Question 1 – "In patients ventilated for 24 hours or more, should the spontaneous breathing trial be conducted with pressure augmentation or without pressure augmentation?"



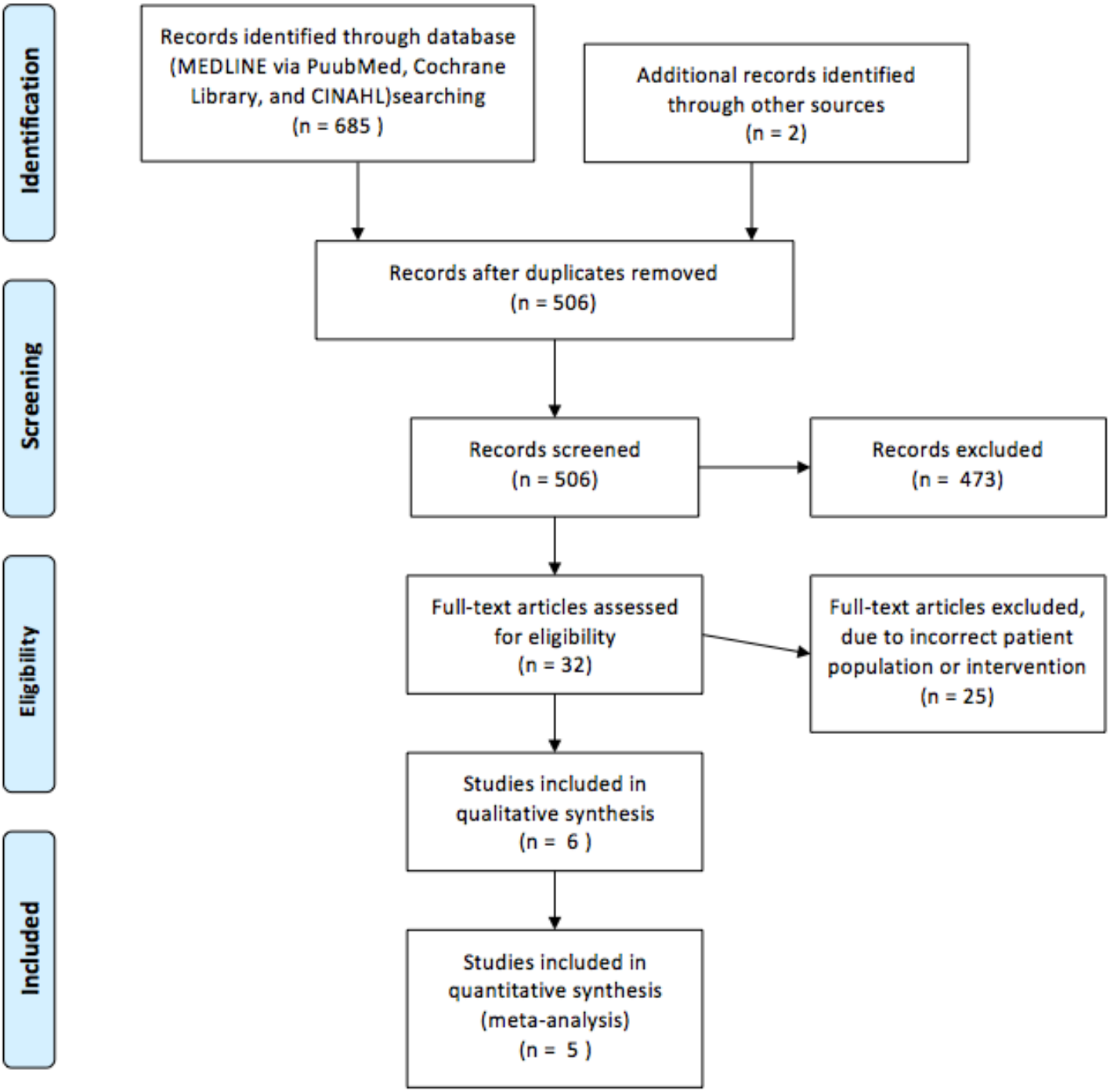
CHEST® Online Supplement

e-Figure 2. PRISMA Flow Diagram for PICO Question 2: "In acutely hospitalized patients ventilated for more than 24 hours, do protocols attempting to minimize sedation compared to an approach that does not attempt to minimize sedation impact duration of ventilation, duration of ICU stay and short-term mortality (60 days)?"



