

Evidence Review for the Use of Non-Invasive Ventilation in a Domiciliary Setting

Question to be addressed

1. In adults with respiratory failure in:
 - a. Chronic obstructive pulmonary disease
 - b. Neuro-muscular disease
 - c. Obstructive Sleep Apnoea

is there evidence to support the use of non-invasive domiciliary ventilation and if so, in what clinical circumstances is the use of domiciliary NIV appropriate?

Reason for review

NHS Birmingham and Solihull CCG, Sandwell and West Birmingham CCG, requested a rapid evidence review of the clinical and cost effectiveness of the use of domiciliary non-invasive ventilation in reducing hospital admissions and preventing death to inform their decisions on commissioning policy development.

Options for commissioners:

1. The Committee considers that due to the limited quality of evidence of clinical and cost effectiveness for the use of domiciliary non-invasive ventilation compared to alternative treatment options, its use should be considered a low priority.
2. The Committee recommends that, due to the limited quality of evidence of its clinical and cost effectiveness, the use of domiciliary non-invasive ventilation should be offered ONLY to patients who have certain clinical diagnoses and have a certain degree of respiratory failure.
3. The Committee considers that there is sufficient evidence to suggest that the use of domiciliary NIV is at least as effective as alternative treatment options and the costs are comparable, therefore the decision to commence non-invasive ventilation should be made after an informed discussion between the clinician and the individual person about the risks and benefits.

Summary

Background

- Respiratory Failure can occur in a number of clinical circumstances and can impact on a patient's ability to carry out activities of daily living and can ultimately result in death.
- Non-invasive ventilation can be undertaken using positive or negative pressure, though the most commonly used form of non-invasive ventilation is positive pressure.
- Positive pressure ventilation can be undertaken through continuous positive airway pressure through to bi-level ventilation.

Clinical effectiveness

- Clinical effectiveness of non-invasive ventilation was clearly identified in number of clinical scenarios:
 - .1 Chronic Obstructive Pulmonary Disease

- .2 Neuromuscular Diseases
- .3 Obstructive Sleep Apnoea
 - NICE clearly supports the use of this intervention in OSA & Motor Neurone Disease.
 - There is strong evidence not only for the clinical effectiveness of the use of NIV in certain clinical circumstances but also for the cost-effectiveness of this intervention in preventing deterioration in patient symptoms, readmission to an acute care setting and death.

Safety

NICE & MHRA support the use of Non-invasive ventilation support in certain clinical circumstances.

Cost effectiveness

A. COPD

No QALY identified within the literature.

B. NMD

Cost-effectiveness of the use of Non-invasive ventilation was supported by NICE (NG 42) with certain cohorts of this patient population diagnosed with NMD

C. OSA

Cost-effectiveness of the use of Non-invasive ventilation was supported by NICE (2012 TA139) with certain cohorts of this patient population diagnosed with OSA.

Equity issues

None were identified within the course of this review for OSA or Neuro-

dependent patient, however COPD was associated with deprivation. Major risk factors for developing COPD are smoking, and occupation dust exposure in patients over the age of 40 years old. Ensuring good smoking cessation support in all ages may help to reduce any inequity issues. Due to the links to smoking and exposure to dust and chemicals more likely to be found in manual labour roles, this would indicate indirect links with deprivation.

Context

1.1 Introduction

A. COPD

Chronic obstructive pulmonary disease (COPD) is the collective name for a group of lung conditions that may cause breathing difficulties.

It includes:

- emphysema – damage to the air sacs in the lungs
- chronic bronchitis – long-term inflammation of the airways

COPD is a common condition that mainly affects middle-aged or older adults who have a smoking history. The breathing problems tend to get gradually worse over time and can limit the patient's normal activities, although treatment can help keep the condition under control.

Symptoms of COPD

The main symptoms of COPD are:

- increasing breathlessness, particularly when the patient is active
- a persistent chesty cough with phlegm
- frequent chest infections
- persistent wheezing

Without treatment, the symptoms usually get slowly worse. There may also be periods when they get suddenly worse, known as a flare-up or exacerbation.

Causes of COPD

COPD occurs when the lungs become inflamed, damaged and narrowed. The main cause is smoking, although the condition can sometimes affect people who have never smoked.

The likelihood of developing COPD increases the more a patient smokes and the longer the patient has smoked. Some cases of COPD are caused by long-term exposure to harmful fumes, or dust or occur as a result of a rare genetic problem that means the lungs are more vulnerable to damage.

The damage to the lungs caused by COPD is permanent, but treatment can help slow down the progression of the condition.

B. NMD

Neuromuscular disorder (NMD) is a very broad term encompassing a range of conditions that impair the functioning of the muscles, either directly, being pathologies of the voluntary muscle, or indirectly, being pathologies of the peripheral nervous system or neuromuscular junctions. Other spinal cord or brain diseases are not considered “neuromuscular” diseases.

NMD affect the nerves controlling voluntary muscles. Voluntary muscles are the ones that can be controlled such as those in arms and legs. Nerve cells, also called neurons, send the messages that control these muscles. When the neurons become unhealthy or die, communication between the nervous system and muscles breaks down. As a result, muscles weaken and waste away. The weakness can lead to twitching, cramps, aches and pains, and joint and movement problems. Sometimes it also affects heart function and the ability to breathe.

Examples of NMD include:

- Motor Neurone Disease
- Multiple sclerosis
- Myasthenia gravis
- Spinal muscular atrophy.

Many NMD are genetic, which means they run in families or there is a gene mutation for example in muscle dystrophies. Sometimes, an immune system disorder can cause them as in myasthenia.

