Health Policy Advisory Committee on Technology

Technology Brief

Non-Invasive Open Ventilation (NIOV™) System for Respiratory Insufficiency

April 2016
Summary of findings

The Non-Invasive Open Ventilation (NIOV™) system by Breathe Technologies Inc. (California, USA) is a lightweight, wearable ventilation system. Outcomes from one randomised controlled trial and two non-randomised comparative studies on the NIOV system are described in this Brief. The randomised controlled trial was in the form of a meeting abstract. At least one of the comparators in each study was standard oxygen therapy using a cannula.

Overall, the three studies reported positive results for the NIOV system. The two non-randomised comparative studies investigated the effects of the NIOV system on exercise tolerance. Of the two studies, one reported significant improvement in all outcomes measured (dyspnoea, endurance, fatigue, discomfort and arterial oxygen saturation), while the other reported significant improvements in endurance, heart rate, arterial oxygen saturation and activation of respiratory muscles, but no improvement in dyspnoea. The randomised controlled trial reported improvements in dyspnoea, however, less improvement in average 6-minute walk test distance for the NIOV system compared with the standard oxygen with cannula treatment.

Several factors need to be taken into account when considering the above results. Sample sizes were small, with the largest study enrolling only 30 patients. One of the non-randomised comparative studies included only men, limiting the generalisability of its results. All studies described in this Brief comprised patients with chronic obstructive pulmonary disease (COPD). It should be noted that Breathe Technologies, Inc. states that indications for the NIOV system include COPD, interstitial lung disease (ILD), neuromuscular conditions and pre- and post-lung transplantation. The safety and efficacy of the NIOV system for other populations is unknown. A range of conflicts of interest were reported in two of the studies, including sponsorship by Breathe Technologies, Inc.

HealthPACT Advice

The Non-Invasive Open Ventilation (NIOV™) system has the potential to support people with COPD outside of a hospital environment, increasing their mobility and quality of life. Treatment with the NIOV™ system may offer an opportunity for clinical redesign that reduces or avoids hospital admissions and readmissions.

Due to the lack of data from large, long-term comparative studies, HealthPACT does not recommend public investment in this technology at this time. However, HealthPACT recommends the evidence for the NIOV™ system be reviewed in 24 months.
Technology, Company and Licensing

Register ID WP193
Technology name Non-Invasive Open Ventilation (NIOV™) system
Patient indication Adult patients with respiratory insufficiency resulting from conditions such as chronic obstructive pulmonary disease, interstitial lung disease and neuromuscular conditions.

Description of the technology

The NIOV system is a non-invasive, positive pressure ventilator (NIPPV) that provides a mixture of oxygen and air when required for patients with respiratory insufficiency. The device was developed as a wearable ventilation system (weighing only 454 g), with the aim of improving exercise tolerance and reducing dyspnoea (breathlessness) for affected patients. It is intended for use by adults capable of spontaneously breathing a minimum tidal volume of 3.5 mL per kg of predicted body weight. It is not indicated for patients who cannot spontaneously breathe, or those who are fully dependent on mechanical ventilation. ¹

The NIOV system consists of a purge tube, oxygen cylinder, oxygen regulator, oxygen supply hose, ventilator, belt clip, battery charger and an open, non-sealing, proprietary nasal pillow interface that leaves the mouth unobstructed (available in four sizes). The oxygen cylinder is not supplied with the device. The system requires a 50 psi oxygen source with a minimum flow of 28 L per minute. Breathe Technologies Inc. advises that the oxygen regulator provided with the NIOV system works with most oxygen cylinders. The battery can be re-charged at any 12 V outlet, such as those available in cars, and lasts for approximately four hours. ¹⁻³

The ventilator system can be worn on a patient’s belt or slung over the shoulder. ¹ When triggered by the patient breathing in (inspiration), the system delivers a pre-set bolus of oxygen (ranging from 50 to 250 mL in volume) according to the patient’s requirement. In addition, ambient air is drawn in through two ports located on the nasal pillow interface. Depending on the volume setting, and factors such as lung compliance and resistance, the total volume of oxygen plus ambient air delivered can exceed 450 mL. Ventilator inspiratory time is set as a function of the patient’s total breath cycle time. ⁴