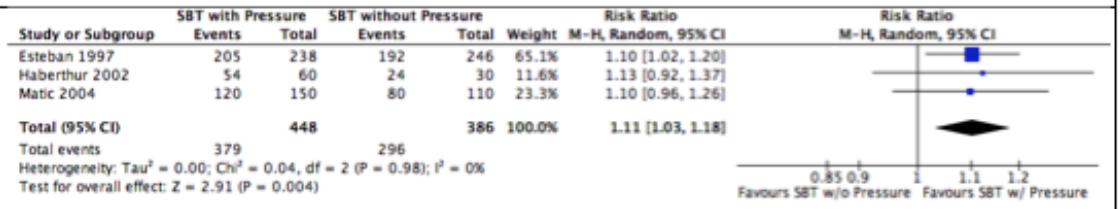
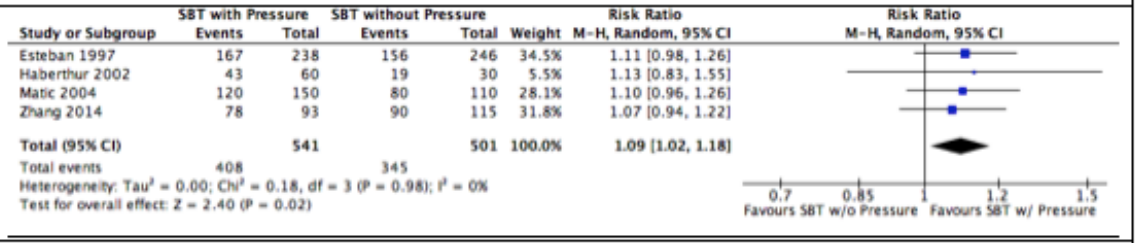
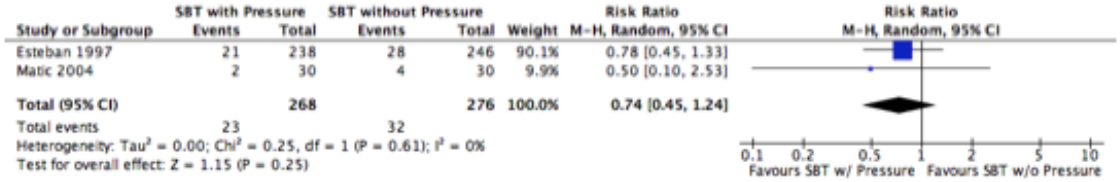
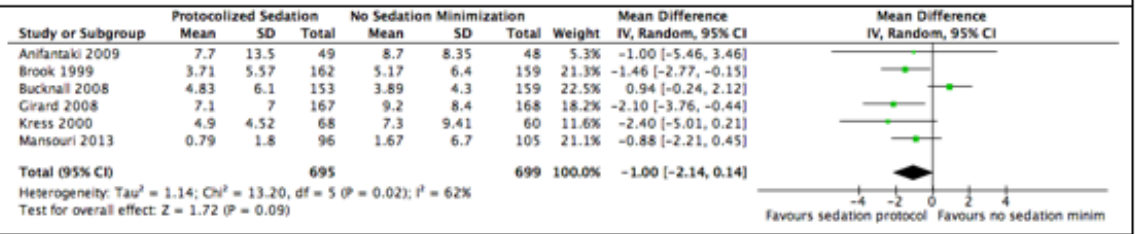
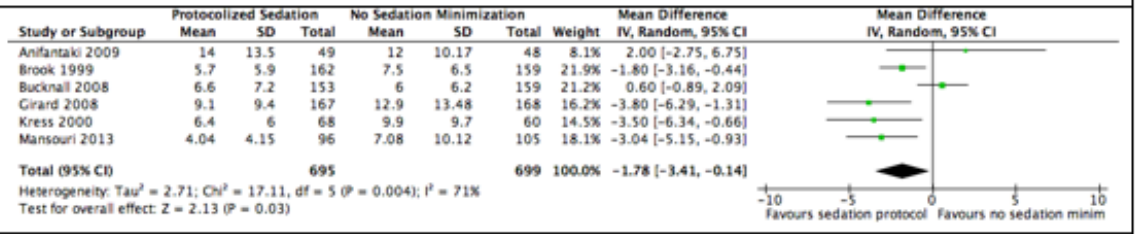
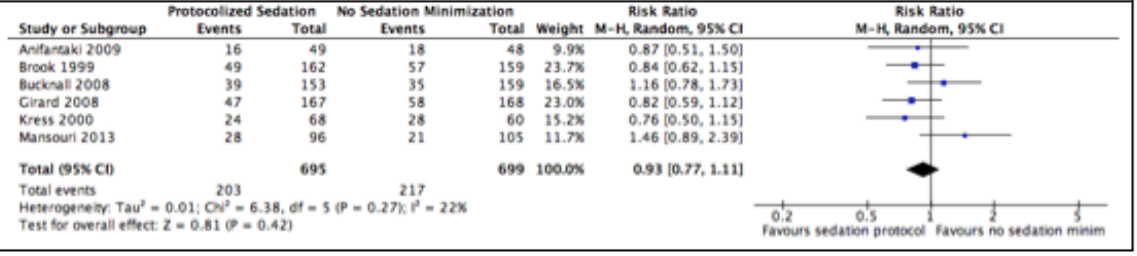
CHEST® Online Supplement