C. OSA

Apnoea is defined as a temporary absence or cessation of breathing. **Obstructive Sleep Apnoea hypopnea syndrome (OSAHS)** is a condition in which a person experiences repeated episodes of apnoea because of a narrowing or closure of the pharyngeal airway during sleep. This is caused by a decrease in the tone of the muscles supporting the airway during sleep. Complete closure (obstruction) stops airflow (apnoea) whereas partial obstruction decreases airflow (hypopnoea). OSAHS results in episodes of brief awakening from sleep to restore normal breathing.

Moderate to severe OSAHS can be diagnosed from patient history and a sleep study using oximetry or other monitoring devices carried out in the person's

home. In some cases, further studies that monitor additional physiological variables in a sleep laboratory or at home may be required, especially when alternative diagnoses are being considered. The severity of OSAHS is usually assessed on the basis of both severity of symptoms (particularly the degree of sleepiness) and the sleep study, by using either the apnoea/hypopnoea index (AHI) or the oxygen desaturation index. OSAHS is considered mild when the AHI is 5–14 in a sleep study, moderate when the AHI is 15–30, and severe when the AHI is over 30. In addition to the AHI, the severity of symptoms is also important.

The symptoms of OSAHS include impaired alertness, cognitive impairment, excessive daytime sleepiness, snoring, nocturia, morning headaches and sexual dysfunction. The sleep quality of partners may also be affected. Excessive daytime sleepiness can adversely affect cognitive function, mood and quality of life. OSAHS is associated with high blood pressure, which increases the risk of cardiovascular disease and stroke. OSAHS has also been associated with an increased risk of road traffic accidents.

Major risk factors for developing OSAHS are increasing age, obesity and being male. OSAHS is also associated with certain specific craniofacial characteristics (such as retrognathia), enlarged tonsils and enlarged tongue. Use of alcohol or sedatives can also increase the risk or severity of the condition. OSAHS has been reported to affect up to 4% of middle-aged men and 2% of middle-aged women in the UK. It is estimated that 1% of men in the UK may have severe OSAHS.

Management

Noninvasive ventilation (NIV) refers to the administration of ventilatory support without using an invasive artificial airway (endotracheal tube or tracheostomy tube). The use of noninvasive ventilation has markedly increased over the past three decades, and noninvasive ventilation has now become an integral tool in the management of both acute and chronic respiratory failure, in both the home setting and in critical care.

In its simplest terms, noninvasive ventilation differs from invasive ventilation by the interface between the patient and the ventilator. Invasive ventilatory support is provided via either an endotracheal tube or tracheostomy tube. Noninvasive ventilatory support uses a variety of interfaces, and these have continued to evolve with modifications based on patient comfort and efficacy. Many of the interfaces or masks were initially used in patients with obstructive sleep apnea before they were adapted for use in patients to provide noninvasive ventilatory support.

Nasal masks and orofacial masks were the earliest interfaces, with subsequent development and use of full-face masks, mouthpieces, nasal pillows, and helmets. Nasal masks and orofacial masks are still the most commonly used interfaces. Orofacial masks are used almost twice as frequently as nasal masks. Both have advantages and disadvantages in the application of noninvasive ventilation.

1.2 Existing national policies and guidance

National Guidance for the provision of aspects of specialist non-ventilation services to patients exists for some individual patient groups e.g. Motor Neurone Disease (MND), Duchene's Muscular Dystrophy; and for broader categories of patients e.g. weaning guidance; and around specific technologies e.g. diaphragmatic pacing and tracheostomies. There are some national standards (NICE, 2010; 2016) available and some specialist society guidance (BTS/ICS 2016).

Provision of complex home ventilation services also falls within the NHS Outcomes Framework Domain 1 - preventing people from dying prematurely where Improvement Area 1a specifically identifies reducing mortality from respiratory disease, and Domain 2 – enhancing quality of life for patients with long term conditions.

Guidance supports delivery of care by respiratory specialists working within MDTs. For example, the National Institute for Health and Clinical Excellence (NICE) clinical guideline (CG) around use of NIV in MND states that “multidisciplinary teams (MDT) should coordinate and provide on-going management and treatment for patients with MND, including regular respiratory assessment and provision of non-invasive ventilation. The team should include a neurologist, a respiratory physician, an MND specialist nurse, a respiratory specialist nurse, a specialist respiratory physiotherapist, a respiratory physiologist, a specialist in palliative care and a speech and language therapist”. The guidance also outlines the support and training which need to be provided to the patient and their family and carers: “support and assistance to manage non-invasive ventilation which should include training on using non-invasive ventilation and ventilator interfaces, for example emergency procedures, night-time assistance if the patient is unable to use the equipment independently (for example, emergency removal or replacement of interfaces), how to use the equipment with a wheelchair or other mobility aids if required, what to do if the equipment fails, assistance with secretion management, information on general palliative strategies, an offer of on-going emotional and psychological support for the patient and their family and carers”.

Ensuring NIV is delivered by competent respiratory professionals is emphasised in NICE MND guidance and also in the National Patient Safety Agency (NPSA) alert which identified cases where problems with administering NIV were stated as causing at least moderate harm: key issues included shortage of staff skills or staff time to set up and monitor NIV.

2 Epidemiology

A. Chronic Obstructive Pulmonary Disease

An estimated 1.2 million people are living with diagnosed COPD (BLF, 2019) – considerably more than the 835,000 estimated by the Department of Health in 2011. In terms of diagnosed cases, this makes COPD the second most common lung disease in the UK, after asthma. Around 2% of the whole population – 4.5% of all people aged over 40 – live with diagnosed COPD.

The number of people who have ever had a diagnosis of COPD has increased by 27% in the last decade, from under 1,600 to nearly 2,000 per 100,000. This could mean that more undiagnosed cases are being found, or that the disease is becoming more common. Changes in record-keeping could also be a factor.

However, prevalence increased by 9% between 2008 and 2012, while record-keeping practices remained the same. Research has indicated that up to two-thirds of people with COPD remain undiagnosed.

