APPENDIXES

Appendix A. Exact Search Strings

PubMed®:

Search date: April 7, 2011

Total number of results: 2541

Strategy:
((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR drug therapy[sh] OR randomly[tiab] OR trial[tiab] OR groups[tiab]) NOT (animals[mh] NOT humans[mh])) AND (positive airway pressure respiration OR continuous positive airway pressure OR bilevel positive airway pressure OR bi-level positive airway pressure OR NPPV OR NIPPV OR BIPAP OR CPAP OR ippv OR ippb OR niv OR niav OR pav OR "proportional assist ventilation" OR "respiratory assist devices" OR ((noninvasive[tiab] OR non-invasive[tiab]) AND (ventilat*[tiab] OR respirat*[tiab])) OR (ventilat* AND helmet[tiab]) OR ((facial[tiab] OR nasal[tiab] OR face[tiab]) AND mask*[tiab]))

Limits: English, All Adult: 19+ years, Publication Date from 1990/01/01

Embase®:

Search date: April 26, 2011

Total number of results: 648

Strategy:
'positive end expiratory pressure'/exp OR 'positive end expiratory pressure' OR 'pressure support ventilation'/exp OR 'pressure support ventilation' OR 'positive airway pressure respiration' OR 'continuous positive airway pressure' OR 'bilevel positive airway pressure' OR 'bi-level positive airway pressure' OR nppv OR nippv OR bipap OR cpap OR ippv OR ippb OR niv OR niav OR pav OR 'proportional assist ventilation' OR 'respiratory assist devices' OR (noninvasive:ti OR 'non invasive':ti AND (ventilat*:ti OR respirat*:ti)) OR (noninvasive:ab OR 'non invasive':ab AND (ventilat*:ab OR respirat*:ab)) OR (ventilat*:ti AND helmet:ti) OR (ventilat*:ab AND helmet:ab) OR (facial:ti OR nasal:ti OR face:ti AND mask*:ti) OR (facial:ab OR nasal:ab OR face:ab AND mask*:ab) AND (random* OR factorial* OR crossover* OR 'cross over' OR 'cross overs' OR placebo* OR doubl* NEAR/1 blind* OR singl* NEAR/1 blind* OR assign* OR allocat* OR volunteer* OR 'double blind procedure'/exp OR 'crossover procedure'/exp OR 'randomized controlled trial'/exp OR 'single blind procedure'/exp) AND [humans]/lim AND [english]/lim AND [embase]/lim NOT [medline]/lim AND [1990-2011]/py

Cochrane Database of Systematic Reviews:

Search date: March 30, 2011

Total number of results: 81

Strategy:
#1 (positive airway pressure respiration OR continuous positive airway pressure OR bilevel positive airway pressure OR bi-level positive airway pressure OR NPPV OR NIPPV OR BIPAP OR CPAP OR ippv OR ippb OR niv OR niav OR pav OR "proportional assist ventilation" OR "respiratory assist devices"):ti,ab,kw
#2 (ventilat* AND helmet):ti,ab,kw
#3 (noninvasive OR non invasive):ti,ab,kw and (respirat* OR ventilat*):ti,ab,kw
#4 (facial OR nasal OR face):ti,ab,kw and (mask):ti,ab,kw
#5 (#1 OR #2 OR #3 OR #4)
#6 (#1 OR #2 OR #3 OR #4), from 1990 to 2011

ClinicalTrials.gov:

Search date: October 18, 2011

Total number of results: 117

Strategy:
(noninvasive OR positive pressure ventilation OR positive airway pressure AND respiration OR continuous positive airway pressure OR bilevel positive airway pressure OR bi-level positive airway pressure OR proportional AND assist ventilation OR respiratory assist AND device) [ALL-FIELDS] AND "Interventional" [STUDY-TYPES] AND respiratory failure [DISEASE] AND ("Adult" OR "Senior") [AGE-GROUP]

Appendix B. Efficacy-Effectiveness Rating Form

Directions: For each article, rate the study along the seven dimensions listed. For each dimension, consider whether, on balance, the study is most consistent with the definition of efficacy or effectiveness. Make your best judgment, but if the article does not give adequate information to make a determination, choose "unclear."

Dimension	Efficacy	Effectiveness
1. Setting [ ] Unclear	Highly specialized setting for administering NPPV (e.g., specialized NPPV unit) or Tertiary care setting (referral population or Academic medical Center) or restricted to highly trained practitioners	Community Hospitals without specialized NPPV units or specifies that practitioners do not have any special training
2. Eligibility criteria [ ] Unclear	Convenience sample or sample selection criteria that excludes typical comorbidities (e.g., mild hemodynamic instability, chronic medical conditions, dysrhythmias, recent surgery) or those less likely to adhere to treatment	Consecutive patients; allows usual comorbidities and those less likely to be adherent
3. Health Outcomes [ ] Unclear	Does not include mortality or health related quality of life	In the methods section, specifies mortality (in hospital or longer) or Health related quality of life outcomes
4. Study Duration/clinically relevant NPPV [ ] Unclear	NPPV administration is fixed (e.g., given for pre-specified, inflexible duration), OR specific respirator settings not based on clinical response, OR outcomes are short-term only (e.g. ICU stay or shorter)	Intervention given to clinical endpoints rather than pre-specified duration. NPPV administration is flexible and responds to clinical status. Outcomes are measured for full hospitalization or longer
5. Assessment of adverse events [ ] Unclear	Report fewer than 2 of the following: discontinuation of NPPV due to intolerance, rates of infection, facial ulcerations	Reports at least 2 of the following: discontinuation of NPPV due to intolerance, rates of infection, facial ulcerations
6. Adequate sample size for health outcomes [ ] Unclear	Sample size not given for mortality or HRQOL	Sample size calculation given for mortality or minimum clinically important difference for HRQOL
7. ITT analysis [ ] Unclear	Completers analysis or excludes those with protocol deviations.	Follows intent-to-treat principle for analysis (includes all patients regardless of compliance, eligibility)

Appendix C. Data Abstraction Elements

I. Study Characteristics

- Additional articles used in this abstraction
  - If an additional article is used to supplement this abstraction, provide the article(s)' full citation(s).
- Study dates
  - Year enrollment started
  - Year enrollment ended
- Study sites
  - Single center
    - Geographic location: Enter City and State (if U.S.) and Country (if outside the U.S.).
  - Multicenter
    - Enter number of sites
    - Select all applicable geographical regions from the following options: US, Canada, UK, Europe, South America, Central America, Asia, Africa, Australia/New Zealand, Not reported/Unclear, Other (specify)
  - Not reported/Unclear
- Funding source (check all that apply): Government, Private foundation, Industry, Not reported, Other (specify)
- Setting (check all that apply): ICUs, Emergency departments, Critical care units, Postoperative settings, General medical units, Not reported/unclear, Other (specify)
- Enrollment approach (check all that apply): Consecutive patients, Convenience sample (not explicitly consecutive), Not reported/Unclear, Other (specify)
- Study inclusion and exclusion criteria
  - Copy/paste criteria as reported in the article
  - Were any of the following exclusion reasons applied?
    - Need for emergent intubation (includes respiratory arrest, severe hemodynamic instability [e.g., SBP < 90, severe bradycardia, severe arrhythmia], other indications)
    - Unable to cooperate with NPPV (includes decreased level of consciousness, encephalopathy, agitation)
    - Acute respiratory failure requiring a specific treatment (e.g. pulmonary embolus, pneumothorax, acute myocardial infarction)
    - Conditions that preclude NPPV face mask or nasal prong application (e.g., tracheostomy; facial deformities; recent oral, esophageal, or gastric surgery)
- Study enrollment and completion
  - Number of subjects assessed for eligibility
  - Number eligible
  - Number randomized
  - Number that completed follow-up
- Comments (if needed)