e-Figure 3. PRISMA Flow Diagram for PICO Question 3: "In acutely hospitalized patients ventilated for more than 24 hours, do protocols attempting to minimize sedation compared to protocols that do not attempt to minimize sedation impact duration of ventilation, duration of ICU stay and short-term mortality (60 days)?"

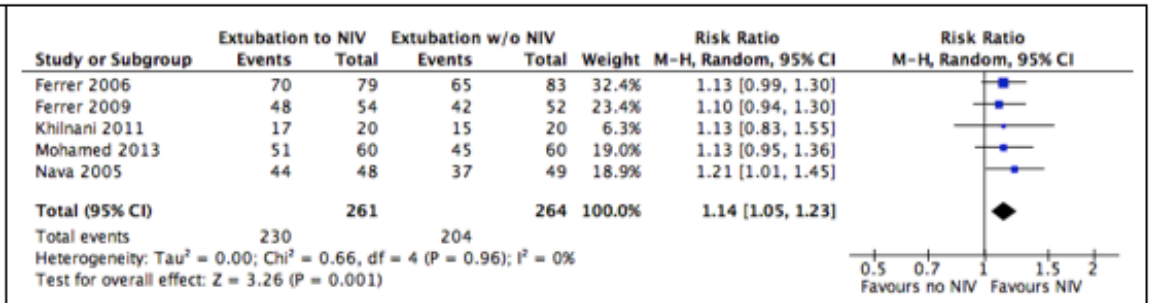
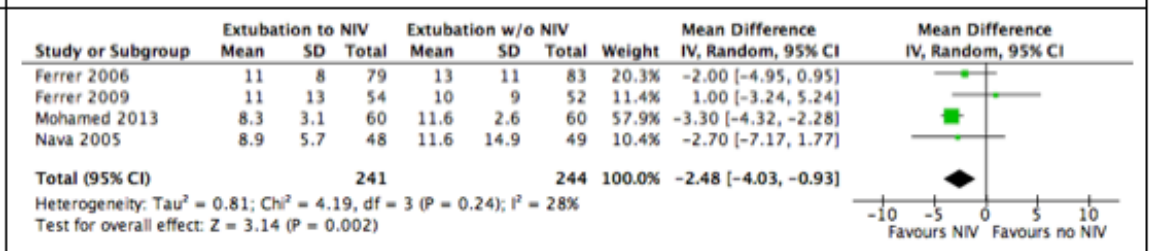
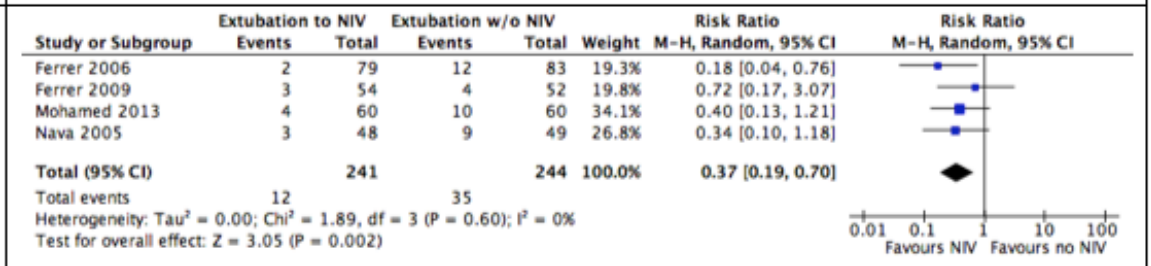
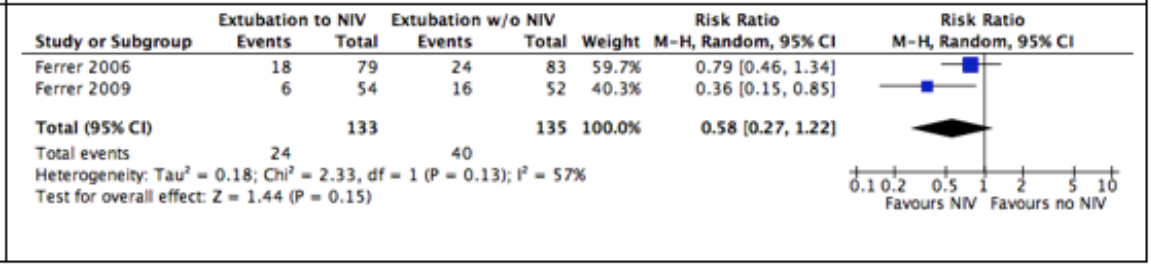


CHEST® Online Supplement

e-Table 2. Forest Plots by Recommendation and Outcome

Topic and Recommendation #	Outcome	Forest Plot
SBT, 1	Successful SBT	
SBT, 1	Extubation Success	
SBT, 1	Short-Term Mortality	
Sedation, 2	Duration of Ventilation	
Sedation, 2	ICU LOS	
Sedation, 2	Short-Term Mortality	

CHEST® Online Supplement

NIV, 3	Extubation Success	
NIV, 3	ICU LOS	
NIV, 3	Short-term Mortality	
NIV, 3	Long-term Mortality	

CHEST® Online Supplement

e-Table 3. Evidence to Decision Framework for PICO 1

<table>
<tr><th></th><th>Criteria</th><th>Judgements</th><th>Research evidence</th><th>Additional considerations</th></tr>
<tr><td>Problem</td><td>Is there a problem priority?</td><td>○ No
○ Probably no
○ Uncertain
○ Probably yes
● Yes
