Introduction

Background

Chronic respiratory failure is a common medical condition characterized by the inability to maintain normal oxygen ($PaO_2 \geq 60$mmHg) and/or carbon dioxide ($PaCO_2 \leq 45$mmHg) levels. Many diseases may lead to chronic respiratory failure including chronic obstructive pulmonary disease (COPD), thoracic restrictive diseases (TRD) such as kyphoscoliosis, neuromuscular diseases (NMD), and obesity hypoventilation. [1] Associated with increased morbidity and mortality, chronic respiratory failure may range from mild to severe and may be stable or progressive.

Chronic respiratory failure may be treated with chronic mechanical ventilation. Mechanical ventilator devices are broadly classified into two categories: home mechanical ventilators (HMV) and bi-level positive airway pressure (BPAP) devices. [1] While both HMV and BPAP devices provide positive pressure ventilation, their technical features may vary and overlap considerably. Variability includes: interface (tracheostomy or mask), mode of ventilation (such as pressure targeted versus volume targeted versus volume preset), respiratory circuit (such as single-limb versus double-limb), monitoring capability, safety and alarm systems, and internal battery life. Devices also differ by level of oversight and servicing. In addition, certain device features (such as the ability to perform lung volume recruitment) may only be available with certain devices and settings.

If deemed to be feasible and safe, using these devices in the home setting is preferred to other settings such as intensive care units (ICUs), ventilator weaning units, or long-term care hospitals. Advantages of home use include lower costs, greater independence, increased quality of life, decreased risk of healthcare associated infections, and reduced use of acute care facilities.[2-4] The number of patients using long-term HMVs and BPAP devices is growing—and this patient population is increasingly differentiated from patients with acute respiratory failure who use such devices in the hospital setting.[5] In addition, the cost of caring for patients with medical conditions associated with chronic respiratory failure is also growing, with estimates as high as $50 billion annually in the United States for COPD alone.[6]

For patients who use home mechanical ventilation through a noninvasive interface, or noninvasive positive pressure ventilation (NIPPV), selecting the optimal device type (HMV versus BPAP versus continuous positive airway pressure [CPAP]) and device settings is imperative. Depending on the severity of illness, patients with chronic hypercapnic respiratory failure may require no, intermittent, or continuous ventilatory support. Failing to adequately treat chronic respiratory failure with the appropriate device could potentially result in sudden or gradual hypoxemia and/or hypercapnia. This can lead to poor quality of life, sleepiness, hospital admission, intubation, and even respiratory arrest and death. [1, 7] Some patients have progressive respiratory failure and may require advanced ventilatory capabilities as their disease progresses.

Currently, substantial variability exists regarding the usage, prescribing patterns, policies, and guidelines among noninvasive HMVs, BPAPs, and CPAPs.[8, 9] While a number of guidelines address home use of BPAPs and HMVs, there is marked variability in the conclusions, recommendations, and evidence basis for these guidelines. [10-13] With current practice and guideline variability, there is a clear need to synthesize the best available evidence to guide prescribing. [14]

This systematic review evaluates home NIPPV in adult patients with chronic respiratory failure primarily due to chronic obstructive pulmonary disease (COPD), thoracic restrictive

disorders, and neuromuscular disease. Other causes of respiratory failure were included due to additional interest.

Scope and Key Questions

Scope of the Review

This systematic review addresses initiation and continuation of home NIPPV including the effectiveness, equipment settings, and related respiratory services for patients with chronic respiratory failure. The systematic review also highlights areas of controversy and identifies needs for future research. NIPPV in other settings were excluded (e.g. long-term acute care hospital, skilled nursing facility, etc.)

Key Questions

The following Key Questions (KQs) were determined based on input from multiple key informants, Centers for Medicare and Medicaid Services (CMS) and the public (drafted KQs were posted for public comment from November 3, 2017 to November 17, 2017). The related PICOTS (population, interventions, comparisons, outcomes, timing, and setting) are listed in Table 1.

KQ1. What are the patient characteristics and/or laboratory criteria and/or target level measurable improvements considered for the initiation and continuation of noninvasive positive pressure ventilation supplied by a Home Mechanical Ventilator (HMV), Bi-level Positive Airway Pressure device (BPAP), and Continuous Positive Airway Pressure device (CPAP) in the home through a noninvasive interface for the population of patients with chronic respiratory failure due to neuromuscular diseases (NMD), thoracic restrictive diseases (TRD), chronic obstructive pulmonary diseases (COPD), or other lung diseases (cystic fibrosis, bronchiectasis)?

a. What are the patient characteristics and/or laboratory criteria and/or target level measurable improvements (e.g., reduction in hypercapnia) considered for the initiation and continuation of noninvasive positive pressure mechanical ventilation supplied by a HMV through a noninvasive interface in the home?
b. What are the patient characteristics and/or laboratory criteria and/or target level measurable improvements (e.g., reduction in hypercapnia) considered for the initiation and continuation of noninvasive positive pressure ventilation supplied as a BPAP through a noninvasive interface in the home?
c. What are the patient characteristics and/or laboratory criteria and/or target level measurable improvements (e.g., reduction in hypercapnia) considered for the initiation and continuation of noninvasive positive pressure ventilation supplied as a CPAP through a noninvasive interface in the home?

