ACI NSW Agency for Clinical Innovation

# Domiciliary Non-Invasive Ventilation in Adult Patients

## A Consensus Statement

ACI Respiratory Network

2010

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This document was reviewed by, and has the support of, The Thoracic Society of Australia and New Zealand and the Australasian Sleep Association.

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# Agency for Clinical Innovation

## ACI Respiratory Network

# Domiciliary Non-Invasive Ventilation in Adult Patients

## A Consensus Statement

## Domiciliary Non-Invasive Ventilation Working Group


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**Statement of intent**: The following consensus statement represents the ideal characteristics for initial and ongoing assessment, implementation and management of adult patients requiring domiciliary non-invasive ventilation. The objective of this document is to provide information to optimise the overall management of individuals with disorders likely to lead to the development of chronic respiratory failure and is aimed at assisting clinicians in informed decision-making. It is not intended to replace clinical decision-making. The consensus recommendations are not a definitive statement on the correct procedures; rather they constitute a general guide to be followed subject to the clinician's judgement in each case.

**- This document is based on current best practice -**

# The Agency for Clinical Innovation

The Agency for Clinical Innovation (ACI) was established in January 2010 as a board-governed statutory health corporation under section 42 of the Health Services Act 1997, in direct response to the Garling Inquiry into Acute Care Services in NSW Public Hospitals.

Reporting to the NSW Minister for Health and Director-General of the NSW Department of Health, the ACI aims to improve healthcare services in NSW by supporting state-wide clinical networks to develop and implement evidence-based clinical guidelines and innovative models of care.

The ACI promotes:

- clinician and community engagement across NSW,
- the development of cost-effective and sustainable healthcare services,
- equity of patient access to, and outcome from, healthcare services across NSW.

The ACI has 24 clinical networks bringing together doctors, nurses, allied health professionals, managers, scientists, researchers and consumers from across NSW. These clinician-led networks harness the clinical expertise of people working in the health system and the practical knowledge of consumers accessing health care. This unique engagement enables clinicians and consumers to meet across service boundaries, identify barriers and opportunities, and to research, design and support the implementation of evidence-based improvements to healthcare services.

The ACI works closely with its partner organisations including the NSW Department of Health, NSW Local Health Networks, the Sax Institute, the Centre for Clinical Governance Research in Health, the Bureau of Health Information, the Clinical Excellence Commission, the Cancer Institute of NSW and the Clinical Education and Training Institute.

# The ACI Respiratory Network

**Purpose and Background**

The ACI Respiratory Network is a collaboration of over 200 members with an interest in thoracic medicine including consumers, administrators, academics and clinicians from all respiratory disciplines across NSW. The Network consists of seven working groups, including a dedicated rural respiratory group, overseen by an executive steering committee. The purpose of the Network is to promote high quality patient care, and to improve equity of access to, and outcome from, respiratory medicine and sleep disorder services for adult and paediatric patients across NSW. Following the amalgamation of the Respiratory Chronic Care Advisory Group into the GMCT Respiratory Steering Committee in November 2007, the Network became the principal source of advice to the NSW Department of Health on clinical respiratory services in NSW.

**Partnership Organisations**

The Respiratory Network has developed collaborative relationships with the NSW Department of Health, the Thoracic Society of Australia & New Zealand, the Australian Sleep Association, the Asthma Foundation, The Lung Foundation, and Cystic Fibrosis NSW.

More information can be found at http://www.health.nsw.gov.au/ACI/

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# LIST OF ABBREVIATIONS

| | |
|---|---|
| **ABGs** | Arterial blood gases |
| **ACBT** | Active cycle of breathing technique (for airways clearance) |
| **AD** | Autosomal dominant |
| **AHI** | Apnoea hypopnoea index |
| **ALS** | Amyotrophic lateral sclerosis |
| **APAP** | Autotitrating (continuous) positive airway pressure |
| **AR** | Autosomal recessive |
| **ASIA** | American Spinal Injury Association (classification system) |
| **ASV** | Adaptive servoventilation |
| **AVAPS** | Average volume assured pressure support (mode of ventilation) |
| **BMI** | Body mass index |
| **BNP** | Brain natriuretic peptide |
| **BVS** | Bilevel ventilatory support |
| **CCHS** | Congenital central hypoventilation syndrome |
| **CF** | Cystic fibrosis |
| **$CO_2$** | Carbon dioxide |
| **CompSAS** | Complex sleep apnoea |
| **COPD** | Chronic obstructive pulmonary disease |
| **CPAP** | Continuous positive airway pressure |
| **CRQ** | Chronic respiratory disease questionnaire |
| **CSA** | Central sleep apnoea |
| **CSR** | Cheyne-Stokes respiration |
| **CVA** | Cardiovascular accident |
| **DMD** | Duchenne muscular dystrophy |
| **EPAP** | Expiratory positive airway pressure |
| **ERV** | Expiratory reserve volume |
| **ESS** | Epworth Sleepiness Scale |
| **$ETCO_2$** | End tidal carbon dioxide |
| **FET** | Forced expiratory technique (for airways clearance) |
| **$FEV_1$** | Forced expiratory volume in one second |
| **$FiO_2$** | Fraction of inspired oxygen |
| **FRC** | Functional residual capacity |
| **FSH** | Fascioscapulohumeral dystrophy |
| **FVC** | Forced vital capacity |
| **GOLD** | Global Initiative for Chronic Obstructive Lung Disease |
| **HF** | Heart failure |

| | |
|---|---|
| **HRQoL** | Health related quality of life |
| **IC** | Inspiratory capacity |
| **ICU** | Intensive care unit |
| **IPAP** | Inspiratory positive airway pressure |
| **IPPV** | Invasive positive pressure ventilation |
| **LGMD1** | Limb girdle muscular dystrophy – autosomal dominant |
| **LGMD2** | Limb girdle muscular dystrophy – autosomal recessive |
| **LMN** | Lower motor neuron |
| **LTOT** | Long term oxygen therapy |
| **LV** | Left ventricle |
| **LVEF** | Left ventricular ejection fraction |
| **MEP** | Maximum expiratory pressure |
| **MIP** | Maximum inspiratory pressure |
| **MND** | Motor neurone disease |
| **MRF-28** | Maugeri Foundation Respiratory item set |
| **NIV** | Non-invasive ventilation |
| **NSW** | New South Wales, Australia |
| **NYHA** | New York Heart Association |
| **OHS** | Obesity hypoventilation syndrome |
| **OSA** | Obstructive sleep apnoea |
| **OSAHS** | Obstructive sleep apnoea hypopnoea syndrome |
| **$PaCO_2$** | Partial pressure of carbon dioxide in arterial blood |
| **$PaO_2$** | Partial pressure of oxygen in arterial blood |
| **PAP** | Positive airway pressure |
| **PCF** | Peak cough flow |
| **$PCO_2$** | Partial pressure of carbon dioxide |
| **PEEP** | Positive end expiratory pressure |
| **PEG** | Percutaneous endoscopic gastrostomy |
| **PEP** | Positive expiratory pressure |
| **PLMs** | Periodic leg movements |
| **PLS** | Primary lateral sclerosis |
| **PMA** | Progressive muscular atrophy |
| **PSG** | Polysomnography |
| **PSQI** | Pittsburgh sleep quality index |
| **PTPdi** | Pressure time product of the diaphragm |
| **RCT** | Randomised controlled trial |
| **REM** | Rapid eye movement sleep |
| **RMW** | Respiratory muscle weakness |
| **RV** | Residual volume |
| **S/T** | Spontaneous timed mode in bilevel pressure pre-set ventilation |

| | |
|---|---|
| **$SaO_2$** | Saturation of haemoglobin with oxygen in arterial blood |
| **SCI** | Spinal cord injury |
| **SDB** | Sleep disordered breathing |
| **SEM** | Standard error of the mean |
| **SF-36** | Medical Outcome Trust 36 item short form health survey status |
| **SMA** | Spinal muscular atrophy |
| **SNP** | Sniff nasal inspiratory pressure |
| **$SpO_2$** | Saturation of haemoglobin with oxygen as measured by pulse oximetry |
| **SRI** | Severe Respiratory Insufficiency questionnaire |
| **SWS** | Slow wave sleep (sleep stage) |
| **TB** | Tuberculosis |
| **$TcCO_2$** | Transcutaneous carbon dioxide |
| **TIPPV** | Tracheostomy intermittent positive pressure ventilation |
| **TLC** | Total lung capacity |
| **UAO** | Upper airway obstruction during sleep |
| **UMN** | Upper motor neuron |
| **V/Q** | Ratio of ventilation to perfusion in the lungs |
| **VC** | Vital capacity |

# EXECUTIVE SUMMARY

With the aim of reducing variation in the assessment, management and on-going care of adult patients requiring domiciliary non-invasive ventilation (NIV) in NSW, a group of expert clinicians directly responsible for the provision of home NIV services was empanelled under the auspice of the Respiratory Network of the Agency for Clinical Innovation (ACI). The Domiciliary NIV Working Group's principle task was to develop best practice guidelines for home NIV based, where possible, on evidence.

This consensus statement reviews the literature in the area of NIV and provides general and disease-specific recommendations for domiciliary NIV in adults.

The recommendations are designed to:

- Standardise criteria for how to **assess / screen** for the need to commence NIV
- Provide **indications** for NIV which reflect the best evidence from the literature and expert opinion
- Identify best practice recommendations for **implementing** NIV and ancillary care measures
- Describe best practice management for **initial review and ongoing follow up** of patients once commenced on NIV

The summary of the main recommendations are listed below in three sections. Section A includes general recommendations for NIV commencement, monitoring and equipment requirements. Section B expands the generic section with disorder specific recommendations. Section C provides further recommendations to assist with the overall management of patients on domiciliary ventilation.

An explanation of the grading recommendations used in this document may be found in the Introduction section.

Full lists of specific recommendations are located at the end of each chapter.

## SECTION A: GENERAL RECOMMENDATIONS

| NEED FOR ASSESSMENT | Grade |
|---|---|
| Hypoxia, hypercapnia, or an elevation in serum bicarbonate indicate the need for additional respiratory assessments and interventions. | D |
| Subjects with progressive respiratory muscle weakness and other restrictive thoracic disorders should be observed regularly with lung function (VC, MIP, MEP, SNP and PCF) and oximetry. An arterial blood gas should be performed especially if VC < 40% predicted or MIP < 60 $cmH_2O$. | C |
| Polysomnography should be performed where there is a history suggestive of sleep disordered breathing or where FVC <40% predicted, base excess > +4mmols/L on arterial blood gases or erect to supine fall in VC of ≥ 25%. | C |
| Consideration for polysomnography also includes symptoms of impaired sleep quality (such as daytime somnolence, waking headache or grogginess, fatigue, impaired cognition, impaired short-term memory, irritability, anxiety and depression) or symptoms of sleep-disordered breathing (such as frequent awakening, snoring, choking, gasping, waking dry mouth, waking dyspnoea or witnessed apnoeas). | D |
| Where there is no overt sign of respiratory compromise, serial VC, respiratory muscle testing, PCF and oximetry should be performed to track baseline pulmonary function in suspected individuals. | D |

| INDICATIONS | Grade |
|---|---|
| Generally NIV should be commenced when there is evidence of:<br>• Daytime hypercapnia, $PaCO_2$ ≥45mmHg<br>*and / or*<br>• Evidence of nocturnal hypoventilation (in order of recommendation), such as<br>i. A rise in $PaCO_2$ of ≥ 8mmHg between evening and morning ABGs or other accurate $CO_2$ surrogate<br>ii. An acute peak rise of ≥ 8mmHg in $TcCO_2$ or $ETCO_2$<br>iii. A rise in $TcCO_2$ or $ETCO_2$ > 50mmHg for more than 50% of total sleep time<br>iv. Whilst not ideal - when a measure of $CO_2$ is not available - nocturnal oximetry demonstrates sustained oxygen desaturation ≤ 88% for 5 consecutive minutes or $SpO_2$ <90% for >10% of total sleep time<br>*or*<br>• Symptoms of significant sleep disordered breathing associated with nocturnal obstructive or hypopneoic events<br>*and / or*<br>• Otherwise unexplained potential co-morbidity of sleep disorders, such as refractory hypertension, pulmonary hypertension, right heart failure, polycythaemia, cardiovascular disease or stroke. | C |
| The institution of NIV is recommended in patients with rapidly progressive respiratory muscle weakness associated with orthopnoea, hypercapnia or symptomatic sleep hypoventilation (sleep fragmentation/ daytime hypersomnolence/ morning headaches and cognitive dysfunction). | B |

| NOCTURNAL MONITORING IN THE DIAGNOSIS AND MANAGEMENT OF SLEEP HYPOVENTILATION SYNDROMES | Grade |
|---|---|
| The minimum requirement for identifying sleep hypoventilation is overnight monitoring of oxygen saturation and, where possible, non-invasive carbon dioxide along with evening to morning arterial blood gases. | B |
| When daytime indicators for NIV have already been met, a full diagnostic PSG measuring sleep quality is not an essential element in determining the need for NIV. | D |
| Periodic nocturnal studies to identify unexpected problems or correct identified ones is indicated, with the frequency influenced by current response to therapy and the nature of the patient's underlying disorder. | D |

| TITRATION | Grade |
|---|---|
| Titration for long term NIV settings should occur when the patient is chronically stable (pH>7.35) and free from exacerbation. | D |
| Adequate IPAP-EPAP difference is required to ameliorate hypoventilation. | A |
| Bi-level ventilation should be commenced in the spontaneous mode, unless there is specific evidence that the patient is unable to trigger the machine once baseline leak and settings have been optimised. | D |
| Complete correction of sleep disordered breathing during the initial titration night is not necessary for improvement of daytime blood gases and symptoms to occur. | B |
| Spontaneous-timed mode flow generator, or a ventilator, to be provided if Spontaneous mode device does not allow correction of sustained hypercapnia in the presence of central apnoea or persisting hypoventilation. | D |
| Ventilators using flow triggering or volume-cycled mandatory ventilation may be required for patients experiencing difficulty in triggering inspiration. | D |

| PATIENT / CARER EDUCATION, TRAINING AND ACCLIMATISATION | Grade |
|---|---|
| Minimum skills and level of knowledge need to be acquired by patients and / or their carers during the process of acclimatisation to NIV. | D |
| Acclimatisation and education for domiciliary NIV should occur at institutions where there is a sufficient through-put of patients requiring long term NIV. | D |
| The patient and/or carer are aware who to contact for medical and technical difficulties. | D |

| REVIEW | Grade |
|---|---|
| Patients can be reviewed at 6 to 8 weeks following the commencement of NIV to determine the clinical response to therapy. After initiation of NIV, clinical review should occur within the first 2 to 3 months to assess symptoms, technical problems, ventilator settings, compliance and success. | D |
| Further clinical reviews should be performed by a Sleep Physician / Respiratory Physician or Respiratory Failure clinic every 6 to 12 months, again assessing symptoms, compliance, technical problems, lung function, oximetry and further investigations (including ABGs and overnight oximetry or PSG) as required. | D |
| At any time, when there are indications of unsatisfactory results like the recurrence of clinical symptoms or awake blood gases deteriorate despite clinical stability (e.g. absence of recent pulmonary infection) and adequate compliance, then inadequate ventilation must be suspected and objective evaluation during sleep must be undertaken. | D |

| OUTCOME | Grade |
|---|---|
| Outcome measures should include awake ABGs, nocturnal $SpO_2$ and assessment of daytime sleepiness, breathlessness and health related quality of life. | C |

| ENTRAINED OXYGEN | Grade |
|---|---|
| If mean oxygen saturations remain ≤ 88% for >30% total sleep time despite optimisation of ventilatory settings, supplemental oxygen should be added. | D |
| If supplemental oxygen is entrained through the bi-level machine at initial commencement, continuation of supplemental oxygen should be reviewed at the subsequent review. | C |

| COMPLIANCE | Grade |
|---|---|
| Usage throughout all sleep periods should be recommended. | D |
| Once established on therapy, regular monitoring of compliance data should be performed and compliance is deemed adequate at > 4 - 6 hours per night. | C |

| SAFETY | Grade |
|---|---|
| Simple bilevel devices are suitable for individuals requiring nocturnal and limited daytime ventilatory support only. However, more sophisticated volume or hybrid devices are indicated for patients requiring more than 18 hours/day or where bilevel devices have proven to be inadequate. | D |
| Ventilator dependent individuals should be titrated on and use ventilators which have been approved for life support and have an alternative battery source to mains power. They also should be supplied with an appropriate back-up ventilator. | D |
| Machines with “mask off” or “low pressure” and “power failure” alarms are recommended for ventilator dependent patients and in disorders where there is a potential inability to arouse from an interruption to ventilation or when there is an absence of ventilatory responses when awake. | D |

