Evidence-based Practice Center Systematic Review Protocol

Project Title: Home Mechanical Ventilators

Project ID: PULT0717

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I. Background and Objectives for the Systematic Review

Chronic respiratory failure is a common condition with important morbidity and mortality and can require long-term home mechanical ventilation. Chronic respiratory failure is defined as the long-term inability to maintain oxygen and carbon dioxide levels within normal limits. Chronic respiratory failure may range from mild to severe and can be characterized as hypoxemic (inability to maintain a PaO_2 • P P + J K \ S 2 H" U F D S Q PL P Hg), or a combination of both. Many disease conditions may lead to chronic respiratory failure including, but not limited to neuromuscular diseases, thoracic restrictive diseases (including thoracic cage abnormalities and morbid obesity), chronic obstructive pulmonary disease, and hypoventilation syndromes such as obesity hypoventilation .[1] Such disease states and the extent of associated respiratory failure may be relatively stable over time or progressive in nature. Mechanical ventilation is used to treat chronic respiratory failure. A mechanical ventilator is "a device capable of delivering pressurized gas (either through a secured artificial airway (tracheostomy) or through a mask or mouthpiece) in a manner that repeatedly supplies a physiological tidal volume to the lungs sufficient to improve or fully sustain respiration." Mechanical ventilator devices are broadly classified into two main categories: 1) home

If deemed to be feasible and safe, long term use of HMVs and BPAPs is preferred in the home setting compared to other settings such as intensive care units (ICUs), ventilator weaning units, or long-term care hospitals. Home use has been associated with lower costs, greater independence, increased quality of life, decreased risk of hospital-acquired infections, and increased space for other acute care patients in acute care facilities.[2-4] The number of patients using long-term HMVs are growing.[5]

Failing to adequately treat chronic respiratory failure in patients who require a ventilator with the appropriate features of an appropriate mechanical ventilator device could potentially result in sudden or gradual hypoxemia and/or hypercarbia. These physiologic aberrations may result in several adverse outcomes that include, but are not limited to: death, respiratory arrest, need for emergency room evaluation, need for hospital admission, need for the intensive care unit admission, need for intubation, deterioration of health, hypersomnolence, and poor quality of life.[1, 6]

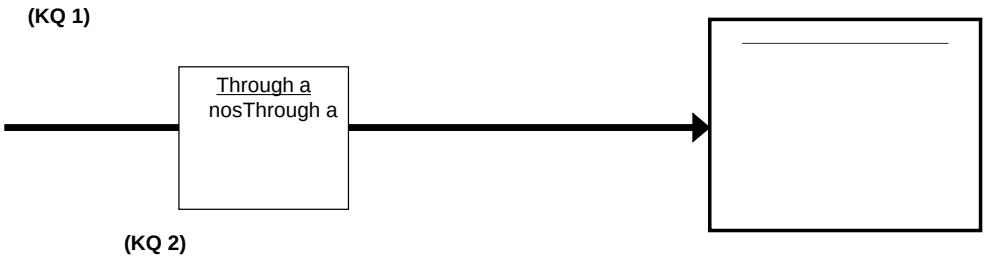
Selecting the most appropriate respiratory device to use for an individual patient is of highest importance. Determining the need for a HMV versus BPAP versus CPAP is complex and may differ based on several important patient level and device level factors such as the underlying disease, interface required (a tight fitting removable mask versus a mouthpiece attachment), type of ventilatory support required, duration of ventilatory support needed per day, and required equipment characteristics

Currently, substantial variability exists regarding the usage, prescribing patterns, policies, and guidelines for HMVs versus BPAPs versus CPAPs.[7, 8] This variability exists, even when accounting for variability in underlying disease processes and severity of chronic respiratory failure. While a number of guidelines address the uses of BPAPs and HMVs in the home for different disease conditions, there is marked variability in the conclusions, recommendations, and evidence basis for such guidelines.[9-12] Many guidelines may address home BPAP usage and other guidelines may address HMV usage, few guidelines address the intricacies of choosing one versus the other. With the current levels of practice variability, and unclear guidelines, there is a clear need to synthesize the best available evidence to clinically guide prescribing of HMVs, BPAPs, and CPAPs.[13] Several challenges contribute to this variability.

1. There is considerable overlap regarding the technical features of HMVs and BPAPs. While HMVs traditionally provided volume targeted ventilation using an invasive tracheostomy interface and BPAPs provided pressure targeted ventilation using a mask interface, the FDA has approved HMVs which can provide pressure targeted ventilation using a mask interface and BPAPs which can be used with an invasive tracheostomy interface.

2. There is considerable variability regarding the continuum of severity of chronic respiratory failure. Depending on the severity of illness, patients with chronic hypercapnic respiratory failure may require no ventilatory support, intermittent ventilatory support (during variable lengths of time at night or day or both), or continuous ventilatory support.