In 2012, 29,776 people died from COPD (5.3 per cent of the total number of UK deaths and 26.1 per cent of deaths from lung disease). Of these, 15,245 were males and 14,531 were females. The total number of deaths was up from 28,344 in 2008.

B. Neuromuscular Disorders

Deenen et al 2015 found incidence rates for ten neuromuscular disorders, ranging from 0.05 to 9 per 100,000/yr. Most NMDs showed prevalence rates between 1 and 10 per 100,000 population, except for multifocal motor neuropathy,

C. Obstructive Sleep Apnoea

OSA is common, affecting an estimated 1.5 million adults in the UK, and yet up to 85% are undiagnosed, therefore untreated. Only an estimated 330,000 adults are currently being treated, out of an OSA population of 1.5 million. (BLF 2015)

3 The interventions

Noninvasive positive-pressure ventilation

Positive-pressure ventilation delivered through a mask, has become the predominant method of providing noninvasive ventilatory support. Early bedside physiologic studies in healthy patients and in patients with respiratory conditions document successful ventilatory support (ie, reduction in respiratory rate, increase in tidal volume, decrease in dyspnea) with reduction in diaphragmatic electromyography (EMG), transdiaphragmatic pressures, work of breathing and improvement in oxygenation with a reduction in hypercapnia.

Ventilatory support can be achieved through a variety of interfaces (mouth piece or nasal, face, or helmet mask), using a variety of ventilatory modes (eg, volume ventilation, pressure support, bilevel positive airway pressure [BiPAP], proportional-assist ventilation [PAV], continuous positive airway pressure [CPAP]) with either ventilators dedicated to noninvasive ventilation (NIV) or those capable of providing support through an endotracheal tube or mask. Older models of noninvasive ventilators required oxygen to be bled into the system, but current models incorporate oxygen blenders for precise delivery of the fraction of inspired oxygen (FIO₂).

Noninvasive negative-pressure ventilation

Negative-pressure ventilators provide ventilatory support using a device that encases the thoracic cage starting from the neck, and devices range from a whole-body tank to a cuirass shell. The general principle is the same with a vacuum device, which lowers the pressure surrounding the thorax, creating sub-atmospheric pressure and thereby passively expanding the chest wall with diaphragmatic descent, all leading to lung inflation. Exhalation occurs with passive recoil of the chest wall.

This was the predominant technology during the polio epidemics, but these devices were bulky and cumbersome to use. Upper airway obstruction was also a problem. These ventilators have been largely supplanted by the more widespread positive-pressure noninvasive ventilators; however, some patients continue to be treated with this modality. While the bulk of the experience lies in patients with chronic respiratory failure, specifically neuromuscular respiratory failure, reports described successful application in patients with acute respiratory failure.

Current use of Non-invasive Ventilation devices.

With respect to the two modes, positive-pressure ventilation has supplanted negative-pressure ventilation as the dominant mode of delivery of noninvasive ventilation. Positive-pressure ventilation is more effective than negative-pressure ventilation in unloading the respiratory muscles, at least under investigational conditions. The primary focus of this policy is domiciliary positive-pressure noninvasive ventilation, and the mention of "noninvasive ventilation" will refer to positive-pressure delivery.

Many patients who are assessed as requiring noninvasive ventilation are provided support with pressure ventilation, i.e. continuous positive airway pressure (CPAP), which is the most basic level of support. CPAP pumps a steady flow of air at constant pressure through the nose to prevent the narrowing or collapse of air passages or to help the lungs to expand. CPAP may be especially useful in patients with congestive heart failure or obstructive sleep apnea.

Bilevel positive airway pressure (BiPAP) is probably the most common mode of noninvasive positive pressure ventilation and requires provisions for inspiratory positive airway pressure (IPAP) and expiratory positive airway pressure (EPAP). The difference between IPAP and EPAP is a reflection of the amount of pressure support ventilation provided to the patient, and EPAP is synonymous with positive end-expiratory pressure (PEEP). Some noninvasive ventilation is provided using proportional-assist ventilation (PAV), which provides flow and volume assistance with each breath. Clinical trials have not demonstrated a significant difference between PAV and pressure-support ventilation with BiPAP.^[5, 6] However, BiPAP is the most commonly available and more frequently used modality for noninvasive ventilation. PAV remains available on many ventilator models, but use is much less common than BiPAP.

4 Findings

4.1 Evidence of effectiveness

4.1.1 Clinical effectiveness

A. COPD

Murphy et al (2017), undertook a randomized clinical trial of patients with persistent hypercapnia ($\text{PaCO}_2 > 53\text{mmHg}$), a total of 116 patients (mean [SD] age of 67 [10] years, 53% female, mean BMI of 21.6 [IQR, 18.2-26.1], mean [SD] forced expiratory volume in the first second of expiration of 0.6 L [0.2 L], and mean [SD] PaCO_2 while breathing room air of 59 [7]mmHg) were randomized. Sixty-four patients (28 in home oxygen alone and 36 in home oxygen plus home NIV) completed the 12-month study period. The median time to readmission or death was 4.3 months (IQR, 1.3-13.8 months) in the home oxygen plus home NIV group vs 1.4 months (IQR, 0.5-3.9 months) in the home oxygen alone group, adjusted hazard ratio of 0.49 (95% CI, 0.31-0.77; $P = .002$). The 12-month risk of readmission or death was 63.4% in the home oxygen plus home NIV group vs 80.4% in the home oxygen alone group, absolute risk reduction of 17.0% (95% CI, 0.1%-34.0%). At 12 months, 16 patients had died in the home oxygen plus home NIV group vs 19 in the home oxygen alone group. Among patients with persistent hypercapnia following an acute exacerbation of COPD, adding home noninvasive ventilation to home oxygen therapy prolonged the time to readmission or death within 12 months.