## SECTION B: DISORDER SPECIFIC RECOMMENDATIONS

| SLOWLY PROGRESSIVE NEUROMUSCULAR DISORDERS | Grade |
|---|---|
| All subjects with DMD should be referred for clinical assessment initially to a paediatric specialist unit for assessment and then care transferred to an adult centre when age >18 years. | C |
| Assessment as to the risk of development of progressive respiratory failure should be considered in all subjects with other progressive neuromuscular disorders. Referral to a specialist centre should occur if significant respiratory muscle weakness or sleep disordered breathing occurs. | D |
| Patients should have access to other specialist health providers, including medical specialists and allied health professionals, preferably in a well co-ordinated multidisciplinary team. | D |

| SPINAL CORD INJURY | Grade |
|---|---|
| NIV is indicated when there is intractable or refractory sputum retention, atelectasis, respiratory tract infection or type-I respiratory failure ($PaO_2$ < 80 mmHg, $SpO_2$ <95%). | D |
| NIV is indicated when there is intolerance of CPAP for treatment of OSA, especially in cases of SCI at C6 or above. | D |
| Use of an abdominal binder may be considered as the initial intervention in cases of mild hypoventilation, or as an adjunct to the use of NIV. | C |
| The implementation of NIV should occur in a specialised centre where there is access to a spinal unit, accredited pulmonary function and sleep laboratory, physician experienced in the use of NIV, NIV service and physiotherapy service trained in secretion removal in patients with spinal cord injury. | D |

| RAPIDLY PROGRESSIVE NEUROMUSCULAR DISEASE | Grade |
|---|---|
| Patients with MND are recommended to have 3 monthly clinical evaluation to monitor for symptoms and signs of respiratory and sleep complications. | D |
| Sniff nasal inspiratory pressure and overnight oximetry are the initial investigations of choice for the assessment of early respiratory muscle compromise and nocturnal hypoventilation. | D |
| A diagnostic polysomnogram should be reserved for patients in whom co-existent upper airway obstruction is suspected on clinical grounds with inconclusive nocturnal oximetry. | D |
| While MND patients with significant bulbar dysfunction should still have the option to trial NIV, it should be recognised that this group of patients may have reduced tolerance to and derive less benefit from NIV. | B |
| The progression to tracheostomy intermittent positive pressure ventilation (TIPPV) should be made on an individual basis, weighing the longer survival advantage with a significantly greater burden of care and cost to the patient, carer and/or community and recognising that HRQoL improvements associated with the use of NIV may not be seen with TIPPV to an equivalent degree. | D |

| RAPIDLY PROGRESSIVE NEUROMUSCULAR DISEASE | Grade |
|---|---|
| The elective commencement of NIV is preferred over non-elective TIPPV despite the improved survival advantage. | D |
| Patients with MND should be managed in a multidisciplinary clinic as this improves survival and HRQoL, and facilitates earlier uptake of interventions including NIV and PEG insertion. | D |
| An advanced care directive should be sought from ALL patients. | D |

| CHEST WALL DISORDERS | Grade |
|---|---|
| NIV in patients with respiratory insufficiency from chest wall disease provides greater physiological and symptomatic relief over oxygen alone. NIV should be trialled in all patients with chest wall disorders with evidence of nocturnal hypoventilation. | C |
| Both pressure and volume preset ventilation is likely to be equally effective in chest wall disease, but there is a subset of patients which may demonstrate the need for volume ventilation if adequately titrated pressure-preset fails to significantly improve diurnal hypercapnia. | C |

| OBESITY HYPOVENTILATION SYNDROME | Grade |
|---|---|
| Simple spirometry, $SpO_2$ and serum bicarbonate should be performed in all patients referred for SDB assessment when BMI is greater than 35kg/m$^2$. | C |
| Arterial blood gases should be obtained in those individuals where $SpO_2$ is ≤ 92% or where the serum bicarbonate is >27mmol/L to confirm the presence and severity of hypoventilation. | C |
| Thyroid function should also be assessed and any airflow limitation treated appropriately. | D |
| Positive airway pressure is first line therapy in patients with OHS, although adjunctive oxygen therapy is likely to be required, at least initially, for a significant number of patients. | C |
| Autotitrating and home studies are not appropriate for this patient group. | D |
| A full PSG should be performed during manual titration in order to identify the nature of the sleep disordered breathing and response to CPAP pressure. | B |
| Many individuals will respond to initial intervention with CPAP. Titration should commence in CPAP mode to document the patient's response to abolition of upper airway obstruction alone. | A |
| Indications for NIV in OHS include an awake $PaCO_2$ >45mmHg and failure of CPAP therapy as evidence by either sustained oxygen desaturation during sleep or an increase in nocturnal daytime or nocturnal $CO_2$ >8mmHg. | D |
| Individuals initially using bilevel support should be reviewed again after 3 months on therapy and CPAP retried, since a significant number may be switched to CPAP without clinical deterioration. | B |
| In patients placed on CPAP in whom awake $PaCO_2$ at baseline was 45-55mmHg, a clinical review at one month with repeat blood gases should be performed. | D |
| Bilevel support should be used as initial therapy in patients presenting with acute decompensated respiratory failure. After 3 months, a CPAP titration should be undertaken to determine long term therapy. | D |
| All patients should be advised on appropriate dietary and lifestyle changes to promote weight loss and referred to appropriate programs where possible. | D |
| The need for and type of nocturnal PAP therapy should be reassessed if significant weight loss occurs. | D |

| CHRONIC OBSTRUCTIVE PULMONARY DISEASE | Grade |
|---|---|
| Nocturnal NIV is indicated in COPD with $PaCO_2$ > 50 mmHg, where there is evidence of signs and symptoms of sleep disordered breathing, and full PSG demonstrates nocturnal hypoventilation (based on a measure of $PaCO_2$) that is not corrected or made worse by LTOT alone. | D |
| Recurrent hospitalisations (2 or more in a year) for acute hypercapnic respiratory failure (especially life threatening events) or difficulty weaning from invasive ventilation are an indicator for assessment for domiciliary NIV. | C |

| | |
|---|---|
| Changes in awake blood gases are not the best measure of effectiveness of NIV in chronic hypercapnic COPD. Changes in symptoms including exertional dyspnoea, control of nocturnal hypoventilation, reduction in hospital admissions and HRQoL (SF-36) are better indicators of the patient's response to therapy. | C |

| CYSTIC FIBROSIS | Grade |
|---|---|
| Individuals with awake $SpO_2$<94% or spirometry ($FEV_1$<65% predicted) are at risk of nocturnal oxygen desaturation. Overnight oximetry should be undertaken in individuals meeting these criteria. | C |
| Non-invasive ventilation is indicated if daytime $CO_2$>45mmHg and nocturnal gas exchange shows $SpO_2$<90% for >5% of TST and/or a rise in $TcCO_2$ / $ETCO_2$ from NREM to REM >5mmHg during room air breathing occurs. | B |
| Nocturnal NIV is more effective than oxygen therapy in controlling nocturnal hypoventilation in patients with hypercapnic CF lung disease. | A |
| Bilevel ventilation should be trialled initially. Volume ventilation may offer additional benefits in some individuals especially if work of breathing is high. | B |
| NIV does not appear to increase the incidence of pneumothorax, but this is a relatively common occurrence in this population. Therefore, patients need to be educated regarding the symptoms of pneumothorax and should seek immediate medical attention should these symptoms arise. | D |
| Changes in awake blood gases are not the best measure of the effectiveness of NIV in CF. Changes in symptoms, exertional dyspnoea and exercise tolerance, and control of nocturnal hypoventilation are better indicators of the patient's response to therapy. | B |
| NIV may be used in patients unsuitable for transplant to relieve symptoms and improve sleep quality. However, alternative methods of symptom relief need to be introduced at the appropriate time. | D |

| HYPERCAPNIC CENTRAL SLEEP APNOEA | Grade |
|---|---|
| Awake $PaCO_2$ > 45 mmHg in the absence of lung and chest wall abnormalities, skeletal malformations and neuromuscular disorders, in combination with symptoms consistent with sleep disordered breathing warrant a full polysomnogram. | D |
| In patients with isolated sleep hypoventilation, titrate NIV settings in a spontaneous-timed mode, during a full polysomnogram. | D |
| Where hypercapnic central apnoea is caused from pharmacological intake (e.g. opioid based derivatives), referrals to chronic pain team or relevant prescribing body should be made with the aim of reducing medication intake in order to improve central events and stabilise oxygen saturations. | D |
| Overall patient management should be performed by specialised teams. | D |
| Any signs of chest infection should be reviewed and managed promptly, especially in the case of CCHS where a lack of dyspnoea in response to pneumonia may mask severe respiratory compromise. | D |

| NON-HYPERCAPNIC CENTRAL SLEEP APNOEA | Grade |
|---|---|
| In patients with CSA in HF, optimisation of HF treatment should be first-line therapy. | D |
| Prior to commencing treatment, patients should have full PSG demonstrating benefit from the chosen treatment. | B |
| If patients are unable to have full PSG then a period of inpatient acclimatisation/titration and overnight oximetry showing attenuation of apnoea-related hypoxia should be performed. | D |
| CPAP therapy should be trialled as a first line ventilatory assistance treatment, with or without oxygen, to attenuate CSA, improve nocturnal oxygenation, exercise capacity and LVEF. | B |
| The most appropriate means to judge the efficacy of CPAP on CSA would be a follow-up sleep study after a trial of 2 to 4 weeks on CPAP. | B |
| ASV should be considered in patients who have not had a resolution of CSA on CPAP and/or oxygen, or have been shown to have better compliance with this mode of therapy. However, it needs to be shown that ASV is able to better control CSA, either on overnight polysomnography or after a period of inpatient acclimatisation with nocturnal oximetry. | B |

| NON-HYPERCAPNIC CENTRAL SLEEP APNOEA | Grade |
|---|---|
| Patients with a persistence of CSA upon the application of CPAP after a period of time ("complex sleep apnoea") may be considered for ASV if adjunctive oxygen can be shown to be ineffective. | C |
| In those with CSA in HF, at least 6 monthly echocardiogram and NYHA class score assessment should be performed to establish response to therapy. Once stable and a plateau is reached at least annual reviews may be undertaken, with interval tests when symptoms recur or worsen. | C |

| RESPIRATORY INSUFFICIENCY FOLLOWING CATASTROPHIC MEDICAL ILLNESS | Grade |
|---|---|
| A multidisciplinary approach to the assessment, management and discharge planning of patients with high level ventilation needs is central to effective and safe discharge. | D |
| The development of specialised 'weaning units' to facilitate the liberation of the patient from ventilatory support. | D |
| Ongoing management in an ICU area is not medically or socially appropriate for a patient requiring long term continuous ventilatory support. | D |
| Facilities for respite care should be available for ventilator dependent patients as well as for those patients requiring nocturnal ventilatory support only but with high level physical care needs. | D |

## SECTION C: OTHER – OVERALL MANAGEMENT OF PATIENTS ON DOMICILIARY VENTILATION

| SECRETION MANAGEMENT IN NEUROMUSCULAR DISEASE | Grade |
|---|---|
| Ability to generate PCF of at least 160 L/min is necessary for non-invasive management of pulmonary secretions. Baseline assisted PCF <270 L/min are likely to decrease to <160 L/min during chest infections, increasing the likelihood of pneumonia and respiratory failure. Patients with a baseline PCF < 270 L/min should have access to equipment which can provide insufflation and a mechanical cough in-exsufflation. | C |
| Training of insufflation should commence when VC < 2L or 50% predicted. | D |
| As manual assisted coughing techniques (e.g. abdominal thrust) further enhance PCF, they should be incorporated with insufflation or mechanical in-exsufflation techniques, where possible. | B |
| For patients with VC < 1 to 1.5L, insufflations should precede manual assisted coughing techniques (e.g. abdominal thrusts). | C |
| In adults, mechanical in-exsufflation settings of +40 $cmH_2O$ and – 40 $cmH_2O$ appear to safely provide adequate PCF for the majority of patients with neuromuscular disease. | B |
| Mechanical in-exsufflation can be ineffective in patients with very poor bulbar dysfunction with insufflation capacity >1L, where dynamic airway collapse occurs. | C |
| Techniques of insufflation, manual assisted coughing and mechanical in-exsufflation require substantial acclimatisation and should be trained when the patient is well and ideally prior to an acute infective requirement. | D |
| Patients should receive regular vaccination against influenza and pneumococcus. | D |
| Early antibiotic treatment to reduce the risk of bacterial super-infection and recurrent infections should be investigated for the source of the pathogen. | D |
| Admission should be arranged if domiciliary insufflation and non-invasive secretion removal techniques are not able to reverse $SpO_2$ < 95% in the presence of continual ventilator use, persisting dyspnoea, suspected dehydration, fever, lethargy or possibility of fatigue. This $SpO_2$ value is based on the absence of ventilation-perfusion mismatch and can be altered by the treating team accordingly. | C |

| NIV AND RELATED RESPIRATORY MANAGEMENT OF PATIENTS ON DOMICILIARY NIV UNDERGOING ANAESTHESIA OR SEDATION | Grade |
|---|---|
| Prior to undergoing anaesthesia or sedation, patients on domiciliary NIV should be assessed by a respiratory physician, anaesthetist and the patient's NIV service. | D |

| | |
|---|---|
| Ensure that patients with chronic respiratory failure on domiciliary NIV receive adequate ventilatory support both during and post sedative procedures or surgical anaesthesia. This is to minimise the risks of the patient potentially developing acute on chronic respiratory failure or other respiratory complications. | C |
| Procedures should be performed at a tertiary hospital where staff have experience in NIV for acute and chronic hypoventilation and that there is access high level monitoring or an ICU. | D |
| A specialised NIV team should be present during and after the procedure to assist with predicting problems that may arise in the peri and post operative period for patients who are usually treated with domiciliary ventilation secondary to respiratory insufficiency. | D |
| Routine administration of oxygen should be avoided. | D |

| NOCTURNAL TO CONTINUOUS NIV USE | Grade |
|---|---|
| While continuous NIV is a therapy option for ventilator dependent patients, such therapy needs to be set up and supervised by centres with expertise in nocturnal and continuous ventilatory support modes, cough assist techniques and tracheostomy care. | D |

| TRANSITION FROM PAEDIATRIC TO ADULT CARE | Grade |
|---|---|
| A Transition Programme needs to be implemented for young people on ventilation to ensure a smooth transition of care and equipment. | D |
| A Transition Case Manager should be appointed to ensure adequate standards are maintained during the transition. | D |

| PALLIATIVE CARE AND END-OF-LIFE ISSUES FOR PATIENTS ON DOMICILIARY NIV | Grade |
|---|---|
| Early and timely discussions involving clinicians, patients and their families to address present and future decision with regards to the use of NIV during the progression of their disease should be held. Focus should be placed on the role of NIV in symptom relief as their disease progresses. | D |
| To ensure adequate time for planning, patients should be referred to palliative care services before they reach the advanced stages of their disease. | D |
| Encourage discussion and documentation of advanced directives:<br>• resuscitation status<br>• treatment end points for NIV (e.g. unacceptable quality of life or when unable to communicate by any means)<br>• attitude towards intubation / tracheostomy ventilation | D |
| NIV can be used in the palliative care / end-of-life setting to: relieve dyspnoea and the sequelae of nocturnal hypoventilation; to allow patient alertness and communication; and to “buy time”. | D |

# INTRODUCTION

## BACKGROUND

Over the past two decades, non-invasive ventilation (NIV) has emerged as a feasible and effective method of managing hypercapnic respiratory failure. While the technique is now widely used in hospitalised patients with acute respiratory failure, it was originally introduced as a method of reversing hypercapnia in patients with chronic respiratory failure. Prior to the introduction of NIV in the mid 1980's, home ventilation was restricted to negative pressure devices used primarily in patients with poliomyelitis, and tracheostomy ventilation used for patients with severe respiratory muscle weakness or total paralysis. Both forms of ventilatory support were associated with significant practical difficulties, which meant that home ventilation was restricted to a small number of individuals usually with complex chronic health care needs. The simplicity, cost and acceptability of NIV has led to this approach being widely adopted by the respiratory community and accepted by patients to the extent that NIV is now considered first line therapy in the management of chronic respiratory failure. Importantly, it is now recognised clinically that ventilatory support during sleep is all that is required to achieve sustained daytime improvements for most patients.