○ Varies</td><td>Several studies have demonstrated that about 75% of mechanically ventilated patients can be successfully extubated after passing a trial of spontaneous breathing. However, controversy still exists on the best technique used to conduct the SBT.</td><td></td></tr>
<tr><td rowspan="3">Benefits & harms of the options</td><td>What is the overall certainty of this evidence?</td><td>○ No included studies
○ Very low
○ Low
● Moderate
○ High</td><td rowspan="3">The relative importance or values of the main outcomes of interest:
<table>
<tr><th>Outcome</th><th>Relative importance</th><th>Certainty of the evidence (GRADE)</th></tr>
<tr><td>Extubation Success</td><td>CRITICAL</td><td>⨁⨁⨁◯ MODERATE</td></tr>
<tr><td>Successful SBT</td><td>IMPORTANT</td><td>⨁⨁⨁◯ MODERATE</td></tr>
<tr><td>Short term Mortality</td><td>IMPORTANT</td><td>⨁⨁◯◯ LOW</td></tr>
<tr><td>ICU LOS</td><td>IMPORTANT</td><td>⨁⨁⨁◯ MODERATE</td></tr>
</table></td><td rowspan="3"></td></tr>
<tr><td>Is there important uncertainty about how much people value the main outcomes?</td><td>○ Important uncertainty or variability
○ Possibly important uncertainty or variability
○ Probably no important uncertainty or variability
● No important uncertainty or variability
○ No known undesirable outcomes</td></tr>
<tr><td>Are the desirable anticipated effects large?</td><td>○ No
○ Probably no
○ Uncertain
● Probably yes
○ Yes
○ Varies</td></tr>
</table>