B. NMD

Very strong recent NICE guidance, and repeated studies which found clinically and statistically significant benefits. Radunovic et al 2017 stated that it would be unethical to have a control group in future RCTs, indicating that equipoise is no longer a question.

A systematic review by Radunovic et al 2017 found good basis for the use of non-invasive ventilation in certain Motor Neurone Disease cohorts of patients:

The conclusions of the review were based on a single RCT on 41 participants. The study provided modest quality evidence that overall median survival was significantly different between the group treated with NIV and the standard care group.

Low-quality evidence indicates that it improves or maintains quality of life in people with ALS.

Survival and quality of life were significantly improved in the subgroup of people with better bulbar function, but not in those with severe bulbar impairment. Adverse effects related to NIV should be systematically reported, as at present there is little information on this subject. More RCT evidence to support the use of NIV in ALS will be difficult to generate, as not offering NIV to the control group is no longer ethically justifiable.

This is also supported by D' Cruz et al. 2018

NIV has been shown to improve quality of life for patients with MND. In a randomised controlled trial, Bourke and colleagues randomised MND patients with orthopnoea, MIP <60% predicted or symptomatic daytime hypercapnia to NIV or standard care. NIV was associated with sustained improvements in quality of life, with the greatest improvements observed in the domains relating to sleep problems, despite an observed reduction in REM sleep. This supports the findings of smaller prospective studies which have demonstrated sustained improvements in patient-reported outcomes amongst MND patients, including sleep quality, duration and efficiency, reduced sleep disturbance and improved and daytime somnolence, following initiation of NIV.

Similar positive impacts have also been identified within the paediatric population by Katz et al 2004:

NPPV can decrease hospitalisations for children with neuromuscular disease and improves sleep related respiratory parameters. A prospective study is now needed to further delineate the role of NPPV in this population of children.

This was supported by Falsaperla et al. in 2014: We found a statistically significant improvement of the lowest oxygen desaturation (nadir SaO₂), apnoea-hypopnoea index (AHI) and oxygen desaturation index (ODI) after NIV treatment in all patients. Mean SaO₂ also improved, although this result was not statistically significant, while the percentage of episodes of desaturation with a SaO₂ <90% and <80% decreased with a statistical significance (P < 0.0001). After NIV, only one patient showed an episode of desaturation lasting more than 5 min (10.6 min length), and we also found an improvement of daytime blood gas parameters with a normalization of these indexes.

C. OSA

Extensive NICE guidance (NICE 2007;2012; 2017) supported by meta-analyses, Cochrane review, and primary studies supports the use of Continuous Positive Airway pressure for the treatment of moderate to severe obstructive sleep apnoea and mild sleep apnoea with certain presenting symptoms. Alternative treatments to CPAP are discussed however the evidence of efficacy for surgery is, as yet, inconclusive.

In the NICE 2012 guidance 139, the Assessment Group identified 23 RCTS that compared CPAP with placebo or usual care using the Epworth Sleepiness Scale (ESS). A meta-analysis of these studies identified a statistically significantly greater reduction in daytime sleepiness with CPAP compared with placebo or usual care (weighted mean difference in ESS score -2.7; 95% confidence interval [CI] -3.5 to -2.0).

The NICE Assessment Group undertook a series of meta-analyses that compared the effect of CPAP on levels of daytime sleepiness in different populations. This showed a statistically significantly greater reduction in daytime sleepiness with CPAP compared

with placebo for moderate and severe categories of OSAHS. For mild OSAHS (meta-analysis of 3 studies; AHI = 5–14 episodes per hour) a weighted mean difference in ESS score of –1.5 (95% CI –3.4 to 0.4) was found. For moderate OSAHS (meta-analysis of 7 studies; AHI = 15–30 episodes per hour) a weighted mean difference in ESS score of –2.0 (95% CI –3.0 to –1.1) was found. For severe OSAHS (meta-analysis of 13 studies; AHI = over 30 episodes per hour) a weighted mean difference in ESS score of –3.4 (95% CI –4.6 to –2.3) was found.

4.1.2 Trials in progress

A search of clinicaltrials.gov using the search terms domiciliary non-invasive ventilation found the following trials currently recruiting:

Terms	Search Results*	Entire Database**
Synonyms		
domiciliary	11 studies	73 studies
non-invasive ventilation	10 studies	402 studies
ventilation	11 studies	6,696 studies
Respiration	6 studies	4,908 studies
breathing	--	894 studies
respiratory assist	--	6 studies
Respiratory function	--	144 studies
non-invasive	11 studies	2,231 studies

1. Assist Control Versus Pressure Support Modes for **Domiciliary Noninvasive Ventilation** in Chronic Respiratory Failure. ClinicalTrials.gov Identifier: NCT00189527
2. Impact of Early **Non Invasive Ventilation** in Amyotrophic Lateral Sclerosis (ALS) Patients
3. Effect of the Integrated Tele-monitoring Management of NIV Treatment
4. Autotitrating Versus Standard **Non-invasive Ventilation** (NIV) in Newly Diagnosed Patients
5. Trial of **Non-invasive Ventilation** for Stable COPD

6. Assessment of Muscular Unloading in Chronic Obstructive Pulmonary Disease (COPD) Patients With NIV
7. **on-invasive Ventilation** Versus Sham **Ventilation** in Chronic Obstructive Pulmonary Disease (COPD)
8. What do built-in Softwares in Home Ventilators Tell us?
9. Prospective Cohort of Respiratory Insufficiency Outcome
10. **Non-invasive** Ventilator Modems: a Qualitative Study
11. Tracheostomized COPD Patients and **Non Invasive** Mechanical **Ventilation**

4.1.3 Cost-effectiveness

A. COPD

None of the studies identified contained QALY measures, however reduction in repeated hospital admissions with the use of domiciliary NIV within this patient cohort was shown in a number of studies. (Murphy et al 2017)

B. NMD

None of the studies identified contained QALY measures so cost effectiveness could not be determined.