Intended applications of the NIOV system include assisting patients to walk and undertake physical, occupational or respiratory therapy or other rehabilitation activities in an institutional or home environment. It should be operated by trained personnel, or by patients or their caregivers under the direction of a physician. ¹

Company or developer

Breathe Technologies Inc., California, USA.
Reason for assessment
The NIOV system is an innovative development in non-invasive ventilation for people with respiratory insufficiency. The wearable system is much smaller and lighter than other non-invasive ventilators (454 g compared to 4.5—5.4 kg), enabling patients to move about freely and participate in daily activities, thereby aiding the recovery process.5

Stage of development in Australia
☐ Yet to emerge
☐ Experimental
☐ Investigational
☐ Nearly established
☐ Established
☐ Established but changed indication or modification of technique
☐ Should be taken out of use

Licensing, reimbursement and other approval
The NIOV system has received 510(k) approval (K1311562) from the United States Food and Drug Administration and the European CE mark.6,7

Australian Therapeutic Goods Administration approval
☐ Yes
☐ No
☐ Not applicable

Technology type Device
Technology use Therapeutic

Patient Indication and Setting
Disease description and associated mortality and morbidity
Breathe Technologies Inc. state that the NIOV system is designed for people with respiratory insufficiency (that is a reduced ability to perform gas exchange) resulting from conditions such as chronic obstructive pulmonary disease (COPD), interstitial lung disease (ILD) and neuromuscular conditions, and for patients before and after lung transplantation.8

The reduced ability to perform gas exchange is also termed ‘respiratory failure’. There are two types of respiratory failure; type one is when not enough oxygen transfers from the lungs into the blood (hypoxaemia); type two is when your lungs can’t remove sufficient carbon dioxide from your blood (hypercarbia). Both of these conditions can occur at the same time.9 Type one is the most common form of respiratory failure, and can be associated with nearly all acute diseases of the lung which generally involve fluid filling or collapse of alveolar units. Causes of type two respiratory failure include drug overdose, neuromuscular...
COPD

COPD is a common preventable and treatable disease, characterised by persistent airflow limitation that is usually progressive and associated with enhanced chronic inflammatory responses in the airways and the lungs to noxious particles or gases. The most common COPD conditions are emphysema (damaged alveoli and bronchi), chronic bronchitis (inflammation of the bronchi) and chronic asthma that isn’t fully reversible with the use of medication.

Usually COPD develops so slowly that people are unaware that their breathing is affected. By the time the main symptoms of breathlessness, chronic cough and sputum production appear, considerable lung damage has already occurred. Some people with COPD have to reduce their physical activity due to breathlessness. With progression of the disease, simple activities like showering, dressing or making a cup of tea become extremely difficult.

Smoking is the main cause of COPD. Other causes include outdoor air pollution, workplace fumes and dust, childhood respiratory infections, and smoke from burning fuels. There is no cure for COPD, and the damaged lung tissue does not repair itself. Diagnosis is based on a breathing test called spirometry. Other tests that may be conducted include physical examination, blood tests, sputum analysis, chest x-ray and CT scans.

ILD

ILD refers to a large group of conditions affecting the lung’s interstitium, the network of tissue that provides support to the microscopic air sacs (alveoli). All forms of ILD cause thickening of the interstitium. The thickening can be due to inflammation, scarring or fluid accumulation. Some forms of ILD are short-lived; others are chronic and irreversible.

The primary signs and symptoms of ILD include a dry cough and shortness of breath at rest or with exertion. ILD can lead to a series of life-threatening complications including acute exacerbation of respiratory insufficiency, high blood pressure in the lungs (pulmonary hypertension), an abnormally low oxygen level in the blood (hypoxaemia) and respiratory failure. Once lung scarring occurs it is generally irreversible. Medications may slow the damage, but many people never regain full use of their lungs.

