Medical Policy

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Title: Home Non-invasive Positive Airway Pressure Devices for the Treatment of Respiratory Insufficiency and Failure

Related Policies:	▪ *Diagnosis and Medical Management of Obstructive Sleep Apnea Syndrome*

Professional / Institutional
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Populations	Interventions	Comparators	Outcomes
Individuals: • with chronic obstructive pulmonary disease and obstructive sleep apnea	Interventions of interest are: • Continuous positive airway pressure	Comparators of interest are: • Oxygenation therapy	Relevant outcomes include: • Mortality • Symptoms • Morbid events • Functional outcomes • Quality of life • Hospitalizations

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Populations	Interventions	Comparators	Outcomes
Individuals: • with chronic obstructive pulmonary disease and chronic respiratory failure	Interventions of interest are: • Bilevel positive airway pressure	Comparators of interest are: • Oxygenation therapy • Continuous positive airway pressure	Relevant outcomes include: • Mortality • Symptoms • Morbid events • Functional outcomes • Quality of life • Hospitalizations
Individuals: • with chronic obstructive pulmonary disease when bilevel positive airway pressure is inadequate	Interventions of interest are: • Non-invasive home mechanical ventilation	Comparators of interest are: • Oxygenation therapy • Continuous or bilevel positive airway pressure	Relevant outcomes include: • Mortality • Symptoms • Morbid events • Functional outcomes • Quality of life • Hospitalizations
Individuals: • with thoracic restrictive disorders due to neuromuscular disease and chronic respiratory failure	Interventions of interest are: • Bilevel positive airway pressure	Comparators of interest are: • Standard medical care without bilevel positive airway pressure	Relevant outcomes include: • Mortality • Symptoms • Morbid events • Functional outcomes • Quality of life • Hospitalizations
Individuals: • with thoracic restrictive disorders due to neuromuscular disease when bilevel positive airway pressure is inadequate	Interventions of interest are: • Non-invasive home mechanical ventilation	Comparators of interest are: • Bilevel positive airway pressure	Relevant outcomes include: • Mortality • Symptoms • Morbid events • Functional outcomes • Quality of life • Hospitalizations
Individuals: • with obesity hypoventilation syndrome and obstructive sleep apnea	Interventions of interest are: • Continuous positive airway pressure	Comparators of interest are: • Oxygenation therapy • Bilevel positive airway pressure	Relevant outcomes include: • Mortality • Symptoms • Morbid events • Functional outcomes • Quality of life • Hospitalizations
Individuals: • with obesity hypoventilation syndrome and chronic respiratory failure	Interventions of interest are: • Bilevel positive airway pressure	Comparators of interest are: • Oxygenation therapy • Continuous positive airway pressure	Relevant outcomes include: • Mortality • Symptoms • Morbid events • Functional outcomes • Quality of life Hospitalizations

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Populations	Interventions	Comparators	Outcomes
Individuals: • with obesity hypoventilation syndrome when bilevel positive airway pressure is inadequate	Interventions of interest are: • Non-invasive home mechanical ventilation	Comparators of interest are: • Oxygenation therapy • Continuous or bilevel positive airway pressure	Relevant outcomes include: • Mortality • Symptoms • Morbid events • Functional outcomes • Quality of life • Hospitalizations
Individuals: • with hypoventilation syndromes unrelated to obesity	Interventions of interest are: • Non-invasive positive airway pressure including bilevel positive airway pressure and non-invasive home mechanical ventilation	Comparators of interest are: • Standard medical care without non-invasive positive airway pressure • Invasive mechanical ventilation	Relevant outcomes include: • Mortality • Symptoms • Morbid events • Functional outcomes • Quality of life • Hospitalizations

DESCRIPTION

Respiratory failure is characterized by low arterial blood oxygen (hypoxemia, PaO_2) and/or high arterial carbon dioxide (hypercapnia, $PaCO_2$ >45 mmHg). Chronic respiratory insufficiency or failure can occur with chronic obstructive pulmonary disease (COPD), thoracic restrictive disorders, and hypoventilation syndromes, and may result in poor quality of life, sleepiness, hospital admission, intubation, and death. Non-invasive positive airway pressure ventilation (NPPV) including continuous positive airway pressure (CPAP), bilevel positive airway pressure (BPAP), and home mechanical ventilators (HMV) that are pressure, rate and volume targeted are proposed for the treatment of COPD and other forms of chronic hypoventilation.

OBJECTIVE

The objective of this evidence review is to determine which features of non-invasive positive airway pressure improve the net health outcome in individuals with chronic obstructive pulmonary disease (COPD) , thoracic restrictive disorders due to neuromuscular disease, or hypoventilation syndromes including obesity hypoventilation syndrome.

BACKGROUND

Chronic Obstructive Pulmonary Disease

Chronic obstructive pulmonary disease (COPD) is a common condition, affecting more than 5% of the population, and is associated with high morbidity and mortality. COPD is the third leading cause of death in the United States. It is a clinical syndrome with multiple etiologies that is characterized by chronic respiratory symptoms, structural pulmonary abnormalities, and/or lung function impairment. Chronic obstructive pulmonary disease is most frequently associated with cigarette smoking or other air pollutants, and a majority of patients with COPD in the United States have a history of cigarette smoking. Chronic obstructive pulmonary disease is progressive, with expiratory airflow limitation, air trapping/hyperinflation, and destruction of alveoli

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(emphysema). The Global Initiative for Chronic Obstructive Lung Disease (GOLD), defines COPD as "a heterogeneous lung condition characterized by chronic respiratory symptoms (dyspnea, cough, sputum production and/or exacerbations) due to abnormalities of the airways (bronchitis, bronchiolitis) and/or alveoli (emphysema) that cause persistent, often progressive, airflow obstruction".[1,2,]

Respiratory failure in patients with COPD is characterized by the inability to sustain normal gas exchange, leading to low arterial blood oxygen (hypoxemia, PaO_2) and/or high arterial carbon dioxide (hypercapnia, $PaCO_2$). Hypercapnia develops in about one-third of patients with COPD and is associated with poor quality of life, sleepiness, frequent hospital admissions due to exacerbations, and an increase in mortality compared to patients with COPD who are normocapnic. The hypercapnia is due in large part to poor lung biomechanics including low inspiratory muscle reserve, high CO_2 production, and a reduced ventilatory capability.[3,] The imbalance between the respiratory load and respiratory capability may in turn affect the ventilatory control center in the brain stem. Physiological changes in responsiveness to hypoxemia and hypercapnia during sleep can be particularly pronounced in patients with COPD, with overnight increases in $PaCO_2$ affecting daytime $PaCO_2$, possibly through bicarbonate retention or changes in cerebrospinal fluid.[4,] Patients with COPD may also have comorbid obstructive sleep apnea and/or obesity hypoventilation syndrome due to decreased ventilatory motor output and upper airway muscle activity during sleep.

Thoracic Restrictive Disorders Due to Neuromuscular Disease
Thoracic restrictive disorders result from a variety of underlying diseases all characterized by restrictive patterns on pulmonary function testing.[5,] Neuromuscular disorders such as muscular dystrophy, amyotrophic lateral sclerosis (ALS), polio, and phrenic neuropathies can result in weakness of the respiratory muscles affecting inspiration and expiration, ultimately resulting in hypoventilation. Impaired cough and swallowing associated with neuromuscular disease increases the risk of respiratory complications in these patients.[6,] Nocturnal hypoventilation due to muscular atonia during sleep leads to nocturnal hypercapnia. Frequent nocturnal episodes can result in renal compensation and ultimately result in daytime hypercapnia. Non-invasive positive airway pressure ventilation (NPPV) is often necessary for patients with thoracic restrictive disorders due to neuromuscular disease.

Hypoventilation Syndromes
Hypoventilation syndromes are nonspecific disorders characterized by hypercapnia ($PaCO_2$ >45 mmHg) that is not otherwise categorized.[7,] Obesity hypoventilation syndrome (OHS), central respiratory depression due to substance or medication use, and decompensated hypercapnic respiratory failure that is not COPD are all included in this category. In patients with OHS, weight loss is useful in normalizing PaCO2; however, NPPV should be initiated early while weight loss is attempted.[8,]

Treatment With Non-invasive Positive Airway Pressure
A major goal of management of patients with chronic hypoventilation is to reduce hospitalizations and mortality. Long-term oxygen therapy is recommended for patients with poor clinical status and NPPV devices for patients with severe chronic hypercapnia and a history of hospitalization for acute respiratory failure. Non-invasive positive airway pressure ventilation devices include nocturnal continuous positive airway pressure (CPAP) for individuals with hypercapnia due to

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obstructive sleep apnea or hypoventilation and bilevel positive airway pressure (BPAP) devices or non-invasive home mechanical ventilators that are pressure, rate, and volume targeted. The objective of this evidence review is to describe which features of NPPV are required to improve the net health outcome in patients with COPD, thoracic restrictive disorders due to neuromuscular disease, or those with hypoventilation syndromes.

Benefits of nocturnal NPPV persist into the daytime with improved breathing patterns (lower frequencies and larger tidal volumes) and improved gas exchange. Explanations for the improvement in daytime respiration with nocturnal NPPV include increased respiratory drive, improved diaphragm function by unloading the respiratory muscles during sleep, increased CO_2 sensitivity, and reduction in air trapping and hyperinflation. It is not known which factors (eg, muscle unloading, gas exchange normalization, decrease in hyperinflation) underlie the benefits of NPPV on health outcomes. It is also unclear if the reduction in $PaCO_2$ has an effect on health outcomes or if it is only a marker of effective ventilation.[4,]

Respiratory Assist Devices

The Centers for Medicare and Medicaid Services (CMS) defines respiratory assist devices (RADs) as bilevel devices with or without back-up respiratory rate capability. While CPAP devices provide continuous air at a pressure that prevents the collapse of the airway during inspiration, BPAP devices work by increasing pressure during inspiration and lowering it during expiration (pressure cycled). In some devices a backup respiratory rate is triggered when the patient's nocturnal respiratory rate decreases below a set threshold. The backup rate is typically set 2 breaths below the patient's spontaneous respiratory rate during wakefulness.

Terminology on device features is described in Table 1.

Table 1. Device Features

Term	Definition	Description
Bilevel-S	Bilevel without a backup rate	Positive airway pressure that is higher during inspiration than expiration that is triggered by patient inspiration.
Bilevel-ST	Bilevel with a backup rate	Positive airway pressure that is higher during inspiration than expiration with a backup respiratory cycle length if the patient's breathing is slower than the preset rate.
VAPS	Volume-assured pressure support modes	Bilevel ST modes that use an algorithm to adjust inspiratory pressure support to meet a set tidal volume.
iVAPS	Intelligent volume-assured pressure support modes	Bilevel ST modes that use an algorithm to adjust inspiratory pressure support within a predetermined range to meet a set target ventilation.

Home Mechanical Ventilators

In some patients, nocturnal respiratory assist devices are insufficient to address the respiratory failure. Non-invasive home mechanical ventilators (HMV) are proposed for the treatment of chronic respiratory failure that is refractory to a respiratory assist device. Mechanical ventilators are devices that deliver more controlled breathing with bilevel ventilation at a higher pressure. The ventilators may also have additional features compared to BPAP machines such as alarms

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and battery backup power. Home mechanical ventilators can be used for patients with tracheostomy in the home, but may also be used with a non-invasive interface such as a mask or mouthpiece in patients who do not depend on 24 hour ventilation for survival. Current technology has decreased the size of home ventilators to around 10 pounds. In addition, some models may be wireless with battery backup, allowing greater mobility during the day.

Titration

Early studies with low intensity NPPV did not demonstrate health benefits in patients with hypercapnia. More recent studies have reinforced the importance of high-intensity NPPV (>18 cm H_2O) that is titrated to decrease hypercapnia. A high respiratory backup rate that is increased to the level of spontaneous breathing has also been shown to be important to achieve positive health outcomes. Manually set, laboratory or hospital titration of NPPV with pressure control and backup rate have been recommended for stable hypercapnic COPD.[9,] The goal of titration of inspiratory positive airway pressure is to achieve normocapnia, a reduction in transcutaneous CO_2, or maximum tolerable inspiratory pressure. A fast rise in inspiratory pressure (rise time) allows enough time for expiration within the normal rate of breathing. In patients with air trapping and hyperinflation, use of positive end-expiratory pressure can also be beneficial.