II. Ventilation Procedures

- Does the study address weaning? (Yes, No)
- Are there significant baseline imbalances between the patient groups? (Yes, No)
- For each treatment arm, indicate type of treatment and answer questions specific to that treatment:
    - Treatment type: NPPV, Supportive care, or Invasive Ventilatory Support
        - If NPPV
            - Interface used: Full face, Nasal prongs, Nasal mask, Not reported, Other (specify)
            - Type of NPPV
                - Bilevel positive airway pressure with supportive care
                - Bilevel upper/inspiratory pressure
                - Bilevel lower/expiratory pressure
                - Continuous positive airway pressure (CPAP) with supportive care
                - Planned CPAP pressure:
                - Fixed pressure
                - Acceptable pressure range
                - Min pressure
                - Max pressure
                - Mean CPAP pressure delivered
                - Other
                - Not reported
            - Other Details:
                - Autotitrating: Yes, No, Not reported/ Not available
                - Duration of ventilation, per protocol (mean hours per day, or if not given, mean and intended duration for Day 1)
                - Protocolized (presence of a structured algorithm for adjusting the non-invasive ventilation): Yes, No, Not reported
        - If Supportive care
            - Is planned supportive care identical for the intervention arm(s) and the comparator arm?
            - Describe supportive care
        - If Invasive Ventilatory Support
            - Autotitrating: Yes, No, Not reported/ Not available
            - Duration of ventilation, per protocol (mean hours per day, or if not given, mean and intended duration for Day 1)
- Staffing/training experience
- Staffing composition (check all that apply): Respiratory therapist, Nurse practitioner, Physician's assistant, Physician (general), Physician (other subspecialty), Physician (critical care trained), Nurse, Not reported
- Adjunctive treatments
    - High flow oxygen: Yes, No, Not reported/Unclear
    - Helium gas mixture: Yes, No, Not reported/Unclear
    - Sedatives and anxiolytics: Yes, No, Not reported/Unclear
        - If yes, was Precedex (dexametomidine) used?

- Comments (if needed)

III. Applicability of Key Questions

- Indicate populations included in the study (check all that apply):
  - Adults with chronic obstructive pulmonary disease (COPD) and acute respiratory failure
  - Adults with acute cardiogenic pulmonary edema (ACPE)
  - Adults with acute respiratory failure due to other causes including pneumonia, asthma, obesity-hypoventilation syndrome, and interstitial lung disease
  - Adults with acute respiratory failure in selective settings including perioperative setting and post-transplant setting
- Indicate applicable Key Questions
  - Key Question 1: Is noninvasive positive-pressure ventilation (NPPV) associated with less morbidity (including from intubation), lower mortality, lower adverse events, or lower medical utilization when compared to supportive medical therapy or invasive ventilation:
    - In adults with chronic obstructive pulmonary disease (COPD) and acute respiratory failure?
    - In adults with acute cardiogenic pulmonary edema (ACPE)?
    - In adults with acute respiratory failure due to other causes including: pneumonia, asthma, obesity-hypoventilation syndrome, and interstitial lung disease?
    - In adults with acute respiratory failure in selective settings including: perioperative setting and post-transplant setting?
  - Key Question 2: Is NPPV with bilevel positive airway pressure (BiPAP™), compared to NPPV with continuous positive airway pressure (CPAP), associated with less morbidity, lower mortality, lower adverse events, or lower medical utilization:
    - In adults with chronic obstructive pulmonary disease (COPD) and acute respiratory failure?
    - In adults with acute cardiogenic pulmonary edema (ACPE)?
    - In adults with acute respiratory failure due to other causes including: pneumonia, asthma, obseity-hypoventilation syndrome, and interstitial lung disease?
    - In adults with acute respiratory failure in selective settings including: perioperative setting and post-transplant setting?
  - Key Question 3: Is early extubation to NPPV, compared to usual care, associated with less morbidity, lower mortality, lower adverse events, or lower medical utilization:
    - In adults with chronic obstructive pulmonary disease (COPD) and acute respiratory failure?
    - In adults with acute cardiogenic pulmonary edema (ACPE)?
    - In adults with acute respiratory failure due to other causes including: pneumonia, asthma, obesity-hypoventilation syndrome, and interstitial lung disease?
    - In adults with acute respiratory failure in selective settings including: perioperative setting and post-transplant setting?
  - Key Question 4: Did this study report a subgroup analysis?
- Comments (if needed)

IV. Baseline Characteristics

- Number of subjects: For the total population and each treatment arm, indicate the following:
    - Treatment type: CPAP, Bilevel, Weaning without NPPV, Weaning with NPPV, Endotracheal intubation, Supportive care
    - N: Total, Female, Male
    - Percentage: Female, Male
- Total population age in years: For the total population and each treatment arm, indicate the following:
    - Treatment type: CPAP, Bilevel, Weaning without NPPV, Weaning with NPPV, Endotracheal intubation, Supportive care
    - Mean
    - Standard deviation
    - Median
    - Interquartile range
- Severity of illness score: Apache II score, Apache III score, Simplified acute physiological score, Other (specify), Not reported
    - For the total population and each treatment arm, indicate the following:
        - Treatment type: CPAP, Bilevel, Weaning without NPPV, Weaning with NPPV, Endotracheal intubation, Supportive care
        - Mean
        - Standard deviation
        - Median
        - Interquartile range
- Ethnicity (indicate total N and percentage of total population)
    - Hispanic or Latino
    - Not Hispanic or Latino
- Race (indicate total N and percentage of total population)
    - Black/African American
    - American Indian or Alaska Native
    - Asian
    - Native Hawaiian or other Pacific Islander
    - White
    - Multiracial
    - Other
- Baseline characteristics: For the total population and each treatment arm, indicate the following:
    - N or Percentage of patients
    - Heart rate: Not reported, or Mean and Standard deviation
    - Respiratory rate: Not reported, or Mean and Standard deviation
    - Systolic blood pressure: Not reported, or Mean and Standard deviation Arterial pH: Not reported, or Mean and Standard deviation
    - PaCO2 : Not reported, or Mean and Standard deviation
    - PaO2: Not reported, or Mean and Standard deviation
    - Ratio of PaO2 to Fraction of inspired O2: Not reported, or Mean and Standard deviation
    - Impaired mental status (Define) : Not reported, or Mean and Standard deviation

    - Mental status changes (Define) : Not reported, or Mean and Standard deviation
    - BMI: Not reported, or Mean and Standard deviation
    - Obesity (e.g. BMI>30) (Define): Not reported, or Mean and Standard deviation
    - Other (Specify): Not reported, or Mean and Standard deviation
- Causes of acute respiratory failure: For the total population and each treatment arm, indicate the following:
    - N or Percentage of patients
    - Chronic obstructive pulmonary disease (COPD): N, Percent
    - Pneumonia: N, Percent
    - Asthma: N, Percent
    - Obesity-hypoventilation syndrome: N, Percent
    - Interstitial lung disease: N, Percent
    - Acute cardiogenic pulmonary edema (ACPE) : N, Percent
    - Acute respiratory failure following a solid organ or bone marrow transplant: N, Percent
    - Acute respiratory failure following surgery requiring general anesthesia other than solid organ or bone marrow transplant: N, Percent
    - Other: N, Percent
- Comments (if needed)

V. Outcomes (repeatable per outcome of interest)

- Select outcome reported:
    - Intermediate Outcome/Respiratory Rate
    - Intermediate Outcome/Heart Rate
    - Intermediate Outcome/Partial Pressure of Oxygen in Arterial Blood (PaO2)
    - Intermediate Outcome/Partial Pressure of Carbon Dioxide in Arterial Blood (PaCO2)
    - Intermediate Outcome/Improved PaO2 to Fraction of inspired oxygen
    - Intermediate Outcome/Intubation Rate (NA for weaning studies)
    - Intermediate Outcome/Reintubation Rate (Post-op: weaning)
    - Intermediate Outcome/Duration of Mechanical Ventilation
    - Intermediate Outcome/Time to Reintubation (Post-op: weaning)
    - Intermediate Outcome/Rates of Discontinuing NPPV secondary to treatment intolerance
    - Intermediate Outcome/Successful Extubation
    - Intermediate Outcome/Myocardial Infarctions
    - Intermediate Outcome/Psychological Distress/Anxiety Validated Measure
    - Intermediate Outcome/AE: Discontinued NPPV-unable to tolerate
    - Final Outcome/Functional Status measured by SF36 or equivalent
    - Final Outcome/Health-related Quality of Life (HRQoL)
    - Final Outcome/Disease-specific functional status measure
    - Final Outcome/Mortality rates
    - Outcome/Ventilator dependent days
    - Days Final Outcome/Rate of Ventilator Dependence at Hospital Discharge
    - Final Outcome/Length of Hospital Stay
    - Final Outcome/Length of Intensive Care Stay
    - Final Outcome/Total Hospital Costs
    - Adverse Event/Aspiration