CHEST® Online Supplement

	Criteria	Judgements	Research evidence	Additional considerations
	Are the undesirable anticipated effects small?	○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies		
	Are the desirable effects large relative to undesirable effects?	○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies		
Resource use	**Are the resources required small?**	○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies		
	Is the incremental cost small relative to the net benefits?	○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies	No data was found on costs of the intervention, however, mean incremental charges of mechanical ventilation in ICU patients has been found to be on average $1,522 per day	
Equity	**What would be the impact on health inequities?**	○ Increased ○ Probably increased ○ Uncertain ○ Probably reduced ○ Reduced ○ Varies		Not relevant.

CHEST® Online Supplement

	Criteria	Judgements	Research evidence	Additional considerations
Acceptability	**Is the option acceptable to key stakeholders?**	○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies		
Feasibility	**Is the option feasible to implement?**	○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies		

Recommendation

Should SBT be conducted with pressure augmentation vs. without pressure augmentation be used in patients ventilated for more than 24hrs?

Balance of consequences	Undesirable consequences *clearly outweigh* desirable consequences in most settings	Undesirable consequences *probably outweigh* desirable consequences in most settings	The balance between desirable and undesirable consequences *is closely balanced or uncertain*	Desirable consequences *probably outweigh* undesirable consequences in most settings	Desirable consequences *clearly outweigh* undesirable consequences in most settings
	○	○	○	●	○

Type of recommendation	We recommend against offering this option	We suggest not offering this option	We suggest offering this option	We recommend offering this option
	○	○	●	○

Recommendation	In patients ventilated for 24 hours or more, we suggest that the initial SBT be conducted with pressure augmentation (5-8cm H2O)
Justification	
Subgroup considerations	This does not take into account the patients who failed the initial SBT. This also does not take into account patients with severe neuromuscular weakness
Implementation considerations	
Monitoring and evaluation	
Research possibilities	

CHEST® Online Supplement

e-Table 4. Evidence to Decision Framework for PICO 2

<table>
<tr><th colspan="5">Assessment</th></tr>
<tr><th></th><th>Criteria</th><th>Judgements</th><th>Research evidence</th><th>Additional considerations</th></tr>
<tr><td>Problem</td><td>Is there a problem priority?</td><td>○ No
○ Probably no
○ Uncertain
○ Probably yes
● Yes
○ Varies</td><td>Patients undergoing mechanical ventilation frequently require sedation and analgesia. There is growing evidence that suggests that over-sedation has been linked to both short-term (longer duration of ventilation, longer ICU and hospital lengths of stay) and long-term (psychological recovery) outcomes.</td><td></td></tr>
<tr><td>Benefits & harms of the options</td><td>What is the overall certainty of this evidence?</td><td>○ No included studies
○ Very low
● Low
○ Moderate
○ High</td><td>The relative importance or values of the main outcomes of interest:<table><tr><th>Outcome</th><th>Relative importance</th><th>Certainty of the evidence (GRADE)</th></tr></table></td><td></td></tr>
</table>