A suggested protocol for in-laboratory titration of NPPV in patients with COPD in the U.S. is described by Orr et al (2020).[4,] Titration of NPPV is usually performed in a monitored environment after the patient has stabilized, as studies have not found an improvement in health outcomes when NPPV is started soon after an acute exacerbation. Polysomnography or respiratory monitoring may be used during titration to evaluate the presence of obstructive sleep apnea or hypoventilation. The inspiratory pressure is typically started at 6 to 8 cm H_2O of pressure support above the expiratory pressure and titrated to reduce hypercapnia. A Bilevel-ST (with backup rate) or a VAPS (volume assured) may be used if a Bilevel-S (without backup rate) fails to adequately reduce hypercapnia. Although titration in European studies has been performed with a hospital stay, this is not feasible in the U.S., and titration might be performed over several weeks in the patient's home by an external durable medical equipment (DME) provider.

Pulmonary Rehabilitation

Pulmonary rehabilitation is a personalized intervention that includes physical activity (eg, activities of daily living, endurance exercises and muscle strengthening), health education, and psychological support. It may be performed in the hospital, outpatient clinic, or home, and has been shown to reduce mortality, exacerbation rate, intensive care admissions, and emergency department visits. Pulmonary rehabilitation is common in Europe but is less frequently provided in the U.S.

REGULATORY STATUS

Numerous CPAP and BPAP devices are available in the U.S. Examples of HMV devices that have both invasive and non-invasive interfaces and are available in the U.S. are described in Table 2.

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Table 2. Select Home Mechanical Ventilators with Non-invasive Interface

Device	Manufacturer	FDA clearance	Date	FDA product code
Trilogy™ Evo Ventilator	Respironics	K181166	2019	NOU, CBK
Vivo 60	Breas	K160481	2016	NOU, CBK, DQA, CCK
Astral 100/150	ResMed	K152068	2016	NOU, CBK
Newport™	Medtronic	K121891	2012	NOU, CBK
iVent	GE Healthcare	K092135	2009	NOU, CBK
LTV	Cardinal Health	K083688	2009	CBK
Puritan Bennett 540	Covidien	K082966	2008	CBK

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POLICY

Bilevel Positive Airway Pressure (BPAP)

A. Nocturnal bilevel positive airway pressure with backup rate may be considered **medically necessary** for individuals with COPD and chronic respiratory failure (see Policy Guidelines) who meet **ONE** of the following:
   1. Chronic stable daytime (awake) hypercapnia ($PaCO_2$> 52 mmHg) **OR**
   2. Daytime (awake) hypercapnia ($PaCO_2$> 52 mmHg) at least 2 weeks after discharge from the hospital for an acute exacerbation with decompensated acidosis.

B. Bilevel positive airway pressure may be considered **medically necessary** for individuals with thoracic restrictive disorders due to neuromuscular disease who meet **ONE** of the following:
   1. Pulmonary function tests with **one** of the following:
      a. Spirometry (upright or supine) with vital capacity <50% predicted or <80% predicted with associated symptoms (orthopnea, dyspnea, morning headaches, excessive daytime sleepiness, or unrefreshing sleep); **OR**
      b. Maximal inspiratory pressure <60 cm H2O or maximum expiratory pressure (MEP) <40 cm H2O; **OR**
      c. Peak cough flow (PCF) <270 L/min for age ≥12 years or PCF <5th percentile for age <12 years; **OR**
      d. Sniff nasal inspiratory pressure (SNIP) <70 cm H_2O in males, SNIP <60 cmH_2O in females for age ≥12 years.

      OR
   2. Hypercapnia with **one** of the following:
      a. Chronic stable daytime (awake) hypercapnia with PaCO2 ≥45 mmHg (capillary blood gas can be used in children); **OR**
      b. Venous blood gas PCO_2, end-tidal PCO_2, or transcutaneous PCO_2, ≥50 mmHg;

      OR
   3. Hypoxia with **one** of the following:
      a. Overnight oximetry in-laboratory or home sleep test with saturation <88% for 5 minutes;
      b. Overnight oximetry: SpO2 ≤90% for ≥2% of sleep time.

C. Bilevel positive airway pressure may be considered **medically necessary** for individuals with hypoventilation syndromes who meet **ALL** of the following criteria:
   1. Awake or sleep hypoventilation with hypercapnia (**one** of the following is met):
      a. Awake hypoventilation with chronic stable daytime (awake) hypercapnia (PaCO2 ≥45 mmHg); **OR**
      b. Venous blood gas PCO2, end-tidal PCO2, or transcutaneous PCO2 ≥50 mmHg; **OR**
      c. Sleep hypoventilation with hypercapnia:
         i. ≥10 mmHg increase from baseline awake PCO_2 and to a value > 50 mmHg for ≥10 min; **OR**

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ii. PCO_2 ≥55 mmHg for ≥10 min;

AND

2. Low clinical suspicion for COPD or neuromuscular disease;

AND

3. **One** of the following conditions are met:
    a. Obesity with body mass index (BMI) ≥30 kg/m2; **OR**
    b. Decreased respiratory drive due to opioid or substance use; **OR**
    c. Advanced lung disease other than COPD (e.g., end-stage or advanced interstitial lung disease);

AND

4. **One** of the following conditions are met:
    a. Individual was discharged from inpatient stay with persistent awake hypoventilation (hypercapnia) on BPAP. (A reassessment with a provider within 3 months (30 to 90 days) is required and an attended polysomnogram (PSG) should be performed to assess appropriateness of positive airway pressure modality (home sleep apnea test is acceptable if attended PSG is not obtainable); **OR**
    b. Individual is ambulatory and sleep study indicates that BPAP is necessary for sleep-disordered breathing, or individual with severe obstructive sleep apnea is continuous positive airway pressure intolerant or continuous positive airway pressure was proven ineffective.

D. Non-invasive positive airway pressure for COPD is considered **experimental / investigational** under all other conditions.

E. Individuals with COPD who are started on bilevel positive airway pressure (BPAP) at discharge from hospitalization may continue for up to 3 months to provide time to stabilize and complete reevaluation.

Non-Invasive Home Mechanical Ventilation

F. Non-invasive home mechanical ventilation may be considered **medically necessary** for individuals with COPD who meet **ALL** of the following criteria:
    1. Qualify for a bilevel positive airway pressure (BPAP) device **AND** meet at least **one** of the following:
        a. Higher pressure (e.g., > 25 cm H2O) is needed to reduce hypercapnia than can be achieved with a bilevel device during titration; **OR**
        b. Severe hypoxemia requiring FIO_2 > 40% or > 5 L/min; **OR**
        c. Daytime use (battery operated unit) is required to reduce hypercapnia.

G. Non-invasive home mechanical ventilation may be considered **medically necessary** for individuals with hypoventilation syndromes who meet **ALL** of the following:
    1. Qualify for a BPAP device and meet at least **one** of the following:
        a. Higher pressure is needed to reduce hypercapnia than can be achieved with a bilevel continuous positive airway pressure device during titration (typically >25 cm H2O); **OR**
        b. Severe hypoxemia requiring FIO2 >40% or >5 L/min; **OR**
        c. Daytime use (battery operated unit) is required to reduce hypercapnia;

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AND

2. Tried and failed BPAP device with persistent hypercapnia despite 3 months of adequate adherence to prescribed positive airway pressure therapy with **one** of the following:
    a. Awake PaCO2 ≥45 mmHg; **OR**
    b. Awake venous blood gas PCO_2, end-tidal PCO_2, or transcutaneous PCO_2 ≥50 mmHg.

H. Non-invasive home mechanical ventilation may be considered **medically necessary** for individuals with thoracic restrictive disorders due to neuromuscular disease who meet **ALL** of the following:
    1. Qualify for a BPAP device;
    AND
    2. **One** of the following:
        a. BPAP fails; **OR**
        b. Have extreme loss in function with vital capacity <30%; **OR**
        c. Non-invasive ventilation is needed for >10 hours per day; **OR**
        d. Severe breathlessness (e.g., with speaking at rest); **OR**
        e. Worsening daytime hypercapnia with need for mouthpiece ventilation; **OR**
        f. Daytime use (battery operated unit) is required to reduce hypercapnia or dyspnea.

POLICY GUIDELINES

A. For individuals with chronic obstructive pulmonary disease (COPD) without hypercapnia ($PaCO_2$ < 52 mmHg) and with obstructive sleep apnea, see BCBSKS medical policy *Diagnosis and Medical Management of Obstructive Sleep Apnea Syndrome.*

B. Respiratory failure in patients with COPD is characterized by the inability to sustain normal gas exchange, leading to low arterial blood oxygen (hypoxemia, PaO_2) and/or high arterial carbon dioxide (hypercapnia, $PaCO_2$). Assessment of hypoxemia would lead to supplemental oxygen administration. Stable clinical state is defined as free of exacerbations for at least 4 weeks with pH over 7.35.

C. Compliance with treatment of at least 4 hours per 24 hours should be documented after the first 3 months of use. There are limited data on which to base compliance assessment. Assessment could be further based on an *average* of at least 4 hours per 24 hours over a consecutive 30-day period or use of 4 hours per 24 hours for at least 65% of the days in a consecutive 30-day period.

D. The Centers for Medicare and Medicaid Services (CMS) classifies a respiratory assist device as a bilevel positive airway pressure device with or without backup respiratory rate capability. Treatment modalities that are reported with the E0471 code include BiPAP ST, ASV, BiPAP AutoSV, iVAPS, AVAPS. BPAP units with batteries have a battery life that is shorter than home mechanical ventilators and are infrequently used in the U.S.

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E. CMS defines non-invasive mechanical ventilators as life supporting/sustaining devices used in various settings, including home, hospital, and institutional settings. The non-invasive mechanical ventilators should have at least 6 pressure modes and 3 volume modes, and allow for both invasive or non-invasive use. For examples, see the Regulatory Status section.

F. Although most patients with comorbid COPD and obstructive sleep apnea can be effectively treated with continuous or auto-adjusting positive airway pressure, approximately 10% of patients will need bilevel positive airway pressure to tolerate the required pressure. These devices are reviewed in medical policy *Diagnosis and Medical Management of Obstructive Sleep Apnea Syndrome.*

Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

RATIONALE

This evidence review was created using a search of the PubMed database. The most recent literature update was performed through January 28, 2026.

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function, including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent 1 or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

CONTINUOUS POSITIVE AIRWAY PRESSURE FOR CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Clinical Context and Therapy Purpose

Sleep-related breathing disorders are common in individuals with chronic obstructive pulmonary disease (COPD). The coexistence of COPD and obstructive sleep apnea (OSA) is associated with

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more pronounced hypoxemia and hypercapnia than either condition individually, and individuals are at greater risk of morbidity and mortality compared to individuals who have either COPD or OSA alone. The purpose of continuous positive airway pressure (CPAP) in individuals with overlap syndrome is to reduce morbidity and mortality in this population.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with COPD who have clinically significant OSA. Obstructive sleep apnea is a partial or intermittent upper airway collapse that results in hypoxemia and arousal during sleep.

Clinically significant OSA in adults that is indicated for treatment is defined as:

- An Apnea/Hypopnea Index (AHI) or Respiratory Disturbance Index of at least 15 events per hour, OR
- An AHI or Respiratory Disturbance Index of at least 5 events per hour in an individual with 1 or more signs or symptoms associated with OSA (eg, excessive daytime sleepiness, hypertension, cardiovascular heart disease, or stroke);

The criterion standard for a diagnosis of sleep disorders is a polysomnogram performed in a sleep laboratory. A standard polysomnogram includes electroencephalogram, submental electromyogram, and electrooculogram (to detect rapid eye movement sleep) for sleep staging. Polysomnography also typically includes electrocardiography and monitoring of respiratory airflow, effort, snoring, oxygen desaturation, and sleep position. A variety of devices have been developed specifically to evaluate OSA at home. They range from portable full polysomnography systems to single-channel oximeters. Available devices evaluate different parameters, which may include oximetry, respiratory and cardiac monitoring, and sleep/wake activity.