Despite this, current evidence about the therapeutic benefit of non-invasive ventilation is weak [1]. However, this is due to a lack of randomised trials in the area, rather than from a lack of clinical benefit. A recent systematic review was able to analyse data from only eight suitable (i.e. randomised) trials involving 144 patients using NIV [1]. In contrast, a European survey of home ventilation identified almost 22,000 users in 16 countries, 87% of whom used non-invasive ventilation [2]. Although the need for larger, randomised trials evaluating the longer term outcomes of NIV in chronic respiratory failure have been voiced [1], the clinical benefits of therapy are so well established that withholding therapy from many patient groups would now be considered unethical [3-5]. However, the data that is available is directionally consistent, suggesting NIV is acceptable to patients on a long-term basis and can alleviate symptoms related to chronic hypoventilation, improving survival and quality of life.

Resources for health care are finite. Therefore, it is important to identify those individuals that will gain benefit from therapy, and establish a management plan to maximise clinical outcomes from therapy. Data from overseas has shown an increase in the number of patients using NIV [6], especially for those with obesity hypoventilation and neuromuscular disorders [7]. Increasing awareness of the benefits of NIV by patients and health care professionals is likely to lead to more referrals for NIV assessment [7]. At present, use of NIV in COPD is generally low, but if evidence in this area improves, it may result in a dramatic increase in demand [8]. Even in homogenous health care systems, there are significant variations in the prescription of NIV [8]. It appears this is due not to different criteria being applied to commence NIV, but rather to a problem of recognition, with experienced individuals and centres more likely to initiate therapy than less experienced ones [8, 9]. This variation in practice also extends to the timing of intervention and the mode of ventilatory support used.

## PURPOSE OF THIS CONSENSUS STATEMENT

In order to establish a cost effective use of this therapy, it is important to develop a management strategy that ensures equity of access and standardisation of care across NSW.

The objective of this document is to provide information to optimise the overall management of individuals with disorders likely to lead to the development of chronic respiratory failure.

**The overall purpose of this consensus statement is to:**

- Provide recommendations regarding best practice management for clinicians involved in the management of adults requiring long-term non-invasive ventilatory support.
- Standardise the overall care of people using non-invasive ventilation.
- Promote the clinical care of individuals with chronic respiratory failure that is based on the best available knowledge.
- Provide a reference tool to support training of health care workers in best practice management of people using non-invasive ventilation in the community.

## CONSULTATION PROCESS

In May of 2006 the Agency for Clinical Innovation (ACI) Respiratory Network, a multi-disciplinary collaboration of clinicians, was established to address certain inadequacies and inequities in the field of respiratory medicine in NSW. This open forum of over one hundred clinicians agreed that six working groups would be formed to consider eight focus issues. The Oxygen and Chronic Ventilatory Support group recommended in August, 2007 that evidenced-based guidelines for domiciliary NIV in adult patients be developed to assist with the standardisation of patient assessment, commencement on NIV, monitoring and follow-up criteria.

To form the Domiciliary Non-Invasive Ventilation Working Group, a letter was sent to clinical representatives from each of the major centres in NSW in November 2007 to invite them to join and contribute to the development of the draft guidelines. This working party met in December 2007, where smaller working parties were assigned specific disease groups. These smaller working parties were responsible for providing a disease specific literature review and recommendations for the standardisation of NIV use in their respective disease category. Initial drafts were sent to all members of the Domiciliary Non-Invasive Ventilation Working Group for comment.

In August 2008, a project officer was employed to complete the literature review and recommendations for the diagnostic groups and to write the sections on the practical aspects for providing domiciliary NIV in adult patients. The second draft of each section was also completed by the project officer, after incorporating comments from its members and chairperson. In April 2009, the document was compiled into one-editorially-consistent text, and the draft of the complete document was circulated to all members of the Respiratory Network, ACI for further comment and review.

By June 2009, all comments and reviews were collated and the Domiciliary Non-Invasive Ventilation Working Group met again in August 2009 to finalise any outstanding consensus statements and the document.

## GRADING RECOMMENDATIONS – LEVELS OF EVIDENCE

Using the National Institute for Health and Clinical Excellence (NICE) guidelines (April 2007) [10] a critical review of the literature in the area of NIV was performed for the formation of this document and its recommendations. As treatment effectiveness was the primary focus of this consensus statement, the grading system for the levels of evidence for intervention studies as described by the Scottish Intercollegiate Guidelines Network (SIGN) was used [10, 11] (see Table 1). Where possible, meta-analyses, systematic reviews and randomised control trials were used to support recommendations. However, a majority of the recommendations rely on cohort, case-control and non-analytic studies or expert opinion, especially in the patient groups where NIV treatment has been well established (e.g. neuromuscular disorders and chest wall disorders) and where it would now be deemed unethical to perform randomised controlled trials in these patients.

**Table 1: Key to level of evidence and grades of recommendations**

| **LEVELS OF EVIDENCE: Used to assist with grading recommendations** | |
|---|---|
| **1++** | High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias. |
| **1+** | Well conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias. |
| **1-** | Meta-analyses, systematic reviews, or RCTs with a high risk of bias. |
| **2++** | High quality systematic reviews of case control or cohort studies.<br>High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal. |
| **2+** | Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal. |
| **2-** | Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal. |
| **3** | Non-analytic studies (for example: case reports; case series) |
| **4** | Expert option, formal consensus |

| **GRADES OF RECOMMENDATIONS**<br>The grade of recommendation relates to the strength of the levels of the evidence on which the recommendation is based. It does not reflect the clinical importance of the recommendation. | |
|---|---|
| **A** | At least one meta-analyses, systematic review, or RCT rated as 1++, and directly applicable to the target population; ***or***<br>A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results |
| **B** | A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; ***or***<br>Extrapolated evidence from studies rated as 1++ or 1+ |
| **C** | A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; ***or***<br>Extrapolated evidence from studies rated as 2++ |
| **D** | Evidence level 3 or 4; ***or***<br>Extrapolated evidence from studies rated as 2+ |

# CHAPTER 1 DEFINITIONS, MODES & GOALS OF NON-INVASIVE VENTILATION

**AMANDA PIPER & DANIEL FLUNT**

## 1.1 DEFINITIONS AND MODES OF NON-INVASIVE VENTILATION

Non-invasive ventilation (NIV) refers to the application of ventilatory assistance without the use of an invasive airway. In the vast majority of cases therapy will be delivered with *positive pressure* devices, although a few individuals around Australia still use *negative pressure* devices, having commenced this therapy prior to the availability of positive pressure devices for home ventilatory support. This is similar to the overseas experience. A large European survey of almost 22,000 home ventilator users found that only 0.005% used devices that were not positive pressure [2]. Negative pressure devices present a number of difficulties with regard to home ventilation including bulkiness, fit and comfort. In addition, they can induce significant upper airway obstruction, rendering therapy ineffective [12-14].

Positive pressure therapy may be delivered with either *volume* or *pressure preset* ventilators [15]. *Volume preset ventilation* delivers a stable tidal volume irrespective of the patient's pulmonary system mechanics (compliance, resistance and active inspiration) [16, 17]. In contrast, *pressure preset ventilation* delivers a set pressure during inspiration and expiration, and changes in the patient's pulmonary mechanics directly influence the flow and the delivered tidal volume [16, 17]. Most studies evaluating these two modes in patients with chronic respiratory failure have shown equivalent effects with respect to maintaining nocturnal gas exchange and improving daytime blood gases [18, 19]. Due to lower cost [20] and greater patient comfort [19, 21], most patients in the majority of centres are now prescribed pressure preset devices, mostly commonly, bilevel machines. However, volume ventilators are recommended for patients with the most severe respiratory failure including those with tracheostomy and when continuous or near continuous ventilatory support is needed. A switch from pressure to volume preset ventilation may also be required in patients who are adherent to pressure preset ventilation but who fail to respond to treatment [21].

Volume preset ventilators are usually set in an *assist/contro*l or *control* mode of support. Only one study has compared these two modes in patients with restrictive chest wall disorders [22]. This was a retrospective study and followed patients established on therapy for a 12 month period. No difference in blood gas improvement, lung function or compliance with therapy was seen between the two modes.

Pressure preset devices may be set in an *assist* ("spontaneous") mode where each breath is patient triggered; an *assist/control* ("spontaneous/timed") mode where breaths may be patient or machine triggered; and a *control* ("timed") mode where all breaths are machine triggered only [15]. The spontaneous mode has been used in patients able to trigger the ventilator consistently, whereas the spontaneous/timed mode is used when the ability of the patient to trigger the device reliably is reduced due to poor or absent inspiratory flows being generated (e.g. respiratory muscle weakness, drive to breathe is reduced or absent, or specific characteristics of the patient's pulmonary mechanics), where the goal of therapy is to control the respiratory pattern [15]. The pressure settings used in bilevel devices include the inspiratory positive airway pressure (IPAP) and expiratory positive airway pressure (EPAP), with the difference between the two determining the level of pressure support [20].

A recent innovation in this area is that of autotitrating bilevel devices. The algorithms of these machines are designed to automatically titrate pressure support levels, and in some devices EPAP, based on minute ventilation or flow targets. There is mounting evidence for the use of these devices in managing sleep disordered breathing in patients with central sleep apnoea/Cheyne–Stokes respiration [23, 24]. In contrast, there is currently a paucity of data and clinical experience with the algorithms and technology to automatically titrate ventilatory support in patients with chronic respiratory failure [25]. Consequently, it is not possible to make recommendations about the role and effectiveness of autotitrating bilevel devices for chronic respiratory failure at the present time, but will be considered in future versions of this document when further information and clinical experience is available.

## 1.2 INTERFACES

Success with NIV is reliant on appropriate selection of equipment and settings. The choice of interface or mask is therefore a major determinant of NIV success or failure [26]. Overall, long term mask choice should be based primarily on patient comfort and acceptance, whilst ensuring that it is both safe and effective [26]. Every effort should be made to ensure that air leaks are minimised, patient comfort is maximised and that the mask can be easily applied and removed.

In this document, specific points of interest relating to mask choice for the various diagnostic groups are discussed in their respective sections on implementation. The term oronasal mask refers to a mask which covers the mouth and the nose. For more specific information on interfaces the reader is referred to a recent review on interfaces and humidification for non-invasive ventilation [26].

## 1.3 GOALS OF NON-INVASIVE VENTILATION

The goals of providing long-term NIV will vary depending of the patient's primary disease process. For those with stable or slowly progressive disorders, the purpose of providing ongoing therapy is to increase survival while maintaining or improving the quality of life [27]. In rapidly progressive disorders, the primary goal is to palliate symptoms [28, 29]. In a small group of individuals, such as those with cystic fibrosis, home NIV may provide a temporising measure until transplantation is possible [30]. In all cases, NIV provides the opportunity to stabilise or improve respiratory insufficiency, allowing patients to return back into the community. The non-invasive approach also permits earlier intervention in the course of the disease than is possible with invasive techniques [31, 32], reduces acute care costs by decreasing hospital length of stay and readmissions [33, 34], and simplifies the burden of care related to managing chronic respiratory failure in the home [20].

# CHAPTER 2 DIAGNOSTIC GROUPS

The main diagnostic groups which develop respiratory insufficiency and subsequently treated and managed with NIV are discussed in this chapter.

**Where possible each diagnostic group contains the following subsections to provide clinicians with diagnostic-specific information to standardise the overall NIV management of their patients:**

- Background information on diagnostic group
- Screening measures and predicting the development of hypercapnic respiratory failure
- Treatment options
- Outcomes
- Indications for NIV
- Implementation of NIV
- Titration of NIV
- Follow up and ancillary care
- Specific issues related to the particular diagnostic group

# CHAPTER 2.1 SLOWLY PROGRESSIVE NEUROMUSCULAR DISORDERS

**PETER WARK, NICHOLAS MURRAY & DANIEL FLUNT**

## 2.1.1 BACKGROUND

Neuromuscular disorders that result in respiratory failure are a diverse group of conditions with varying aetiologies. However, all share the same physiological consequence, namely the development of progressive hypercapnic respiratory failure secondary to progressive muscle weakness. These disorders can be arbitrarily divided into those with rapid or acute progression (Motor neurone disease, which will not be discussed in this section) and those that have variably slow progression or are non-progressive. The most common of these are summarised below in Table 2.

**Table 2: Conditions causing neuromuscular weakness that result in chronic respiratory failure of variable and slow progression** (adapted from [35]).

| Variable progression | Slowly progressive or non-progressive |
|---|---|
| Duchenne's Muscular dystrophy | Previous poliomyelitis or post-polio syndrome |
| Congenital myopathies (including nemaline and metabolic causes) | Fascio-scapular humeral dystrophy |
| Merosin negative congenital muscular dystrophy | Spinal muscular atrophy |
| Limb girdle muscular dystrophy | Primary diaphragmatic paralysis |
| Myotonic dystrophy | Spinal cord injury (traumatic, malignant and vascular causes) |

## 2.1.2 RESPIRATORY FAILURE FROM NEUROMUSCULAR DISEASE

The development of respiratory failure in these disorders follows a highly variable course (see Table 3 for reference table for the degree of respiratory involvement across the slowly progressive neuromuscular disorders). In some conditions such as Duchenne muscular dystrophy (DMD) the clinical course is inevitable and well documented with all subjects developing respiratory failure by their late teenage years [36]. Whereas, in other disorders, the course is not so clear and patients may present more slowly and often much later in life, inevitably increasing the risk of delay in diagnosis and referral. Whilst treatment should always be based on individual patient assessment, common progression of some of the slowly progressive neuromuscular disorders are discussed below.

### Dystrophinopathy

DMD has an X-linked recessive pattern of inheritance with mutations occurring in chromosome Xp21 causing an absence of dystrophin [37], and affects up to 1 in 3300 live male births [38]. After a normal rise in childhood, vital capacity generally plateaus at 10 years of age, which is a similar time at which they become wheelchair dependent (typically by 10 to 12 years of age). After this plateau, with the development of worsening respiratory muscle weakness, VC declines at approximately 8% per year [39]. When it reaches <1L, 5 year survival has been reported as 8% [40]. In DMD the development of daytime hypercapnic respiratory failure indicates a mean survival of only 9.7 months [41]. Life expectancy has generally been in the early 20's, however, the use of NIV has increased survival beyond age 24 to 53% in one study [36].

Becker's muscular dystrophy is a less severe allelic version of DMD where there is only a reduction in dystrophin [37]. Symmetrical proximal weakness occurs and there is also cardiac involvement [42]. The progression of this condition is less predictable and respiratory failure is less common, with some patients remaining asymptomatic until their 60's [43]. It has been recommended to monitor lung function at yearly intervals [42].

### Myotonic Dystrophy

Myotonic dystrophy (DM1) results from an abnormal cytosine-thymidine-guanine expansion at chromosome 19q13 and is the most common dystrophy in the adult population, with an incidence of 1 in 8000 [44]. The disorder is inherited in an autosomal dominant manner and despite being a multisystem disorder, the clinical features are highly variable across different patients. The typical clinical presentation includes bilateral facial weakness, ptosis and distal muscle weakness with myotonia [44]. Respiratory muscle weakness and dysfunction of the respiratory centres in the brain can result in alveolar hypoventilation [42]. Whilst daytime sleepiness can be a strong symptom of sleep disordered breathing from nocturnal hypoventilation, it also occurs in this group in the absence of respiratory failure [45, 46], with some studies suggesting a central nervous system dysfunction of sleep regulation [47, 48]. When there is evidence of nocturnal hypoventilation, NIV can improve symptoms and survival in these patients. However, alterations of personality and cognitive function can hinder compliance to the extent that adherence to treatment is generally poor [45, 49]. Due to significant bulbar weakness, aspiration pneumonia is common [50] and pneumonia is the most common reason for mortality in this cohort of patients [51].

### Limb girdle muscular dystrophy

Limb girdle muscular dystrophy is an expanding set of autosomal dominant (LGMD1) and recessive (LGMD2) myopathies which have in common weakness of the shoulder girdle and pelvic girdle muscles [42, 49] (see Table 3). Due to rarity, there is little evidence in the literature regarding respiratory involvement in LGMD1, although scoliosis and spinal rigidity can occur which could lead to a restrictive respiratory impairment and therefore this subgroup should be closely monitored [42].

LGMD2, on the other hand accounts for 90% of cases and many subtypes have been described, including the sarcoglycanopathies (LGMD2 C to F) which present in a similar way to the dystrophinopathies [52]. In the sarcoglycanopathies, an evaluation has suggested that over 70% of individuals have reduced FVC. Particularly in γ and α sarcoglycanopathies, severe respiratory insufficiency, with FVC being reduced to <40% predicted have been observed. In LGMD2 A, respiratory muscle involvement is a rare occurrence and in LGMD2 I, patients typically present in adulthood with proximal limb weakness and diaphragmatic weakness is often observed. In the latter group this respiratory muscle weakness can even occur in ambulant patients [42] and in one series respiratory muscle involvement occurred in 10 of 16 patients, with NIV being required in 5 patients [53].