Some types of ILD are caused by inhaling dust or other particles in the air (e.g. coal dust, asbestos, farm dust and silica dust). Other causes of ILD include autoimmune diseases or exposure to moulds, gases or fumes. In some cases the cause of ILD is unknown. Diagnosis can include imaging tests (e.g. chest x-ray, computerised tomography scan and echocardiogram) and pulmonary function tests (e.g. oximetry and spirometry).
Neuromuscular conditions

Diseases that affect the neuromuscular system are classified into four main groups: motor neurone diseases, neuropathies, neuromuscular junction disorders, and myopathies, including muscular dystrophies. There are a range of causes for these conditions including genetic abnormalities, viral infections, autoimmune disorders, metabolic disorders, dietary deficiencies, and certain drugs and poisons.\(^{17}\)

Some neuromuscular conditions can result in respiratory muscle weakness, which can cause breathing difficulty and coughing. Symptoms, which may not become apparent until there is a complication (e.g. lung infection), can include recurrent chest infection, chronic headache, constant fatigue and increased muscle weakness.\(^{18}\)

Neuromuscular conditions are diagnosed using a range of tests including nerve conduction studies, electromyography, blood tests, muscle biopsies and genetic testing.\(^{17}\)

Number of patients

COPD

In 2012, COPD caused 5,923 deaths in Australia, making it the fifth leading cause of death.\(^{19}\) An estimated 530,000 Australians had COPD in 2011-12.\(^{20}\) In New Zealand, COPD is the fourth most common cause of death, and was responsible for an estimated 12,000 hospital admissions and greater than 50,000 bed-days in 2011. In New Zealand, COPD affects an estimated 15 per cent of the adult population over the age of 45 years (at least 200,000 people).\(^{21,22}\)

ILD

No statistics could be identified on the incidence or prevalence of ILD in Australia or New Zealand. Based on registries in other countries, the estimated incidence of ILD in Australia is 30 in 100,000 people per year.\(^{23}\)

Neuromuscular conditions

It is estimated that there are greater than 20,000 people in Australia who have some form of neuromuscular disease.\(^{24}\) An estimate of the number of people with neuromuscular conditions in New Zealand could not be found.

Speciality | Respiratory medicine
--- | ---
Technology setting | Multiple, including general hospital, community and ambulatory care
Impact

Alternative and/or complementary technology
The NIOV ventilation system is a substitute for other NIPPV (non-invasive, positive pressure ventilator systems).

Current technology
The NIOV system is a type of NIPPV. These devices deliver a mixture of air and oxygen through a non-invasive interface (nasal mask, face mask or nasal plugs) rather than via a breathing tube (endotracheal or tracheostomy tube).\(^\text{25}\) The ventilator helps or does the work of the respiratory muscles by exerting a positive pressure on the airways during inhalation.

Collectively, NIPPV includes several modalities of non-invasive ventilation that can be delivered via a standard intensive care unit ventilator or a portable device like the NIOV system.\(^\text{25}\) There is a wide range of portable ventilators currently on the market, however, the NIOV system is reported to be the first and only wearable form of portable NIPPV ventilator to receive CE mark and FDA approval.\(^\text{26, 27}\)

Diffusion of technology in Australia
At the time of writing this Brief there was no evidence that the NIOV system is being used in Australia.

International utilisation
According to Breathe Technologies, Inc., the NIOV system is currently being used by clinicians and patients across the USA in public and private hospitals, Veterans Affairs healthcare facilities, pulmonary rehabilitation centres and in patients’ homes.\(^\text{28}\)

<table>
<thead>
<tr>
<th>Country</th>
<th>Level of Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA</td>
<td>Trials underway or completed</td>
</tr>
</tbody>
</table>

Cost infrastructure and economic consequences
The only expected cost of the NIOV system is the cost of the device. The manufacturer were contacted regarding the cost of the device but did not respond. There are no infrastructure costs. Regarding costs to the healthcare system, one meeting abstract was identified that included a retrospective study describing changes in healthcare utilisation before and after NIOV implementation in 16 patients with chronic respiratory insufficiency.\(^\text{29}\) The study reported that the number of emergency department visits, inpatient admissions, inpatient days and intensive care unit days significantly decreased following NIOV implementation.
Although the study was retrospective and involved only a small number of patients, it indicates that the NIOV system may result in reduced costs to the healthcare system.