A definition of terms and scoring criteria for OSA are described in Table 3.

Table 3. Definitions of Terms and Scoring Criteria for Obstructive Sleep Apnea

Terms	Definition
Respiratory event	
Apnea	The frequency of apneas is measured from channels assessing oxygen desaturation, respiratory airflow, and respiratory effort. In adults, apnea is defined as a drop in airflow by 90% or more of pre-event baseline for at least 10 seconds.
Hypopnea	Hypopnea in adults is scored when the peak airflow drops by at least 30% of pre-event baseline for at least 10 seconds in association with either at least 3% or 4% arterial oxygen desaturation (depending on criteria) or an arousal.
Positive airway pressure	
APAP	Auto-adjusting positive airway pressure may be used either to provide treatment or to determine the most effective pressure for CPAP.
BPAP	Bilevel positive airway pressure that is higher on inspiration than expiration.

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Terms	Definition
CPAP	Continuous positive airway pressure provides the same pressure throughout the breathing cycle.
PAP	Positive airway pressure that may be continuous (CPAP), auto-adjusting (APAP), or bilevel (BPAP).

Comparators
The following therapies are currently being used to make decisions about individuals with overlap of COPD and OSA: medical treatment for COPD without treatment for OSA.

Outcomes
The general outcomes of interest are mortality, symptoms, morbid events, functional outcomes, quality of life, and hospitalization. These are measured with a variety of tools as shown in Table 4.

Table 4. Health Outcome Measures Relevant to Patients with Chronic Obstructive Pulmonary Disease

Outcome	Measure (Units)	Description
Readmission	Measured as readmission-free survival or time to readmission	May be part of a composite of readmission or death
Mortality	Measured as time to death or percent mortality within a set period	May be specific to chronic obstructive pulmonary disease or overall
PaO_2	Partial pressure of oxygen (kPa or mmHg)	The level of arterial oxygen.
$PaCO_2$	Partial pressure of carbon dioxide (kPa or mmHg)	The level of arterial carbon dioxide. Some studies have used a threshold of 45 mmHg. Severe hypercapnia is $PaCo_2$ > 7.3 kPa or > 52 mmHg.
6MWD	Six-minute walking distance (meters)	The distance that can be walked in 6 minutes.
HRQL	Health-related quality of life	Severe Respiratory Insufficiency Questionnaire (SRI) or the St George's Respiratory Questionnaire (SGRQ)

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Consistent with a 'best available evidence approach,' within each category of study design, studies with larger sample sizes and longer durations were sought.
- Studies with duplicative or overlapping populations were excluded.

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REVIEW OF EVIDENCE

Systematic Reviews

A 2021 evidence review by the American Thoracic Society found several studies suggesting that identification and treatment with CPAP in patients with overlap syndrome improves outcomes.[2,] However, no trials were identified that compared an OSA screening strategy with no screening strategy in patients with stable hypercapnic COPD or with use of CPAP in patients already on other modes of positive airway pressure (PAP).

Srivali et al 2023 conducted a systematic review of 5 observational studies evaluating CPAP in patients with overlap syndrome.[10,] Definitions of OSA, COPD, and CPAP use were inconsistent among the studies, and the data were not pooled. However, all-cause mortality was reported in 3 studies and was significantly reduced with CPAP in each study (hazard ratios [HRs], 0.19 to 0.71).

Observational Studies

Marin et al (2010) evaluated outcomes of patients who have both COPD and OSA from a prospective database of patients referred to a university sleep clinic.[11,] The authors analyzed 3 groups of patients; those with overlap syndrome who were started on CPAP (n=228), those with overlap syndrome not treated with CPAP (n=213), and patients with COPD who did not have OSA (n=210). Patients were seen at least once a year or until death, and the primary outcome was time to death from any cause. The secondary outcome was the time to first severe COPD exacerbation requiring hospitalization. There were 589 patients with overlap syndrome and 210 with COPD and simple snoring. Positive pressure was recommended for 468 patients, another 121 patients did not qualify for CPAP and were given other options for treatment.

Of the 468 patients with overlap syndrome who received a recommendation for PAP, 228 were treated with CPAP, 27 were treated with bilevel positive airway pressure (BPAP), and 213 did not accept treatment. The AHI was similar (35 vs. 34) in the 2 groups; these patients would have received a recommendation for treatment based on presence of clinically significant OSA. Median follow-up was 9.4 years (range, 3.3 to 12.7). When compared to patients with COPD only, patients with overlap syndrome who were not treated with PAP had a higher mortality risk (42.2% vs. 24.2%; relative risk [RR] 1.79; 95% confidence interval [CI]: 1.16 to 2.77) and were more likely to suffer a severe COPD exacerbation leading to hospitalization (RR 1.70; 95% CI: 1.21 to 2.38). Patients with overlap syndrome treated with CPAP did not have a statistically significant increased risk for death from any cause (31.6%) compared to patients with COPD only (24.2%). There were a number of baseline differences between the COPD only and the overlap syndrome groups which may impact mortality, but the 2 overlap groups were well matched for baseline characteristics. The main conclusion of the study was that patients with COPD should be screened for OSA and offered treatment.

Similar findings were reported by Machado et al (2010), who reported a prospective comparative study of 95 patients with moderate to severe OSA and hypoxemic COPD who were offered CPAP treatment.[12,] Of the 95 patients, 61 (64%) accepted CPAP and were adherent while 34 did not accept or were not adherent. After adjusting for confounders, patients treated with CPAP had a significantly lower risk of death (HR, 0.19; 95% CI: 0.08 to 0.48).

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Other studies have evaluated the patient characteristics that show most benefit from PAP. Jaoude et al (2014) evaluated 271 consecutive patients with overlap syndrome who were seen at a Veterans Administration sleep center.[13,] Of the 271 overlap patients identified, 104 were considered hypercapnic (mean partial pressure of arterial carbon dioxide [$PaCO_2$] = 51.6 + 4.3 mmHg), indicating that the level of hypercapnia was lower than in other studies that had a threshold of 52 mmHg. The normocapnic and hypercapnic patients had similar AHI (29.3 + 23.8 and 35.2 + 29.2 events per hour, respectively; p=.07) and similar adherences rates to CPAP (43% and 42%, respectively). During a median follow-up of 71 months, mortality was higher in patients who were hypercapnic (35%) compared to patients who were normocapnic (17%, p=.001). Mortality in patients who were hypercapnic was lower in those who w ere adherent to CPAP compared to those who were not (p=.04), but adherence to CPAP had little impact on mortality in normocapnic patients (p=.42)

Singh et al (2019) evaluated the impact of PAP therapy on emergency room visits and hospitalization rates in Medicare beneficiaries with overlap syndrome.[14,] Using a 5% Medicare sample of claims data from 2010 to 2012, they identified 319 patients with overlap syndrome who were new users of PAP therapy in 2011. Subjects were categorized by age (66 to 74 years, 75 to 84 years, >85 years), gender, race, socioeconomic status, Centers for Medicare and Medicaid Services (CMS) geographic region, comorbidity score, COPD complexity, tobacco use, and selected comorbidities. Comorbidities included hypertension (84%), diabetes (42%), and congestive heart failure (32%); 63% of individuals had 3 or more comorbidities. COPD complexity was based on pulmonary and non-pulmonary comorbid conditions and the prevalence of exacerbations and utilization of healthcare services; 26.0% of individuals were considered low complexity, 57.7% moderate complexity, and 16.3% high complexity. When compared with the year before PAP initiation, hospitalization for COPD-related conditions was significantly reduced (19.4% vs. 25.4%, p=.03). Rates of emergency room visits and hospitalization for any cause were not significantly different for the pre- and post-initiation periods. Although the benefit was seen primarily in patients who were considered to be of higher complexity, no information could be obtained from the claims data on the severity of COPD and OSA.

Section Summary: Continuous Positive Airway Pressure for Chronic Obstructive Pulmonary Disease

The evidence on use of CPAP in patients with COPD includes observational studies of patients with both COPD and OSA who do or do not use CPAP and a systematic review of those studies. Studies show a mortality benefit in patients with overlap syndrome who are treated with PAP. The greatest benefits occur in patients with COPD and hypercapnia and in older adults, and individuals with more comorbid conditions and higher complexity ratings. It should be noted that the mean $PaCO_2$ was 51.6 + 4.3 mmHg in at least 1 study, indicating that the threshold for what was considered hypercapnia was lower than the threshold for hypercapnia in other studies (see below). Although the literature indicates that patients with COPD should be screened for OSA due to increased mortality in overlap syndrome, no studies were identified to indicate that CPAP would be prescribed in any manner other than would typically be recommended for patients with clinically significant OSA.

BILEVEL POSITIVE AIRWAY PRESSURE FOR CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Clinical Context and Therapy Purpose

Morbidity and mortality are high in individuals with COPD and chronic respiratory failure. Despite maximal medical therapy, the occurrence of acute exacerbations requiring hospitalizations is high, and a substantial percentage of individuals will die within 1 year. The purpose of BPAP in individuals who have COPD and chronic respiratory failure is to improve function and quality of life and to reduce acute exacerbations and death.

The following PICO was used to select literature to inform this review.

Populations

The relevant populations of interest are individuals with COPD who have chronic respiratory failure or who have had an acute exacerbation.

Interventions

The therapy being considered is BPAP with or without a backup rate.

Comparators

The following therapies are currently being used to treat COPD with chronic respiratory failure: medications and home oxygen therapy.

Outcomes

The general outcomes of interest are mortality, symptoms, morbid events, functional outcomes, quality of life, and hospitalization. These are measured with a variety of tools as shown in Table 4.

This is a chronic treatment in a population with a high mortality rate. Therefore, follow-up at 12 months is of interest to measure readmissions and mortality and at 3 to 6 months to measure blood gasses and health outcomes. It is not known whether $PaCO_2$ has an effect on health outcomes, or if it is only a marker of effective ventilation.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Consistent with a 'best available evidence approach,' within each category of study design, studies with larger sample sizes and longer durations were sought.
- Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE

Systematic Reviews

An updated Cochrane review by Raveling et al (2021) evaluated the evidence for nocturnal non-invasive positive pressure ventilation (NPPV) for the treatment of either stable COPD or COPD

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after an acute exacerbation.[15,] The primary outcomes were arterial blood gas and exercise capacity measured with the 6-minute walk distance (6MWD) as well as readmissions for acute exacerbations. Where available, the meta-analysis included individual patient data (chronic: n=778; acute exacerbation: n=364) along with missing data from the primary RCTs. Criteria for inclusion were RCT, NPPV prescribed for at least 4 hours per night, and use for greater than 3 weeks; trials that allowed daytime use were excluded from the review. Most of the trials were conducted in Europe and excluded patients with OSA or high body mass index (BMI).

The update included 17 trials on stable COPD and 4 trials on NPPV after an acute exacerbation of COPD. Bilevel positive airway pressure with a backup rate was used in 3 studies, including the trials by Kohnlein et al (2014), Murphy et al (2017) and Struik et al (2014) described below. Eight studies were judged to be at low risk of bias, including the 3 by Kohnlein et al, Murphy et al, and Struik et al. Sources of heterogeneity were baseline hypercapnia ($PaCO_2$ <55 mmHg vs. >55 mmHg) and the mean inspiratory pressure of NPPV (<18 cm H_2O vs. >18 cm H_2O). Sensitivity analysis removing studies with high or unclear risk of bias in the chronic COPD cohort increased the treatment effects for partial pressure of arterial oxygen (PaO_2), $PaCO_2$, 6MWD, and health related quality of life (HRQL). The authors concluded that the addition of chronic NPPV to standard treatment improves diurnal hypercapnia (high certainty), and there was evidence that NPPV improved PaO_2 and all cause mortality (moderate certainty) and HRQL (very low certainty). In patients with stable COPD, the effect on gas exchange seemed to be larger in people with more severe hypercapnia ($PaCO_2$ >55 mmHg), better treatment compliance (>5 hours per night), and treated with a high inspiratory pressure (IPAP >18 cm H_2O). The uncertain contribution of improvements in gas exchange, along with possible mechanisms, for an improvement in health outcomes were discussed.