    - Adverse Event/Secondary Infections
    - Adverse Event/Facial Ulcerations
    - Adverse Event/Other (specify)
    - Other (specify)
- Provide the following data for the indicated outcome
    - Timing of the outcome data: 2 hours, 6 hours, 24 hours, At discharge, 30 days, In hospital, Other (Specify)
    - For each treatment arm, record the following:
        - N or Percentage of patients
        - Result, recorded as one of the following:
            - Mean
            - Median
            - Number of points with outcome
            - Percentage of points with outcome
            - Events per denominator
            - Other (specify)
        - Variability, recorded as one of the following:
            - Standard error
            - Standard deviation
            - Range
            - Interquartile range
            - Other (specify)
        - Comparative result, recorded as one of the following:
            - Relative risk
            - Relative hazard
            - Odds ratio
            - Risk difference
            - Other (specify)
            - Comparator: Treatment arm 1, Treatment arm 2, Treatment arm 3
        - Confidence interval (CI) or interquartile range (IQR)
            - Indicate measure (select one): 95% CI, Other percent CI (specify), IQR
            - Lower level (25% if IQR)
            - Upper level (75% if IQR)
- Comments (if needed)

VI. Subgroup Analyses (if applicable)

- Indicate the factor being considered: Setting, Experience and training of clinicians, Use of protocols, Morbid obesity, Mental status changes, Overall disease burden, Other patient characteristic (specify)
- Define the categories considered in this subgroup analysis.
- For each category described, provide data by outcome. Clearly indicate units (number of patients, %, hazard ratio, etc.). Include values for confidence intervals, p values, standard error, standard deviation, etc. when available.
    - Outcomes (provide data for all that apply):
        - Intermediate Outcome/Respiratory Rate
        - Intermediate Outcome/Heart Rate

        - Intermediate Outcome/Partial Pressure of Oxygen in Arterial Blood (PaO2)
        - Intermediate Outcome/Partial Pressure of Carbon Dioxide in Arterial Blood (PaCO2)
        - Intermediate Outcome/Improved PaO2 to Fraction of inspired oxygen
        - Intermediate Outcome/Intubation Rate (NA for weaning studies)
        - Intermediate Outcome/Reintubation Rate (Post-op: weaning)
        - Intermediate Outcome/Duration of Mechanical Ventilation
        - Intermediate Outcome/Time to Reintubation (Post-op: weaning)
        - Intermediate Outcome/Rates of Discontinuing NPPV secondary to treatment intolerance
        - Intermediate Outcome/Successful Extubation
        - Intermediate Outcome/Myocardial Infarctions
        - Intermediate Outcome/Psychological Distress/Anxiety Validated Measure
        - Intermediate Outcome/AE: Discontinued NPPV-unable to tolerate
        - Final Outcome/Functional Status measured by SF36 or equivalent
        - Final Outcome/Health-related Quality of Life (HRQoL)
        - Final Outcome/Disease-specific functional status measure
        - Final Outcome/Mortality rates
        - Outcome/Ventilator dependent days
        - Days Final Outcome/Rate of Ventilator Dependence at Hospital Discharge
        - Final Outcome/Length of Hospital Stay
        - Final Outcome/Length of Intensive Care Stay
        - Final Outcome/Total Hospital Costs
        - Adverse Event/Aspiration
        - Adverse Event/Secondary Infections
        - Adverse Event/Facial Ulcerations
        - Adverse Event/Other (specify)
        - Other (specify)
- Comments (if needed)

VII. Quality Assessment

- Rate each individual risk of bias item as Yes, No, or Unclear
    - Randomization and allocation concealment:
        - Was the allocation sequence adequately generated?*
        - Was the allocation adequately concealed?*
    - Study performance
        - Did variation from the study protocol compromise the conclusion of the study?
    - Outcomes
        - Were outcome assessors blind to treatment assigned for “hard outcomes” such as mortality?*
        - Were outcome assessors blind to treatment assignments for “soft outcomes” such as symptoms?*
        - Were the measures used reliable and valid? If so, choose “Yes,” indicating no important measurement bias.
    - Data analysis

        - Are reports of the study free of suggestion of selective outcome reporting (systematic differences between planned and reported findings)?*
        - Was incomplete outcome data adequately addressed?*
            - Yes (no systematic differences between groups in withdrawals from a study and no high overall loss to follow-up; all eligible patients that were randomized are included in analysis ("intention-to-treat" [ITT] analysis; note – mixed models and survival analyses are in general ITT)
            - No
            - Unclear
        - Was there adequate power for main effects?
    - Results
        - Were systematic differences observed in baseline characteristics and prognostic factors across the groups compared?
        - Were comparable groups maintained? Consider issues of crossover (e.g., from one intervention to another), adherence (major differences in adherence to the interventions being compared), contamination (e.g., some members of control group get intervention), or other systematic differences in care that was provided.*
    - Conflict of interest
        - Was there the absence of potential important conflict of interest? The focus is financial conflict of interest. If no financial conflict of interest (e.g., if funded by government or foundation and authors do not have financial relationships with drug/device manufacturer), then answer "Yes."

    *Items contained in the Cochrane Risk of Bias Tool (Chapter 8 in the *Cochrane Handbook,* www.cochrane-handbook.org/)
- Overall study rating: Good, Fair, Poor
    - Assign each study an overall quality rating based on the following definitions:
        - Good. A "Good" study has the least bias, and results are considered valid. A good study has a clear description of the population, setting, interventions, and comparison groups; uses a valid approach to allocate patients to alternative treatments; has a low dropout rate; and uses appropriate means to prevent bias, measure outcomes, and analyze and report results.
        - Fair. A "Fair" study is susceptible to some bias but probably not enough to invalidate the results. The study may be missing information, making it difficult to assess limitations and potential problems. As the fair-quality category is broad, studies with this rating vary in their strengths and weaknesses. The results of some fair-quality studies are possibly valid, while others are probably valid.
        - Poor. A "Poor" rating indicates significant bias that may invalidate the results. These studies have serious errors in design, analysis, or reporting; have large amounts of missing information; or have discrepancies in reporting. The results of a poor-quality study are at least as likely to reflect flaws in the study design as to indicate true differences between the compared interventions.
    - If the study is rated as "Fair" or "Poor," provide rationale for decision.
- Comments (if needed)

VIII. Applicability

- Use the PICOTS format to identify specific issues that may limit the applicability of the study. Indicate the most important limitations affecting applicability, if any, from the list below.
    - Population (P)
        - Study population poorly specified
        - Overly narrow definition of acute respiratory failure
    - Intervention (I)
        - Intervention not well described
        - Highly selected intervention team or level of training/proficiency not widely available
    - Comparator (C)
        - Inadequate comparison therapy
        - Comparator(s) not well described
    - Outcomes (O)
        - Composite outcomes that mix outcomes of different significance
    - Timing (T)
        - No outcomes at 72 hours or greater
    - Setting (S)
        - Conducted outside of the US and practices not well described or widely divergent relative to US practices
        - Not widely accessible technology
- Comments (if needed)

Appendix D. Analyses of Potential Publication Bias

Testing for publication bias is difficult at best. In effect, one is testing for the number of studies that have not been reported based on the results of those that have been reported. For comparisons with at least 10 studies, we used three tools to look for bias: (1) the funnel plot, which looks for an uneven number of studies falling to the left or right of the funnel; (2) Begg and Mazumdar's test[1] based on the rank correlation between the observed effect sizes and observed standard errors; and (3) Egger's regression intercept, which is similar to Begg and Mazumdar's but uses actual values instead of ranks. For Begg and Egger's test statistics, we report two-sided p-values. When the funnel plot or test statistics suggested publication bias, we used Duval and Tweedie's trim-and-fill method to estimate an effect, corrected for publication bias.[2]