The NIOV system may be an alternative treatment option for COPD presentation in the Intensive Care Unit setting. This may result in reduced healthcare costs.

**Ethical, cultural, access or religious considerations**

No ethical, cultural, access or religious considerations were identified that may limit the use of this technology.

**Evidence and Policy**

**Safety and effectiveness**

One randomised controlled trial (level II interventional evidence) reported in a meeting abstract and two non-randomised comparative studies (two level III-2 interventional evidence) were identified for inclusion in this Technology Brief. An abstract detailing the longer term results of a subset of patients from one of the non-randomised comparative studies is also summarised. An overview of the studies is provided in Table 1.

<table>
<thead>
<tr>
<th>Study details/location</th>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
<th>Number of patients; length of follow up; losses to follow up</th>
<th>Conflicts of interest</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obi et al 2015&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Patients with COPD</td>
<td>NR</td>
<td>n = 12&lt;br&gt;Length of follow up: 10 weeks&lt;br&gt;Losses: 3</td>
<td>None disclosed</td>
</tr>
<tr>
<td>Level II interventional evidence&lt;br&gt;Single centre&lt;br&gt;USA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carlin et al 2015&lt;sup&gt;4&lt;/sup&gt;</td>
<td>Stable COPD with current use of supplemental oxygen during rest and exertion, self-reported dyspnoea-related activity limitation, and ability to perform ADL such as walking, cleaning and climbing stairs</td>
<td>Tobacco smokers, patients with acute respiratory symptoms</td>
<td>n = 30&lt;br&gt;Length of follow up: measurement recorded same day as test&lt;br&gt;Losses: 1</td>
<td>Study sponsored by Breathe Technologies, Inc. One author serves as a consultant to Breathe Technologies, Inc. and another author was an employee of the same company</td>
</tr>
<tr>
<td>Prospective level III-2 interventional evidence&lt;br&gt;Single centre&lt;br&gt;USA</td>
<td></td>
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</tbody>
</table>
### Study details/location

<table>
<thead>
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</tr>
</thead>
<tbody>
<tr>
<td>Porszasz et al 2013⁴¹</td>
<td>Patients with spirometric COPD criteria</td>
<td>Women and obese patients</td>
<td>n = 15 (all male) Length of follow up: Not reported* Losses: 0</td>
<td>Study sponsored by Breathe Technologies, Inc. All but one author reported conflicts of interest involving Breathe Technologies, Inc. including consulting fees, support for travel, and fees for writing or reviewing the manuscript or data analysis. One author is employed by Breathe Technologies, Inc.</td>
</tr>
</tbody>
</table>

ADL: activities of daily living; COPD: chronic obstructive pulmonary disease; NR: not reported

*Study involved four visits in total. Interval between visits was 2—7 days in 70% of cases and 2—14 days in 82% of cases

†Presented in the form of a meeting abstract

### Obi et al 2015³⁰

A randomised controlled trial published in the form of a meeting abstract reported on the effects of the NIOV system on dyspnoea severity and exercise capacity in 12 COPD patients undergoing standard pulmonary rehabilitation (level II intervention evidence). Patients were randomly assigned to receive oxygen through either a nasal cannula or the NIOV device. Outcomes assessed at the beginning and end of the 10-week pulmonary rehabilitation program included the mMRC dyspnoea score, CAT score and 6-minute walk test distance. Data were collected from nine patients in total (five from the nasal cannula treatment group and four from the NIOV treatment group). Reasons were not provided for the three patients lost to follow up.