Wilson et al (2020) published a meta-analysis that included 21 RCTs and 12 observational studies (N=51,085) on patients with COPD and hypercapnia treated with NPPV.[16,]. Of these, 15 RCTs and 6 observational studies evaluated BPAP compared with no device. The BPAP modes were spontaneous/timed, volume-assured pressure support, pressure-controlled ventilation, or the mode was not specified. The primary outcomes were mortality, all-cause hospital admissions, intubation, and quality of life. Analysis indicated that overall, use of BPAP, compared with no device, was significantly associated with a lower risk of mortality (odds ratio [OR] 0.66), fewer patients with hospital admissions (OR 0.22), and lower need for intubation (OR 0.34). There was no significant difference in quality of life, and sensitivity analysis indicated that observational studies were driving the significant results. Further analysis of subgroups evaluated the timing of the initiation of NPPV (stable vs. recent exacerbation) and separated the $PaCO_2$ threshold categories as 45 to 49 mmHg, 50 to 51 mmHg, and at least 52 mmHg. Post-hoc subgroup analysis found no significant differences in mortality or all-cause hospital admissions based on $PaCO_2$ levels, but improved quality of life in patients with higher $PaCO_2$ levels.

A 2020 evidence review by the American Thoracic Society evaluated NPPV on health outcomes in patients with stable hypercapnic COPD (Table 5).[2,] Studies varied in the severity of baseline hypercapnia and lung disease, mode of ventilation, pressure settings, and comparator, all of which may have contributed to the imprecision of the studies.

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Table 5. Effect of Non-invasive Positive Pressure Ventilation on Health Outcomes in Patients With Stable Hypercapnic COPD

Outcome	Effect	Level of Certainty
Mortality	RR: 0.86 (0.58 to 2.27)	Low
Hospitalizations	MD: -1.26 (-2.59 to 0.08)	Low
Quality of Life	MD: 0.48 (0.09 to 0.88)	Low
Dyspnea	SMD: -0.51 (-0.95 to -0.06)	Moderate

COPD: chronic obstructive pulmonary disease; MD: mean difference; RR: relative risk; SMD: standardized mean difference

RANDOMIZED CONTROLLED TRIALS

Chronic Hypercapnic Respiratory Failure

Kohnlein et al (2014) conducted a multicenter RCT to determine whether BPAP would improve survival in patients with COPD and stable hypercapnic respiratory failure when ventilator settings were targeted to reduce hypercapnia.[17,] Patients (N=195) with Global Initiative for Chronic Obstructive Lung Disease (GOLD) stage IV COPD, $PaCO_2$ 51.9 mmHg or higher, and pH higher than 7.35 were randomized into treatment as usual (including O_2), or BPAP plus treatment as usual. Excluded were patients with BMI of 35 kg/m2 or greater, abnormalities of the lung or thorax other than COPD, or other conditions resulting in hypercapnia. Titration was performed in the hospital over a mean of 5.6 days with pressure targeted to reduce the baseline $PaCO_2$ by at least 20% or to achieve $PaCO_2$ <48.1 mmHg. The mean inspiratory pressure in the NPPV group was 21.6 cm H_2O with a backup rate of 16.1. Patients in both groups were admitted to the hospital at 3, 6, 9, and 12 months after randomization to ensure optimized treatment and additionally contacted by telephone every 4 weeks to ensure adherence to therapy. At 12 months, the $PaCO_2$ was 48.8 mmHg in the NPPV group (mean use of 5.9 hours per day) compared to 55.5 in the control group. The primary outcome of 1-year all cause mortality was 12% in the NPPV group compared to 33% in the control group, with a HR of 0.24 (95% CI: 0.11 to 0.49; p=.004). Emergency hospital admissions were limited to 3 patients (3%) in the control group. The study utilized intention-to-treat analysis with blinded outcomes assessors. Previous studies that had not shown a significant improvement in survival with NPPV included patients with mild hypercapnia who did not have reduced hypercapnia or improved blood gases with treatment.[18,]

Post-Acute Hypercapnic Respiratory Failure

Murphy et al (2017) reported an RCT on the use of BPAP in addition to home oxygen therapy in patients with persistent hypercapnia following acute respiratory failure in the Home Oxygen Therapy Home Mechanical Ventilation (HOT-HMV) trial.[19,] Patients (N=116) who had persistent hypercapnia following hospitalization for an acute exacerbation of COPD were randomized to a BPAP device with home oxygen therapy (NPPV+O_2) or to oxygen therapy alone (O_2). Randomization occurred between 2 to 4 weeks after resolution of decompensated acidosis (arterial pH >7.30) in patients who had persistent hypercapnia ($PaCO_2$ >53 mmHg) and hypoxemia (PaO_2 <55 mmHg or <60 mmHg; ≥1 of polycythemia, pulmonary hypertension, or cor pulmonale; >30% of sleep time with oxygen saturation <90% as measured by pulse

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oximetry) and arterial pH greater than 7.30 while breathing room air. Patients were admitted for inpatient titration with either the Harmony 2 ST (Philips-Respironics) or VPAP IIIST (ResMed) with pressure support and backup rate. Settings were adjusted during overnight sleep studies to control hypoventilation and hypoxemia with a median inspiratory positive airway pressure of 24 cm H_2O. Respiratory failure was attributed to COPD if forced expiratory volume in 1 second (FEV_1) was less than 50% predicted, the FEV_1/forced vital capacity (FVC) ratio was less than 60%, and the patient had a smoking history in the absence of 1) obesity (BMI >35), 2) clinically significant obstructive sleep apnea, or 3) neuromuscular or chest wall disease. $PaCO_2$ levels improved significantly more in the NPPV group at 6 weeks (between group difference of -5.0; 95% CI: -9.0 to -1.3) and 3 months (-4.0; 95% CI:-7.1 to -0.8) but not at 6 or 12 months. Improvements in PaO_2 levels were not significantly different in the 2 groups. There was a significant reduction in the composite endpoint of readmission or death within 12 months (63.4% in the NPPV+O_2 group vs. 80.4% in the O_2 alone group), with an adjusted HR of 0.49 (95% CI: 0.31 to 0.77; p=.002) and a number needed to treat of 5.8 to prevent 1 readmission or death. The median time to readmission or death was 4.3 months in the NPPV+O_2 group and 1.4 months in patients receiving oxygen alone, and the exacerbation rate in 12 months was reduced to 3.8 for the NPPV+O2 group compared to 5.1 with O_2 alone (adjusted rate ratio 0.66; 95% CI: 0.46 to 0.95, p=.02). Twelve month mortality was not significantly different between the groups. The study utilized intention-to-treat analysis with blinded outcomes assessors.

Several differences were noted between the results of the HOT-HMV trial and the RESCUE trial, which failed to demonstrate an improvement in hospitalizations or mortality.[20,] In the RESCUE trial there was less stringent $PaCO_2$ criteria (>45 mmHg) and treatment began immediately following cessation of acute ventilation rather than after a 2 week stabilization period, so that patients with spontaneously reversible hypercapnia would have been included in the study. For example, in the HOT-HMV trial 21% of potential patients were excluded due to not meeting the $PaCO_2$ criteria 2 weeks after the acute exacerbation. The GOLD guideline notes that several factors may account for discrepancies in study results, including differences in patient selection, underpowered studies, NPPV settings, and poor adherence.[1,]

Section Summary: Bilevel Positive Airway Pressure for Chronic Obstructive Pulmonary Disease

The evidence on bilevel NPPV includes RCTs and systematic reviews of those RCTs. The primary limitation of the evidence base is the heterogeneity of patient selection criteria and treatment parameters. The most recent trials indicate that bilevel NPPV improves hypercapnia in both patients with stable hypercapnia and in patients who have stabilized following an acute exacerbation. There is evidence that some health outcomes including function, readmissions, and death are improved, although the strength of evidence is low. Notable differences between the results of the HOT-HMV trial and the RESCUE trial, which failed to demonstrate an improvement in hospitalizations or mortality, are that in the RESCUE trial there was less stringent $PaCO_2$ criteria (>45 mmHg) and treatment began immediately following cessation of acute ventilation, so that patients with spontaneously reversible hypercapnia may have been included in the study. Meta-analysis of individual patient data supports the importance of the level of hypercapnia and intensity of the pressure on outcomes in patients with COPD. Other factors that are reported to be important to achieve benefit of NPPV include use for at least 5 hours per night, and for patients with hypercapnia following an acute exacerbation, titration should occur at least 2 weeks after hospitalization when hypercapnia has stabilized.

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HOME MECHANICAL VENTILATION FOR CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Clinical Context and Therapy Purpose

The purpose of non-invasive home mechanical ventilation (HMV) in individuals who have COPD is to provide a treatment option that is an improvement over high flow oxygen or BPAP.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with COPD and chronic respiratory failure that is refractory to pharmacologic management, oxygen, and BPAP.

Interventions

The therapy being considered is HMV. Mechanical ventilators are devices that deliver more controlled breathing with bilevel ventilation. They can be used either invasively with tracheostomy or non-invasively with a mask. Compared to BPAP, HMVs have additional ventilatory modes and ventilatory control along with features such as alarms and battery backup power for individuals who require backup at night or daytime use with mobility. HMVs are classified by the U.S. Food and Drug Administration as life support devices.

Comparators

BPAP with high flow oxygen may be used to treat individuals with COPD and chronic respiratory failure.

Outcomes

The general outcomes of interest are mortality, symptoms, morbid events, functional outcomes, quality of life, and hospitalization. These are measured with a variety of tools as shown in Table 4.

This is a chronic treatment in a population with a high mortality rate. Therefore, follow-up at 12 months is of interest to measure readmissions and mortality and at 3 to 6 to measure blood gasses and health outcomes. It is not known whether $PaCO_2$ has an effect on health outcomes, or if it is only a marker of effective ventilation.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Consistent with a 'best available evidence approach,' within each category of study design, studies with larger sample sizes and longer durations were sought.
- Studies with duplicative or overlapping populations were excluded.

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REVIEW OF EVIDENCE

Systematic Reviews

A technology assessment by the Agency for Healthcare Research and Quality (AHRQ, 2019) for CMS identified 5 studies on the initiation of HMV.[21,] No studies were identified that compared initiation criteria for HMV versus BPAP. The AHRQ systematic review found low quality evidence that HMV compared to BPAP, CPAP, or no device was associated with significantly fewer hospital admissions. This was based on 2 observational studies that compared HMV to no device and a large study of administrative claims data (Vasquez et al, 2017, described below) that compared HMV, BPAP, and CPAP.

In 2020 the AHRQ authors published a meta-analysis of RCTs and comparative observational studies of patients with COPD and hypercapnia treated with BPAP or HMV.[16,] The primary outcomes were mortality, all-cause hospital admissions, intubation, and quality of life. Based on 2 observational studies, HMV was significantly associated with fewer all-cause hospital admissions (rate ratio, 0.50; 95% CI, 0.35 to 0.71) compared with no device, but there was not a statistically significant difference in mortality (21.84% vs. 34.09%; OR, 0.56; 95% CI, 0.29 to 1.08). However, the evidence was low to moderate in quality and based on small numbers of studies.