CHEST® Online Supplement

Assessment				
	Criteria	**Judgements**	**Research evidence**	**Additional considerations**
	Is there important uncertainty about how much people value the main outcomes?	○ Important uncertainty or variability ○ Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ● No important uncertainty or variability ○ No known undesirable outcomes	Duration of Ventilation — IMPORTANT — ⨁◯◯◯ VERY LOW ICU Length of Stay — IMPORTANT — ⨁◯◯◯ VERY LOW Short-term Mortality — IMPORTANT — ⨁⨁⨁◯ MODERATE	
	Are the desirable anticipated effects large?	○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies		
	Are the undesirable anticipated effects small?	○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies		

CHEST® Online Supplement

Assessment				
	Criteria	**Judgements**	**Research evidence**	**Additional considerations**
	Are the desirable effects large relative to undesirable effects?	○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies		
Resource use	**Are the resources required small?**	○ No ○ Probably no ● Uncertain ○ Probably yes ○ Yes ○ Varies		Workload.
	Is the incremental cost small relative to the net benefits?	○ No ○ Probably no ● Uncertain ○ Probably yes ○ Yes ○ Varies	A systematic review of seven studies reported the impact of sedation protocols on the costs of sedative agents used; all found a reduction in the costs of sedative agents with protocolised sedation, which was reported as significant in four studies with values ranging from 22% to 94% of the cost for non-protocol managed sedation	

CHEST® Online Supplement

Assessment				
	Criteria	**Judgements**	**Research evidence**	**Additional considerations**
Equity	**What would be the impact on health inequities?**	○ Increased ○ Probably increased ○ Uncertain ○ Probably reduced ○ Reduced ○ Varies		
Acceptability	**Is the option acceptable to key stakeholders?**	○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies		
Feasibility	**Is the option feasible to implement?**	○ No ○ Probably no ○ Uncertain ○ Probably yes ○ Yes ● Varies		Practical issues - culture, staffing, etc.

CHEST® Online Supplement

Recommendation

Should Protocolized sedation vs. no attempt to minimize sedation be used for patients mechanically ventilated for 24 hours or more?

Balance of consequences	Undesirable consequences *clearly outweigh* desirable consequences in most settings	Undesirable consequences *probably outweigh* desirable consequences in most settings	The balance between desirable and undesirable consequences *is closely balanced or uncertain*	Desirable consequences *probably outweigh* undesirable consequences in most settings	Desirable consequences *clearly outweigh* undesirable consequences in most settings
	○	○	○	●	○

Type of recommendation	We recommend against offering this option	We suggest not offering this option	We suggest offering this option	We recommend offering this option
	○	○	●	○

Recommendation	For acutely hospitalized patients ventilated for more than 24 hours, we suggest protocols attempting to minimize sedation. (Weak recommendation, Low quality of evidence)
Justification	
Subgroup considerations	
Implementation considerations	
Monitoring and evaluation	
Research possibilities	

CHEST® Online Supplement

e-Table 5. Evidence to Decision Framework for PICO 3

<table>
<tr><th colspan="5">Assessment</th></tr>
<tr><th></th><th>Criteria</th><th>Judgements</th><th>Research evidence</th><th>Additional considerations</th></tr>
<tr><td>Problem</td><td>Is there a problem priority?</td><td>○ No
○ Probably no
○ Uncertain
○ Probably yes
● Yes
○ Varies</td><td>Reintubation occurs in 4-23% of mechanically ventilated patients within 48-72 hours of planned extubation. Extubating patients to noninvasive ventilation (NIV) could provide a means of avoiding reintubation in high risk patients.</td><td>Harms associated with the need of reintubation</td></tr>
<tr><td>Benefits & harms of the options</td><td>What is the overall certainty of this evidence?</td><td>○ No included studies
○ Very low
○ Low
● Moderate
○ High</td><td>The relative importance or values of the main outcomes of interest:<table><tr><th>Outcome</th><th>Relative importance</th><th>Certainty of the evidence (GRADE)</th></tr></table></td><td>There is not much concern from patients or physicians in identifying important variability in these outcomes. These outcomes are universally important.</td></tr>
</table>