**Effectiveness**

Results for effectiveness varied (Table 2). The average dyspnoea score decreased in the NIOV treatment group by week 10, meaning that patients perceived themselves to be less breathless. In contrast, the average dyspnoea score increased in the nasal cannula treatment group, meaning that patients perceived themselves to be more breathless. However, patients in the cannula group had a greater average improvement in 6-minute walk test distance by week 10 than those in the NIOV treatment group. Both treatment groups showed an improvement in average CAT scores by week 10, meaning that patients felt there was a reduction in the impact of COPD on their lives. No statistical analyses of the data were reported.
<table>
<thead>
<tr>
<th>Test</th>
<th>Week 1 (NIOV)</th>
<th>Week 1 (Nasal cannula)</th>
<th>Week 10 (NIOV)</th>
<th>Week 10 (Nasal Cannula)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean mMRC dyspnoea score</td>
<td>2.12</td>
<td>2.2</td>
<td>1.75</td>
<td>3.0</td>
</tr>
<tr>
<td>Mean CAT score (average)</td>
<td>26.5</td>
<td>21.4</td>
<td>21.3</td>
<td>18.8</td>
</tr>
<tr>
<td>Mean 6-MWT distance</td>
<td></td>
<td>250 feet</td>
<td>362 feet</td>
<td></td>
</tr>
</tbody>
</table>

6-MWT: 6-minute walk test; CAT: Chronic Obstructive Pulmonary Disease Assessment Test; mMRC: modified Medical Research Council

Safety

Not reported.

Carlin et al 2015

In this prospective, non-randomised comparative study, Carlin et al 2015 compared the effect of the NIOV system with standard oxygen therapy in 30 patients with stable, oxygen-dependent COPD (level III-2 Intervention evidence). It is not stated whether patient enrolment was consecutive. The study involved a crossover design whereby patients first performed a self-selected activity of daily living (ADL), such as walking, stair climbing or cleaning, for as long as tolerable using standard oxygen therapy. Following a rest of at least 15 minutes, the patients then performed the same ADL for as long as tolerable using the NIOV system. For the standard oxygen treatment, the patients used their existing nasal cannula at the prescribed flow rates for rest and exertion. For the NIOV treatment, patients were familiarised with the system on the day of testing. This involved a fitting with the NIOV nasal pillow interface and optimising the ventilator’s volume, inspiratory time and trigger sensitivity settings for both rest and activity. Approximately five minutes before each test, baseline values were collected for heart rate, respiratory rate, dyspnoea, fatigue, discomfort and the amount of oxygenated haemoglobin in the blood (SpO$_2$).

The primary outcome measured in the study was ADL endurance time. Secondary outcomes included SpO$_2$ and dyspnoea (measured using the Borg Dyspnoea Scale), fatigue and discomfort scores. A per-protocol approach, defined as having at least minimal use of both study treatments, was used for data analyses. Of the 30 enrolled patients, 29 successfully completed both study treatment arms. Data from the patient who dropped out were excluded from the efficacy, but included in the safety analyses.

Effectiveness

Significantly better responses for all outcomes were reported in the NIOV treatment compared with standard oxygen therapy treatment (Table 3).
A meeting abstract\textsuperscript{32} reported interim results for 12 patients (mean age 72.3 years) from the Carlin et al 2015\textsuperscript{4} study. Mean time from diagnosis to initiation of the NIOV system treatment was 16.8 months. Both modified Medical Research Council (mMRC) dyspnoea scores and COPD Assessment Test (CAT) scores improved in patients using the NIOV system for an average of 11 months. The mean mMRC dyspnoea score reduced from 3.3 (range 2-4) to 1.7 (range 0-4), whilst the mean CAT score reduced from 27.2 (range 10-37) to 14.5 (range 4-27).

\textbf{Safety}

A single adverse event was observed in one patient who was unable to use the NIOV system treatment owing to nasal congestion and rhinorrhea. \textsuperscript{4} The patient did not require treatment, and the event was deemed unrelated to the study interventions.