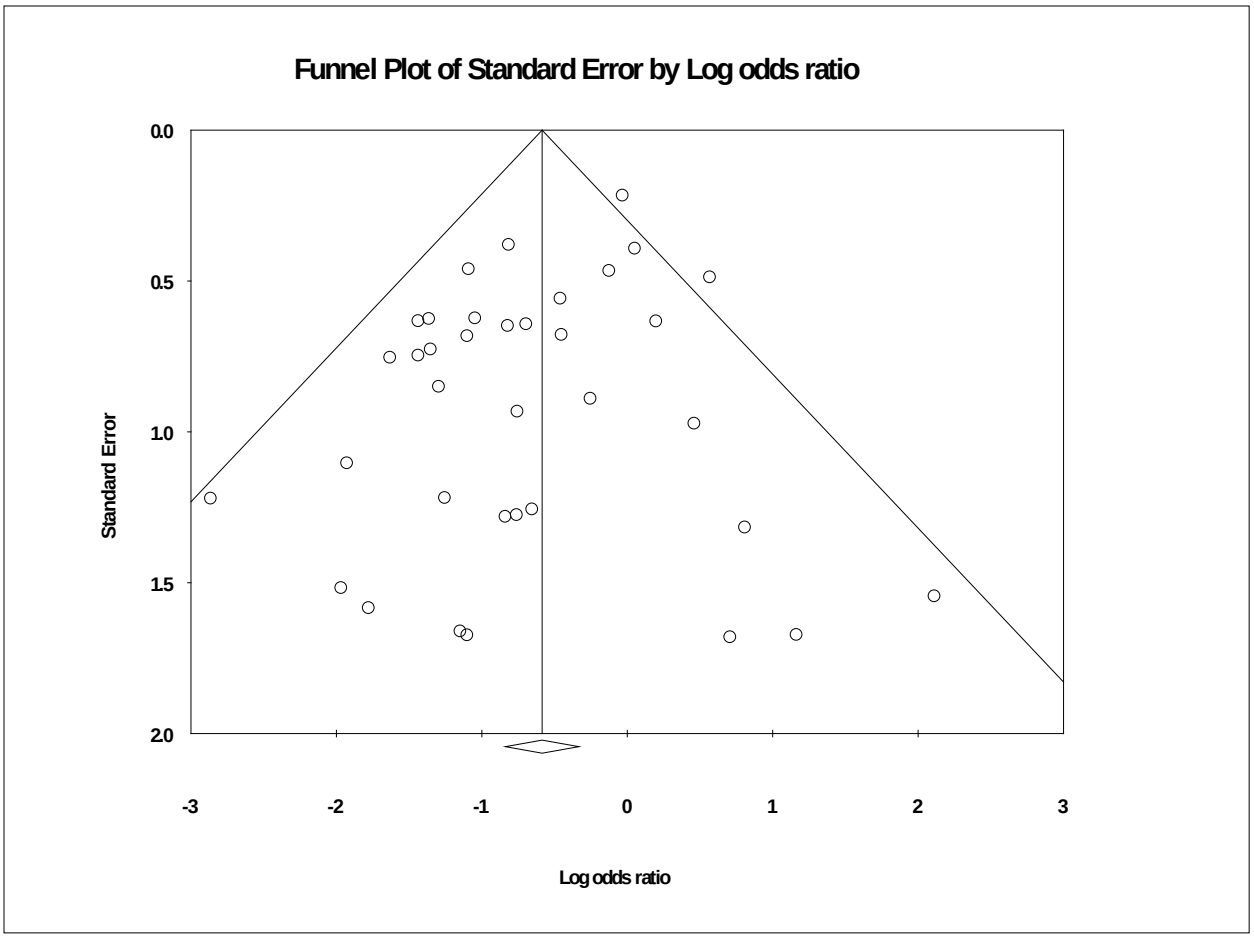
We used Comprehensive Meta-Analysis (Version 2; Biotstat, Englewood, NJ) to test for potential publication bias for the outcomes described below.

Key Question 1

Mortality Outcomes

We used Comprehensive Meta-Analysis to examine any potential publication bias in the studies of mortality outcomes. The resulting funnel plot is shown in Figure D-1.

Figure D-1. Funnel plot for studies of mortality outcomes

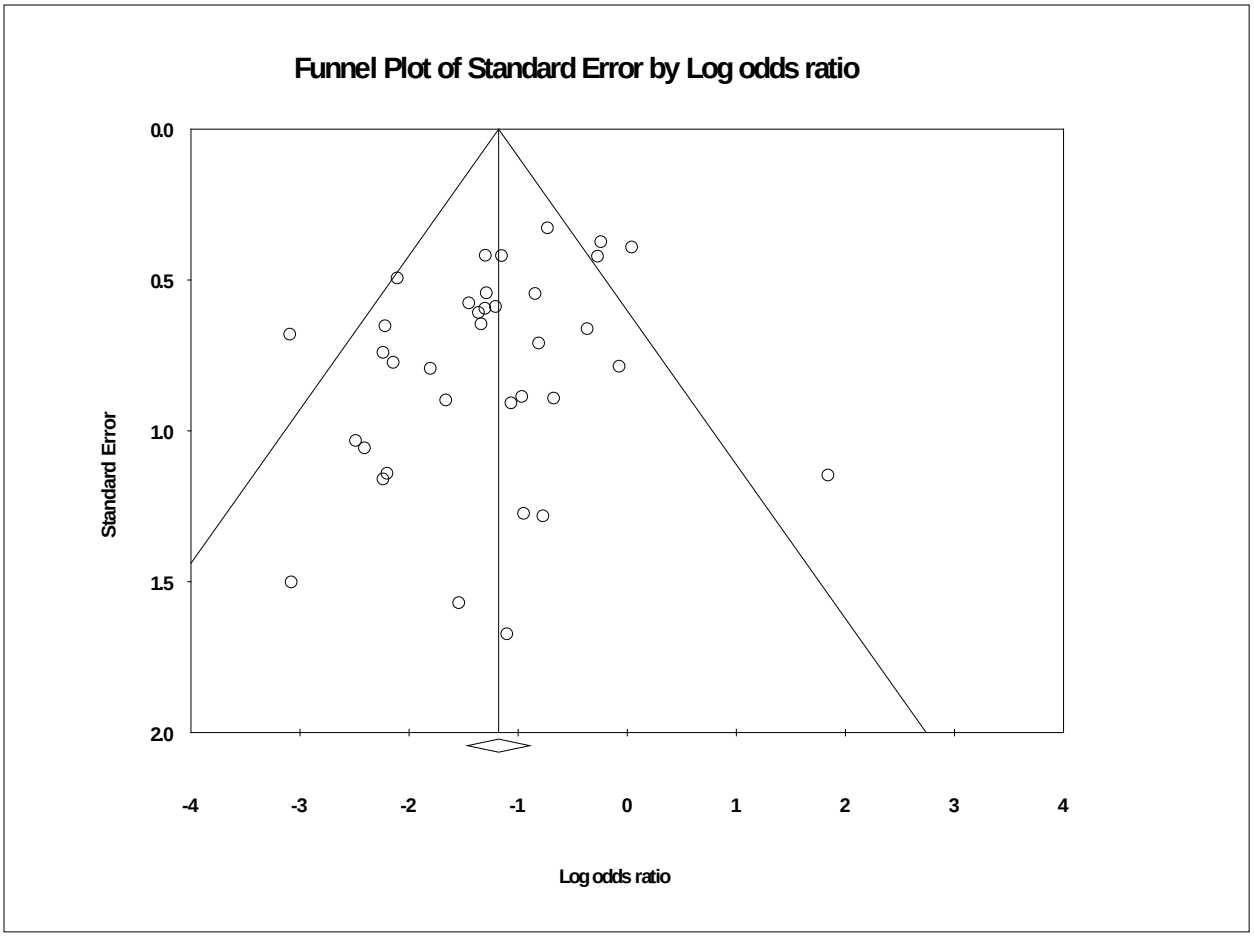


The funnel plot does not suggest significant publication bias. Begg's test statistic, p = 1.0; Eggers test statistic, p = 0.05.

Intubation Rate Outcomes

We used Comprehensive Meta-Analysis to examine any potential publication bias in the studies of intubation rate outcomes. The resulting funnel plot is shown in Figure D-2.