Observational Studies

Vasquez et al (2017) performed a retrospective analysis of claims data of hospitalization in patients with COPD who did or did not receive therapy with CPAP, BPAP, or HMV.[22,] Differences in COPD-related hospitalization were compared from 6 months before the prescription of a device to 6 months after prescription of a device across the device types. Models were stratified by sleep disordered breathing, congestive heart failure, age less than or greater than 65 years, and chronic respiratory failure. There were 1,881,652 enrollees with at least 2 COPD-related claims; 28,774 were on BPAP, 112,119 on CPAP, and 1011 enrolled on HMV. After exclusion criteria (health plan coverage for 12 month before and 6 months after the index date) were applied, there were 39,385 patients on CPAP, 9,156 patients on BPAP, and 315 patients on HMV who were included in the analysis. Propensity matching was used to compare the NPPV groups to medication groups. Most patients (92.5%) were not receiving any form of NPPV. Continuous positive airway pressure was prescribed for 5.6% of patients, BPAP for 1.5% of patients, and HMV in less than 1% of patients. Most patients prescribed HMV were older and there was high geographic variability; a majority (59.1%) of HMV users resided in the south. A majority of patients prescribed CPAP or BPAP had co-morbid sleep-disordered breathing (57.4% and 59.1%, respectively), while HMV was prescribed most frequently in patients with acute respiratory failure (56.5%), hypoxemia (30.2%), and chronic respiratory failure (28.3%). Sleep disordered breathing was present in 20.3% of patients using HMV. Hospitalization rates were highest in the HMV group. While all forms of NPPV reduced hospitalization rates, HMV was associated most strongly with a reduction in hospitalizations ($p<.001$).

Section Summary: Home Mechanical Ventilation for Chronic Obstructive Pulmonary Disease

There is low strength of evidence based on observational studies and claims data that HMV reduces the number of hospital admissions or number of patients with hospitalization compared to either no device or BPAP. Analysis of claims data also suggests that HMV is prescribed most

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frequently in patients with acute and chronic respiratory failure or hypoxemia. Due to the severity of the condition, high quality prospective controlled trials are unlikely in patients who have failed BPAP. It was also observed that there is high geographic variability in prescribing HMV. This finding suggests a possibility of inappropriate use in some areas of the country. Due to the severity of the condition, high quality prospective controlled trials are unlikely in patients who have failed BPAP. Therefore, HMV may be appropriate in situations where BPAP is not adequate to obtain needed pressures or when daytime use and battery backup is needed.

BILEVEL POSITIVE AIRWAY PRESSURE FOR RESTRICTIVE THORACIC DISORDER DUE TO NEUROMUSCULAR DISEASE

Clinical Context and Therapy Purpose

The purpose of BPAP in individuals who have restrictive thoracic disorder due to neuromuscular disease is to reduce morbidity and mortality in this population.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with restrictive thoracic disorder due to neuromuscular disease who have chronic respiratory failure.

Interventions

The therapy being considered is NPPV with BPAP.

Comparators

Standard medical care without BPAP may be used to treat individuals with chronic respiratory failure due to neuromuscular disease.

Outcomes

The general outcomes of interest are mortality, symptoms, morbid events, functional outcomes, quality of life, and hospitalization.

This is a chronic treatment in a population with a high mortality rate. Therefore, follow-up at 12 months is of interest to measure readmissions and mortality and at 3 to 6 to measure blood gasses and health outcomes. It is not known whether $PaCO_2$ has an effect on health outcomes, or if it is only a marker of effective ventilation.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Consistent with a 'best available evidence approach,' within each category of study design, studies with larger sample sizes and longer durations were sought.

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- Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE

Systematic Reviews

A Cochrane systematic review by Annane et al (2014) identified 10 clinical trials (N=173) evaluating nocturnal mechanical ventilation (volume-cycled mechanical ventilation or BPAP) in patients with hypoventilation due to neuromuscular or chest wall disorders.[23,] The included trials enrolled patients with motor neuron disease (n=3), chest wall deformity (n=3), Duchenne muscular dystrophy (n=1), or mixed populations (n=3). Trials comparing mechanical ventilation to standard of care or those evaluating different methods of ventilation were included. Only 2 trials evaluated HMV; thus, the majority of the evidence is for BPAP. The largest study (N=70) was conducted specifically in patients with Duchenne muscular dystrophy. Studies included in the systematic review are summarized in Table 6. Tables 7 and 8 describe the characteristics and results of the systematic review. Although the quality of the studies was low, nocturnal mechanical ventilation lowered mortality among patients with neuromuscular or chest wall disorders.

Table 6. Studies Included in Cochrane Review

Study	Annane (2014)
Struik et al (2011)[24,]	●
Jaye et al (2009)[25,]	●
Bourke et al (2006)[26,]	●
Tuggey and Elliott (2005)[27,]	●
Ward et al (2005)[28,]	●
Willson et al (2004)[29,]	●
Laserna et al (2003)[30,]	●
Jackson et al (2001)[31,]	●
Pinto et al (1995)[32,]	●
Raphael et al (1994)[33,]	●

Table 7. Cochrane Systematic Review Characteristics

Study	Dates	Trials	Participants	N (Range)	Design	Duration
Annane et al (2014)[23,]	Through June 2014	10	Chronic, stable hypoventilation due to diseases of the nerves, muscles, or chest wall	173 (10 to 70)	RCT (or quasi-RCT)	NR

NR: not reported; RCT: randomized controlled trial.

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Table 8. Cochrane Systematic Review Results

Study	1-Year Mortality Rate	Hospital Admission	Symptom Improvement
Annane et al (2014)[23,]			
N	109	38	51
Risk ratio (95% CI)	0.62 (0.42 to 0.91)	0.25 (0.08 to 0.82)	0.43 (0.18 to 1.03)
I^2	*30%*	*0%*	NR

CI: confidence interval; NR: not reported.

Other systematic reviews have included only observational studies. AlBalawi et al (2022) evaluated long-term non-invasive ventilation in children with neuromuscular disease.[34,] A total of 57 studies in 1948 children were identified. Neuromuscular diseases were classified as spinal muscular atrophy, Duchenne muscular dystrophy, or other/multiple neuromuscular diseases. Methods of ventilation were either not reported or specific to BPAP. Overall, NPPV resulted in lower mortality compared with standard care (risk ratio, 0.30; 95% CI, 0.19 to 0.46; p<.00001; I^2=68%), but mortality was not significantly improved compared with invasive mechanical ventilation (risk ratio, 0.91; 95% CI, 0.24 to 3.48; p=.89; I^2=88%*).*

Section Summary: Bilevel Positive Airway Pressure Ventilation for Restrictive Thoracic Disorder Due to Neuromuscular Disease

The evidence for the use of BPAP for hypoventilation as a result of neuromuscular disorders includes systematic reviews. A systematic review of 10 randomized or quasi-randomized clinical trials evaluated the use of nocturnal mechanical ventilation (volume-cycled mechanical ventilation or BPAP) in 173 patients with neuromuscular or chest wall disorders. One-year mortality rates were significantly reduced with NPPV use (risk ratio, 0.62; 95% CI, 0.42 to 0.91). Patients treated with NPPV also had lower hospital admission rates and greater symptom improvement. Although the studies were limited by heterogeneity, nocturnal NPPV was found to improve outcomes in patients with restrictive thoracic disorders including neuromuscular disease. In a systematic review of observational studies conducted in children with neuromuscular disorders, NPPV (BPAP or method unreported) improved mortality compared with standard of care.

HOME MECHANICAL VENTILATION FOR RESTRICTIVE THORACIC DISORDER DUE TO NEUROMUSCULAR DISEASE

Clinical Context and Therapy Purpose

The purpose of non-invasive HMV in individuals who have restrictive thoracic disorder due to neuromuscular disease is to reduce morbidity and mortality in this population.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with restrictive thoracic disorder due to neuromuscular disease who have chronic respiratory failure.

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Interventions
The therapy being considered is NPPV with non-invasive HMV.

Comparators
BPAP may be used to treat individuals with chronic respiratory failure due to neuromuscular disease.

Outcomes
The general outcomes of interest are mortality, symptoms, morbid events, functional outcomes, quality of life, and hospitalization.

This is a chronic treatment in a population with a high mortality rate. Therefore, follow-up at 12 months is of interest to measure readmissions and mortality and at 3 to 6 to measure blood gasses and health outcomes. It is not known whether $PaCO_2$ has an effect on health outcomes, or if it is only a marker of effective ventilation.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:
- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Consistent with a 'best available evidence approach,' within each category of study design, studies with larger sample sizes and longer durations were sought.
- Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE

Systematic Reviews
A technology assessment by the AHRQ (2019) for CMS identified 3 observational studies on the initiation of HMV in patients with neuromuscular disease.[21,] One study (N=144) compared HMV versus BPAP in patients with amyotrophic lateral sclerosis (ALS) (see Sancho et al 2014 below).[35,] The other studies were not relevant to this review of evidence.

Nonrandomized Studies
Sancho et al (2014) retrospectively compared BPAP with volume-cycled ventilation in patients with ALS.[35,] A total of 144 patients were identified with 82 receiving BPAP and 62 receiving HMV. No differences in survival were found between groups (median 15.00 months in both groups; p=.533). More patients had effective ventilation (gas exchange and hypoventilation symptoms) with HMV than BPAP (72.41% vs. 48.78%; p<.001).

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Section Summary: Home Mechanical Ventilation for Restrictive Thoracic Disorder Due to Neuromuscular Disease
The evidence for the use of HMV for hypoventilation as a result of neuromuscular disease includes observational studies. One observational study comparing BPAP to HMV found no difference in survival between these ventilation methods, although more patients received effective ventilation with HMV.

CONTINUOUS POSITIVE AIRWAY PRESSURE FOR OBESITY HYPOVENTILATION SYNDROME

Clinical Context and Therapy Purpose
Sleep-related breathing disorders are common in individuals with obesity hypoventilation syndrome (OHS). The coexistence of OHS and OSA is associated with more pronounced hypoxemia and hypercapnia than either condition individually, and individuals are at greater risk of morbidity and mortality compared to individuals who have either OHS or OSA alone. The purpose of CPAP in these individuals is to reduce morbidity and mortality in this population.

The following PICO was used to select literature to inform this review.

Populations
The relevant population of interest is individuals with OHS who have clinically significant OSA. Obstructive sleep apnea is a partial or intermittent upper airway collapse that results in hypoxemia and arousal during sleep.

Clinically significant OSA in adults that is indicated for treatment is defined as:
- An AHI or Respiratory Disturbance Index of at least 15 events per hour, OR
- An AHI or Respiratory Disturbance Index of at least 5 events per hour in an individual with 1 or more signs or symptoms associated with OSA (eg, excessive daytime sleepiness, hypertension, cardiovascular heart disease, or stroke);

The criterion standard for a diagnosis of sleep disorders is a polysomnogram performed in a sleep laboratory. A standard polysomnogram includes electroencephalogram, submental electromyogram, and electrooculogram (to detect rapid eye movement sleep) for sleep staging. Polysomnography also typically includes electrocardiography and monitoring of respiratory airflow, effort, snoring, oxygen desaturation, and sleep position. A variety of devices have been developed specifically to evaluate OSA at home. They range from portable full polysomnography systems to single-channel oximeters. Available devices evaluate different parameters, which may include oximetry, respiratory and cardiac monitoring, and sleep/wake activity.

A definition of terms and scoring criteria for OSA are described in Table 3.

Interventions
The therapy being considered is CPAP.

Comparators
Oxygen therapy may be used for OHS with OSA.