\textbf{Porszasz et al 2013\textsuperscript{31}}

In this prospective, non-randomised comparative study Porszasz et al 2013\textsuperscript{31} investigated the effects of the NIOV system on exercise tolerance in 15 men with COPD (level III-2 intervention evidence). The study did not explain why only men were included, nor whether they were consecutively enrolled.

The experiment involved four visits. On the first visit, patients performed incremental exercise testing (5 to 10 minutes in duration) and then, following 1.5 hours’ rest, performed constant work rate (CWR) endurance testing at 80 per cent peak work rate. Exercise was conducted with patients breathing air through a mouthpiece. All tests were performed to each patient’s limit of tolerance. Ventilation and gas exchange were measured breath by breath. On visit two, patients exercised at the CWR determined at the first visit, whilst subjected to the following breathing treatments: unassisted breathing of ambient air; breathing using the NIOV system driven by compressed air; and breathing using the NIOV system driven by compressed oxygen. On visit three, the tests conducted on the second visit were repeated. On visit four, patients performed CWR tests whilst subjected to the
following breathing treatments: breathing oxygen via a standard nasal cannula; or breathing using the NIOV system plus oxygen. The interval between visits was two to seven days in 70 per cent of cases and two to 14 days in 82 per cent of cases.

Outcomes assessed included exercise duration, surface inspiratory muscle electromyography (EMG) (measures the activity of the rib muscles and diaphragm), \( \text{SpO}_2 \), transcutaneous partial pressure of carbon dioxide in the blood (TcPCO\(_2\)) and Borg dyspnoea score. Each outcome, excluding exercise duration, was compared at isotime (the shortest CWR test during visits 1 to 4) and peak exercise. Results for the breathing of oxygen through a nasal cannula were unavailable for one patient, with no reason provided for this loss to follow up. Data for the remaining treatments are based on the results from all 15 patients.

**Effectiveness**

Patients using the NIOV system driven by compressed oxygen had significantly better responses for rib muscle EMG (reduced activation of rib muscles), heart rate (reduced) and \( \text{SpO}_2 \) (increased), compared with breathing ambient air unassisted, breathing using the NIOV system driven by compressed air and breathing oxygen via a nasal cannula (\( p<0.05; \) Table 4).

Significant reductions were also recorded in breathing frequency and Borg Dyspnoea scores in patients using the NIOV system driven by compressed oxygen, compared with patients using the NIOV system driven by compressed air and those breathing ambient air unassisted (\( p<0.05 \)), but not compared with patients breathing oxygen via a cannula (\( p>0.05; \) Table 4).