### Fascioscapulohumeral dystrophy

Fascioscapulohumeral dystrophy (FSH) is generally inherited in an autosomal pattern with the prevalence being 1 in 20000. Presentation is typically in the second decade with associated weakness in facial, scapular fixator, bicep, finger, dorsiflexor, abdominal, hip girdle and foot extensor muscles. However, there is a typical sparing of the extra-ocular, bulbar and respiratory muscles [42], with one study showing that only 1% of patients with FSH requiring ventilatory support [54]. Patients requiring ventilatory support had a more severe form of the disorder with kyphoscoliosis and wheelchair dependence. Due to oro-facial weakness, respiratory function testing using a mouth piece can be difficult and spirometry and mouth pressures may be less accurate and unreliable if there is not an adequate seal. Using a face mask attached to the measuring devices may be required.

**Table 3: Respiratory involvement in various slowly progressive neuromuscular disorders** (from [42], with adaptations from [49])

| Condition | Respiratory involvement |
|---|---|
| Duchenne muscular dystrophy | Inevitable, usually in teens, due to respiratory weakness |
| Becker muscular dystrophy | Less known but can occur with disease progression |
| Myotonic dystrophy | Common, due to:<br>Sleep disordered breathing<br>Respiratory muscle weakness and myotonia<br>Alveolar hypoventilation<br>Aspiration pneumonia due to bulbar weakness |
| Fascioscapulohumeral dystrophy | Respiratory insufficiency reported in severe disease |
| Autosomal dominant limb-girdle muscular dystrophy | Can occur due to scoliosis and spinal rigidity |
| Autosomal recessive limb-girdle muscular dystrophy<br>LGMD 2A (calpainopathy)<br>LGMD 2B (dysferlinopathy)<br>LGMD 2C (γ sarcoglycanopathy)<br>LGMD 2D (α sarcoglycanopathy)<br>LGMD 2E (β sarcoglycanopathy)<br>LGMD 2F (δ sarcoglycanopathy)<br>LGMD 2G<br>LGMD 2H<br>LGMD 2I | <br>Late involvement<br>Not reported<br>Common<br>Common<br>Common<br>Common<br>Not reported<br>Not reported<br>Common |
| Emery-Dreifuss muscular dystrophy | Occurs in association with skeletal deformities |
| Oculopharyngeal muscular dystrophy | Aspiration pneumonia and sleep disordered breathing reported |
| Spinal muscular atrophy<br>Type 1<br>Type 2<br>Type 3 | <br>Inevitable<br>Variable extent<br>Uncommon |
| Myasthenia gravis | Rapid respiratory failure and fatal hypercapnic can develop over hours, often in the setting of respiratory infection |
| Bethlem myopathy | Common |
| Autosomal dominant Distal myopathy<br>Laing<br>Welander<br>Markesbery–Griggs–Udd | <br>Rare |
| Autosomal recessive Distal myopathy<br>Nonaka<br>Miyoshi | <br>Rare |
| Myofibrillar myopathy with abnormal desmin | Common |
| *Metabolic myopathy* | |
| Glycogenosis type II (Acid Maltase Deficiency)<br>Infantile<br>Childhood<br>Adults | <br>Common, death usually before age 2<br>Common, respiratory involvement in first years of life<br>Common, *de novo* presentation with acute-on-chronic respiratory failure |
| Glycogenosis type V (McArdle's) | Respiratory failure with acidosis reported |
| Fatty acid metabolism disorder | Uncommon unless severe rhabdomyolysis |
| Mitochondrial disorders | Can present with:<br>Respiratory muscle weakness<br>Hyperventilation syndrome secondary to acidosis<br>Central hypoventilation |
| *Congenital myopathy* | |
| Nemaline myopathy<br>Infantile/childhood<br>Adult | <br>Inevitable<br>Common |
| Central core disease | Rare |
| Minicore myopathy | Inevitable |
| Myotubular myopathy | Inevitable |
| *Congenital muscular dystrophy* | |
| Normal cognition, merosin negative<br>Congenital muscular dystrophy 1A, 1B, 1C | <br>Inevitable |
| Normal cognition, merosin positive<br>Ullrich Congenital muscular dystrophy<br>Early spine rigidity | <br><br>Inevitable |
| Associated mental abnormality<br>Fukuyama<br>Muscle–eye–brain<br>Walker–Warburg | <br><br>Inevitable, early onset |

### Emery-Dreifuss muscular dystrophy

Emery-Dreifuss muscular dystrophy is characterised by slowly progressive muscle weakness and wasting in a scapulohumeroperoneal distribution, early contractures of the elbow, ankle and posterior neck and cardiac conduction defects. Respiratory insufficiency is dependent on the development of scoliosis, contractures and spinal rigidity [42].

### Congenital myopathies

Congenital myopathies include nemaline myopathy, central core diseases, minicore myopathy and myotubular myopathy. Respiratory muscle involvement is best recognised in myotubular myopathy, multicore myopathy, nemaline myopathy, and is rare in central core disease [42, 49]. In X-linked myotubular myopathies, onset of hypotonia and weakness occurs early in life and is associated with severe respiratory insufficiency causing early death [42].

With regards to multi-minicore myopathy, respiratory involvement can occur even when patients are still ambulant. In a group of 19 patients, respiratory failure was found in more than half of the patients over the age of ten years and was correlated to the severity of scoliosis [55]. In small cohort of ambulant patients with multi-core myopathy also demonstrated symptomatic nocturnal hypoventilation, which was adequately ameliorated by the early intervention of NIV [56].

In nemaline myopathy, the severity of respiratory involvement depends in the time of disease onset and severity. When it occurs in infancy, marked respiratory insufficiency has been treated with early intervention [57]. Whilst usually occurring in the neonatal period, a rare variant of nemaline myopathy, (sporadic late-onset nemaline myopathy) the onset of limb and muscle weakness can occur in adult life [58] and in some cases, respiratory weakness has been the initial presentation [59].

### Spinal muscular atrophy

Spinal Muscular Atrophy (SMA) has an incidence of 1/10000 [60]. It is characterised by degeneration of alpha neurons in the anterior horn cells of the spinal cord leading to progressive muscle atrophy and premature death, usually from respiratory failure. There are many different types of SMA, based predominantly on the age of onset, severity of presenting symptoms and the absence of milestones (see Table 4). Type 1 SMA (the most severe) presents with weakness at birth or in the first six months of life. Type 2 SMA presents between six and 18 months of age with weakness of muscles in the legs and trunk and failure to meet motor milestones (crawling and walking). Type 3 SMA with onset after 18 months of age, and ability to walk which may be lost in time [60].

In the three classic forms of SMA, respiratory complications are inevitable in type 1, occurs to a variable extent in type 2 and are rare in type 3 [61]. When intercostal muscles (along with other accessory muscles of respiration) are involved [61], inspiration becomes reliant on the diaphragm alone and the lack of these stabilising muscles of the chest wall causes rib recession, pectus deformity and scoliosis. These factors if severe enough produce a weak, stiff chest wall which is operating at a mechanical disadvantage. Prognosis is dependent on the extent and timing of respiratory complications. Inspiratory muscle weakness predisposes the individual to ventilatory failure and expiratory muscle impairment causes an ineffective cough, which can lead to secretion retention and chronic atelectasis [62]. In SMA, expiratory muscle weakness may be more marked than inspiratory muscle weakness, which can lead to the recurrent infections prior to the development of respiratory failure [61]. Advancements in technology, assessment, ventilation and secretion removal techniques has produced an increase in survival to the extent that authors have recommended that the current classifications which use age of onset and age of death to describe a type of SMA, as inadequate [60].

**Table 4: Types of Spinal Muscular Atrophy** (from page 785 [63], with additions from [60] and [64])

| Type | Inheritance pattern[§] | Age of Onset | Presenting symptoms | Hallmark | Prognosis |
|---|---|---|---|---|---|
| SMA type I (severe infantile SMA, acute or fatal SMA, Werdnig-Hoffman, Oppenheim disease, amyotonia congentia) | AR | In utero to 6 months | Hypotonia and weakness; problems with sucking, swallowing, and breathing | Never able to sit | Traditionally suggested death usually occurs at 2 years but with improvements in medical technologies (including NIV) and assessment ), Survivals at 1, 2, 4, 10, and 20 years are 50%, 40%, 30%, 30% and 30% respectively [60]. |
| SMA type II (intermediate) | AR | Generally between 3 and 15 months | Proximal leg weakness, fasciculations, fine hand tremor | Never able to stand; facial muscles spared | *Dependent on extent and timing of respiratory complications*<br>Survival has been noted at 98.5% at 5 years and 68.5% at 25 years in one study [64] and 92% at 10 years and 92% at 20 years in another study [60]. |
| SMA type III (chronic SMA, Kugelberg-Welander) | AR, AD | 15 months to teen years | Proximal leg weakness, delayed motor milestones | Kyphoscoliosis and tongue fasciculations appear late | *Dependent on extent and timing of respiratory complications*<br>Life expectancy is not significantly less than the normal population [64] |
| SMA type IV (adult-onset SMA) | AD, AR, or very rarely X-linked recessive | Median age of onset, 37 years | Proximal weakness; variable within families; more severe in AD form | | Life expectancy not markedly reduced |
| Distal SMA (progressive SMA, Charcot-Marie-Tooth–type SMA) | AR, AD | AR: birth or infancy; AD: adulthood | Distal weakness | | Very slow clinical progression; does not alter life span |

[§]AD, autosomal dominant; AR, autosomal recessive.

### Acid maltase deficiency

Acid maltase deficiency, also named Pompe's disease or glycogen storage disorder type II, follows an autosomal recessive pattern which is characterised by a deficiency in the lysosomal enzyme acid α-glucosidase which leads to an intracellular accumulation of glycogen, causing progressive muscle weakness throughout the body and affecting various body tissues, particularly the heart, skeletal muscles, liver and nervous system [42, 49, 65]. Three clinical syndromes of acid maltase disease have been described: infantile form, childhood form and adult form.

In the infantile form, there is particular involvement of skeletal muscle, heart and liver, with death usually occurring before the age of two from respiratory failure. The childhood form presents in the first years of life with limb or respiratory muscle weakness. In the adult form, presentation occurs after childhood, usually with an indolent axial and proximal myopathy and involvement of the respiratory muscles is common [42, 49]. In an analysis of 29 adults with acid maltase deficiency (mean age 55 ± 11 years), and age of symptom onset 41 ± 11 years, showed that 16 patients required mechanical ventilation with the age of initiation being 50 ± 12 years [65]. Whilst ventilation was commenced during an episode of acute respiratory failure in five of these patients, the other 11 patients were commenced on ventilation secondary to diurnal hypercapnia or evidence of nocturnal hypoventilation. Sixty-nine percent of these patients were treated with NIV.

### Post-poliomyelitis syndrome

The poliovirus (an enterovius) infects the spinal motor neurons and/or the brainstem nuclei which results in a widely variable distribution of weakness of the skeletal or bulbar muscles leaving affected patients with variable residual permanent impairments after maximal recovery. The impairments can range from minor muscle weaknesses or deformities in the affected limbs, through to functional deficits in ambulation and self-care, to quadriplegia or need for mechanical ventilation [66, 67].

Whilst the degree of the initial recovery from the acute paralysing effects of poliomyelitis depends on the survival of sufficient numbers of infected and non-infected motor neurons to re-innervate some or all of the orphaned muscle fibres [66], postpolio syndrome affects polio survivors 20-40 years after the acute process has subsided and is characterised by a diffuse complex array of symptoms including fatigue, pain, and muscular atrophy with slowly progressive loss of function and weakness in previously affected muscles [66, 68]. In a survey of 551 survivors of poliomyelitis (response rate 66.5%) the risk of post-polio syndrome was significantly higher among patients who sustained substantial permanent impairment after polio and among females. However, the incidence did not vary with the age of onset, severity during the acute stage, or level of physical activity after recovery [66]. The prevalence of post-polio was 28.5% of all paralytic cases and of all cases of post-polio syndrome, 79% reported no major change in impairment status since onset.

As worsening respiratory function may occur in those individuals where the breathing muscles were involved during the initial episode [68], a detailed history, careful monitoring of lung function and measures of respiratory muscle strength, as well as being vigilant for signs of nocturnal hypoventilation should occur, especially if the patient is not already established on ventilation. Where the respiratory muscles were not involved in the initial disease process, the development of post-polio respiratory impairment is uncommon [68, 69]. Bulbar function should also be continually monitored in patients with poliomyelitis to ensure that if ventilation is required, NIV remains a suitable option.

### General progression to diurnal respiratory failure

In disorders that result in progressive respiratory muscle weakness the end result is daytime hypercapnic respiratory failure from hypoventilation. This is preceded by the development of nocturnal hypoventilation which results from progressive respiratory pump weakness and sleep induced decreased respiratory drive [70]. This usually begins in rapid eye movement (REM) sleep and then progresses into non-REM phases. In addition, upper airway obstructive events may also occur as a result of bulbar weakness and/or obesity.

Therefore, it is reasonable to assume that sleep related hypoventilation will precede and may even influence the development of daytime hypercapnic respiratory failure.

### 2.1.3 PREDICTING THE DEVELOPMENT OF HYPERCAPNIC RESPIRATORY FAILURE

Hukins et al [70] investigated the relationship between daytime measures of respiratory function ($FEV_1$, FVC, TLC, maximal inspiratory pressures (MIP) and maximal expiratory pressures (MEP)), arterial blood gases and full polysomnography in subjects with DMD. Total sleep time below 90% saturation exceeding 2% was used to define nocturnal hypoventilation. Lower lung function, elevated arterial $PaCO_2$ and arterial base excess were all related to nocturnal hypoventilation. An FVC <40% of predicted was found to be a sensitive indicator for hypoventilation but not specific (sensitivity 91%, specificity 50%), while base excess > 4mmols/L was highly specific but not sensitive (sensitivity 55%, specificity 100%). These authors recommended monitoring lung function regularly in this population, performing a blood gas when FVC<40% predicted, and undertaking sleep studies when base excess > 4mmols/L. However, a cautionary warning was sounded by Suresh et al [71] who found that 64% of younger patients with milder weakness reported symptoms suggestive of sleep disordered breathing, indicating that obstructive sleep apnoea could develop prior to nocturnal hypoventilation. The impact this may have on progression of respiratory failure or survival is unclear.

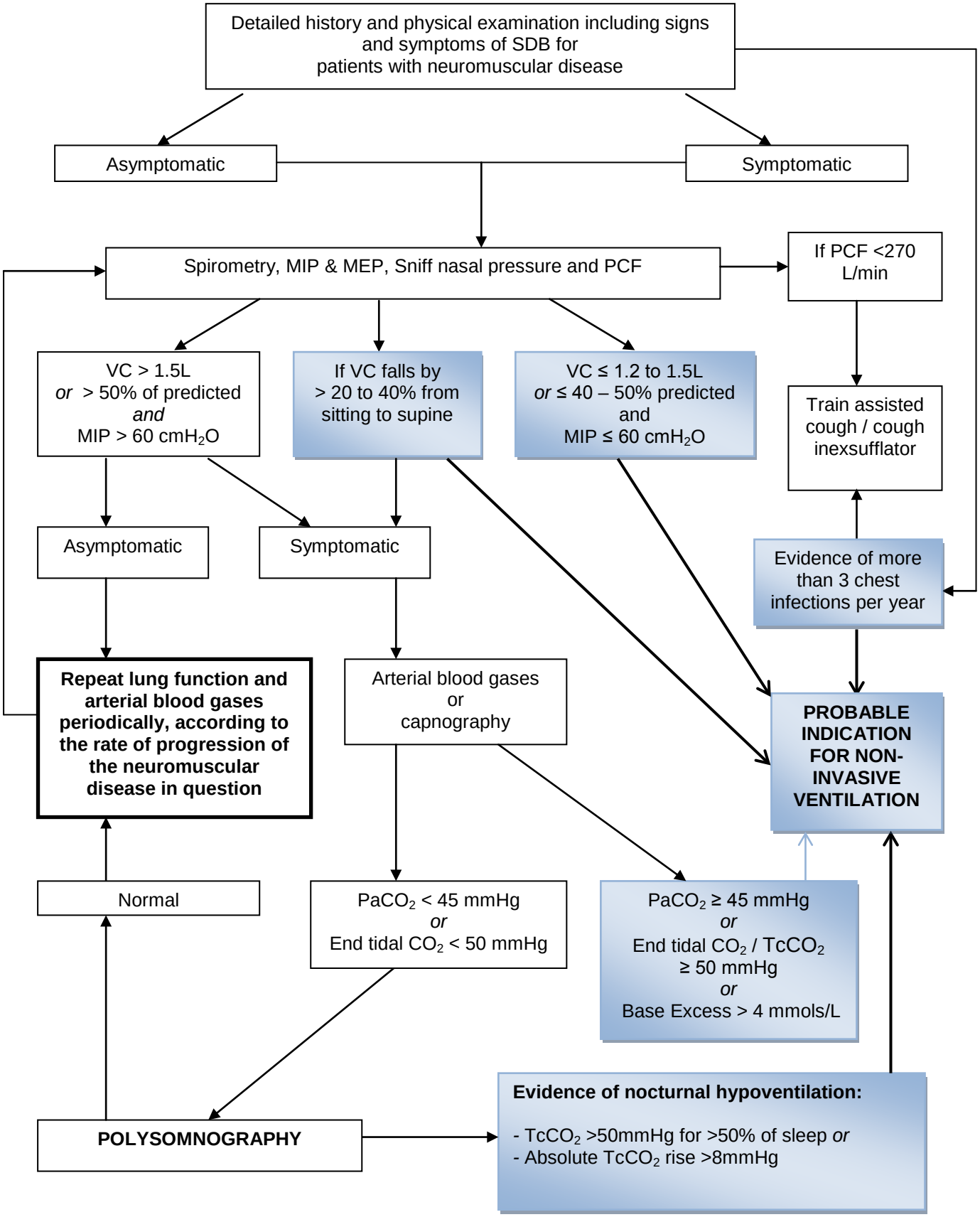
Monitoring VC can provide helpful diagnostic information when comparing erect and supine measures in patients with suspected diaphragm weakness [72]. One study demonstrated that the specificity and sensitivity of a greater than 25% fall in VC (from sitting to supine) for diaphragmatic weakness were 90% and 79% respectively [73]. Patients with significant diaphragmatic weakness may report that they are not able to lie flat due to sensations of orthopnoea. Compared to other diagnostic groups which frequently report exertional dyspnoea, patients with very limited mobility will not be able to exercise to the extent to experience or report exertional dyspnoea [49]. (See Figure 1 for Protocol for functional evaluation of patients with Neuromuscular Diseases).