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Outcomes
The general outcomes of interest are mortality, symptoms, morbid events, functional outcomes, quality of life, and hospitalization.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:
- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Consistent with a 'best available evidence approach,' within each category of study design, studies with larger sample sizes and longer durations were sought.
- Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE

Systematic Reviews
A technology assessment by the AHRQ (2019) for CMS identified 1 trial comparing CPAP to no device in patients with OHS and OSA.[21,] This study by Masa et al (2015) is summarized below.[36,]

Randomized Controlled Trials
Masa et al (2015, 2016, 2019, 2020) conducted a series of open-label, multicenter RCTs evaluating NPPV in patients with OHS.[37,36,38,39,] The initial study, Masa et al (2015), enrolled patients with concomitant OHS and OSA. Patients (N=221) were randomized to NPPV (as mixed mechanical ventilation/BPAP), CPAP, or lifestyle modification.[36,] Lifestyle modifications included a low-calorie diet, sleep hygiene, and avoidance of alcohol or tobacco. NPPV was administered throughout the entire sleep period at bilevel pressure. Daytime use was to be adjusted to normal oxygen saturation (if possible). Both CPAP and NPPV resulted in greater improvements in $PaCO_2$ compared with lifestyle interventions, but no significant difference in $PaCO_2$ was found between CPAP and NPPV. Other outcomes including HRQL, 6MWD, and spirometry had greater improvement with NPPV than CPAP. The trial was limited by a short follow-up duration of 2 months and lack of comparative risk calculations. After this 2 month trial, patients were enrolled in the long-term extension trial.[39,] Patients treated with only lifestyle interventions were re-randomized to NPPV or CPAP. At a median follow up of 5.44 years, patients treated with NPPV had lower mean hospitalization days compared with CPAP treatment, but the difference was nonsignificant. Mortality was also similar between groups (15% with CPAP vs. 11% with NPPV; HR , 0.92, 95% CI, 0.36 to 1.87; p=.631).

Howard et al (2017) compared CPAP and BPAP for initial treatment in patients with OHS and severe OSA in a double-blind RCT.[40,] A total of 57 patients were treated for 3 months. Outcomes were similar between groups, but the trial is limited by the small sample size and short duration of follow-up prohibiting any conclusions regarding differences in mortality.

Tables 9 and 10 summarize RCT characteristics and results, respectively.

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Table 9. Summary of Key RCT Characteristics

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
Masa et al (2015)[36,]	Spain	16	2009-2013	OHS and OSA without COPD	NPPV (n=71)/CPAP (n=80)	Lifestyle (n=70)
Masa et al (2019)[39,]	Spain	16	2009-2013	OHS and OSA without COPD	NPPV (n=97)	CPAP (n=107)
Howard et al (2017)[40,]	Australia	2	2011-2013	OHS and OSA	CPAP (n=31)	BPAP (n=29)

BPAP: bilevel positive airway pressure; COPD: chronic obstructive pulmonary disease; CPAP: continuous positive airway pressure; NPPV: non-invasive positive airway pressure ventilation; OHS: obesity hypoventilation syndrome; OSA: obstructive sleep apnea; RCT: randomized controlled trial.

Table 10. Summary of Key RCT Results

Study	$PaCO_2$ (mmHg) Change from Baseline	PaO_2 (mmHg) Change from Baseline	FEV_1 (%) Change from Baseline	6MWD (m) Change from Baseline	Hospitalization Days (Per Year Per Patient)	Treatment Failure[a]
Masa et al (2015)[36,]	N=221	N=221	N=221	N=221		
CPAP	-3.7	5.5	-1.8	6.0		
NPPV	-5.5	4.8	4.8	32		
Control	-3.2	1.9	-1.5	16		
Masa et al (2019)[39,]					N=204	
NPPV					1.44	
CPAP					1.63	
Adjusted rate ratio (95% CI)					0.78 (0.34 to 1.77)	
p-value					.561	
Howard et al (2017)[40,]						
CPAP						13.3%
BPAP						14.8%
Difference (95% CI)						1.5% (-16.6 to 19.6)
p-value						.87

6MWD: 6-minute walk distance; BPAP: bilevel positive airway pressure; CI, confidence interval; CPAP: continuous positive airway pressure; FEV_1: forced expiratory volume in 1 second; NPPV: non-invasive positive airway pressure

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ventilation; $PaCO_2$: partial pressure of arterial carbon dioxide; PaO_2: partial pressure of arterial oxygen; RCT: randomized controlled trial.
[a] Defined as device usage <2 hours per night at 2 consecutive reviews, a hospital admission during the trial, or $PaCO_2$ >60 mmHg.

Tables 11 and 12 describe limitations of the RCTs.

Table 11. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Duration of Follow-up[e]
Masa et al (2015)[36,]	4. Conducted only in Spain			1. Morbidity/mortality data lacking	1,2. 2 months of follow-up insufficient for outcomes of chronic treatment
Howard et al (2017)[40,]	4. Conducted only in Australia				1,2. 3 months of follow-up insufficient for outcomes of chronic treatment

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Population key: 1. Intended use population unclear; 2. Study population is unclear; 3. Study population not representative of intended use; 4, Enrolled populations do not reflect relevant diversity; 5. Other.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest (e.g., proposed as an adjunct but not tested as such); 5: Other.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively; 5. Other.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. Incomplete reporting of harms; 4. Not establish and validated measurements; 5. Clinically significant difference not prespecified; 6. Clinically significant difference not supported; 7. Other.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms; 3. Other.

Table 12. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Masa (2015)[36,]		1,2. Trial was open-label				3,4. Lacking comparative treatment effects and CIs
Howard et al (2017)[40,]						

CI: confidence interval.
The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias; 5. Other.
[b] Blinding key: 1. Participants or study staff not blinded; 2. Outcome assessors not blinded; 3. Outcome assessed by treating physician; 4. Other.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication; 4. Other.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials); 7. Other.
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on

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clinically important difference; 4. Other.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated; 5. Other.

Nonrandomized Studies

Arellano-Maric et al (2020) conducted a prospective observational trial to determine whether patients with OHS and OSA could be switched from NPPV to CPAP.[41,] Patients were recruited from the sleep units of 3 hospitals in Germany. All patients had received successful NPPV ($PaCO_2$ ≤45 mmHg and <20% total sleep time with oxygen saturation <20%) for at least 3 months. Those patients who were successfully switched to CPAP (n=37) continued CPAP for 4 to 6 weeks. Five patients who did not meet criteria for CPAP switch requested to be switched to CPAP for a total sample size of 42 patients. During the study period, 30 of 42 patients (71%) maintained daytime $PaCO_2$ ≤45 mmHg. Quality of life, sleep parameters, and lung function were similar after the switch to CPAP. The authors concluded that CPAP is a feasible alternative to NPPV in patients with concomitant OHS and OSA.

Section Summary: Continuous Positive Airway Pressure Ventilation for Obesity Hypoventilation Syndrome

The evidence for use of CPAP in patients with OHS includes RCTs, a long-term extension study, and an observational study of patients with both OHS and OSA. The largest randomized trial showed improvement in outcomes with CPAP compared with lifestyle interventions and similar $PaCO_2$ outcomes with CPAP and NPPV. Long-term extension of this trial found similar hospitalization and mortality outcomes with these modalities. Observational data found that select patients with OHS and OSA can be successfully switched from BPAP to CPAP and maintain adequate $PaCO_2$.

BILEVEL POSITIVE AIRWAY PRESSURE VENTILATION FOR OBESITY HYPOVENTILATION SYNDROME

Clinical Context and Therapy Purpose

The purpose of BPAP in individuals who have OHS is to reduce morbidity and mortality in this population.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with OHS.

Interventions

The therapy being considered is NPPV with BPAP.

Comparators

Oxygenation therapy or CPAP may be used to treat individuals with hypoventilation syndromes.

Outcomes

The general outcomes of interest are mortality, symptoms, morbid events, functional outcomes, quality of life, and hospitalization.

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This is a chronic treatment in a population with a high mortality rate. Therefore, follow-up at 12 months is of interest to measure readmissions and mortality and at 3 to 6 to measure blood gasses and health outcomes. It is not known whether $PaCO_2$ has an effect on health outcomes, or if it is only a marker of effective ventilation.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Consistent with a 'best available evidence approach,' within each category of study design, studies with larger sample sizes and longer durations were sought.
- Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE

Systematic Reviews

Multiple systematic reviews have evaluated various NPPV methods in patients with hypoventilation syndromes (Tables 13 to 15). Xu et al (2022) conducted a network meta-analysis evaluating various NPPV methods (CPAP and BPAP) in patients with OHS.[42,] Trials enrolled obese patients (BMI ≥30 mg/m^2) with hypercapnia ($PaCO_2$ ≥45 mmHg) who had no other causes for the hypercapnia. BPAP-average volume-assured pressure support (AVAPS) and BPAP-spontaneous timed (ST) pressure support were the most effective methods for improving sleep and $PaCO_2$.

Afshar et al (2020) conducted a systematic review of 25 studies (3 RCTs) evaluating NPPV (CPAP and BPAP) in patients with OHS.[43,] Table 13 identifies the 3 RCTS included in the analysis (the 12 nonrandomized comparative studies and 10 studies without a comparator group are not included). Overall, NPPV was associated with improved mortality, daytime sleepiness, and hospital visits; however, the evidence had low to very low certainty and was considered very low quality.

Table 13. Comparison of Trials Included in the Systematic Reviews

Study	Xu (2022)[42,]	Afshar (2020)[43,]
Borel et al (2012)[44,]	●	●
Howard et al (2017)[40,]	●	
Masa et al (2015)[36,]	●	●
Masa et al (2016)[38,]	●	●
Masa et al (2019)[39,]	●	
Masa et al (2020)[37,]	●	

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Study	Xu (2022)[42,]	Afshar (2020)[43,]
Murphy et al (2012)[45,]	●	
Patout et al (2020)[46,]	●	
Piper et al (2008)[47,]	●	
Storre et al (2006)[48,]	●	

Table 14. Systematic Review and Meta-Analyses Characteristics

Study	Dates	Trials	Participants	N (Range)	Design	Duration
Xu et al (2022)[42,]	Through Feb 2021	10	Obese patients with OHS receiving treatment	845 (20 to 204)	RCT	1 to 36 months
Afshar et al (2020)[43,]	Jan 1946 to Mar 2019	25 (3 RCTs)	Patients with OHS with or without OSA	342 (35 to 221)	RCT	1 to 2 months

OHS: obesity hypoventilation syndrome; OSA: obstructive sleep apnea; RCT: randomized controlled trial.

Table 15. Systematic Review and Meta-Analyses Results

Study	Daytime $PaCO_2$ (mmHg)	ESS		
Xu et al (2022)[42,]				
N	693	673		
BPAP-AVAPS (MD; 95% CI)	-3.02[a] (-4.42 to -1.62); -1.49[b] (95% CI, -2.82 to -0.16)	-3.36 (-4.62 to -2.10)		
BPAP-ST (MD; 95% CI)[a]	-2.06 (-3.83 to -0.29)	-2.43 (-4.29 to -0.57)		
CPAP (MD; 95% CI)		-3.03 (-4.46 to -1.60)		
BPAP-S		-6.03 (-10.62 to -1.44)		
Afshar et al (2020)[43,]				
	Daytime $PaCO_2$ (mmHg)	**Functional Outcomes of Sleep Questionnaire**	**AHI**	**Hypercapnia resolution**
N	342	229	342	342
RR (95% CI)[c]				1.39 (0.97 to 2.00)

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Study	Daytime $PaCO_2$ (mmHg)	ESS		
MD (95% CI)[c]	-2.40 (-3.77 to -1.03)	6.59 (2.47 to 10.70)	-33.99 episodes/hour (-65.45 to -2.53)	
I^2	10%	0%	97%	

AHI: apnea-hypopnea index; BPAP-AVAPS: bilevel positive airway pressure-average volume-assured pressure support; BPAP-S: bilevel positive airway pressure-spontaneous; BPAP-ST: bilevel positive airway pressure-spontaneous timed; CI: confidence interval; CPAP: continuous positive airway pressure; ESS: Epworth Sleep Scale; MD: mean difference; $PaCO_2$: partial pressure of arterial carbon dioxide; RCT: randomized controlled trial; RR: relative risk.
[a] Compared with lifestyle.
[b] Compared with CPAP.
[c] Data from 3 RCTs compared with control.