**Table 4  Mean physiologic responses to constant work rate exercise at isotime**

<table>
<thead>
<tr>
<th>Variable</th>
<th>CWR (breathing air through a mouthpiece) (V1)</th>
<th>Unassisted ambient air breathing (V2 and V3)</th>
<th>NIOV + air breathing (V2 and V3)</th>
<th>Oxygen by cannula breathing (V4)</th>
<th>NIOV + oxygen breathing (V2, V3 and V4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scalene EMG, ( \mu \text{V/s} \pm \text{SD} ) n/a</td>
<td>9.3 ± 6.3</td>
<td>8.1 ± 6.5</td>
<td>5.7 ± 6.5*</td>
<td>3.1 ± 2.6**</td>
<td></td>
</tr>
<tr>
<td>Intercostal EMG, ( \mu \text{V/s} \pm \text{SD} ) n/a</td>
<td>3.5 ± 2.7</td>
<td>2.9 ± 2.1*</td>
<td>2.6 ± 2.5†</td>
<td>1.7 ± 2.1**</td>
<td></td>
</tr>
<tr>
<td>Diaphragmatic EMG, ( \mu \text{V/s} \pm \text{SD} ) n/a</td>
<td>4.8 ± 2.2</td>
<td>4.5 ± 1.8</td>
<td>3.2 ± 1.8†</td>
<td>2.5 ± 1.5**</td>
<td></td>
</tr>
<tr>
<td>Breathing frequency, breaths/minute ± SD</td>
<td>31.1 ± 10.4</td>
<td>29.6 ± 8.1</td>
<td>27.5 ± 7.1§</td>
<td>23.5 ± 6.5§</td>
<td>23.8 ± 7.7§</td>
</tr>
<tr>
<td>Heart rate, beats/minute ± SD</td>
<td>121 ± 16</td>
<td>112 ± 14§</td>
<td>114 ± 15 §</td>
<td>110 ± 13 §</td>
<td>105 ± 12**§</td>
</tr>
<tr>
<td>( \text{SpO}_2 ) % ± SD</td>
<td>86.9 ± 2.9</td>
<td>88.2 ± 2.2</td>
<td>87.9 ± 3.8 §</td>
<td>92.7 ± 3.9§</td>
<td>98.5 ± 1.0**§</td>
</tr>
<tr>
<td>TcPCO(_2), mmHg ± SD</td>
<td>45.9 ± 6.8</td>
<td>45.4 ± 7.4</td>
<td>43.4 ± 6.4</td>
<td>42.7 ± 5.6</td>
<td>45.2 ± 6.5</td>
</tr>
<tr>
<td>Borg CR10 score ± SD</td>
<td>4.7 ± 2.8</td>
<td>4.6 ± 2.0</td>
<td>3.3 ± 1.8§</td>
<td>2.5 ± 1.7§</td>
<td>1.8 ± 1.3**§</td>
</tr>
</tbody>
</table>

Borg CR10 score: dyspnoea rating on a 10-point scale; CWR: constant work rate test performed at visit 1; EMG: electromyography (reported relative to resting level. For studies performed on more than one visit, responses were averaged); n/a: not applicable; NIOV: non-invasive open ventilation; SD: standard deviation; \( \text{SpO}_2 \): arterial oxygen saturation measured by transcutaneous oximetry; TcPCO\(_2\): transcutaneous partial pressure of carbon dioxide in the blood; V1–V4: data from visit 1 through to visit 4

*\( p<0.05 \) (vs. air unassisted); †\( p<0.05 \) (vs. NIOV plus air); ‡\( p<0.05 \) (vs. oxygen via cannula); §\( p<0.05 \) (vs. CWR)
For physiologic responses to CWR at limit of tolerance, patients using the NIOV system driven by compressed oxygen had significantly better exercise endurance than with any other treatments ($p<0.05$; Table 5). Compared with using oxygen breathed through a nasal cannula, exercise endurance using the NIOV system driven by compressed oxygen was improved by an average of 6.1 minutes ($p<0.001$). In addition, patients using the NIOV system driven by compressed oxygen had significantly better $\text{SpO}_2$ than all other treatments ($p<0.05$). No significant differences were seen among any of the treatments with respect to heart rate, Borg Dyspnoea Scale score or $\text{TcPCO}_2$ ($p>0.05$; Table 5).