**Key points:**

- In conditions associated with progressive respiratory muscle weakness the development of daytime hypercapnic respiratory failure is indicative of increased mortality.
- The development of daytime hypercapnic respiratory failure is preceded by nocturnal hypercapnia.
- Subjects with progressive respiratory muscle weakness should have regular monitoring of lung function. When FVC<40% predicted, arterial blood gases should be performed, and a sleep study undertaken when base excess > 4mmols/L.
- A fall of 25% from erect to supine VC may be helpful in detecting severe or predominant diaphragmatic weakness.
- If symptoms suggestive of sleep disordered breathing develop despite lung function >40% predicted, a sleep study should be considered.

**Figure 1: Protocol for functional evaluation of patients with Neuromuscular Diseases**

(from Paschoal 2007 [74] with additions)



### 2.1.4 TREATMENT OPTIONS

As the main cause of respiratory insufficiency in neuromuscular patients is caused by alveolar hypoventilation, the use of oxygen therapy alone to treat acute or chronic respiratory failure is generally inappropriate and may actually cause an iatrogenic worsening of the patient's hypoventilation [75, 76]. It is for this reason that mechanical ventilation (including NIV) is the primary treatment option for hypoventilation in neuromuscular disorders and that oxygen alone is not recommended to treat alveolar hypoventilation. In the absence of parenchymal lung disease, oxygenation should be normal in uncomplicated neuromuscular disease. However, supplementing oxygen to NIV may be required during episodes of hypoxaemia which are not amenable to ventilation alone, such as episodes of acute pneumonia [68]. If supplemental oxygen is required, close monitoring of $PaCO_2$ is indicated and it should be ceased as soon as it is no longer required [75].

### 2.1.5 OUTCOMES

Controlled trials on NIV in neuromuscular disease documenting its efficiency and ability to prolong survival are lacking and for ethical reasons these are unlikely to be performed in the future. Despite this, the clinical evidence and experience supporting its use in this diagnostic group of patients with chronic respiratory failure is overwhelming [3].

The evidence for the use of NIV in these disorders largely comes from observational trials. The Cochrane systematic review only included 4 studies of neuromuscular patients on NIV and included subjects with MND [1]. They could only conclude that NIV consistently improved symptoms of chronic hypoventilation in the short term and suggested further long term studies were needed. Clearly, important differences exist between subjects with MND and other slowly progressive neuromuscular disorders in terms of prognosis and the application of NIV. For this reason the conditions have been considered separately. The diagnoses that compromise the slowly progressive disorders also are disparate, but share more common ground.

Even in the most prevalent single disorder, DMD, controlled trials are few due its relative rarity and extremely poor prognosis if untreated. To assess survival in DMD from 1960 onwards and the impact of the introduction of NIV in 1991 a specialist unit in the north of England conducted an observational retrospective review of cases [36]. They introduced NIV in all patients once daytime hypercapnic respiratory failure had occurred. They found that multidisciplinary care increased the chance of surviving to 25 years of age from 0% in 1960 to 12% in 1981, but the advent of NIV further increased this to 53% in those who received treatment.

In contrast the only randomised trial of NIV in DMD occurred in subjects who had daytime eucapnia [77] and an FVC 20-50% predicted. Prophylactic use of NIV did not improve lung function and the NIV group had increased mortality. While the numbers were small and the adverse mortality may have in part related to an increase in cardiomyopathy in the intervention group, this study highlights the importance of adequately identifying suitable subjects for treatment.

In uncontrolled observational study of DMD subjects with daytime hypercapnic the application of nocturnal NIV led to a significant improvement in daytime $PaCO_2$ despite deteriorating respiratory muscle weakness [70]. In another uncontrolled study of children with DMD and other congenital myopathies who had presented with daytime respiratory failure, use of nocturnal NIV improved daytime gas exchange, nocturnal hypoventilation and sleep architecture [78].

To determine if nocturnal NIV applied to subjects with DMD who had daytime normocapnia, but evidence of nocturnal hypoventilation would be of benefit Ward et al [79] randomised subjects to NIV or routine follow-up, with intervention only occurring when daytime hypercapnia developed. NIV was provided using bilevel positive pressure ventilators or volume support ventilators, with settings established by sleep study to correct $SaO_2$ >90% and keep transcutaneous $CO_2$ <50mmHg. Nocturnal NIV reduced nocturnal transcutaneous $CO_2$, improved daytime arterial blood gases and improved some features of quality of life. In the control group, nine of the 10 subjects had progressed to daytime hypercapnic respiratory failure and required NIV within an average time period of 8.3 ± 7.3 months.

Recent retrospective reviews of subjects with neuromuscular disease using NIV have shown there are fewer episodes of lower respiratory tract infection including episodes requiring hospitalisation [80].

**Key points:**

- The introduction of nocturnal NIV in specialist clinics for subjects with DMD who have developed daytime hypercapnic respiratory failure has been associated with a significant improvement in mortality.
- The introduction of nocturnal NIV in subjects with DMD who have developed daytime hypercapnic respiratory failure improves daytime gas exchange, nocturnal hypoventilation and improves sleep architecture.
- The introduction of NIV when nocturnal hypercapnia first appears even if daytime normocapnia is present, prevents the development of acute daytime respiratory failure, and improves some aspects of quality of life scores.

### 2.1.6 INDICATIONS FOR NIV

Home ventilation for patients with respiratory failure secondary to neuromuscular disease is now regarded as standard practice [79]. However, as previously discussed, this group encompasses a wide variety of disorders, with varying levels of disability, rates of progression and prognosis. While some neuromuscular disorders are relatively stable once therapy is introduced (e.g. post polio syndrome, limb girdle dystrophy, spinal muscular atrophy), other disorders will continue to demonstrate ongoing muscle weakness (e.g. Duchenne muscular dystrophy). In this latter group, changes in the type of home respiratory equipment and the way in which ventilatory support is delivered can alter significantly over time, and this needs to be taken into account and met as the patient's medical condition progresses. Although the majority of patients will present with chronic respiratory failure, careful respiratory monitoring of all patients with neuromuscular disease should occur, so that the appropriate introduction of NIV and techniques to promote insufflation and peak cough flows are not delayed.

**Recommendations for referral**

Recommendations for the review and use of NIV in patients with slowly progressive neuromuscular disease should occur at a specialist centre which has the skills to investigate and manage these patients on NIV. All subjects with a slowly progressive neuromuscular disorder who are <18 years of age should be referred for clinical assessment to a paediatric specialist unit and transitional care to an adult centre should be planned between 16-18 years.

Assessment by all treating physicians and clinicians as to the risk of development of respiratory failure should be considered in all subjects with other progressive neuromuscular disorders. Referral to a specialist centre should occur if the following develop:

i) History of possible sleep disordered breathing including poor sleep quality, insomnia, nightmares, frequent arousals, daytime drowsiness and sleepiness, nocturnal or early morning headaches, loss of energy, decrease in intellectual performance, loss of appetite or weight loss.

ii) Regular measurement of basic lung function should be undertaken. An FVC < 70% predicted or MIP < 60cm$H_2O$ (<50% predicted) should trigger referral

Urgent referral for NIV assessment should occur in these subjects where there is:

i) Development of hypercapnic respiratory failure, $PaCO_2$ > 45mmHg

ii) FVC < 50% predicted

iii) Progressive symptoms of dyspnoea and orthopnoea

iv) Recurring chest infections

v) Clinical signs of cor pulmonale

**INDICATIONS FOR TRIAL OF DOMICILIARY NIV**

Indications for a trial of home ventilation in patients with slowly progressive neuromuscular disorders include:

i) a clinical diagnosis of a neuromuscular disorder with appropriate clinical history

***AND***

ii) symptoms of significant sleep disordered breathing associated with nocturnal or hypopnoeic events or severe sleep fragmentation

***OR***

iii) an awake $PaCO_2 \geq 45$ mmHg

***OR***

evidence of nocturnal hypoventilation (e.g. sustained falls in $SpO_2$ such as $SpO_2 < 90\%$ for greater than 5% of the night *or* increase of peak $TcCO_2$ / $ETCO_2 \geq 8$ mmHg above awake resting values [81, 82] or peak $TcCO_2$ / $ETCO_2$ value being > 50mmHg for 50% or more of sleep time [62, 79]) **on** PSG *or* nocturnal respiratory monitoring which includes $SpO_2$ and carbon dioxide monitoring, despite daytime normocapnia

***OR***

iv) more than 3 chest infections per year [79]

v) In progressive disorders, a fall in VC below 50%, MIP < 40% predicted and/or nocturnal oximetry demonstrating a fall in $SpO_2$ below 90% for a period of more than 2 consecutive minutes [83]

vi) an acute event with respiratory decompensation where complete weaning off ventilatory support is not possible

vii) where upper airway obstruction is the primary abnormality but weakness of the respiratory muscles makes tolerance of adequate CPAP levels not possible.

## 2.1.7 IMPLEMENTATION

**Level of assessment required & definition of a specialist centre**

The assessment of patients with neuromuscular disorders should be ongoing, with the review process frequency being based on the usual process of the disease progression and individual patient changes. Clinical experience and provision of a multidisciplinary service are necessary for optimal management and specialised service provision. Services required for a hospital to be considered as a specialist centre include:

i) A team experienced in the use of NIV

ii) Access to complex pulmonary function tests and arterial blood gas analysis in an accredited pulmonary function laboratory

iii) Access to an accredited sleep laboratory with experience in monitoring transcutaneous $CO_2$ and initiating NIV

iv) Access to allied health services such as physiotherapists who have been specifically trained in sputum clearance in neuromuscular disorders, speech pathology for swallowing assessment and dietetics for nutritional support

v) Access to sub-specialities such as neurology, gastroenterology and palliative care, preferably with the ability for close consultation and multidisciplinary care

The initial assessments which occur at the Specialist centre should include:

i) History of possible sleep disordered breathing including poor sleep quality, insomnia, nightmares, frequent arousals, daytime drowsiness and sleepiness, nocturnal or early morning headaches, loss of energy, decrease in intellectual performance, loss of appetite or weight

ii) History of dyspnoea and orthopnoea, symptoms and signs suggesting the development of cor-pulmonale

iii) Lung function tests: FVC, MIP, MEP or alternative respiratory muscle strength testing, peak cough flow (PCF)

iv) Consideration for arterial blood gases, overnight oximetry or polysomnography

Subsequent reviews and assessments should include:

i) History of possible sleep disordered breathing

ii) Lung function tests: FVC, MIP, MEP or alternative respiratory muscle strength testing, PCF

iii) Arterial blood gases where FVC <40% predicted or MIP < 60cm$H_2O$ (50% predicted)

iv) Polysomnography where there is a history suggestive of sleep disordered breathing or where FVC <40% predicted and base excess > 4mmols/L

v) Training in assisted cough techniques including manual insufflation (e.g. using a resuscitation bag with a one-way valve or breath stacking on a volume ventilator), manually assisted cough manoeuvres and cough in-exsufflation

**Commencing non-invasive ventilation**

Acclimatisation of patients with neuromuscular disorders to NIV is a detailed process which requires significant amounts of education and training for the patient and their carers. Whilst some patients and carers prefer to have this performed as an intensive regime of outpatient appointments to avoid the discomfort of being away from their highly specialised home environmental set-up and specialised care, most acclimatisation occurs as an inpatient admission. This is particularly so when patients live a distance away from the hospital, have difficulty accessing transport due to severe limitations to mobility or have a preference for this method. It also has the benefit of ensuring that new skills are consolidated and provides full multi-disciplinary support during the initial assessment and training stage for NIV and other non invasive adjuncts (e.g. maximal insufflation and assisted peak cough flows).

A randomised controlled trial has showed comparable results between inpatient and outpatient acclimatisation in highly selected stable patients with neuromuscular disease (i.e. without significant bulbar weakness or cognitive impairment) and near normal daytime $PaCO_2$ [84]. Similar findings have been found in observational studies which also included mixed diagnostic groups [85, 86]. The location of acclimatisation therefore relies on clinical judgement based on the severity of diurnal hypoventilation, the likelihood of individuals experiencing problems with acclimatisation, associated medical co-morbidities, patient preference and clinical expertise [84, 85].

**Considerations for mask choice in patients with neuromuscular disorders**

Success with NIV is reliant on appropriate selection of equipment and settings. With regards to masks, whilst comfort and minimising air leaks are very important, other considerations need to be explored in patients with neuromuscular disease who are not able to independently remove their mask in the case of equipment malfunction, power loss or vomit. While nasal masks have less risk of aspiration, are easier for secretion clearance and may be easier for speech, they are more prone to mouth leak which may cause problems with machine triggering or cycling which can result in less effective ventilation and disrupt sleep architecture [87]. On the other hand whilst oro-nasal masks are able to better control for leak and are more effective for mouth breathers, they have increase aspiration risk, increase the difficulty with speaking and eating and increase the risk of asphyxiation with ventilator malfunction [87]. All oro-nasal masks should have an anti-asphyxial valve, which significantly reduce the resistance that the patient has to breathe in and out of, should the machine stop working. The ultimate mask choice will depend on safety, comfort and efficacy. Where possible, if a patient is unable to independently remove their mask in an emergency situation, a call system which can be activated by the patient should be installed.

**Key points:**

- Clinical experience and provision of a multidisciplinary service are necessary for optimal management and specialised service provision. This service at a baseline should have primary access to respiratory physicians, sleep physicians, a dedicated respiratory failure service, allied health (including physiotherapy, speech pathology and occupational therapy) and access to sub-specialities such as neurology, gastroenterology and palliative care.
- Regular respiratory assessment should include VC, MIP, MEP, PCF, and signs and symptoms of sleep disordered breathing or respiratory failure.
- Arterial blood gases should be performed where FVC < 40% predicted or MIP < 60 $cmH_2O$ (50% predicted), or fall in erect to supine VC ≥ 25%.
- Polysomnography should be performed where there is a history suggestive of sleep disordered breathing or where FVC <40% predicted and base excess > 4mmols/L.
- The patient / carer should be comfortable with NIV prior to home use.
- Where PCF < 270 L/min, training should also include assisted cough techniques including manual insufflation, manually assisted cough manoeuvres and mechanical in-exsufflation.
- Training/ education would come from the in-patient acclimatisation or be conducted in the specialist clinic.
- Extra consideration for choice of mask is required for patients who do not have sufficient upper limb and manipulation function to independently remove their mask.

### 2.1.8 TITRATION

Titration principles for slowly progressive neuromuscular disorders include:

i) Establish whether the patient is able to trigger the device consistently during sleep. Where diaphragm weakness has been identified either by a significant fall in erect to supine VC, an inspiratory muscle pressures less than 40% predicted or on specific diaphragm testing, a spontaneous-timed mode is likely to be required.

ii) Nocturnal monitoring during NIV to ensure settings are appropriate to control sleep hypoventilation.

iii) Titrate EPAP to prevent upper airway obstruction. Care should be taken not to use EPAP pressures over and above the requirements of the patient as excessive EPAP can be difficult or uncomfortable to breathe out against especially when there is significant muscle weakness.

iv) Titrate IPAP-EPAP difference to provide enough support for ventilation.

v) A pressurisation time which is comfortable and natural for the patient should be chosen.

vi) In order to improve patient triggering and cycling in the presence of weak inspiratory efforts, care should be taken to minimise mask leaks.

vii) Where a spontaneous-timed mode is required, the initial rate may be based around quiet and relaxed wakefulness when in the spontaneous mode.