Randomized Trials

In 2016, Masa et al published a trial conducted in patients with OHS but without severe OSA (Tables 16 and 17).[38,] Patients (N=86) were randomized to BPAP or lifestyle modification. Patients treated with BPAP had greater improvement in PaCO2 than those who received lifestyle modification. Daytime sleepiness and some health-related quality of life parameters were also improved. Similar to the 2015 study previously described,[36,] the follow-up was limited to 2 months.[38,] Long-term outcomes were also published by Masa et al (2020) in patients (N=98) without severe OSA.[37,] Compared with control, BPAP did not significantly reduce mean hospitalization days per year, cardiovascular events, or mortality but did improve $PaCO_2$, quality of life, and daytime sleepiness at a median follow-up of 4.98 years.

Table 16. Summary of Key RCT Characteristics

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
Masa et al (2016)[38,]	Spain	16	2009-2013	OHS without OSA	BPAP (n=40)	Lifestyle (n=46)
Masa et al (2020)[37,]	Spain	16	2009-2016	OHS without OSA	BPAP (n=48)	Lifestyle (n=48)

BPAP: bilevel positive airway pressure; OHS: obesity hypoventilation syndrome; OSA: obstructive sleep apnea; RCT: randomized controlled trial.

Table 17. Summary of Key RCT Results

Study	$PaCO_2$ (mmHg) Change from Baseline	PaO_2 (mmHg) Change from Baseline	FEV_1 (%) Change from Baseline	6MWD (m) Change from Baseline	Hospitalization Days (Per Year Per Patient)
Masa et al (2016)[38,]					
BPAP	-6	4.6	1.8	29	
Control	-2.8	1.4	1.9	-7.2	
Masa et al (2020)[37,]					N=96

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Study	$PaCO_2$ (mmHg) Change from Baseline	PaO_2 (mmHg) Change from Baseline	FEV_1 (%) Change from Baseline	6MWD (m) Change from Baseline	Hospitalization Days (Per Year Per Patient)
BPAP					2.71
Control					2.60
Adjusted rate ratio (95% CI)					1.07 (0.44 to 2.59)
p-value					.882

6MWD: 6-minute walk distance; BPAP: bilevel positive airway pressure; CI, confidence interval; FEV_1: forced expiratory volume in 1 second; $PaCO_2$: partial pressure of arterial carbon dioxide; PaO_2: partial pressure of arterial oxygen; RCT: randomized controlled trial.

The limitations of the Masa RCT are summarized in Tables 18 and 19.

Table 18. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Duration of Follow-up[e]
Masa et al (2016)[36,38,]	4. Conducted only in Spain			1. Morbidity/mortality data lacking	1,2. 2 months of follow-up insufficient for outcomes of chronic treatment

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Population key: 1. Intended use population unclear; 2. Study population is unclear; 3. Study population not representative of intended use; 4, Enrolled populations do not reflect relevant diversity; 5. Other.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest (e.g., proposed as an adjunct but not tested as such); 5: Other.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively; 5. Other.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. Incomplete reporting of harms; 4. Not establish and validated measurements; 5. Clinically significant difference not prespecified; 6. Clinically significant difference not supported; 7. Other.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms; 3. Other.

Table 19. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Masa et al (2016)[38,]		1,2. Trial was open-label				3,4. Lacking comparative treatment effects and CIs

CI: confidence interval.
The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias; 5. Other.
[b] Blinding key: 1. Participants or study staff not blinded; 2. Outcome assessors not blinded; 3. Outcome assessed by treating physician; 4. Other.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication; 4.

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Other.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials); 7. Other.
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference; 4. Other.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated; 5. Other.

Section Summary: Bilevel Positive Airway Pressure Ventilation for Obesity Hypoventilation Syndrome

The evidence for BPAP in OHS consists of systematic reviews of NPPV with either CPAP or BPAP and an RCT specific to BPAP in patients with OHS but without OSA. Masa et al (2016) enrolled patients who had OHS but not OSA and randomized them to BPAP or lifestyle interventions. In patients with OHS and without OSA, BPAP resulted in better $PaCO_2$ outcomes than lifestyle modifications in the short-term, but long-term outcomes failed to find significant improvement in hospitalization days between groups.

HOME MECHANICAL VENTILATION FOR OBESITY HYPOVENTILATION SYNDROME

Clinical Context and Therapy Purpose

The purpose of non-invasive HMV in individuals who have OHS is to provide a treatment option that is an improvement over other treatments including high flow oxygen or BPAP.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with OHS that is refractory to pharmacologic management, oxygen, and BPAP.

Interventions

The therapy being considered is HMV. Mechanical ventilators are devices that deliver more controlled breathing with bilevel ventilation. They can be used either invasively with tracheostomy or non-invasively with a mask. Compared to BPAP, HMVs have additional ventilatory modes and ventilatory control along with features such as alarms and battery backup power for individuals who require backup at night or daytime use with mobility. HMVs are classified by the U.S. Food and Drug Administration as life support devices.

Comparators

BPAP with high flow oxygen may be used to treat individuals with OHS and chronic respiratory failure.

Outcomes

The general outcomes of interest are mortality, symptoms, morbid events, functional outcomes, quality of life, and hospitalization.

This is a chronic treatment in a population with a high mortality rate. Therefore, follow-up at 12 months is of interest to measure readmissions and mortality and at 3 to 6 to measure blood

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gasses and health outcomes. It is not known whether $PaCO_2$ has an effect on health outcomes, or if it is only a marker of effective ventilation.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Consistent with a 'best available evidence approach,' within each category of study design, studies with larger sample sizes and longer durations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence
No randomized or nonrandomized studies specific to HMV in patients with OHS, but without concomitant OSA or COPD were identified.

Section Summary: Home Mechanical Ventilation for Obesity Hypoventilation Syndrome
Clinical trials specific to HMV in OHS are lacking.

NON-INVASIVE POSITIVE AIRWAY PRESSURE FOR HYPOVENTILATION SYNDROMES UNRELATED TO OBESITY

Clinical Context and Therapy Purpose
The purpose of NPPV including BPAP or HMV in individuals who have hypoventilation syndromes without obesity is to provide a treatment option that is an improvement over standard medical care including invasive mechanical ventilation.

The following PICO was used to select literature to inform this review.

Populations
The relevant population of interest is individuals with hypoventilation syndromes unrelated to obesity.

Interventions
The therapy being considered is NPPV with BPAP or HMV.

Comparators
Oxygen may be used to treat individuals with hypoventilation syndromes and chronic respiratory failure. Individuals with hypoventilation syndromes may require invasive ventilation.

Outcomes
The general outcomes of interest are mortality, symptoms, morbid events, functional outcomes, quality of life, and hospitalization.

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This is a chronic treatment in a population with a high mortality rate. Therefore, follow-up at 12 months is of interest to measure readmissions and mortality and at 3 to 6 to measure blood gasses and health outcomes. It is not known whether $PaCO_2$ has an effect on health outcomes, or if it is only a marker of effective ventilation.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Consistent with a 'best available evidence approach,' within each category of study design, studies with larger sample sizes and longer durations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence
The evidence for NPPV in patients with hypoventilation syndromes unrelated to obesity is limited to case reports and case series primarily in patients with congenital central hypoventilation. In some cases NPPV may avoid the need for invasive mechanical ventilation.[49,50,42,]

Section Summary: Non-Invasive Positive Airway Pressure for Hypoventilation Syndromes Unrelated to Obesity
Case series and case reports support that NPPV may be useful to limit invasive mechanical ventilation in some patients with hypoventilation syndromes unrelated to obesity.

SUPPLEMENTAL INFORMATION
The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Practice Guidelines and Position Statements
Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American College of Chest Physicians
In 2023, the American College of Chest Physicians (ACCP) published clinical practice guidelines for respiratory management of patients with neuromuscular weakness.[51,] Most evidence is based on observational data from patients with amyotrophic lateral sclerosis. The guidelines recommend non-invasive ventilation (NIV) for patients with neuromuscular disease and chronic respiratory failure for patients who meet the following pulmonary function test criteria:

- Forced vital capacity (FVC) <80% predicted with symptoms or FVC <50% predicted without symptoms;

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- Maximum inspiratory pressure (MIP) <60 cm H_2O or maximum expiratory pressure (MEP) <40 cm H_2O;
- Peak cough flow (PCF) <270 L/min for age ≥12 years or PCF <5th percentile for age <12 years;
- Sniff nasal inspiratory pressure (SNIP) <70 cm H_2O in male patients, SNIP <60 cmH_2O in female patients for age ≥12 years.

The panel found no strong evidence to support one method of NIV over another.

American College of Chest Physicians et al
In 2021, the ACCP, the American Association for Respiratory Care, the American Academy of Sleep Medicine, and the American Thoracic Society published a technical expert panel report on optimal NIV for chronic obstructive pulmonary disease (COPD), thoracic restrictive disorders, and hypoventilation syndromes.[52,53,54,]

Chronic Obstructive Pulmonary Disease
For COPD the panel recommends that overnight oxygen saturation should not be part of the criteria for bilevel positive airway pressure (BPAP) and that home mechanical ventilators be considered when patients need any of the following:[52,]

- "Higher inspiratory pressures than those deliverable by E0471,
- FIO_2 [fraction of inspired oxygen] higher than 40% or 5 L/min nasally,
- Ventilator support for 10 h per day or greater (ie, daytime use),
- Both sophisticated alarms and accompanying internal battery (high-dependency patient),
- Mouthpiece ventilation during the day,
- Persistence of hypercapnia with $PaCO_2$ [arterial blood carbon dioxide] > 52 mmHg despite adequate adherence to BPAP therapy"
- The panel strongly recommended the use of respiratory therapists in the home for initiation and ongoing support for positive pressure ventilation with either BPAP or home ventilators.

Thoracic Restrictive Disorders
For thoracic restrictive disorders, the panel recommends BPAP for patients with any of the following:[53,]

- "Spirometry (upright or supine) with vital capacity <50% predicted or <80% predicted with associated symptoms (i.e., orthopnea, dyspnea, morning headaches, excessive daytime sleepiness, or unrefreshing sleep),
- Force testing with maximal inspiratory pressure <60 cm H_2O,
- Hypercapnia:
    - Chronic stable daytime (awake) hypercapnia with $PaCO_2$ >45 mmHg,
    - Venous blood gas PCO_2, end-tidal PCO_2, or transcutaneous PCO_2, >50 mmHg, or
- Hypoxia:
    - Overnight oximetry in-laboratory or home sleep test with saturation <88% for 5 minutes."

Home mechanical ventilation is recommended in patients with vital capacity <30% or if BPAP fails.

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Hypoventilation Syndromes

For patients with hypoventilation syndromes who are obese the recommendations include:[54,]

- BPAP (spontaneous/timed) or volume-assured pressure support (VAPS) for those who are discharged from the hospital, for those with obesity hypoventilation syndrome (OHS) without obstructive sleep apnea, and for those who have failed continuous positive airway pressure (CPAP).

For patients with hypoventilation syndromes due to reduced respiratory drive or advanced lung disease that is not COPD, BPAP (spontaneous/timed) or VAPS is recommended. Patients with hypoventilation syndromes who fail BPAP/VAPS should receive home mechanical ventilation.

AMERICAN THORACIC SOCIETY

Chronic Obstructive Pulmonary Disease

In 2020, the American Thoracic Society published an evidence-based clinical practice guideline on long-term non-invasive ventilation in chronic stable hypercapnic COPD.[2,] The society included the recommendations in Table 20, all of which were conditional due to moderate to very low certainty in the evidence base.

Table 20. American Thoracic Society Recommendations for COPD

Recommendation	Strength of Recommendation	Level of Certainty
"We suggest the use of nocturnal noninvasive ventilation (NIV) in addition to usual care for patients with chronic stable hypercapnic COPD."	Conditional	Moderate
"We suggest that patients with chronic stable hypercapnic COPD undergo screening for obstructive sleep apnea before initiation of long-term NIV."	Conditional	Very low
"We suggest not initiating long-term NIV during an admission for acute on-chronic hypercapnic respiratory failure, favoring instead reassessment for NIV at 2 to 4 weeks after resolution."	Conditional	Low
"We suggest not using an in-laboratory overnight polysomnogram (PSG) to titrate NIV in patients with chronic stable hypercapnic COPD who are initiating NIV."	Conditional	Very low
"We suggest NIV with targeted normalization of $PaCO_2$ in patients with hypercapnic COPD on long-term NIV."	Conditional	Low

COPD: chronic obstructive pulmonary disease; NIV: non-invasive ventilation; PaCO2: pressure of arterial carbon dioxide; PSG: polysomnogram.
Hypercapnic COPD defined as PaCO2 > 45 mmHg.