CHEST® Online Supplement

<table>
<tr><th colspan="5">Assessment</th></tr>
<tr><th></th><th>Criteria</th><th>Judgements</th><th>Research evidence</th><th>Additional considerations</th></tr>
<tr>
<td></td>
<td>Is there important uncertainty about how much people value the main outcomes?</td>
<td>○ Important uncertainty or variability
○ Possibly important uncertainty or variability
○ Probably no important uncertainty or variability
● No important uncertainty or variability
○ No known undesirable outcomes</td>
<td rowspan="4">
<table>
<tr><td>Extubation Success</td><td>CRITICAL</td><td>⨁⨁⨁◯ MODERATE</td></tr>
<tr><td>ICU LOS</td><td>IMPORTANT</td><td>⨁⨁⨁◯ MODERATE</td></tr>
<tr><td>Short-term Mortality (ICU Mortality)</td><td>IMPORTANT</td><td>⨁⨁◯◯ LOW</td></tr>
<tr><td>Long-term Mortality</td><td>IMPORTANT</td><td>⨁⨁◯◯ LOW</td></tr>
</table>
</td>
<td rowspan="4">physicians.

Patients on NIV could deteriorate and develop organ failure, so they get reintubated. Studied local complications seem to be unlikely but more serious effects of organ failure that have yet to be studied may occur

Possible harms/complications associated with NIV - nasal bridge damage, conjunctivitis, nasal ulceration</td>
</tr>
<tr>
<td></td>
<td>Are the desirable anticipated effects large?</td>
<td>○ No
○ Probably no
○ Uncertain
○ Probably yes
● Yes
○ Varies</td>
</tr>
<tr>
<td></td>
<td>Are the undesirable anticipated effects small?</td>
<td>○ No
○ Probably no
○ Uncertain
● Probably yes
○ Yes
○ Varies</td>
</tr>
</table>

CHEST® Online Supplement

Assessment				
	Criteria	**Judgements**	**Research evidence**	**Additional considerations**
	Are the desirable effects large relative to undesirable effects?	○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies		
Resource use	**Are the resources required small?**	○ No ○ Probably no ● Uncertain ○ Probably yes ○ Yes ○ Varies	No data was found on the cost of the intervention	
	Is the incremental cost small relative to the net benefits?	○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies	Mean incremental charges of mechanical ventilation in ICU patients has been found to be on average $1,522 per day. Total ICU costs have been found to be approximately $3,000/day	Reduced ICU LOS, and reduced ventilation may offer a cost benefit.

CHEST® Online Supplement

Assessment				
	Criteria	**Judgements**	**Research evidence**	**Additional considerations**
Equity	**What would be the impact on health inequities?**	○ Increased ○ Probably increased ● Uncertain ○ Probably reduced ○ Reduced ○ Varies		ICU access?
Acceptability	**Is the option acceptable to key stakeholders?**	○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies		Some practitioners may not choose to extubate
Feasibility	**Is the option feasible to implement?**	○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies		

CHEST® Online Supplement

Recommendation

Should Extubation to noninvasive ventilation vs. extubation without noninvasive ventilation be used for pts ventilated for >24hrs who have passed an SBT and who are at high risk for extubation failure?

Balance of consequences	Undesirable consequences *clearly outweigh* desirable consequences in most settings	Undesirable consequences *probably outweigh* desirable consequences in most settings	The balance between desirable and undesirable consequences *is closely balanced or uncertain*	Desirable consequences *probably outweigh* undesirable consequences in most settings	Desirable consequences *clearly outweigh* undesirable consequences in most settings
	○	○	○	○	●

Type of recommendation	We recommend against offering this option	We suggest not offering this option	We suggest offering this option	We recommend offering this option
	○	○	○	●

Recommendation	In patients who have been ventilated for 24 or more hours who have passed a spontaneous breathing trial and who are at high risk for extubation failure, we recommend that patients be treated with noninvasive ventilation immediately after extubation.
Justification	Reduced LOS, reduced mortality, extubation success outcomes
Subgroup considerations	The majority (80-90%) of ventilated patients are successfully extubated and do not need reintubation. This recommendation specifically addresses the high risk subset of patients.
Implementation considerations	
Monitoring and evaluation	
Research possibilities	