Figure D-2. Funnel plot for studies of intubation rate outcomes



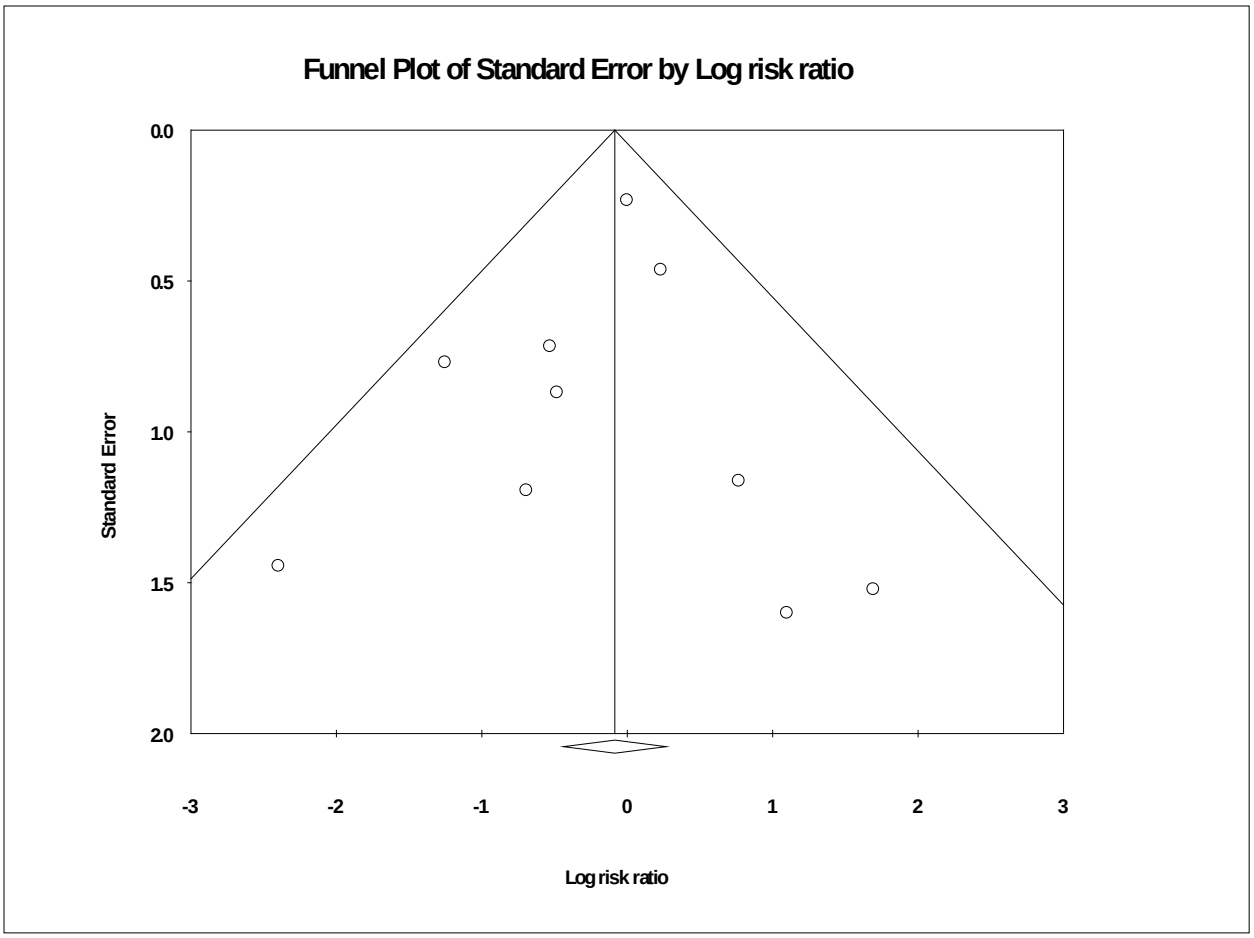
The funnel plots suggest possible publication bias with expected studies missing to the right of the summary effect. Begg's test statistic, p = 0.26; Egger's test statistic, p = 0.03. Trim-and-fill adjusted estimate OR = 0.42 (95% CI, 0.34 to 0.51).

Key Question 2

Mortality Outcomes

We used Comprehensive Meta-Analysis to examine any potential publication bias in the studies of mortality outcomes. The resulting funnel plot is shown in Figure D-3.

Figure D-3. Funnel plot for studies of mortality outcomes

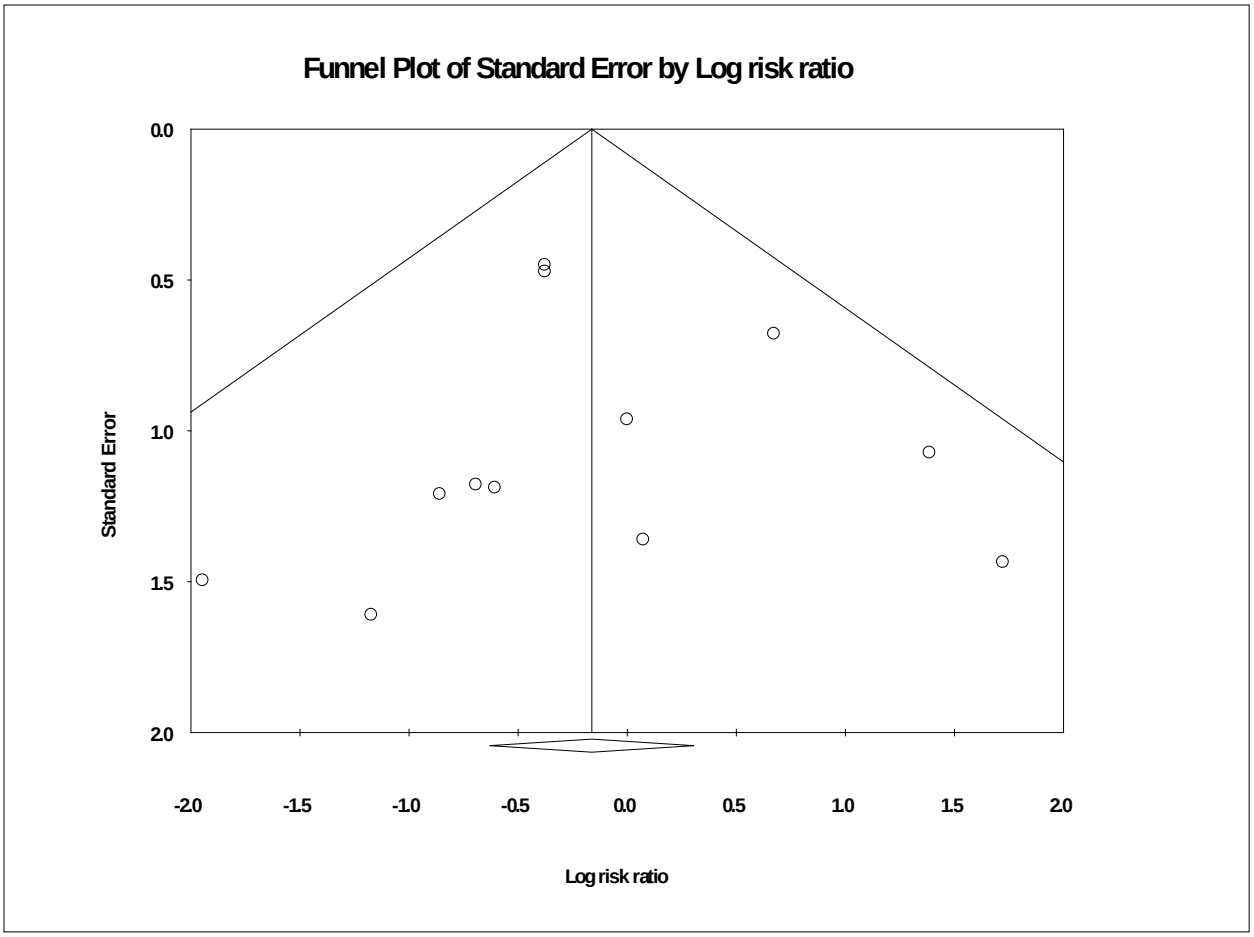


The funnel plot does not suggest publication bias. Begg's test statistic, $p = 0.65$; Egger's test statistic, $p = 0.62$.