### 2.1.9 FOLLOW UP AND ANCILLARY CARE

After the successful initiation of NIV, the following should occur:

i) A home trial of NIV to establish compliance and response to therapy

ii) Clinical review within the first 3 months to assess symptoms, success and compliance and patient's willingness and ability to continue therapy long term

iii) Patients should be using NIV >4 hrs / day [79]

iv) Over time, if there is a change in the patient's condition such that ventilatory support is required for more than 18 hours / day, the management of the patient should follow the guidelines outlined for continuous ventilatory support *(see Nocturnal to Continuous Ventilatory Support in the Home section)*

Once a patient with slowly progressive neuromuscular disease has been established on treatment the following should occur:

i) Annual electrical safety checks or as per manufacturers instructions.

ii) Written information regarding client responsibilities with respect to the care and maintenance of the equipment, and the need for regular clinical review to ensure benefit from therapy and identify changes to treatment that need to occur.

iii) Clear documentation of current settings should be provided to the patient to keep with the machine.

iv) Once the patient has demonstrated stability on their current settings, they should be monitored regularly either by the service that established therapy or an appropriately trained sleep physician closer to home. This should include:

- check of filters, mask and tubing
- confirmation that machine settings remain as documented.
- regular monitoring should include lung function, arterial blood gases and consideration for overnight oximetry
- weight should be measured periodically

v) Regular 6-12 monthly review by clinic or specialist sleep/respiratory physician to trouble shoot equipment problems, identify disease progression or change in the patient's circumstances.

vi) Repeat polysomnography / nocturnal monitoring will be required but the frequency determined by the clinical need and practical difficulties and will be determined by the treating service or physician.

vii) The patient / carer should receive information regarding the disease, likely prognosis, implications for surgery, anaesthesia, use of respiratory suppressants, uncontrolled oxygen therapy, care of equipment, and ongoing reviews should be given to the patient / carer. They should receive information on who to contact in the event of equipment failure as well as what steps to take.

viii) Training of carer's regarding secretion clearance techniques should be undertaken *(see Secretion Management section).*

ix) If bi-level pressure support is ineffective in controlling nocturnal blood gases, a trial of volume ventilation is warranted.

Access to a multidisciplinary service is crucial in order to provide adequate level of care. Referrals to other clinical services should include:

i) Access to physiotherapy for aid in sputum clearance in stable disease and with acute lower respiratory tract infection via manual insufflation, abdominal thrusts and/or mechanical in-exsufflation devices

ii) Specialist and regular dietetics nutritional support. Weight control is often necessary in patients with myopathy or post-poliomyelitis syndrome or in other neuromuscular conditions where patients become overweight through a combination of inactivity, reduced basal energy expenditure in wasted muscle or erroneous desire to improve muscle mass by increasing calorific intake alone [88]. This is important to control as obesity has adverse effects on a respiratory system which is already compromised. Conversely, some patients lose excessive weight especially when there are swallowing difficulties as a result of neurological dysfunction or if the patient has difficulty coordinating swallowing with their pattern of breathing. Due to the adverse effects of malnutrition on respiratory muscle

function, patients are generally advised to maintain a high protein, low calorie diet with the ultimate aim of achieving a body mass which suitable and stable for their requirements.

iii) Review by a speech pathologist to assess and manage swallowing difficulties, especially where there is a risk of aspiration (e.g. bulbar dysfunction).

iv) Access to a respiratory home care programme for advice in the management of stable disease and as a contact for acute problems such as lower respiratory tract infection.

v) Depending on the patient's social circumstances and degree of disability, assessment for other home support programs should be undertaken

vi) Cardiology review as appropriate

vii) Access to sub-specialities such as neurology, gastroenterology and palliative care, preferably with the ability for close consultation and multidisciplinary care.

**Key points:**

- Clinical review should occur within three months of commencement.
- Compliance should be at least 4 hours per night.
- If conditions change such that ventilatory support is required for greater than 18 hours per day, the management of the patient should follow the guidelines outlined for continuous ventilatory support *(see Nocturnal to Continuous Ventilatory Support in the Home section).*
- Regular 6-12 monthly review by clinic or specialist sleep/respiratory physician.
- Access to physiotherapy for aid in sputum clearance in stable disease and with acute lower respiratory tract infection via manual insufflation, abdominal thrusts and/or mechanical in-exsufflation devices.
- Access to a respiratory home care programme for advice in the management of stable disease and as a contact for acute problems such as lower respiratory tract infection.
- Specialist and regular dietetics nutritional support for weight control or optimisation as required.
- Review by a speech pathologist to assess and manage swallowing difficulties.
- Access to sub-specialities such as neurology, gastroenterology, cardiology and palliative care.

| RECOMMENDATIONS FOR SLOWLY PROGRESSIVE NEUROMUSCULAR DISORDERS | Grade |
|---|---|
| All subjects with DMD should be referred for clinical assessment initially to a paediatric specialist unit for assessment and then care transferred to an adult centre when age >18 years. | C |
| Assessment as to the risk of development of progressive respiratory failure should be considered in all subjects with other progressive neuromuscular disorders. Referral to a specialist centre should occur if significant respiratory muscle weakness or sleep disordered breathing occurs. | D |
| Subjects with progressive respiratory muscle weakness should be observed regularly with lung function, when FVC<40% predicted or MIP <60cm$H_2O$ arterial blood gases should be performed and when base excess > +4mmols/L, polysomnography should be performed. | C |
| Polysomnography should be performed where there is a history suggestive of sleep disordered breathing or where FVC <40% predicted, base excess > +4mmols/L on arterial blood gases or erect to supine fall in VC of ≥ 25%. | C |
| In subjects with progressive respiratory muscle weakness, nocturnal NIV should be commenced when:<br>• Daytime hypercapnia, $PaCO_2$ >45mmHg<br>• Evidence of nocturnal hypoventilation with $SaO_2$ <90% for >5% of the night or where there is a rise in $TcCO_2$ / $ETCO_2$ > 50mmHg for more than 50% of total sleep time or peak rise ≥ 8 mmHg.<br>• Symptoms of significant sleep disordered breathing associated with nocturnal obstructive or hypopneoic events. | C |
| After initiation of NIV clinical review should occur within the first 3 months to assess symptoms, success and compliance.<br>Regular monitoring should then occur and include lung function, arterial blood gases and consideration for overnight oximetry. | D |
| The patient and or carer should receive adequate training with equipment and be aware who to contact for medical and technical difficulties. | D |
| Patients should have access to other specialist health providers, including medical specialists and allied health professionals, preferably in a well co-ordinated multidisciplinary team. | D |

# CHAPTER 2.2 SPINAL CORD INJURY

**NICHOLAS MURRAY & PETER WARK**

## 2.2.1 BACKGROUND

The prevalence of spinal cord injury (SCI) in Australia was estimated at ~10,000 in 1997 and this is projected to rise to ~12,000 in 2021 [89]. Respiratory disease is the major cause of death in the first 12 years following SCI [90]. SCI is associated with a variable amount of respiratory compromise due to the fact that there is widespread variation in both the level and the completeness of the injury. A lesion causing segmental or long-tract injury at or above the level of C5 will compromise all relevant muscles including, most importantly, the diaphragm. SCI below C5 will leave the diaphragm intact but may paralyse other inspiratory muscles including the parasternal intercostals, the external intercostals and the scalenes. This can cause paradoxical movement of the thorax during inspiration, an abnormality which reduces the mechanical advantage of the diaphragm [91]. SCI below the level of T12 will leave the inspiratory muscles intact, but may still compromise muscles of expiration, leading in particular to impairment of cough. Cough is most impaired following cervical and upper thoracic injuries. Loss of inspiratory capacity in SCI can lead to considerable reduction in vital capacity (VC) and total lung capacity (TLC). Changes in both pulmonary compliance and chest wall recoil also tend to reduce the functional residual capacity (FRC), but much less markedly [92]. Abdominal wall tone can also be altered, resulting in alteration of the mechanical advantage of the diaphragm through increase in the radius of curvature of the diaphragmatic dome and altering the working segment of the diaphragmatic length/tension curve, especially with the patient sitting upright, but also when supine [93]. No direct measurements of work of breathing in SCI patients exist, but the consensus is that work of breathing is substantially elevated, leading to increased risk of respiratory muscle fatigue.

Central control of ventilation and central ventilatory drive should not be altered, except in the instance of coexisting brainstem injury as a consequence of vertebral arterial dissection, or in the presence of pre-existing morbidity such as severe chronic airflow limitation, significant heart failure or obesity. Disruption of the sympathetic nervous system in the instance of lesions above T1 can lead to unopposed vagal tone acting on the airways and consequently the excessive production of hyperviscous mucus [94].

Almost all SCI patients ultimately requiring non-invasive ventilation (NIV) will deteriorate acutely following the injury and then demonstrate a prolonged period of slow recovery of ventilatory function [95]. Acute ventilatory deterioration may be observed as a result of the phenomena of ascending spinal shock, inspiratory muscle fatigue, progressive atelectasis, progressive sputum retention and supervening pneumonia. Chronic deterioration in ventilatory function is not always seen and, when present, tends to be minor with the exception of progressive post-traumatic cervical or thoracic syringomyelia, recurrent severe chest infections or deteriorating thoracic spine or chest wall morphology. Work from other neuromuscular disease states suggests that pulmonary compliance decreases with time, potentially in association with a progressive increase in work of breathing [96, 97]. Paradoxical thoracic movement tends, fortunately, to diminish with chronicity of the injury as spasticity of the chest wall muscles increases and as the chest wall skeletal apparatus stiffens [96, 98].

In the SCI patient population, NIV usage might be considered in the case of stable nocturnal hypoventilation or obstructive sleep apnoea (OSA). It may also be used in mild wakeful hypoventilation, although opinion is divided with regard to this indication. Hypothetically, abdominal wall flaccidity may allow pathologically large expansion of the FRC through diaphragmatic flattening as a result of the application of positive airway pressure (PAP), leading to impaired tolerance of continuous positive airway pressure (CPAP) or positive end expiratory pressure (PEEP), or at least the effect of increased work of breathing when such therapies are applied. Abdominal binders may alleviate this effect.

In patients using NIV, there may be benefit from the concomitant usage of humidification and the intermittent usage of mechanically assisted cough (MAC) devices [99, 100].

**Key points:**

- The amount of respiratory compromise in SCI is dependent on both the level and completeness of the injury.
- Respiratory disease is still the major cause of death in the first 12 years following injury.
- SCI at or above C5 will compromise all relevant respiratory muscles, most importantly the diaphragm.
- Mechanical disadvantage of the diaphragm results from paradoxical movement of the thorax which occurs when the parasternal intercostal, external intercostal and scalene muscles are involved.
- Cough is impaired with expiratory muscle involvement.
- Reduced abdominal wall tone may allow pathologically large expansion of the FRC when continuous positive airway pressures are applied.

### 2.2.2 TREATMENT OPTIONS FOR RESPIRATORY INSUFFICIENCY IN SCI

As the incidence of neurological deterioration more than 7 days after a spinal cord injury is well under 5% [101, 102], it may be inferred that the overwhelming majority of patients who ultimately demonstrate nocturnal or wakeful hypoventilation will do so within that first week. Current Australian practice is that almost all such patients will be intubated and ventilated. Thoracic SCI patients should all be able to be weaned from ventilatory support, as should most patients with a level from C6-C8. Lesions at C4 and C5 can sometimes achieve ventilator independence, but many patients will continue to require ventilation. Complete (ASIA A) lesions at C3 or above will be associated with complete ventilator dependence. When weaning is possible in cervical SCI, the process is often prolonged (mean 87 days in weanable C2–C6 SCI patients) [103] and NIV will often be used as a weaning aid.

SCI is different from other neuromuscular disease in that the onset is hyper-acute and the long-term ventilatory status of most patients will be clear within a few months of presentation. Consequently, the usual progression from ventilatory competence to NIV usage to invasive IPPV usage is not followed. This means, firstly, that fewer SCI patients will use NIV than in other neuromuscular disorders because the most dependent patients will be on IPPV from the beginning and patients with ventilatory competence can expect to remain independent of NIV for a long time. The standard management of patients with complete dependence on assisted ventilation is IPPV, with few current exceptions in this country, so current candidates for NIV demonstrate partial or complete wakeful ventilatory independence and nocturnal hypoventilation. This group will consist mostly of C4-C6 SCI patients.

#### Obstructive Sleep Apnoea

The prevalence of OSA in tetraplegic patients who avoid IPPV acutely has been found to be ~60% [104, 105]. This disease is managed with CPAP in patients without SCI. While there is no doubt that most SCI patients can tolerate CPAP long-term, hypothetical concerns exist regarding the use of high CPAP pressures without inspiratory pressure support in c-spine SCI patients, as the FRC may be expected to increase considerably, reducing the mechanical advantage of the diaphragm and moving ventilation to a less advantageous segment of the pulmonary compliance curve. No published data are available to support a decision either for or against the use of CPAP in cervical spine SCI patients at the present time.

**Key points:**

- Complete lesions at C3 or above are associated with complete ventilator dependence and generally are treated with invasive positive pressure ventilation.
- Lesions at C4 and C5 can be associated with ventilator independence in some individuals.
- Thoracic level and most C6 to C8 SCI should be able to be weaned from ventilatory support.
- Long term ventilatory status of most patients with SCI will be clear within a few months of onset of injury.
- NIV is generally used when nocturnal hypoventilation is present but when partial or completely independent ventilation during wakefulness has been demonstrated (usually C4 to C6 SCI patients).
- OSA is very prevalent in tetraplegic patients. However, CPAP alone may not be tolerated due to its potential effect of increasing FRC in patients with reduced abdominal and chest wall muscle tone.

### 2.2.3 PREDICTING THE DEVELOPMENT OF NOCTURNAL RESPIRATORY FAILURE IN SCI

The assessment of nocturnal ventilation in SCI patients is made easier by the fact that the overwhelming majority of patients are managed as acute medical inpatients in a tertiary / quaternary referral centre for some weeks or months after their injury or after leaving intensive care. Consequently, direct measures of ventilatory insufficiency such as overnight oximetry, overnight capnography, evening and morning arterial blood gas assessment and partial or even full polysomnography may be performed without logistical difficulty. Unfortunately, and in keeping with several other neuromuscular diseases, little published work addresses the prediction of ventilatory failure in a SCI population. Such predictive measures would be particularly useful in the event of slow neurological deterioration, in the event of increasing BMI or sedative usage in an outpatient, or in an outpatient who is experiencing the onset of cardiorespiratory comorbidity.

Extrapolation from other neuromuscular disease states and from studies of able-bodied subjects suggests that the sensible monitoring of SCI patients, from a ventilatory viewpoint, would include the regular subjective assessment of markers of sleep-disordered breathing and sleep deprivation, serial measurement of maximal inspiratory pressure (MIP), inspiratory capacity (IC) and wakeful arterial $PaCO_2$, and intermittent serial overnight studies that might include capnography, oximetry or partial or full polysomnography. The ability to perform some of these measurements in this patient population is possessed only by a limited number of centres.

### 2.2.4 OUTCOMES

The benefits of NIV in SCI patients may accrue from respiratory muscle resting, resetting of the central $CO_2$ control mechanism, normalising tissue acidosis and hypoxia, improving the objective physiology of sleep, the beneficial effects of pulmonary distension and improved sputum clearance [106], and in comparison with IPPV, from improvements in appearance, comfort, swallowing and speech and reduced tracheal irritation and obstruction. However, a recent randomised study of NIV in the setting of cervical SCI failed to show improvements in respiratory function, pulmonary mechanics or work of breathing [107]. A randomised interventional study of NIV in ventilator-independent cervical SCI, examining clinical and quality of life outcomes rather than physiological parameters only, has yet to be performed in either an acute or a chronic setting.

Several low-level studies have suggested higher patient satisfaction, and fewer complications, in selected, completely ventilator-dependent SCI patients treated with NIV rather than IPPV [108-110], so the paradigm of treating these patients in Australia may change in the future.

### 2.2.5 INDICATIONS FOR NIV

When NIV is indicated, referral to a specialist centre with skills to investigate and manage NIV should take place. Many patients will not need consideration of NIV, but the following should lead to appropriate referral [16, 106, 111, 112]:

i) Symptoms of impaired sleep quality, such as daytime somnolence, waking headache or grogginess, fatigue, impaired cognition, impaired short-term memory, irritability, anxiety and depression.