KQ2. In each of the above groups, what is the effect of HMV, BPAP, or CPAP use on patient outcomes, including mortality, hospitalization, admission/readmission to intensive care unit (ICU), need for intubation, outpatient visits, emergency room visits, disease exacerbations, quality of life (QoL), activities of daily living (ADL), dyspnea, sleep quality, exercise tolerance, and adverse events?

KQ3. What are the equipment parameters that are used in each of the above groups?

a. What are the parameters of ventilator usage (e.g., mode as determined by trigger, control and cycling variables)?
b. What are the equipment parameters that are necessary to achieve desired outcomes (e.g., flow capabilities, settings, etc.)?
c. What are the parameters of prescribed patient usage (e.g., frequency of use, duration of use throughout the day, other)?
d. In each of the above populations, what are the parameters of patient compliance with the prescribed usage of the equipment?

KQ4. What respiratory services, other than the technical support of the use of the prescribed equipment, are being provided to the above patients in the home (e.g., patient education, ongoing smoking cessation, respiratory therapist led home care)?

KQ5. What are the professional guidelines and statements that address KQ1 to KQ4?

Table 1. PICOTS (population, interventions, comparisons, outcomes, timing, and setting)

PICOTS Elements	Inclusion Criteria	Exclusion Criteria
Populations	Humans Adults 18 years and older Patients with: COPD Obesity hypoventilation syndrome Neuromuscular disease Thoracic cage abnormality Interstitial lung disease Cystic fibrosis Bronchiectasis	Animals Children (age < 18 years) Patients in whom the indication for the device was the lone diagnosis of: Any sleep apnea (obstructive, central, complex) Congestive heart failure
Interventions	Noninvasive mask or mouthpiece: HMV BPAP CPAP	Mechanical insufflation and exsufflation device / cough assist device High flow nasal cannula oxygen Negative pressure ventilators Patients with tracheostomy
Comparators	Usual care (i.e. no HMV/BPAP/CPAP) Different type of noninvasive mechanical ventilation Different modes of same equipment Other noninvasive ventilation (Studies that reported outcomes of interest (e.g. mortality) in two or more groups of patients based on different patient characteristics, laboratory criteria, ventilator parameters, or respiratory services will also be included)	Invasive ventilation (e.g. tracheostomy)
Outcomes	Mortality Hospitalization Admission/readmission to intensive care unit (ICU) Need for intubation Outpatient visits Emergency room visits Disease exacerbations Quality of life (QoL) Activities of daily living (ADL) Dyspnea Sleep quality Exercise tolerance Adverse events	None

PICOTS Elements	Inclusion Criteria	Exclusion Criteria
Timing	At least 1 month of treatment in home settings	None
Settings	Therapy (BPAP, CPAP, HMV) administered and studied at home or assisted living. Therapy could have been started at hospital / ICU but must be evaluated in the study as an outpatient treatment.	Therapy (BPAP, CPAP, HMV) administered only in: • Nursing home/skilled nursing facility (SNF) • Long term acute care facility (LTACH) • Hospital step down unit • Hospital chronic ventilator unit / ventilator weaning unit
Study design	Original data Any sample size RCTs, nonrandomized comparative studies (prospective and retrospective) Relevant systematic reviews, or meta-analyses (used for identifying additional studies) Clinical guideline	*In vitro* studies Non-original data (e.g. narrative reviews, editorials, letters, or erratum) Non-comparative observational studies, case series Qualitative studies Cost-benefit analysis Cross-sectional (i.e., non-longitudinal) studies Before-after studies Survey
Publications	Studies published in 1995 and after	Studies published before 1995

BPAP: bi-level positive airway pressure, COPD: chronic obstructive pulmonary disease, CPAP: continuous positive airway pressure, HMV: home mechanical ventilation, KQ: key question, PICOTS: populations, interventions, comparators, outcomes, timing, and settings, RCT: randomized controlled trial

Organization of the Report

In this report, we first presented the methods used to collect, screen, and synthesize the literature. The results section was organized first by disease conditions (chronic obstructive pulmonary disease, thoracic restrictive diseases, neuromuscular disease, obesity hypoventilation syndrome, other lung diseases, and mixed disease conditions) and then by KQs. Adverse events were summarized at the end of the results, regardless of disease conditions. After the results section, we summarized our findings, findings in relation to what is known, limitations, applicability of the findings, future research needs, and conclusion.