Intubation Rate Outcomes

We used Comprehensive Meta-Analysis to examine any potential publication bias in the studies of intubation rate outcomes. The resulting funnel plot is shown in Figure D-4.

Figure D-4. Funnel plot for studies of intubation rate outcomes



The funnel plot does not suggest publication bias. Begg's test statistic, p = 0.58; Egger's test statistic, p = 0.89.

Key Question 3

No funnel plots or test statistics were performed because no set of comparisons had at least 10 studies.

References

1. Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. Biometrics 1994;50(4):1088-101. PMID: 7786990.
2. Duval S, Tweedie R. Trim and fill: A simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. Biometrics 2000;56(2):455-63. PMID: 10877304.

Appendix E. List of Included Studies

Anonymous. Early use of non-invasive positive pressure ventilation for acute exacerbations of chronic obstructive pulmonary disease: a multicentre randomized controlled trial. Chin Med J (Engl) 2005;118(24):2034-40. 16438899

Anonymous. Pulmonary infection control window in treatment of severe respiratory failure of chronic obstructive pulmonary diseases: a prospective, randomized controlled, multi-centred study. Chin Med J (Engl) 2005;118(19):1589-94. 16232342

Antonelli M, Conti G, Bufi M, et al. Noninvasive ventilation for treatment of acute respiratory failure in patients undergoing solid organ transplantation: a randomized trial. JAMA 2000;283(2):235-41. 10634340

Antonelli M, Conti G, Rocco M, et al. A comparison of noninvasive positive-pressure ventilation and conventional mechanical ventilation in patients with acute respiratory failure. N Engl J Med 1998;339(7):429-35. 9700176

Auriant I, Jallot A, Herve P, et al. Noninvasive ventilation reduces mortality in acute respiratory failure following lung resection. Am J Respir Crit Care Med 2001;164(7):1231-5. 11673215

Barbe F, Togores B, Rubi M, et al. Noninvasive ventilatory support does not facilitate recovery from acute respiratory failure in chronic obstructive pulmonary disease. Eur Respir J 1996;9(6):1240-5. 8804944

Bellone A, Monari A, Cortellaro F, et al. Myocardial infarction rate in acute pulmonary edema: noninvasive pressure support ventilation versus continuous positive airway pressure. Crit Care Med 2004;32(9):1860-5. 15343013

Bellone A, Vettorello M, Monari A, et al. Noninvasive pressure support ventilation vs. continuous positive airway pressure in acute hypercapnic pulmonary edema. Intensive Care Med 2005;31(6):807-11. 15871011

Bersten AD, Holt AW, Vedig AE, et al. Treatment of severe cardiogenic pulmonary edema with continuous positive airway pressure delivered by face mask. N Engl J Med 1991;325(26):1825-30. 1961221

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Appendix F. List of Excluded Studies

All studies listed below were reviewed in their full-text version and excluded. Following each reference, in italics, is the reason for exclusion. Reasons for exclusion signify only the usefulness of the articles for this study and are not intended as criticisms of the articles.

Aguilo R, Togores B, Pons S, et al. Noninvasive ventilatory support after lung resectional surgery. Chest 1997:112(1);117-21. *Full-text Exclude - Does not include intervention/comparators of interest.*

Agusti AG, Carrera M, Barbe F, et al. Oxygen therapy during exacerbations of chronic obstructive pulmonary disease. Eur Respir J 1999:14(4);934-9. *Full-text Exclude - Does not include intervention/comparators of interest.*

Allan PF, Thomas KV, Ward MR, et al. Feasibility study of noninvasive ventilation with helium-oxygen gas flow for chronic obstructive pulmonary disease during exercise. Respir Care 2009:54(9);1175-82. *Full-text Exclude - Does not include clinical or utilization-related outcomes of interest.*

Ambrogio C, Lowman X, Kuo M, et al. Sleep and non-invasive ventilation in patients with chronic respiratory insufficiency. Intensive Care Med 2009:35(2);306-13. *Full-text Exclude - Does not include a study population of interest.*

Ambrosino N, Nava S, Bertone P, et al. Physiologic evaluation of pressure support ventilation by nasal mask in patients with stable COPD. Chest 1992:101(2);385-91. *Full-text Exclude - Does not include clinical or utilization-related outcomes of interest.*

Ambrosino N, Vitacca M, Polese G, et al. Short-term effects of nasal proportional assist ventilation in patients with chronic hypercapnic respiratory insufficiency. Eur Respir J 1997:10(12);2829-34. *Full-text Exclude - Does not include clinical or utilization-related outcomes of interest.*

Anderson J and Groth M. Usefulness of noninvasive positive-pressure ventilation in postextubation respiratory distress. Clinical Pulmonary Medicine 2003:10(2);123-4. *Full-text Exclude - Not a full publication (abstract only), not original data, not peer-reviewed literature published 1990 to present, or not grey lit meeting specified criteria.*

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Anonymous. Non-invasive ventilation in acute respiratory failure. Thorax 2002:57(3);192-211. *Full-text Exclude - Study type is not RCT.*

Anton A, Tarrega J, Giner J, et al. Acute physiologic effects of nasal and full-face masks during noninvasive positive-pressure ventilation in patients with acute exacerbations of chronic obstructive pulmonary disease. Respir Care 2003:48(10);922-5. *Full-text Exclude - Does not include intervention/comparators of interest.*

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Baillard C, Fosse JP, Sebbane M, et al. Noninvasive ventilation improves preoxygenation before intubation of hypoxic patients. Am J Respir Crit Care Med 2006:174(2);171-7. *Full-text Exclude - Does not include clinical or utilization-related outcomes of interest.*

Bardi G, Pierotello R, Desideri M, et al. Nasal ventilation in COPD exacerbations: early and late results of a prospective, controlled study. Eur Respir

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Baser S, Kiter G, Kavas M, et al. Binasal cannula versus face mask for oxygen therapy in patients with chronic pulmonary disease. Adv Ther 2006:23(6);1068-74. *Full-text Exclude - Does not include intervention/comparators of interest.*

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Bolton J and Russell WJ. Are nasal spectacles adequate for supplementary oxygen in patients after anaesthesia? Int J Nurs Pract 2001:7(5);329-35. *Full-text Exclude - Does not include intervention/comparators of interest.*

Bourke SC, Bullock RE, Williams TL, et al. Noninvasive ventilation in ALS: indications and effect on quality of life. Neurology 2003:61(2);171-7. *Full-text Exclude - Does not include a study population of interest.*

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Casanova C, Celli BR, Tost L, et al. Long-term controlled trial of nocturnal nasal positive pressure ventilation in patients with severe COPD. Chest 2000:118(6);1582-90. *Full-text Exclude - Not conducted in a hospital or ED setting.*

Celebi S, Koner O, Menda F, et al. Pulmonary effects of noninvasive ventilation combined with the recruitment maneuver after cardiac surgery. Anesth Analg 2008:107(2);614-9. *Full-text Exclude - Does not include a study population of interest.*

Chadda K, Annane D, Hart N, et al. Cardiac and respiratory effects of continuous positive airway pressure and noninvasive ventilation in acute cardiac pulmonary edema. Crit Care Med 2002:30(11);2457-61. *Full-text Exclude - Does not include clinical or utilization-related outcomes of interest.*

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Chermont S, Quintao MM, Mesquita ET, et al. Noninvasive ventilation with continuous positive airway pressure acutely improves 6-minute walk distance in chronic heart failure. J Cardiopulm Rehabil Prev 2009:29(1);44-8. *Full-text Exclude - Does not include a study population of interest.*

Cheung AP, Chan VL, Liong JT, et al. A pilot trial of non-invasive home ventilation after acidotic respiratory failure in chronic obstructive pulmonary disease. Int J Tuberc Lung Dis 2010:14(5);642-9. *Full-text Exclude - Not conducted in a hospital or ED setting.*

Coimbra VR, Lara Rde A, Flores EG, et al. Application of noninvasive ventilation in acute respiratory failure after cardiovascular surgery. Arq Bras Cardiol 2007:89(5);270-6, 98-305. *Full-text*

Exclude - Does not include clinical or utilization-related outcomes of interest.