C. OSA

NICE assessment group (2012) identified four published economic evaluations all of which compared CPAP with a 'do nothing' alternative. The resulting incremental cost-effectiveness ratios (ICERs) were: (1) US \$3354 (approximately £1688; currency conversions were calculated in August 2007) per quality-adjusted life year (QALY) gained from a third-party payer perspective and US \$314 (£158) per QALY gained from a societal perspective; (2) €7861 (£5348) per QALY gained over a 5-year time horizon and €4938 (£3359) per QALY gained for a lifetime time horizon; (3) £8300 per QALY gained at 1 year and £5200 per QALY gained at 2 years; (4) Can \$9809 (£4654) per QALY gained for the high-cost estimate and Can \$3523 (£1672) per QALY gained for the low-cost estimate.

Only two of the NICE Assessment Group's subgroup and scenario analyses resulted in pronounced changes to the base-case ICERs. When the lifespan of the device was changed from 7 to 5 years and an auto-titrating device plus humidifier was used instead of a fixed-pressure device, the ICER was £16,362 per QALY gained. When cardiovascular events and road traffic accidents were excluded in the analysis for the total population (all severities of OHAHS), the ICER was approximately £8000 per QALY gained.

4.2 Safety

NICE

Support of use in: a subset of section B. patients with Motor Neurone Disease & C. OSA

Medicines and Healthcare Products Regulatory Authority (MHRA) support the use of a number of NIV devices.

5 Equity issue

A. COPD

Major risk factors for developing COPD are smoking, and occupation dust exposure in patients over the age of 40 years old. Ensuring good smoking cessation support in all ages may help to reduce any inequity issues. Due to the links to smoking and exposure to dust and chemicals more likely to be found in manual labour roles, this would indicate indirect links with deprivation.

B. NMD

None of the studies identified discussed health inequality measures.

C. OSA

Major risk factors for developing OSAHS are increasing age, obesity and being male. OSAHS is also associated with certain specific craniofacial characteristics (such as retrognathia), enlarged tonsils and enlarged tongue. Use of alcohol or sedatives can also increase the risk or severity of the condition. OSAHS has been reported to affect up to 4% of middle-aged men and 2% of middle-aged women in the UK. It is estimated that 1% of men in the UK may have severe OSAHS.

6 Discussion and conclusions

A. COPD

There is evidence to support the addition to patients with persistent hypercapnia following an acute exacerbation of COPD, of home non-invasive ventilation to home oxygen therapy prolonged the time to readmission or death within 12 months.

B. NMD

High quality evidence to support the use of non-invasive ventilation within certain patient groups within this cohort of patients. Clinical review should be ensured with patients with severely impaired bulbar function to ensure tolerance of the intervention.

C. OSA

Clinical and cost-effective use of CPAP in more moderate / severe instances of OSA are clearly demonstrated within the literature. Use in those with a mild diagnosis of OSA is demonstrated when the patient is symptomatic.

7 Search Strategy

A. COPD

Population: Person with COPD (and similar conditions) Breathing Impairment Having Experienced a Recent Exacerbation

Intervention: Self-Administered / Home-Based Routine Non-Invasive Ventilation / Continuous Positive Airway Pressure (excludes acute episodes and Long Term Oxygen Therapy)

Comparator / Control: No intervention / Alternative treatments

Outcome: Quality of Life and Survival Benefit

B. NMD

Population: Person with Neurologically Dependent Breathing Impairment

Intervention: Self-Administered / Home-Based Routine Non-Invasive Ventilation / Continuous Positive Airway Pressure (excludes acute episodes and Long Term Oxygen Therapy)

Comparator / Control: No intervention

Outcome: Quality of Life and Survival Benefit

C. OSA

Population: Persons with Sleep Apnoea

Intervention: Self-Administered / Home-Based Routine Non-Invasive Ventilation / Continuous Positive Airway Pressure (excludes acute episodes and Long Term Oxygen Therapy)

Comparator / Control: No intervention / Alternative treatments

Outcome: Quality of Life and Wider Health Benefits

8 References

1. British Lung Foundation (BLF) 2019. Chronic obstructive pulmonary disease (COPD) statistics. https://www.blf.org/?_ga=2.219377177.1205961109.1564051606-1530561031.1560162537&_gac=1.247269040.1564051606.EAlalQobChMI5q78tLP4wIVzLTtCh3j-QJkEAYASAAEgLNfD_BwE
2. British Lung Foundation (BLF) 2015 Obstructive Sleep Apnoea: Toolkit for commissioning and planning local NHS services in the UK. https://www.blf.org.uk/sites/default/files/OSA_Toolkit_2015_BLF_0.pdf
3. Deenen et al. 2015 The Epidemiology of Neuromuscular Disorders: A Comprehensive Overview of the Literature. *Journal of Neuromuscular Diseases* 2 (2015) 73–85
DOI 10.3233/JND-140045
<https://pdfs.semanticscholar.org/edf8/cb210b7371b45811ab221dd1c31233079191.pdf>
4. NICE 2017 Hypoglossal nerve stimulation for moderate to severe obstructive sleep apnoea (2017) - <https://www.nice.org.uk/guidance/ipg598>
5. NICE 2007 Soft-palate implants for obstructive sleep apnoea (2007) - <https://www.nice.org.uk/guidance/ipg241>
6. NICE 2012 Continuous positive airway pressure for the treatment of obstructive sleep apnoea/hypopnoea syndrome (2008, reviewed 2012) - <https://www.nice.org.uk/guidance/ta139>
7. Khan et al. 2018. A meta-analysis of continuous positive airway pressure therapy in prevention of cardiovascular events in patients with obstructive sleep apnoea. *European Heart Journal*, Volume 39, Issue 24, 21 June 2018, Pages 2291–2297, <https://doi.org/10.1093/eurheartj/ehx597>
8. Corrado A, Gorini M, Melej R, et al. Iron lung versus mask ventilation in acute exacerbation of COPD: a randomised crossover study. *Intensive Care Med.* 2009 Apr. 35(4):648-55.
9. Parke RL, McGuinness SP. Pressures delivered by nasal high flow oxygen during all phases of the respiratory cycle. *Respir Care.* 2013 Oct. 58 (10):1621-4.