***AND / OR***

ii) Symptoms of sleep-disordered breathing, such as frequent awakening, snoring, choking, gasping, waking dry mouth, waking dyspnoea or witnessed apnoeas.

***AND***

iii) Wakeful hypoventilation ($PaCO_2 \geq 45$ mmHg) [113, 114],

***OR***

Polysomnogram, capnography or oximetry suggesting nocturnal hypoventilation (such as one or more episodes of $SpO_2$ <88% for >5 min, or $SpO_2$ <88% for >10% of total sleep time [106], or $TcCO_2$/ $ETCO_2$ >50mmHg for more than 50% of TST [79].

***OR***

iv) Patients being weaned from invasive ventilation.

v) Otherwise unexplained potential co-morbidity of sleep disorders, such as refractory hypertension, pulmonary hypertension, right heart failure, cardiovascular disease or stroke.

vi) Intractable or refractory sputum retention, atelectasis, respiratory tract infection or type-I respiratory failure ($PaO_2$ < 80 mmHg, $SpO_2$ <95%).

vii) Intolerance of CPAP for treatment of OSA, especially in cases of SCI at C6 or above.

viii) The presence of a tracheostomy is not a contraindication.

### 2.2.6 IMPLEMENTATION OF NIV

The implementation of NIV should occur in a specialised centre. The specialised centre should include:

i) A team experienced in the use of NIV.

ii) Access to an accredited pulmonary function laboratory providing spirometry, maximum inspiratory pressure measurement (mouthpiece, mask and sniff nasal), and arterial or arterialised capillary blood gas analysis.

iii) Access to an accredited sleep laboratory with experience in monitoring transcutaneous or end-tidal $CO_2$, and in providing and adjusting NIV.

iv) Access to a respiratory failure/physiotherapy service for aid in bronchial secretion clearance.

v) Access to a spinal unit.

vi) Respiratory units caring for SCI patients to have at least one staff member designated in charge of patient and carer education and involved in equipment purchase.

The initial assessments which occur at this Specialist Centre should include:

i) History of possible sleep disordered breathing, impaired sleep quality, dyspnoea, cough, sputum retention, symptoms of right heart failure, and symptoms of vascular morbidity.

ii) Lung function tests: vital capacity (VC), maximum inspiratory pressure (MIP), sniff nasal inspiratory pressure (SNP) and peak cough flow (PCF).

iii) Consideration of spot wakeful arterial or arterialised capillary blood gases, or evening and morning ABGs, especially if FVC < 40% predicted or MIP < 60 $cmH_2O$.

iv) Polysomnography with capnography.

Subsequent reviews and assessments should include:

i) History as above.

ii) Lung function tests: FVC/VC (MIP if deteriorating symptoms).

iii) ABG if FVC < 40% predicted, or MIP < 60 $cmH_2O$.

iv) Polysomnography if symptoms or ventilatory physiology deteriorating. For patients established on ventilation a treatment-review PSG should occur at least every two years. In patients on CPAP a routine investigation should occur every two years. Other patients (not on CPAP or ventilation) can be reviewed with polysomnography every five years or as indicated.

### 2.2.7 TITRATION

**Specific issues to consider when commencing or titrating NIV in SCI include:**

i) In the instance of wakeful hypoventilation, IPPV via tracheostomy and ventilator, or at least the provision of NIV via a volume ventilator rather than flow-generator, should be considered. The use of NIV in chronic wakeful hypoventilation or in a state of "ventilator dependence" has been supported [110, 115, 116].

ii) Early pressure-titration polysomnography should occur, ideally based on capnography rather than oximetry. In the absence of capnography, evening and early morning ABGs may be helpful.

iii) Use of an abdominal binder may be considered as the initial intervention in cases of mild hypoventilation, or as an adjunct to the use of NIV [91].

iv) The patient should sleep supine if possible. Abdominal binders may improve ventilation in patients unable to sleep supine [117].

v) Adequate non-invasive assistance with sputum clearance must be demonstrated before decannulation of a tracheostomy.

**Equipment considerations for NIV in SCI are as follows:**

i) NIV flow generator to be capable of providing an IPAP of at least 22 $cmH_2O$.

ii) Spontaneous-timed mode flow generator, or a volume ventilator, to be provided if spontaneous mode device does not allow correction of sustained hypercapnia.

iii) In the case of wakeful hypoventilation, the use of a ventilator, with internal battery and low minute volume alarm, needs to be considered.

iv) Ventilators using flow triggering or volume cycled ventilation may be required for patients experiencing difficulty in triggering inspiration.

v) Volume-cycled ventilators may allow more effective coughing through the use of breath-stacking techniques.

vi) "Warm-pass" humidification to be provided, with or without internal coil heating.

vii) Nasal interface to be preferred for patients with inadequate arm function to allow autonomous mask removal and for patients with a history of ongoing vomiting or aspiration pneumonia. However, there is a risk of intermittent large oral air leaks with a nasal interface during sleep [118]. Pressure support or pressure-controlled, time-cycled ventilation is to be preferred over volume-cycled ventilation for nasal interface users.

v) The interface must contain an exhalation port if this is required by the NIV system.

vi) Patient and carers must be experienced with the application and maintenance of NIV equipment before home usage.

vii) The provision of equipment for allowing intermittent lung insufflation, or mechanical inexsufflation, should be considered desirable [99, 100]

**Key points:**

- Implementation of NIV should occur in a specialised centre with access to a spinal centre.
- Perform arterial blood gases if VC < 40% or MIP < 60 $cmH_2O$.
- If indicated, an early pressure determination titration polysomnography which includes a measure of carbon dioxide should be performed.
- Spontaneous-timed mode flow generator, or a volume ventilator, to be provided if spontaneous mode device does not allow correction of sustained hypercapnia.
- Abdominal binders may be used in the initial intervention of mild hypoventilation or assist with supine sleep.
- Adequate non-invasive assistance with sputum clearance must be demonstrated before decannulation of tracheostomy.
- A ventilator appropriate for life support is recommended for patients with wakeful hypoventilation.

### 2.2.8 FOLLOW-UP AND ANCILIARY CARE

**After the successful initiation of NIV, the following should occur:**

i) Initial clinical review should occur within the first 3 months to assess symptoms, adequacy of adherence and potential technical problems [106].

ii) Further review should occur every 6-12 months, again assessing symptoms, adherence and spirometry; further investigation as required.

iii) Objective decline of ventilatory function in a patient already on NIV should result in consideration of volume ventilation.

iv) Repeat treatment-review polysomnography to occur at least biennially and will be determined by the treating service or physician.

v) If the patient is requiring ventilatory support more than 18 hrs/day, a reassessment of equipment needs and re-categorisation to ***continuous ventilator dependent*** status should occur (See Continuous Ventilatory Support in the Home section). If the patient wishes to continue non-invasive ventilatory support, training with a mouthpiece must be undertaken.

**Once a patient with spinal cord injury has been established on NIV treatment the following should occur:**

i) Annual electrical safety checks or as per manufacturers instructions.

ii) Written information regarding patient responsibilities with respect to the care and maintenance of the equipment, and the need for regular clinical review to ensure benefit from therapy and identify changes to treatment that need to occur

iii) Clear documentation of current settings should be provided to the patient to keep with the machine

iv) Once the patient has demonstrated stability on their current settings, they should be monitored regularly either by the service that established therapy or an appropriately trained sleep physician closer to home. This should include:

- checking the filters, mask and tubing
- confirming machine settings remain as documented.
- regular monitoring should include lung function, arterial blood gases and consideration for overnight oximetry.
- weight should be measured periodically.

v) The patient / carer should receive information regarding the disease, likely prognosis, implications for surgery, anaesthesia, use of respiratory suppressants or recreational drug use, uncontrolled oxygen therapy, care of equipment, and ongoing reviews should be given to the patient / carer. They should receive information on who to contact in the event of equipment failure as well as what steps to take.

vi) Carers should be trained in manual insufflation and secretion removal techniques (including mechanical in-exsufflation) [99, 100]. These techniques should be practised with the patient regularly.

**Referrals to other clinical services should include:**

i) Physiotherapist service to be consulted in the event of persistent cough, sputum retention, respiratory tract infection, unexplained fevers or type I respiratory failure. Carers should be trained in manual insufflation and secretion removal techniques.

ii) Dietetics, Endocrinology or Obesity service to be consulted if patient's BMI >30 kg / $m^2$.

iii) Access to a targeted respiratory outpatient care programme, or an appropriately educated spinal outpatient care programme, is desirable but not essential.

iv) Access to spinal, neurosurgical, orthopaedic, plastic surgery, gastroenterology and palliative care services within a formal multidisciplinary framework.

**Key points:**

- Carers should be trained in manual insufflation and secretion removal techniques (including mechanical in-exsufflation). These techniques should be practised with the patient regularly.
- Access to a targeted respiratory outpatient care programme is desirable and access to a multidisciplinary care model is essential.

| RECOMMENDATIONS FOR SPINAL CORD INJURY | Grade |
|---|---|
| Consideration for NIV in SCI includes symptoms of impaired sleep quality (such as daytime somnolence, waking headache or grogginess, fatigue, impaired cognition, impaired short-term memory, irritability, anxiety and depression) or symptoms of sleep-disordered breathing (such as frequent awakening, snoring, choking, gasping, waking dry mouth, waking dyspnoea or witnessed apnoeas). | D |
| Full lung function tests should be performed including VC, MIP or SNP. An arterial blood gas should be performed especially if VC < 40% predicted or MIP < 60 $cmH_2O$. | D |
| NIV is indicated when there is evidence of hypoventilation when awake ($PaCO_2$ ≥ 45 mmHg) or evidence of nocturnal hypoventilation (such as one or more episodes of $SpO_2$ <88% for >5 min, or $SpO_2$ <90% for >10% of total sleep time, or $ETCO_2$ /$TcCO_2$ >50 mmHg for >50% of the total sleep time). | C |
| NIV is indicated when there are otherwise unexplained potential co-morbidity of sleep disorders, such as refractory hypertension, pulmonary hypertension, right heart failure, cardiovascular disease or stroke. | D |
| NIV is indicated when there is intractable or refractory sputum retention, atelectasis, respiratory tract infection or type-I respiratory failure ($PaO_2$ < 80 mmHg, $SpO_2$ <95%). | D |
| NIV is indicated when there is intolerance of CPAP for treatment of OSA, especially in cases of SCI at C6 or above. | D |
| The implementation of NIV should occur in a specialised centre where there is access to a spinal unit, accredited pulmonary function and sleep laboratory, physician experienced in the use of NIV, NIV service and physiotherapy service trained in secretion removal in patients with spinal cord injury. | D |
| In the instance of wakeful hypoventilation which does not require invasive ventilation, NIV should be supplied by a ventilator which has been approved for life support. | D |
| Use of an abdominal binder may be considered as the initial intervention in cases of mild hypoventilation, or as an adjunct to the use of NIV. | C |
| Spontaneous-timed mode flow generator, or a ventilator, to be provided if Spontaneous mode device does not allow correction of sustained hypercapnia in the presence of central apnoea or persisting hypoventilation. | D |
| Ventilators using flow triggering or volume-cycled mandatory ventilation may be required for patients experiencing difficulty in triggering inspiration. | D |
| Nasal interface to be preferred for patients with inadequate arm function to allow autonomous mask removal and for patients with a history of ongoing vomiting or aspiration pneumonia. As this may lead to intermittent large oral air leaks with a nasal interface during sleep, pressure support or pressure-controlled, time-cycled ventilation is to be preferred over volume-cycled ventilation when this type of mask is used. | D |
| Initial clinical review should occur within the first 3 months to assess symptoms, adherence and potential technical problems. Further review should occur every 6-12 months, again assessing symptoms, adherence and spirometry; further investigation as required. | D |
| Minimum compliance levels have not been established. In patients without wakeful hypoventilation, usage throughout all sleep periods should be recommended. | D |
| Carers should be trained in manual insufflation and secretion removal techniques (including mechanical in-exsufflation). These techniques should be practised with the patient regularly. | C |

# CHAPTER 2.3 RAPIDLY PROGRESSIVE NEUROMUSCULAR DISORDERS

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## 2.3.1 BACKGROUND

The archetypal rapidly progressive neuromuscular disorder is Motor Neuron Disease (MND), and hence it serves as the disease model for these NIV guidelines.

Motor Neuron Disease is a term used to describe a number of progressive neurological conditions that selectively affect motor neurons. Forms of MND include: amyotrophic lateral sclerosis (ALS), primary lateral sclerosis (PLS), progressive muscular atrophy (PMA), psuedobulbar palsy, progressive bulbar palsy and spinal muscular atrophy (SMA). ALS is the most common adult motor neuron disease and is characterised by a progressive deterioration of the corticospinal tract, brainstem and anterior horn cells of the spinal cord. Patients with MND usually have a variable combination of upper motor neuron (UMN) and lower motor neurone (LMN) features, although their clinical presentation can either be LMN or UMN predominant, leading to the clinical heterogeneity that is typical for the disease. The incidence is 1 in 40-50 thousand. There are approximately 1,300 to 1,400 people living in Australia with MND at any given time [119].

The presentations, clinical phenotypes and outcomes of MND are diverse. Presentations include: MND, presenting with a combination of upper and lower motor neurone (UMN and LMN) signs in the limbs; bulbar onset MND (30%), presenting with speech and swallowing difficulties, (sometimes with limb and cognitive features developing later in the course of the disease); less commonly PLS with pure UMN involvement; and progressive muscular atrophy, with purely LMN signs. More recent sub-classifications include the flail limb variant of MND, marked by prolonged disease duration [120].

The key respiratory symptoms and co-morbidities in MND include respiratory muscle weakness (dyspnoea, ineffective cough), sleep-disordered breathing (sleep fragmentation, morning headache and daytime sleepiness), and aspiration risk related to bulbar involvement. Respiratory failure, when it occurs, is a direct consequence of respiratory muscle weakness. While a small percentage of patients with MND initially present with severe respiratory muscle involvement, there is no reliable method to predict when respiratory muscle impairment will occur. There is a high incidence of sleep-related hypoventilation in MND, although the underlying mechanisms are not entirely defined [121]. This can occur despite normal or near normal awake lung function, with a proportion of patients developing early sleep-related hypoventilation independent of respiratory muscle weakness [83]. Sleep-related hypoventilation impacts on quality of life, and is an independent predictor of survival [122]. Hence, it is generally recommend that MND patients with excessive daytime sleepiness or insomnia should undergo sleep monitoring to diagnose nocturnal respiratory insufficiency and/or sleep disturbance [123].

The natural history of MND results in the death of approximately 500 Australians per year with a median survival of only 2 to 3 years from diagnosis. The progression of the disease varies greatly between patients however, with up to 25% of affected individuals surviving for 5 years or more. A reliable marker of disease progression is still unavailable and remains a challenge. No single algorithm combines the findings of functional assessments and rating scales with biological markers of disease activity and findings from imaging and neurophysiological assessments. Each MND case demonstrates the same pathology and ultimately a similar death from respiratory failure as a result of muscle weakness.

**Key points:**

- MND will be used as the general model for progressive neuromuscular disease in this section.
- In MND, it is difficult to predict when respiratory muscle involvement will occur.
- A proportion of patients develop early sleep-related hypoventilation, independent of respiratory muscle weakness.
- There is a high incidence of sleep related hypoventilation in MND, which in turn impacts on quality of life and is an independent predictor of survival.
- There are no reliable markers of disease progression in MND and median survival is only 2 to 3 years from initial diagnosis.

## 2.3.2 RESPIRATORY ASSESSMENT AND SCREENING IN MND

Recognition of respiratory muscle weakness and nocturnal hypoventilation facilitates appropriate and timely discussion regarding ventilatory support. Thus appropriate assessment of respiratory function in an individual with MND is important, particularly given that the course of MND commonly ends in respiratory failure. The assessment consists of the evaluation of symptoms and signs, pulmonary function testing of respiratory muscle strength and evidence of nocturnal hypoventilation.

The evaluation of symptoms relating to respiratory muscle weakness (RMW) and sleep disordered breathing (SDB) is important to identify patients who may benefit from intervention with NIV. Patients with asymptomatic impairment of respiratory function are associated with higher failure rates using NIV due to poor compliance [124-126]. Conversely, in a prospective study of 22 patients with MND addressing the indications for and effect of NIV on quality of life, the best predictor of compliance and benefit from NIV was the presence of orthopnoea [127]. Thus symptoms form an essential component in the decision to commence a trial of NIV. The main symptoms of RMW consist of dyspnoea and orthopnoea, whilst symptoms of SDB include sleep fragmentation, daytime hypersomnolence and fatigue, morning headaches and cognitive dysfunction. Respiratory symptoms are commonly noted when the VC has fallen to $\leq$ 50% predicted, and respiratory failure is imminent when the VC is $\leq$ 30% predicted [128].