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Corrado A, Gorini M, Melej R, et al. Iron lung versus mask ventilation in acute exacerbation of COPD: a randomised crossover study. Intensive Care Med 2009:35(4);648-55. *Full-text Exclude - Does not include intervention/comparators of interest.*

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Fagevik Olsen M, Wennberg E, Johnsson E, et al. Randomized clinical study of the prevention of pulmonary complications after thoracoabdominal resection by two different breathing techniques. Br J Surg 2002:89(10);1228-34. *Full-text Exclude - Does not include a study population of interest.*

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Gaszynski T, Tokarz A, Piotrowski D, et al. Boussignac CPAP in the postoperative period in morbidly obese patients. Obes Surg 2007:17(4);452-6. *Full-text Exclude - Does not include intervention/comparators of interest.*

Gay PC, Hess DR and Hill NS. Noninvasive proportional assist ventilation for acute respiratory insufficiency. Comparison with pressure support ventilation. Am J Respir Crit Care Med 2001:164(9);1606-11. *Full-text Exclude - Does not include intervention/comparators of interest.*

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Girault C, Chevron V, Richard JC, et al. Physiological effects and optimisation of nasal assist-control ventilation for patients with chronic obstructive pulmonary disease in respiratory failure. Thorax 1997:52(8);690-6. *Full-text Exclude - Does not include clinical or utilization-related outcomes of interest.*

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Hawker F, Breen D, Torzillo P, et al. Randomized prospective trial of noninvasive positive pressure ventilation in acute respiratory failure. Am J Respir Crit Care Med 1996:153(3);1188-9. *Full-text Exclude - Not a full publication (abstract only), not original data, not peer-reviewed literature published 1990 to present, or not grey lit meeting specified criteria.*

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Khayat RN, Abraham WT, Patt B, et al. Cardiac effects of continuous and bilevel positive airway pressure for patients with heart failure and obstructive sleep apnea: a pilot study. Chest 2008:134(6);1162-8. *Full-text Exclude - Does not include a study population of interest.*

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Appendix G. Characteristics of Included Studies

Table. Characteristics of included studies (ordered first by KQ, then alphabetically by first author)

Study	KQ Applicability	Location; Setting; Total N	ARF Etiology[a]	Demographics	Disease Severity	Type of NPPV	Comparator	Quality Assessment Rating
Anonymous 2005[1]	KQ 1 KQ 4	Asia GMU 342	COPD	Mean age: 69.5 % Male: 38.0	Apache II score: 10.9	BPAP	Supportive	Good
Antonelli 1998[2]	KQ 1 KQ 4	Italy ICUs 64	Mixed	Mean age: 54.5 % Male: 59.4	SAPS: 12.5	BPAP	IVS	Good
Antonelli 2000[3]	KQ 1 KQ 4	Italy ICUs 40	Transplant	Mean age: 44.5 % Male: 37.5	SAPS: 13	BPAP	Supportive	Good
Auriant 2001[4]	KQ 1 KQ 4	France ICUs 48	Post-op	Mean age: 61.0 % Male: NR	SAPS: 16.25	BPAP	Supportive	Good
Barbe 1996[5]	KQ 1 KQ 4	Spain Respiratoryward 24	COPD	Mean age: 68.0 % Male: NR	NR	BPAP	Supportive	Poor
Bersten 1991[6]	KQ 1 KQ 4	Australia ICUs 39	ACPE	Mean age: 75.5 % Male: 33.3	Apache II score: 20.51	CPAP	Supportive	Fair
Bott 1993[7]	KQ 1 KQ 4	UK NR 60	COPD	Mean age: NR % Male: NR	NR	BPAP	Supportive	Poor
Brochard 1995[8]	KQ 1 KQ 4	Europe ICUs 85	COPD	Mean age: 70.0 % Male: NR	SAPS: 12.49	BPAP	Supportive	Good
Carrera 2009[9]	KQ 1	Europe Respiratoryward 75	COPD	Mean age: 70.5 % Male: NR	NR	BPAP	Supportive	Good
Celikel 1998[10]	KQ 1 KQ 4	Turkey ICUs 30	COPD (≥ 70%)	Mean age: NR % Male: NR	NR	BPAP	Supportive	Poor

Study	KQ Applicability	Location; Setting; Total N	ARF Etiology[a]	Demographics	Disease Severity	Type of NPPV	Comparator	Quality Assessment Rating
Confalonieri 1999[11]	KQ 1 KQ 4	Europe ICUs 56	Mixed	Mean age: 63.5 % Male: 71.4	Apache II score: 19	Other	Supportive	Good
Conti 2002[12]	KQ 1	Italy ICUs 49	COPD	Mean age: 71.9 % Male: NR	SAPS: 38.22	Other	IVS	Fair
Delclaux 2000[13]	KQ 1 KQ 4	Europe; Africa ICUs 123	Mixed	Mean age: NR % Male: 63.4	NR	CPAP	Supportive	Good
Dhamija 2005[14]	KQ 1 KQ 4	India NR 29	COPD	Mean age: NR % Male: NR	NR	BPAP	Supportive	Poor
Dikensoy 2002[15]	KQ 1 KQ 4	Turkey ED 34	COPD	Mean age: 64.7 % Male: 58.8	NR	BPAP	Supportive	Poor
Ferrer 2003[16]	KQ 1 KQ 4	Europe ICUs 105	Mixed	Mean age: 61.5 % Male: 55.2	SAPS: 33.49	BPAP	Supportive	Fair
Gupta 2010[17]	KQ 1	India ICUs 53	Asthma	Mean age: 43.8 % Male: 20.8	NR	BPAP	Supportive	Good
Hilbert 2001[18]	KQ 1 KQ 4	France ICUs 52	Transplant	Mean age: 49.0 % Male: 71.2	SAPS: 43.5	BPAP	Supportive	Good
Holley 2001[19]	KQ 1	Jacksonville, FL ED 35	Asthma	Mean age: 36.8 % Male: 28.6	NR	BPAP	Supportive	Fair
Honrubia 2005[20]	KQ 1 KQ 4	Europe ICUs 64	Mixed	Mean age: 67.4 % Male: 70.3	Apache II score: 24.48	BPAP	IVS	Fair
Jurjevic 2009[21]	KQ 1 KQ 4	Croatia ICUs 156	COPD	Mean age: NR % Male: 66.0	NR	BPAP	IVS	Fair

Study	KQ Applicability	Location; Setting; Total N	ARF Etiology[a]	Demographics	Disease Severity	Type of NPPV	Comparator	Quality Assessment Rating
Keenan 2005[22]	KQ 1 KQ 4	Canada Respiratoryward 52	COPD	Mean age: 70.0 % Male: 46.2	Apache II score: 18.04	BPAP	Supportive	Good
Kelly 2002[23]	KQ 1 KQ 4	NR ED; Stepdown unit 58	ACPE	Mean age: 77.5 % Male: 44.8	NR	CPAP	Supportive	Fair
Khilnani 2010[24]	KQ 1 KQ 4	India ICUs 40	COPD	Mean age: 57.5 % Male: 77.5	Apache II score: 16.44	BPAP	Supportive	Fair
Kramer 1995[25]	KQ 1 KQ 4	U.S. ICUs; GMU; Stepdown unit 30	COPD(≥ 70%)	Mean age: 68.5 % Male: 60.0	Apache II score: 18.48	BPAP	Supportive	Good
Levitt 2001[26]	KQ 1 KQ 4	Oakland, California ED 38	ACPE	Mean age: 67.9 % Male: 34.2	NR	BPAP	Supportive	Fair
L'Her 2004[27]	KQ 1 KQ 4	Europe ED; GMU 89	ACPE	Mean age: 84.0 % Male: 41.6	NR	CPAP	Supportive	Fair
Lin 1991[28]	KQ 1	Taiwan ICUs 55	ACPE	Mean age: 73.8 % Male: 90.9	NR	CPAP	Supportive	Fair
Lin 1995[29]	KQ 1 KQ 4	Asia ED; ICU 100	ACPE	Mean age: 72.5 % Male: 90.0	NR	CPAP	Supportive	Fair
Martin 2000[30]	KQ 1 KQ 4	Pittsburg, PA ICU 61	COPD	Mean age: 61.1 % Male: 47.5	Apache III score: 61.33	BPAP	Supportive	Fair
Masip 2000[31]	KQ 1 KQ 4	Europe ICUs 142	ACPE	Mean age: 76.9 % Male: 13.4	Apache II score: 16	BPAP	Supportive	Fair
Matic 2007[32]	KQ 1 KQ 4	Croatia ICUs 72	COPD	Mean age: NR % Male: 66.7	NR	BPAP	IVS	Fair