10. Spoletini G, Alotaibi M, Blasi F, Hill NS. Heated Humidified High-Flow Nasal Oxygen in Adults: Mechanisms of Action and Clinical Implications. *Chest*. 2015 Jul. 148 (1):253-61.
11. Ozsancak A, Sidhom S, Liesching TN, Howard W, Hill NS. EVALUATION OF THE TOTAL FACE MASK™ FOR NONINVASIVE VENTILATION TO TREAT ACUTE RESPIRATORY FAILURE. *Chest*. 2011 Feb 17.
12. Wysocki M, Richard JC, Meshaka P. Noninvasive proportional assist ventilation compared with noninvasive pressure support ventilation in hypercapnic acute respiratory failure. *Crit Care Med*. 2002 Feb. 30 (2):323-9.
13. Fernández-Vivas M, Caturla-Such J, González de la Rosa J, Acosta-Escribano J, Alvarez-Sánchez B, Cánovas-Robles J. Noninvasive pressure support versus proportional assist ventilation in acute respiratory failure. *Intensive Care Med*. 2003 Jul. 29 (7):1126-33.
14. Hoo, G. 2018. Noninvasive Ventilation. Medscape. <https://emedicine.medscape.com/article/304235-overview#a5>
15. British Thoracic Society/Intensive Care Society Acute Hypercapnic Respiratory Failure Guideline Development Group. 2016. BTS/ICS Guidelines for the Ventilatory Management of Acute Hypercapnic Respiratory Failure in Adults. Journal of the British Thoracic Society. <http://thorax.bmj.com/site/about/guidelines.xhtml#open>
16. National Institute for Health and Clinical Excellence (NICE). Motor neurone disease: assessment and management. NICE guideline [NG42] Published date: February 2016 Last updated: July 2019
17. National Institute for Health and Clinical Excellence (NICE). *Chronic Obstructive Pulmonary Disease in Over 16s: Diagnosis and Management [CG101]*. London, England: NICE; 2010. <https://www.nice.org.uk/guidance/ng42>

18.Guidance – A: COPD

19. Brochard L, Mancebo J, Wysocki M, et al. Noninvasive ventilation for acute exacerbations of chronic obstructive pulmonary disease. *N Engl J Med*. 1995;333(13):817-822.
20. Bott J, Carroll MP, Conway JH, et al. Randomised controlled trial of nasal ventilation in acute ventilatory failure due to chronic obstructive airways disease. *Lancet*. 1993;341(8860):1555-1557.
21. Connors AF Jr, Dawson NV, Thomas C, et al; SUPPORT Investigators (Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments). Outcomes following acute exacerbation of severe chronic obstructive lung disease. *Am J Respir Crit Care Med*. 1996;154(4 pt 1): 959-967.
22. Murray I, Paterson E, Thain G, Currie GP. Outcomes following non-invasive ventilation for hypercapnic exacerbations of chronic obstructive pulmonary disease. *Thorax*. 2011;66(9):825-826.

23. 5. Chu CM, Chan VL, Lin AW, Wong IW, Leung WS, Lai CK. Readmission rates and life threatening events in COPD survivors treated with non-invasive ventilation for acute hypercapnic respiratory failure. *Thorax*. 2004;59(12):1020-1025.
24. Suh ES, Mandal S, Harding R, et al. Neural respiratory drive predicts clinical deterioration and safe discharge in exacerbations of COPD. *Thorax*. 2015;70(12):1123-1130.
25. Nickol AH, Hart N, Hopkinson NS, et al. Mechanisms of improvement of respiratory failure in patients with COPD treated with NIV. *Int J Chron Obstruct Pulmon Dis*. 2008;3(3):453-462.
26. Meecham Jones DJ, Paul EA, Jones PW, Wedzicha JA. Nasal pressure support ventilation plus oxygen compared with oxygen therapy alone in hypercapnic COPD. *Am J Respir Crit Care Med*. 1995;152(2):538-544.
27. Elliott MW, Mulvey DA, Moxham J, Green M, Branthwaite MA. Domiciliary nocturnal nasal intermittent positive pressure ventilation in COPD: mechanisms underlying changes in arterial blood gas tensions. *Eur Respir J*. 1991;4(9):1044-1052.
28. Lloyd-Owen SJ, Donaldson GC, Ambrosino N, et al. Patterns of home mechanical ventilation use in Europe: results from the Eurovent survey. *Eur Respir J*. 2005;25(6):1025-1031.
29. Clini E, Sturani C, Rossi A, et al; Rehabilitation and Chronic Care Study Group, Italian Association of Hospital Pulmonologists (AIPO). The Italian multicentre study on noninvasive ventilation in chronic obstructive pulmonary disease patients. *Eur Respir J*. 2002;20(3):529-538.
30. McEvoy RD, Pierce RJ, Hillman D, et al; Australian trial of non-invasive Ventilation in
31. Chronic Airflow Limitation (AVCAL) Study Group. Nocturnal non-invasive nasal ventilation in stable hypercapnic COPD: a randomised controlled trial. *Thorax*. 2009;64(7):561-566.
32. 13. Windisch W. Noninvasive positive pressure ventilation in COPD. *Breathe*. 2011;8(2):114-123.
33. Köhnlein T, Windisch W, Köhler D, et al. Non-invasive positive pressure ventilation for the treatment of severe stable chronic obstructive pulmonary disease: a prospective, multicentre, randomised, controlled clinical trial. *Lancet Respir Med*. 2014;2(9):698-705.
34. Struik FM, Sprooten RT, Kerstjens HA, et al. Nocturnal non-invasive ventilation in COPD patients with prolonged hypercapnia after ventilatory support for acute respiratory failure: a randomised, controlled, parallel-group study. *Thorax*. 2014;69(9):826-834.
35. Altman DG, Bland JM. Treatment allocation by minimisation. *BMJ*. 2005;330(7495):843.
36. Murphy PB, Brignall K, Moxham J, Polkey MI, Davidson AC, Hart N. High pressure versus high intensity noninvasive ventilation in stable hypercapnic chronic obstructive pulmonary disease: a randomized crossover trial. *Int J Chron Obstruct Pulmon Dis*. 2012;7:811-818.
37. National Institute for Health and Clinical Excellence (NICE). Motor neurone disease: assessment and management. NICE guideline [NG42] Published date: February 2016 Last updated: July 2019