3. A significant newer body of literature has been published which necessitates a reexamination of recommendations, guidelines, and policies regarding HMVs, BPAPs, and CPAPs. Such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(KQ 2)

PICOTS Elements	Inclusion Criteria	Exclusion Criteria
Abbreviations: KQ = key question; PICOTS = populations, interventions, comparators, outcomes, timing, and settings; RCT = randomized controlled trial		

Searching for the Evidence: Literature Search Strategies for Identification of Relevant Studies To Answer the Key Questions - We plan to conduct a comprehensive literature search of eight databases, including National Guideline Clearinghouse, Embase, Epub Ahead of Print, In-Process & Other Non-Indexed Citations, MEDLINE Daily, MEDLINE, Cochrane Central Registrar of Controlled Trials, Ovid Cochrane Database of Systematic Reviews, and Scopus from January 1, 1995 to the present. We have developed a preliminary database search strategy (Appendix A) and found that these databases can adequately identify the relevant literature. We will use relevant systematic reviews and meta-analysis to identify additional existing and new literature. We will also search FDA Establishment Registration & Device Listing, ClinicalTrials.gov, Health Canada, ITJ EMCchito.0br, Healc1.150(T)-e-1.1iTto.6 (er)-c4

observational studies, we will select appropriate items from the Newcastle-Ottawa Scale.[16] Additional criteria will be adopted from other quality appraisal tools if deemed appropriate.

Data Synthesis - We will qualitatively summarize key features/characteristics (e.g. study populations, design, intervention, outcomes, device model, equipment parameters, and conclusions) of the included studies and present in evidence tables for each KQs.

We will determine whether meta-analysis is appropriate (i.e., more than 2 studies address the same PICOTS and provide point estimates and dispersion measures) to quantitatively summarize study findings based on the similarities of PICOTS presented by the studies. If meta-analysis is deemed appropriate, we plan to use the DerSimonian and Laird random effect method to combine direct comparisons between treatments if the number of studies included in the analysis is larger than 18[17]; otherwise, the DerSimonian and Laird random effect method with the Knapp and Hartung adjustment of the variance will be adopted[18]. We will evaluate heterogeneity between studies using I^2 indicator. To further explore heterogeneity, we plan to conduct subgroup analyses based on factors listed in Section II. We will conduct sensitivity analyses to evaluate robustness of our findings by excluding studies with high risk of bias.

We will evaluate potential publication bias by evaluating funnel plots symmetry and using statistical tests such as Egger linear regression test if the number of studies included in a direct comparison is large (n>=20).

Grading the Strength of Evidence (SOE) for Major Comparisons and Outcomes

We will grade the strength of the body of evidence as per the EPC methods guide on assessing the strength of evidence. We will grade the strength of evidence for the outcomes we classified as most important or critical such as mortality, hospitalization, outpatient visits. These outcomes are chosen because they are either clinically important from a patient's perspective or highly relevant for CMS's decision making.

Grading the SOE will be done for each comparison and for each outcome. Randomized trials start as high strength of evidence and observational studies start as low strength of evidence. The domains to be used for all KQs will be: the methodoll-7 (orhi[l4 (.) (l)-v (nd us(t)-10 (f)5 Tw -27.79 -1

review. Can Respir J. 2015 Sep 30 PMID: 26422402.

8.

Key Informants must disclose any financial conflicts of interest greater than $5,000 and any other relevant business or professional conflicts of interest. Because of their role as end-users, individuals are invited to serve as Key Informants and those who present with potential conflicts may be retained. The AHRQ Task Order Officer (TOO) and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

IX. Technical Experts

Not applicable

X. Peer Reviewers

Peer reviewers are invited to provide written comments on the draft report based on their clinical, content, or methodological expertise. The EPC considers all peer review comments on the draft report in preparation of the final report. Peer reviewers do not participate in writing or editing of the final report or other products. The final report does not necessarily represent the views of individual reviewers. The EPC will complete a disposition of all peer review comments. The disposition of comments for systematic reviews and technical briefs will be published three months after the publication of the evidence report.

Potential Peer Reviewers must disclose any financial conflicts of interest greater than $5,000 and any other relevant business or professional conflicts of interest. Invited Peer Reviewers may not have any financial conflict of interest greater than $5,000. Peer reviewers who disclose potential business or professional conflicts of interest may submit comments on draft reports through the public comment mechanism.

XI. EPC Team Disclosures

EPC core team members must disclose any financial conflicts of interest greater than $1,000 and any other relevant business or professional conflicts of interest. Related financial conflicts of interest that cumulatively total greater than $1,000 will usually disqualify EPC core team investigators.

XII. Role of the Funder

This project was funded under Contract No. 290-2015-00013-I

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