Study	KQ Applicability	Location; Setting; Total N	ARF Etiology[a]	Demographics	Disease Severity	Type of NPPV	Comparator	Quality Assessment Rating
Nava 2003[33]	KQ 1 KQ 4	ER ED 130	ACPE	Mean age: 72.6 % Male: 77.7	SAPS: 21.1	BPAP	Supportive	Good
Nava 2011[34]	KQ 1 KQ 4	Europe ICU 82	COPD	Mean age: 81.3 % Male: 65.9	SAPS: 33.5	Other	Supportive	Good
Pastaka 2007[35]	KQ 1 KQ 4	Greece Respiratoryward 42	COPD	Mean age: 68.4 % Male: 78.6	NR	BPAP	Supportive	Fair
Plant 2000[36]Plant 2001;[37]	KQ 1 KQ 4	UK GMU; Respiratoryward 236	COPD	Mean age: 69.0 % Male: 49.6	NR	BPAP	Supportive	Good
Soroksky 2003[38]	KQ 1	Tel Aviv, Israel ED 30	Asthma	Mean age: 33.3 % Male: 50.0	NR	BPAP	Supportive	Fair
Squadrone 2005[39]	KQ 1 KQ 4	Europe Postoperative 209	Post-op	Mean age: 65.5 % Male: 64.6	SAPS: 27.5	CPAP	Supportive	Good
Takeda 1997[40]	KQ 1 KQ 4	Japan ICU 30	ACPE	Mean age: 66.5 % Male: 73.3	Apache II score: 14.65	CPAP	Supportive	Fair
Takeda 1998[41]	KQ 1 KQ 4	Tokyo, Japan ICU 22	ACPE	Mean age: 74.5 % Male: 77.3	Apache II score: 10.65	CPAP	Supportive	Fair
Thys 2002[42]	KQ 1 KQ 4	Belgium ED 20	Mixed	Mean age: 73.5 % Male: 55.0	NR	BPAP	Supportive	Good
Wood 1998[43]	KQ 1 KQ 4	St. Louis, MO ED 27	Mixed	Mean age: 58.7 % Male: 59.3	Apache II score: 17.08	BPAP	Supportive	Good
Wysocki 1995[44]	KQ 1 KQ 4	France ICUs 41	Mixed	Mean age: 63.0 % Male: 58.5	SAPS: 12	Other	Supportive	Good

Study	KQ Applicability	Location; Setting; Total N	ARF Etiology[a]	Demographics	Disease Severity	Type of NPPV	Comparator	Quality Assessment Rating
Crane 2004[45]	KQ 1 KQ 2 KQ 4	UK ED 60	ACPE	Mean age: 75.2 % Male: 38.3	NR	CPAP BPAP	Supportive	Good
Gray 2008;[46] Gray 2009[47]	KQ 1 KQ 2 KQ 4	UK ED 1069	ACPE	Mean age: 78.0 % Male: 43.3	NR	CPAP BPAP	Supportive	Good
Park 2001[48]	KQ 1 KQ 2 KQ 4	Sao Paulo, Brazil NR 26	ACPE	Mean age: NR % Male: 38.5	NR	CPAP BPAP	Supportive	Poor
Park 2004[49]	KQ 1 KQ 2 KQ 4	Brazil ED 80	ACPE	Mean age: 64.0 % Male: 42.5	Apache II score: 19.34	CPAP	BPAP	Fair
Bellone 2004[50]	KQ 2	Italy ED 46	ACPE	Mean age: 77.1 % Male: 50.0	Apache II score: 18.26	CPAP	BPAP	Fair
Bellone 2005[51]	KQ 2	Italy ED 36	ACPE	Mean age: 76.8 % Male: 33.3	Apache II score: 18.15	CPAP	BPAP	Fair
Cross 2003[52]	KQ 2	Australia/N.Z. ED 101	COPD (≥ 70%)	Mean age: 72.5 % Male: NR	NR	CPAP	BPAP	Fair
Ferrari 2007[53]	KQ 2	Turin, Italy High dependency unit 52	ACPE	Mean age: 75.5 % Male: 44.2	SAPS: 45.97	CPAP	BPAP	Fair
Ferrari 2010[54]	KQ 2	Europe ED 80	ACPE	Mean age: 77.0 % Male: NR	SAPS: 41.6	CPAP	BPAP	Good
Mehta 1997[55]	KQ 2	Providence, RI NR 27	ACPE	Mean age: 76.5 % Male: 40.7	Apache II score: 17.93	BPAP	CPAP	Poor
Moritz 2007[56]	KQ 2	Europe ED 109	ACPE	Mean age: 77.6 % Male: 52.3	NR	CPAP	BPAP	Fair

Study	KQ Applicability	Location; Setting; Total N	ARF Etiology[a]	Demographics	Disease Severity	Type of NPPV	Comparator	Quality Assessment Rating
Nouira 2011[57]	KQ 2	Africa ED 200	ACPE	Mean age: 69.0 % Male: 43.5	Apache II score: 16	CPAP	BPAP	Good
Anonymous 2005[58]	KQ 3	Asia ICUs 90	COPD	Mean age: 68.6 % Male: 66.7	Apache II score: 9	BPAP	IVS	Fair
Esteban 2004[59]	KQ 3	U.S.; Canada; Europe; S. America; Middle East ICUs 221	Mixed	Mean age: 59.5 % Male: 57.5	Apache II score: 36.52	BPAP	Supportive	Good
Ferrer 2003[60]	KQ 3	Europe ICUs 43	Mixed	Mean age: 70.7 % Male: 69.8	Apache II score: 18.16	BPAP	IVS	Fair
Ferrer 2006[61]	KQ 3	Spain ICUs 162	Mixed	Mean age: 71.0 % Male: 71.0	Apache II score: 13.49	BPAP	Supportive	Fair
Ferrer 2009[62]	KQ 3	Europe ICUs 106	COPD(≥ 70%)	Mean age: 68.5 % Male: 75.5	Apache II score: 11	BPAP	Supportive	Good
Girault 1999[63]	KQ 3	Rouen, France ICUs 33	Mixed	Mean age: 64.2 % Male: NR	SAPS: 38.42	BPAP	IVS	Fair
Girault 2011[64]	KQ 3	Europe ICUs 208	Mixed	Mean age: NR % Male: 71.6	NR	Other	Supportive IVS	Good
Jiang 1999[65]	KQ 3	Taiwan ICUs 93	Mixed	Mean age: 72.8 % Male: 63.4	Apache II score: 16.8	BPAP	Supportive	Poor
Keenan 2002[66]	KQ 3	Canada ICUs 81	ACPE	Mean age: 68.5 % Male: NR	Apache II score: 23.28	BPAP	Supportive	Good
Nava 1998[67]	KQ 3	Europe ICUs 50	COPD	Mean age: 67.9 % Male: NR	Apache II score: 23.7	BPAP	IVS	Good

Study	KQ Applicability	Location; Setting; Total N	ARF Etiology[a]	Demographics	Disease Severity	Type of NPPV	Comparator	Quality Assessment Rating
Nava 2005[66]	KQ 3	Europe ICUs 97	Mixed	Mean age: 54.6 % Male: 62.9	SAPS: 32.45	BPAP	Supportive	Good

[a]In instances where a single ARF etiology made up 70% or more of the population, that etiology has been listed, along with the notation "(≥ 70%)." ARF etiology has been listed as "Mixed" if no single etiology made up at least 70% of the population.

Abbreviations: ACPE = acute cardiogenic pulmonary edema; ARF = acute respiratory failure; BPAP = bilevel positive airway pressure; COPD = chronic obstructive pulmonary disease; CPAP = continuous positive airway pressure; ICU = intensive care unit; IVS = invasive ventilatory support; KQ = key question; N = number of participants; NPPV = noninvasive positive-pressure ventilation; NR = not reported; SAPS = Simplified Acute Physiology Score

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