Obesity Hypoventilation Syndrome

In 2019, the American Thoracic Society published a clinical practice guideline on OHS.[55,] These guidelines recommend positive airway pressure for patients with OHS. Generally CPAP is recommended over other NIV because the majority (>70%) of patients have concomitant obstructive sleep apnea (OSA). The guidelines do recommend non-invasive positive airway pressure ventilation (NPPV) initiation at discharge for patients hospitalized with respiratory failure

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suspected of having OHS until they undergo outpatient workup and titration of positive airway pressure therapy. Both recommendations were conditional with very low level of certainty in the evidence.

Global Initiative for Chronic Obstructive Pulmonary Disease
The Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD) published a revised report for 2026. [1,] GOLD guidelines recommend at least 1 of the following as an indication for non-invasive mechanical ventilation :

- Respiratory acidosis ($PaCO_2$ ≥45 mmHg and arterial pH ≤7.35);
- Severe dyspnea with clinical signs suggestive of respiratory muscle fatigue, increased work of breathing, or both;
- Persistent hypoxemia despite supplemental oxygen therapy.

National Institute for Health and Care Excellence Global
In 2019, the United Kingdom's NICE published a guideline for the diagnosis and management of COPD.[56,] NICE recommends that patients with COPD who have chronic hypercapnic respiratory failure despite adequate pharmacologic and oxygen therapy should be referred to a specialist center for consideration of long-term, non-invasive ventilation.

U.S. Preventive Services Task Force Recommendations
Not applicable.

Ongoing and Unpublished Clinical Trials
Some currently unpublished trials that might influence this review are listed in Table 21.

Table 21. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT01037387	Effect of the Noninvasive Mechanical Ventilation on the Daily Physical Activity and the Inflammatory Biomarkers in Stable Patients With COPD	50	Dec 2025
NCT02811588[a]	Registry of Stable Hypercapnic Chronic Obstructive Pulmonary Disease Treated With Non-Invasive Ventilation Amendment: Home Tele-Monitoring of Non-Invasive Ventilation in Chronic Obstructive Pulmonary Disease	169	Jun 2026
NCT03647462	The Impact of Early Diagnosis and Treatment of OSA on Hospital Readmission in Hospitalized Chronic Obstructive Pulmonary Disease Patients: the COPD Readmit Clinical Trial	100	Apr 2025
NCT03221101	Home Non Invasive Ventilation Versus Long Term Oxygen Therapy Alone in COPD Survivors After Acute Hypercapnic Respiratory Failure. A French Multicenter Randomized Controlled Trial	86	Dec 2025

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NCT No.	Trial Name	Planned Enrollment	Completion Date
NCT05805293	High-Velocity Nasal Insufflation Therapy Versus Non-Invasive Ventilation In Management Of Acute Hypercapnic Respiratory Failure In Obesity Hypoventilation Syndrome: A Randomized Controlled Trial	56	Jun 2024
Unpublished			
NCT03766542	Optimal Positive Airway Pressure in Overlap Syndrome: a Randomized Controlled Trial	70	Sep 2020 (unknown)

NCT: national clinical trial.
[a] Denotes industry-sponsored or cosponsored trial.

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CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. This may not be a comprehensive list of procedure codes applicable to this policy.

Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

The code(s) listed below are medically necessary ONLY if the procedure is performed according to the "Policy" section of this document.

CPT/HCPCS	
E0466	Home ventilator, any type, used with non-invasive interface, (e.g., mask, chest shell)
E0470	Respiratory assist device, bi-level pressure capability, without backup rate feature, used with noninvasive interface, e.g., nasal or facial mask (intermittent assist device with continuous positive airway pressure device)
E0471	Respiratory assist device, bi-level pressure capability, with back-up rate feature, used with noninvasive interface, e.g., nasal or facial mask (intermittent assist device with continuous positive airway pressure device)

REVISIONS	
10-25-2019	New policy published to medical policy webpage 09-25-2019. Policy effective 10-25-2019.
05-21-2021	Medical policy reviewed; no revisions made.
02-25-2022	Changed Title to: Non-Invasive Positive Airway Pressure for Chronic Obstructive Pulmonary Disease
	Update Description Section
	Updated Policy Section ▪ Change entire Policy Section to read as: A. For patients with chronic obstructive pulmonary disease (COPD) without hypercapnia ($PaCO_2$ < 52 mmHg) and with obstructive sleep apnea, see BCBSKS medical policy *Diagnosis and Medical Management of Obstructive Sleep Apnea Syndrome.* B. Nocturnal bilevel positive airway pressure with backup rate may be considered medically necessary for patients with COPD and chronic respiratory failure (see Policy Guidelines) who meet either of the following: 1. Chronic stable daytime (awake) hypercapnia ($PaCO_2$> 52 mmHg) OR 2. Daytime (awake) hypercapnia ($PaCO_2$> 52 mmHg) at least 2 weeks after resolution of an acute exacerbation with decompensated acidosis. C. Non-invasive home mechanical ventilation may be considered medically necessary for patients with COPD who meet the following criteria: 1. Qualify for a bilevel positive airway pressure device AND 2. meet at least one of the following:

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	a. Higher pressure (e.g., > 25 cm H2O) is needed to reduce hypercapnia than can be achieved with a bilevel device during titration; OR b. Severe hypoxemia requiring FIO_2 > 40% or > 5 L/min; OR c. Daytime use (battery operated unit) is required to reduce hypercapnia. D. Individuals with COPD who are started on bilevel positive airway pressure at discharge from hospitalization may continue for up to 3 months to provide time to stabilize and complete reevaluation. E. Non-invasive positive airway pressure for COPD is considered experimental / investigational under all other conditions.
	Updated Policy Guidelines Section
	Updated Rationale Section
	Updated Code Section ▪ Added HCPCS code E0471 ▪ Added ICD-10 Code G47.33
	Update References Section
Posted 04-23-2024 Effective 05-23-2024	Updated Title ▪ Changed Title to: "Home Non-invasive Positive Airway Pressure Devices for the Treatment of Respiratory Insufficiency and Failure"
	Updated Description Section
	Updated Policy Section ▪ Changed statement B2 from "after resolution to "after discharge from the hospital" F. Added Section F: Bilevel positive airway pressure may be considered medically necessary for individuals with thoracic restrictive disorders due to neuromuscular disease who meet any of the following: 1. Pulmonary function tests: a. Spirometry (upright or supine) with vital capacity <50% predicted or <80% predicted with associated symptoms (orthopnea, dyspnea, morning headaches, excessive daytime sleepiness, or unrefreshing sleep); OR b. Maximal inspiratory pressure <60 cm H2O or maximum expiratory pressure (MEP) <40 cm H2O; OR c. Peak cough flow (PCF) <270 L/min for age ≥12 years or PCF <5th percentile for age <12 years; OR d. Sniff nasal inspiratory pressure (SNIP) <70 cm H_2O in males, SNIP <60 cmH_2O in females for age ≥12 years. 2. Hypercapnia a. Chronic stable daytime (awake) hypercapnia with PaCO2 ≥45 mmHg (capillary blood gas can be used in children); OR b. Venous blood gas PCO_2, end-tidal PCO_2, or transcutaneous PCO_2, ≥50 mmHg; OR 3. Hypoxia a. Overnight oximetry in-laboratory or home sleep test with saturation <88% for 5 minutes; b. Overnight oximetry: SpO2 ≤90% for ≥2% of sleep time. G. Added Section G: Non-invasive home mechanical ventilation may be considered medically necessary for individuals with thoracic restrictive disorders due to neuromuscular disease who meet the following: 1. Qualify for a BPAP device; AND a. BPAP fails; OR b. Have extreme loss in function with vital capacity <30%; OR

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	c. Non-invasive ventilation is needed for >10 hours per day; OR d. Severe breathlessness (e.g., with speaking at rest); OR e. Worsening daytime hypercapnia with need for mouthpiece ventilation; OR f. Daytime use (battery operated unit) is required to reduce hypercapnia or dyspnea. ▪ Added Section H: Bilevel positive airway pressure may be considered medically necessary for individuals with hypoventilation syndromes who meet the following criteria: 1. Awake or sleep hypoventilation with hypercapnia (one of the following is met): a. Awake hypoventilation with chronic stable daytime (awake) hypercapnia (PaCO2 ≥45 mmHg); OR b. Venous blood gas PCO2, end-tidal PCO2, or transcutaneous PCO2 ≥50 mmHg; OR c. Sleep hypoventilation with hypercapnia: i. ≥10 mmHg increase from baseline awake PCO_2 and to a value > 50 mmHg for ≥10 min; OR ii. PCO_2 ≥55 mmHg for ≥10 min; AND 2. Low clinical suspicion for COPD or neuromuscular disease; AND 3. One of the following conditions are met: a. Obesity with body mass index (BMI) ≥30 kg/m2; OR b. Decreased respiratory drive due to opioid or substance use; OR c. Advanced lung disease other than COPD (e.g., end-stage or advanced interstitial lung disease); AND 4. Individual was discharged from inpatient stay with persistent awake hypoventilation (hypercapnia) on BPAP. a. A reassessment with a provider within 3 months (30 to 90 days) is required and an attended polysomnogram (PSG) should be performed to assess appropriateness of positive airway pressure modality (home sleep apnea test is acceptable if attended PSG is not obtainable); OR 5. Individual is ambulatory and sleep study indicates that BPAP is necessary for sleep-disordered breathing, or individual with severe obstructive sleep apnea is continuous positive airway pressure intolerant or continuous positive airway pressure was proven ineffective. ▪ Added Section I: Non-invasive home mechanical ventilation may be considered medically necessary for individuals with hypoventilation syndromes who meet the following: 1. Qualify for a BPAP device and at least one of the following: a. Higher pressure is needed to reduce hypercapnia than can be achieved with a bilevel continuous positive airway pressure device during titration (typically >25 cm H2O); OR b. Severe hypoxemia requiring FIO2 >40% or >5 L/min; OR c. Daytime use (battery operated unit) is required to reduce hypercapnia; OR 2. Tried and failed BPAP device with persistent hypercapnia despite 3 months of adequate adherence to prescribed positive airway pressure therapy with: a. Awake PaCO2 ≥45 mmHg; OR b. Awake venous blood gas PCO_2, end-tidal PCO_2, or transcutaneous PCO_2 ≥50 mmHg.
	Updated Policy guidelines ▪ Statement B added "There are limited data on which to base compliance assessment. Assessment could be further based on an average of at least 4 hours per 24 hours over a consecutive 30-day period or use of 4 hours per 24 hours for at least 65% of the days in a consecutive 30-day period." to the end of the statement.

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	Updated Rationale Section
	Updated Coding Section ▪ Added E0470 ▪ Removed ICD-10 Codes
	Updated References Section
05-13-2025	Updated Description Section
	Updated Rationale Section
	Updated References Section
05-14-2026	Updated Description Section
	Updated Rationale Section
	Updated References Section
11-10-2026	Updated Policy Section ▪ Statement A: Changed to read "ONE" of the following ▪ Statement B1, B2 and B3: Added "with one of the following:" ▪ Statement C: Added C ▪ Statement C4: Added "one of the following conditions are met: " ▪ Statement F: Added "ALL" of the following ▪ Statement F1: Added "meet at least one of the following: " ▪ Statement G: Added ALL ▪ Added: AND between G1c and G2 ▪ Statement G2: Added "with one of the following:" ▪ Statement H: Added "ALL" of the following ▪ Added: AND between H1 and H2 ▪ Added Statement H2: Added "one of the following"

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