38. National Institute for Health and Clinical Excellence (NICE). *Chronic Obstructive Pulmonary Disease in Over 16s: Diagnosis and Management [CG101]*. London, England: NICE; 2010. <https://www.nice.org.uk/guidance/ng42>
39. Bestall JC, Paul EA, Garrod R, Garnham R, Jones PW, Wedzicha JA. Usefulness of the Medical Research Council (MRC) dyspnoea scale as a measure of disability in patients with chronic obstructive pulmonary disease. *Thorax*. 1999;54(7): 581-586.
40. Ghosh D, Rzehak P, Elliott MW, Windisch W. Validation of the English Severe Respiratory Insufficiency Questionnaire. *Eur Respir J*. 2012;40 (2):408-415.
41. Jones PW, Quirk FH, Baveystock CM. The St George's Respiratory Questionnaire. *Respir Med*. 1991;85(suppl B):25-31.
42. Jones PW. St George's Respiratory Questionnaire: MCID. *COPD*. 2005;2(1):75-79.
43. Kahan BC, Morris TP. Improper analysis of trials randomised using stratified blocks or minimisation. *Stat Med*. 2012;31(4):328-340.
44. Costello R, Deegan P, Fitzpatrick M, McNicholas WT. Reversible hypercapnia in chronic obstructive pulmonary disease: a distinct pattern of respiratory failure with a favourable prognosis. *Am J Med*. 1997;102(3):239-244.
45. Seemungal TA, Donaldson GC, Paul EA, Bestall JC, Jeffries DJ, Wedzicha JA. Effect of exacerbation on quality of life in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 1998;157(5 pt 1):1418-1422.
46. De Backer L, Vos W, Dieriks B, et al. The effects of long-term noninvasive ventilation in hypercapnic COPD patients: a randomized controlled pilot study. *Int J Chron Obstruct Pulmon Dis*. 2011;6:615-624.
47. Gates KL, Howell HA, Nair A, et al. Hypercapnia impairs lung neutrophil function and increases mortality in murine pseudomonas pneumonia. *Am J Respir Cell Mol Biol*. 2013;49(5):821-828.
48. Pepperell JC, Ramdassingh-Dow S, Crosthwaite N, et al. Ambulatory blood pressure after therapeutic and subtherapeutic nasal continuous positive airway pressure for obstructive sleep apnoea: a randomised parallel trial. *Lancet*. 2002;359(9302):204-210.
49. Saatci E, Miller DM, Stell IM, Lee KC, Moxham J. Dynamic dead space in face masks used with noninvasive ventilators: a lung model study. *Eur Respir J*. 2004;23(1):129-135.
50. Rodway GW, Weaver TE, Mancini C, et al. Evaluation of sham-CPAP as a placebo in CPAP intervention studies. *Sleep*. 2010;33(2):260-266.
51. Djavadkhani Y, Marshall NS, D'Rozario AL, et al. Ethics, consent and blinding: lessons from a placebo/sham controlled CPAP crossover trial. *Thorax*. 2015;70(3):265-269.
52. Schwartz SW, Cimino CR, Anderson WM. CPAP or placebo-effect? *Sleep*. 2012;35(12):1585- 1586.
53. Murphy, P, Rehal, S. et al. 2017. Effect of Home Noninvasive Ventilation With Oxygen Therapy vs Oxygen Therapy Alone on Hospital Readmission or Death After an Acute COPD Exacerbation: A Randomized Clinical Trial. *JAMA*. 2017;317(21):2177-2186. doi:10.1001/jama.2017.4451. <https://jamanetwork.com/journals/jama/issue/317/21>
54. Murphy P, Arbane G, Phillips R, Hart N. S37 Home mechanical ventilation (HMV) and home oxygen therapy (HOT) following an acute exacerbation of COPD in patients with persistent hypercapnia: results of the per protocol analysis from the HOT-HMV

UK trial. *Thorax* 2017; 72: A25– A6.
<https://onlinelibrary.wiley.com/doi/full/10.1111/resp.13484>