**Table 5  Mean physiologic responses to constant work rate exercise at limit of tolerance**

<table>
<thead>
<tr>
<th></th>
<th>CWR (breathing air through a mouthpiece) (V1)</th>
<th>Unassisted ambient air breathing (V2 and V3)</th>
<th>NIOV + air breathing (V2 and V3)</th>
<th>Oxygen by cannula breathing (V4)</th>
<th>NIOV + oxygen breathing (V2, V3 and V4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scalene EMG, µV/s ± SD</td>
<td>n/a</td>
<td>9.7 ± 6.8</td>
<td>9.5 ± 7.0</td>
<td>7.7 ± 6.5</td>
<td>6.8 ± 5.1†</td>
</tr>
<tr>
<td>Intercostal EMG, µV/s ± SD</td>
<td>n/a</td>
<td>3.8 ± 3.1</td>
<td>3.3 ± 2.3*</td>
<td>3.7 ± 3.3</td>
<td>2.8 ± 2.3†</td>
</tr>
<tr>
<td>Diaphragmatic EMG, µV/s ± SD</td>
<td>n/a</td>
<td>5.1 ± 2.3</td>
<td>5.3 ± 2.2</td>
<td>4.1 ± 2.3†</td>
<td>4.0 ± 2.2†</td>
</tr>
<tr>
<td>Breathing frequency, breaths/minute ± SD</td>
<td>33.8 ± 9.8</td>
<td>28.8 ± 7.8†</td>
<td>26.7 ± 7.3†</td>
<td>27.1 ± 7.8†</td>
<td>26.6 ± 6.7†</td>
</tr>
<tr>
<td>Heart rate, beats/minute ± SD</td>
<td>125 ± 17</td>
<td>118 ± 14†</td>
<td>120 ± 13†</td>
<td>120 ± 17</td>
<td>119 ± 13</td>
</tr>
<tr>
<td>$\text{SpO}_2$, % ± SD</td>
<td>85.1 ± 3.4</td>
<td>86.0 ± 2.9</td>
<td>85.9 ± 4.1</td>
<td>91.2 ± 4.2††</td>
<td>97.4 ± 1.8††</td>
</tr>
<tr>
<td>$\text{TcPCO}_2$, mmHg ± SD</td>
<td>47.3 ± 6.7</td>
<td>46.3 ± 7.6</td>
<td>44.8 ± 7.0</td>
<td>43.5 ± 4.5</td>
<td>47.5 ± 7.4</td>
</tr>
<tr>
<td>Borg CR10 score ± SD</td>
<td>6.7 ± 2.3</td>
<td>6.6 ± 2.5</td>
<td>6.3 ± 2.5</td>
<td>6.3 ± 3.6</td>
<td>6.1 ± 2.9</td>
</tr>
<tr>
<td>$\text{Tlim}$, minutes ± SD</td>
<td>5.1 ± 1.1</td>
<td>5.6 ± 1.9</td>
<td>6.3 ± 4.1</td>
<td>11.4 ± 6.8††</td>
<td>17.6 ± 5.7††</td>
</tr>
</tbody>
</table>

Borg CR10 score: dyspnoea rating on a 10-point scale; CWR: constant work rate test performed at visit 1; EMG: electromyography (reported relative to resting level. For studies performed on more than one visit, responses are averaged); n/a: not applicable; NIOV: non-invasive open ventilation; SD: standard deviation; $\text{SpO}_2$: arterial oxygen saturation measured by transcutaneous oximetry; $\text{TcPCO}_2$: transcutaneous partial pressure of carbon dioxide in the blood; $\text{Tlim}$: endurance time; V1–V4: data from visit 1 through to visit 4

* $p<0.05$ (vs. air unencumbered)
† $p<0.05$ (vs. NIOV plus air)
‡ $p<0.05$ (vs. CWR)
§ $p<0.05$ (vs. oxygen via cannula)

**Safety**

Safety data were not reported.

**Economic evaluation**

No economic evaluation studies on the NIOV system were identified.

**Ongoing research**

No ongoing trials for the NIOV system were identified from a search of ClinicalTrials.gov and the Australian and New Zealand Clinical Trials Registry.
Other issues

Two of the three studies included in this Brief (Porszasz et al 2013 and Carlin et al 2015) were funded by Breathe Technologies Inc. Furthermore, authors of three of the included studies (Porszasz et al 2013, Carlin et al 2015 and Carlin et al 2014) declared conflicts of interest involving Breathe Technologies, Inc. (Table 1).

Number of studies included

All evidence included for assessment in this Technology Brief has been assessed according to the revised NHMRC levels of evidence. A document summarising these levels may be accessed via the HealthPACT web site.

Total number of studies: 3
Total number of Level II studies: 1
Total number of Level III-2 studies: 2

Search criteria to be used (MeSH terms)

Noninvasive open ventilation OR NIOV OR open ventilation system OR open ventilator system or open ventilation device OR open ventilator device

AND

COPD OR chronic obstructive pulmonary disease OR ‘pulmonary disease, chronic obstructive’ (MeSH)

Date searched

26/10/2015

References