Guidance B. - NMD

55. Joshua O. Benditt¹ and Louis J. Boitano. Pulmonary Issues in Patients with Chronic Neuromuscular Disease. *Am J Respir Crit Care Med* Vol 187, Iss. 10, pp 1046–1055, May 15, 2013
56. Miller RG, Jackson CE, Kasarskis EJ, England JD, ForsheW D, Johnston W, Kalra S, Katz JS, Mitsumoto H, Rosenfeld J, et al.; Quality Standards Subcommittee of the American Academy of Neurology. Practice parameter update: the care of the patient with amyotrophic lateral sclerosis: drug, nutritional, and respiratory therapies (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology* 2009;73: 1218–1226.
57. Bourke SC, Gibson GJ. Sleep and breathing in neuromuscular disease. *Eur Respir J* 2002;19:1194–1201.
58. Birnkrant DJ, Panitch HB, Benditt JO, Boitano LJ, Carter ER, Cwik VA, Finder JD, Iannaccone ST, Jacobson LE, Kohn GL, et al. American College of Chest Physicians consensus statement on the respiratory and related management of patients with Duchenne muscular dystrophy undergoing anesthesia or sedation. *Chest* 2007; 132:1977–1986.
59. Mehta S, Hill NS. Noninvasive ventilation. *Am J Respir Crit Care Med* 2001;163:540–577.
60. Eagle M, Baudouin SV, Chandler C, Giddings DR, Bullock R, Bushby K. Survival in Duchenne muscular dystrophy: improvements in life expectancy since 1967 and the impact of home nocturnal ventilation. *Neuromuscul Disord* 2002;12:926–929.
61. Toussaint M, Steens M, Wasteels G, Soudon P. Diurnal ventilation via mouth-piece: survival in end-stage Duchenne patients. *Eur Respir J* 2006; 28:549–555
62. Radunovic A, Annane D, Jewitt K, Mustfa N. Mechanical ventilation for amyotrophic lateral sclerosis/motor neuron disease. *Cochrane Database Syst Rev* 2009;4:CD004427. Update in: *Cochrane Database Syst Rev* 2013;3:CD004427.
63. Motor neurone disease: assessment and management (2016) - <https://www.nice.org.uk/guidance/ng42/chapter/Recommendations#non-invasive-ventilation>
64. Outcome of non-invasive positive pressure ventilation in paediatric neuromuscular disease (2004) - <https://www.ncbi.nlm.nih.gov/pubmed/14736624>
65. Effects of non-invasive ventilation on survival and quality of life in patients with amyotrophic lateral sclerosis: a randomised controlled trial (2006) - <https://www.ncbi.nlm.nih.gov/pubmed/16426990>
66. Non-invasive ventilation in amyotrophic lateral sclerosis: a 10 year population based study (2012) - <https://www.ncbi.nlm.nih.gov/pubmed/22013242>

67. Mechanical ventilation for amyotrophic lateral sclerosis/motor neuron disease (2017) - <https://www.ncbi.nlm.nih.gov/pubmed/28982219>
68. Outcome of non-invasive positive pressure ventilation in paediatric neuromuscular disease (2004) - <https://www.ncbi.nlm.nih.gov/pubmed/14736624>
69. Polysomnographic evaluation of non-invasive ventilation in children with neuromuscular disease (2014) - <https://www.ncbi.nlm.nih.gov/pubmed/24033486>
70. Mechanical ventilation for amyotrophic lateral sclerosis/motor neuron disease (2017) - <https://www.ncbi.nlm.nih.gov/pubmed/28982219>
71. Sleep disordered breathing in motor neurone disease (2018) - <http://jtd.amegroups.com/article/view/18178/14526>
72. The use of non-invasive ventilation at end of life in patients with motor neurone disease: a qualitative exploration of family carer and health professional experiences (2013) - <https://www.ncbi.nlm.nih.gov/pubmed/23462702>
73. Sheehan, D. Birnkrant, J. et al. 2018. Respiratory Management of the Patient With Duchenne Muscular Dystrophy Paediatrics, October 2018, vol 142 https://pediatrics.aappublications.org/content/142/Supplement_2/S62
74. Hamada et al. 2011. Indicators for ventilator use in Duchenne muscular dystrophy. *Respiratory Medicine*. Volume 105, Issue 4, April 2011, Pages 625-629. <https://www.sciencedirect.com/science/article/pii/S0954611110005317#tbl1>
75. Birnkrant et al 2010. The Respiratory Management of Patients With Duchenne Muscular Dystrophy: A DMD Care Considerations Working Group Specialty Article. *Pediatric Pulmonology*. DOI 10.1002/ppul.21254. http://muscle.ca/wp-content/uploads/2012/11/Respiratory_Management_DMD_Publication_2010.pdf

Guidance – C. - OSA

76. NICE. 2008. Continuous positive airway pressure for the treatment of obstructive sleep apnoea/hypopnoea syndrome. Technology appraisal guidance. Published: 26 March 2008. Updated Feb 2014. [nice.org.uk/guidance/ta139](https://www.nice.org.uk/guidance/ta139)
77. Hypoglossal nerve stimulation for moderate to severe obstructive sleep apnoea (2017) - <https://www.nice.org.uk/guidance/ipg598>
78. Soft-palate implants for obstructive sleep apnoea (2007) - <https://www.nice.org.uk/guidance/ipg241>
79. A meta-analysis of continuous positive airway pressure therapy in prevention of cardiovascular events in patients with obstructive sleep apnoea (2017) - <https://academic.oup.com/eurheartj/article-abstract/39/24/2291/4563763?redirectedFrom=fulltext>
80. Sleep-disordered Breathing in Heart Failure (2015) - <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6159414/>
81. The official website of The Epworth Sleepiness Scale (ESS) - <http://epworthsleepinessscale.com/about-the-ess/>
82. The Epworth Sleepiness Scale: Minimum Clinically Important Difference in Obstructive Sleep Apnea (2018) - <https://www.atsjournal.org/doi/abs/10.1164/rccm.201704-0672LE>
83. Minimum important difference of the Epworth Sleepiness Scale in obstructive sleep apnoea: estimation from three randomised controlled trials (2018) - <https://thorax.bmj.com/content/early/2018/08/11/thoraxjnl-2018-211959>
84. Cardiorespiratory interaction with continuous positive airway pressure (2018) - <http://jtd.amegroups.com/article/view/18553/14525>
85. Continuous positive airway pressure for the treatment of obstructive sleep apnoea/hypopnoea syndrome (2008, reviewed 2012) - <https://www.nice.org.uk/guidance/ta139>