A number of pulmonary function tests are used to evaluate respiratory function. There have been no studies addressing the frequency of interval testing to assess deterioration over time.

### Spirometry

The FVC has been identified as a good overall prognostic indicator of disease progression in MND, and is a more accurate predictor of mortality than the neuromuscular score [129]. A VC of < 49% was predictive of hypercapnia in non-bulbar patients in a prospective study of 59 patients with a sensitivity of 90% and a specificity of 73.5% [130]. However, the FVC is not sensitive to early RMW and did not correlate with respiratory symptoms in a prospective study of patients with relatively preserved FVC (70-100%) [131]. The supine FVC was significantly lower in these patients and may be more sensitive in detecting early diaphragmatic weakness. This is supported by a prospective study by Lechtzin et al. demonstrating supine FVC as the most highly correlated predictor of diaphragmatic pressure (Pdi), although sniff nasal inspiratory pressure was not assessed in the study [132]. The erect – supine %FVC has also been used to assess RMW, and has been demonstrated to correlate with symptoms of orthopnoea, dyspnoea and daytime fatigue [129].

### Static mouth occlusion pressure

The maximum inspiratory pressure (MIP) and maximum expiratory pressure (MEP) are more sensitive to early changes in respiratory muscle strength than FVC. Difficulty in testing may cause unreliable results in patients with advanced disease (inability to generate sustained inspiratory or expiratory pressures for > 1 second) or with bulbar dysfunction (leak around the mouthpiece) [130, 133].

### Sniff nasal inspiratory pressure (SNP)

This has a linear deterioration over time at a similar rate to FVC, while being more sensitive in detecting early RMW [133]. Whilst some studies report ease of use in patients with significant bulbar disease, this is conflicting with other reports that describe difficulties in testing due to mouth leak. A SNP < 26% in non-bulbar patients was predictive of hypercapnia with a sensitivity of 90% and a specificity of 73.5%, but there was no significant relationship in patients with bulbar disease [130]. SNP has also been shown to predict survival in MND, with a force less than 40 $H_2O$ having a sensitivity of 97% and a specificity of 79% for death within 6 months [134].

### Arterial blood gases

Hypercapnia only occurs as respiratory weakness becomes profound. It initially occurs during sleep with nocturnal hypoventilation and progresses to daytime hypercapnia with progressive RMW. VC, MIP, MEP and SNP all have predictive power for the detection of hypercapnia, however the SNP has greater discriminatory power. The predictive power of all tests is significantly reduced in patients with significant bulbar dysfunction [135].

### Overnight oximetry

Investigation of SDB can be made using overnight oximetry or polysomnography. Nocturnal hypoxia is recognised as a predictor of survival in MND, independent of RMW. Velasco et al. showed that a mean nocturnal arterial oxygen saturation of < 93% is predictive of a dramatically shortened mean survival time of less than 6 months [122]. Thus regular assessment of nocturnal saturations has been recommended to guide initiation of NIV in MND, given that the first signs of hypoventilation can occur during sleep, and that symptoms relating to SDB appear insidiously. Nocturnal pulse oximetry has been shown to be a sensitive indicator of early respiratory insufficiency and that this can occur despite relatively normal lung function [83, 136]. Interpretation of nocturnal pulse oximetry is not standardised, but should be based on time spent with $SpO_2$ <90%, the value of mean $SpO_2$, visual analysis of graphs and number of episodes of desaturation [137]. Screening of patients with nocturnal pulse oximetry alone appears sufficient to detect early respiratory insufficiency. It is also non invasive and can be performed in an outpatient setting, which can be more efficient and timely than inpatient assessment.

### Polysomnography

Formal polysomnography (PSG) demonstrates hypoventilation secondary to RMW. The incidence of co-existent OSA is low although has been described [135]. This may be in part due to insufficient negative intrathoracic pressure being generated to cause upper airway obstruction [135]. Formal PSG has also shown disrupted sleep architecture in patients with MND, with reduced total sleep time, reduced proportion of REM and SWS with an increase in stage 1 sleep and arousal index. In a study addressing the relation between health related quality of life (HRQoL) and PSG and tests of RMW, the relation between PSG indices and HRQoL were weaker and less consistent than those of respiratory muscle function [121]. Respiratory muscle strength testing with SNP has been shown to correlate with indices of sleep disturbance, but no significant correlation was observed with %VC and MIP [135].

**Key points:**

- Patients experiencing symptoms relating to respiratory muscle weakness (especially orthopnoea) and sleep disordered breathing are likely to benefit most, and be more compliant with NIV.
- VC < 49% is predictive of hypercapnia in non-bulbar MND patients.
- Patients may have respiratory symptoms at relatively preserved VC (70 to 100%).
- MIP and MEP are more sensitive to early changes in respiratory muscle strength than VC.
- In the absence of significant bulbar dysfunction, whilst VC, MIP, MEP and SNP all have predictive power to detect hypercapnia, SNP has the greatest power for the detection of hypercapnia.
- In MND, mean overnight oximetry of $SpO_2$ < 93% is predictive of a mean survival time of less than 6 months.
- In MND, SNP < 40 $cmH_2O$ has a sensitivity of 97% and a specificity of 79% for death within 6 months.
- SNP testing correlates with indices of sleep disturbances.

### 2.3.3 OUTCOMES

The potential benefits of NIV include improvements sleep quantity and quality, cognition and daytime sleepiness, overall HRQoL and survival. However, the negative impacts of this treatment need to be borne in mind, including physical discomfort, the intrusiveness of NIV and cost. There is also the potential for NIV to prolong life in the setting of an intolerable disease burden, adding to the already high workload for the caregiver and consequently impacting negatively on their quality of life.

Respiratory muscle function is an important determinant of HRQoL in MND [121], possibly more than overall MND severity [138], and represents a key predictor of survival [134]. It has also been shown that RMW is a much more important factor in determining HRQoL than any measure of sleep disordered breathing [121]. Several studies have examined the effect of NIV on HRQoL and have shown clinically and statistically significant benefit. Particular improvements have been demonstrated in measures of vitality, mental health and role emotional domain in the Short Form 36 (SF-36) [139, 140] and in all domains of the Chronic Respiratory Disease Questionnaire (CRQ), especially fatigue and mastery [139, 141]. Importantly, this improvement in HRQoL appears to be maintained, at least in the medium term [139], and may be related to improved daytime cognition, with statistically significant increments in measures of memory and executive function being demonstrated in one study [142]. The literature also demonstrates improvement in symptoms of fatigue, sleep quality, and headaches [28, 127].

Earlier uncontrolled studies suggested that NIV may prolong survival in patients who tolerated this treatment compared to those who did not [127, 143]. However, the role of NIV remained unclear until a randomised controlled study by Bourke et al [139]. The authors randomised 41 patients with MND with either orthopnoea associated with a maximum inspiratory pressure of < 60% predicted or daytime hypercapnia, to receive NIV or to a control group. Patients were divided into two groups - normal to moderate bulbar dysfunction, and severe bulbar dysfunction. This study demonstrated a statistically significant median survival benefit of 205 days (p=0.006) in those subjects without severe bulbar disease. This result was, however, significantly influenced by 6 patients in the control group who died very early, within 2 weeks of randomisation. Importantly, there was no survival advantage found in the group with severe bulbar dysfunction.

Mustfa et al have studied the potential added load that NIV may place on caregivers [144]. In this study, no impact of NIV was seen on most aspects of caregiver quality of life and NIV did not significantly increase caregiver burden or stress.

In summary, although all studies are limited by the small numbers of patients involved and some by their lack of an adequate control group, the vast majority strongly support the role of NIV in MND. Improvements in most aspects of HRQoL are sustained for meaningful periods of time, regardless of deterioration in muscle weakness, which might be expected to counter any positive effects NIV confers.

Uncontrolled studies have also hinted at an improvement in survival with NIV and the single randomised controlled trial has confirmed this improvement. The greatest benefit of NIV appears to occur in those with orthopnoea or symptomatic hypercapnia. Patients with severe bulbar weakness demonstrated poorer compliance and less overall benefit.

**Key points:**

- Respiratory muscle weakness is a much more important factor in determining HRQoL than any measure of sleep disordered breathing.
- Over the medium term, NIV improves measures of vitality, mental health and role emotional domain (SF36) and all domains of the Chronic Respiratory Disease Questionnaire, especially fatigue and mastery.
- Improvements in HRQoL have been attributed from NIV improving daytime cognition, memory and executive function, symptoms of fatigue, sleep quality and headaches.
- NIV increases survival in patients with MND with normal to moderate bulbar dysfunction.

### 2.3.4 INDICATIONS FOR NON-INVASIVE VENTILATION

The aim of commencing NIV in patients with MND is to provide treatment that will optimise quality of life. The continual monitoring of symptoms and respiratory function have been the guide for clinicians to commence NIV [145], however, there are no clear guidelines to define the optimal timing.

**Timing of referral for respiratory assessment and monitoring**

At presentation, the patient should be referred for baseline respiratory function testing [146]. This ideally should occur prior to the patient developing symptoms such as dyspnoea, orthopnoea or sleep disordered breathing. The following information should be obtained at baseline and assessed at regular intervals [29, 146]:

i) Respiratory function testing
   - VC (erect and supine)
   - SNP
   - MIP and MEP
   - Serum bicarbonate
   - Oximetry

ii) Ongoing clinical review every 3-6 months either through a Respiratory Failure/Ventilation clinic or Respiratory/Sleep specialist.
   - Dyspnoea / Orthopnoea
   - Sleep disordered breathing

Based on the worsening of these serial measurements, considerations of when to commence NIV can be discussed. This information may also allow the clinician to establish the patient on NIV prior to the commencement of significant orthopnoea, dyspnoea or sleep disordered breathing, or to ensure that the commencement of NIV is not excessively delayed.

**Timing of NIV commencement**

In clinical practice, tolerance and efficacy of NIV is extremely variable in this group of patients. Bourke and colleagues attempted to examine the optimal criteria for initiating NIV and potential predictors of efficacy in a group of 22 MND subjects [127]. They demonstrated that the presence of orthopnoea was the best predictor of benefit and compliance with NIV, with 9 out of 11 patients continuing with NIV after the initial trial with a large improvement in HRQoL and excellent compliance. Daytime hypercapnia and nocturnal desaturation also predicted benefit but were less sensitive factors. Sleep related symptoms proved less sensitive still and an isolated AHI> 10 was unhelpful as a predictor of tolerance and

efficacy. Patients without symptoms were poorly compliant. In addition, moderate or severe bulbar weakness was associated with poorer compliance and less improvement in HRQoL than those with no or mild bulbar weakness. It would therefore appear reasonable to consider ventilation particularly in patients with orthopnoea or symptomatic hypercapnia, being conscious that patients with bulbar dysfunction may be limited in their tolerance and benefit from NIV.

### 2.3.5 IMPLEMENTATION AND TITRATION OF NIV

As previously discussed, nocturnal ventilation is used in patients with motor neurone disease to improve symptoms and quality of life [139]. Although survival is also improved in those with normal or only moderately impaired bulbar function, it is still often less than 12 months from presentation with symptoms [139]. Therefore, initiation and titration of nocturnal ventilation guided by symptoms rather than PSG variables or the presence of awake hypercapnia is justified.

**Key points:**

- Indications, implementation and titration of NIV in MND should be guided by symptoms, particularly those of orthopnoea or symptomatic hypercapnia.
- Patients with moderate to severe bulbar dysfunction may be limited in their tolerance and benefit from NIV.

### 2.3.6 FOLLOW-UP AND ANCILLARY CARE

After initial acclimatisation to non-invasive ventilation the following should be performed and assessed:

i) Clinical review of patient within 1-2 months to determine compliance and response to therapy. Changes in symptoms and sleep quality should be documented.

ii) Ongoing clinical review every 3-6 months either through a Respiratory Failure/Ventilation clinic or Respiratory/Sleep specialist.

iii) Therapy should be used at least 4 hrs/day but less than 18hrs/day. If >18hrs/day of use is occurring, the management of the patient should follow the guidelines outlined for continuous ventilatory support *(See Nocturnal to Continuous Ventilatory Support section).*

iv) Assessment of cough and swallowing and the implementation of techniques to assist any deficiencies identified.

v) Ensure discussions regarding alternate feeding options have been undertaken.

vi) Overnight PSG or nocturnal respiratory monitoring should be performed at the discretion of the treating team based on the patient's clinical progression, problems and blood gas levels.

vii) The patient should be highly encouraged to contact a local supportive association, e.g. Motor Neurone Disease Association of NSW.

viii) If the patient develops bulbar dysfunction or if blood gases cannot be controlled non-invasively or there are insurmountable interface problems, nocturnal ventilatory support via a tracheostomy needs to be discussed *(See Role of Tracheostomy, later in this section).*

Once a patient with progressive neuromuscular disease has been established on treatment the following should occur:

i) Annual electrical safety checks or as per manufacturers instructions.

ii) Written information regarding client responsibilities with respect to the care and maintenance of the equipment, and the need for regular clinical review to ensure benefit from therapy and identify changes to treatment that need to occur.

iii) Regular clinical review either by the service that established therapy or an appropriately trained sleep or respiratory physician closer to home. This should include checking of filters and mask/tubing as well as confirming machine settings remain as documented. Arterial blood gases and weight should be measured periodically at the discretion of the treating service or physician. When it becomes difficult for patients to attend outpatient appointments, home visits by clinicians should be encouraged.

iv) Clear documentation of current settings should be provided to the patient to keep with the machine.

v) Written information for the patient explaining hypoventilation syndromes and the implications for surgery, sedative procedures or uncontrolled oxygen therapy. Also, the patient and relatives should be instructed to bring in their NIV equipment if they are admitted for either planned or unplanned admissions.

vi) Establish initial and ongoing discussions regarding the patient's wishes with respect to medical management in case of acute deterioration, need for tracheostomy and end-of-life care issues.

vii) Regular 3-6 monthly review by clinic or specialist sleep/respiratory physician to trouble-shoot equipment problems, identify disease progression or a change in the patient's circumstances.

viii) If the patient is requiring ventilatory support more than 18 hrs/day, a reassessment of equipment needs and re-categorisation to ***continuous ventilator dependent*** status should occur. If the patient wishes to continue non-invasive ventilatory support, training with a mouthpiece should be undertaken.

ix) Arrange a multidisciplinary review, including speech therapy, physiotherapy, occupational therapy and dietitian to ensure adequate swallow, nutritional status, mobility aids and home care management.

x) Review of the patient's domiciliary circumstances and refer to additional services as deemed appropriate.

xi) Training of carer's regarding secretion clearance techniques should be undertaken *(See Secretion Management Section).*

xii) Management plan and back up systems in case of power supply loss or machine breakdown for patients using NIV >18hrs/day.

### 2.3.7 SPECIFIC ADVANCED CARE INITIATIVES IN MND

Specific advanced care initiatives in MND include:

- Role of Tracheostomy
- Role of Carers
- Special circumstances (PEG, intercurrent acute non-respiratory illness)
- Role of the multidisciplinary Clinic
- End of Life determinations

**Role of Tracheostomy**

There is a limited evidence base for determining the role of tracheostomy and, therefore, permanent ventilation in the setting of MND. The timing of the formation of an end-tracheostomy has not been determined, and there is no current published data to help in the derivation of guidelines for physicians to determine patient characteristics which may best select those who may benefit. There is not a single prospective randomised study into the role of TIPPV (tracheostomy-intermittent positive pressure ventilation) and only limited studies to ascertain the benefits in terms of HRQoL measures and survival improvements. These studies can only be compared to historical cohorts further diminishing their power in any analysis of value [147-149].

The current published papers have been reviewed for their contribution in the area albeit that their supportive level of evidence is low and should be considered as such with some caution. In essence, TIPPV offers longer survival but a significantly greater burden of care and cost to the patient and/or community. HRQoL improvements as determined by NIV are not inferred by TIPPV to an equivalent degree and perceived dissatisfaction with treatment outcomes is greater. Issues related to placement and ongoing care of an individual with a tracheostomy and deteriorating physical function needs to be clearly discussed.

### Carer's Role

In a study from the US [28], fewer than 10% of MND patients had chosen home ventilation, and fewer than 5% were still on it. Family caregivers report major burdens despite the fact that the patients reported satisfaction with the therapy. Patient satisfaction is least in those receiving permanent ventilation in emergent circumstances despite survival advantages. Carer burden is considerably less and satisfaction considerably greater in the group selected for elective NIV or those self-selecting for non-ventilatory support [144]. The burden to the carers should be considered with significant weight in determining the progression to TIPPV. The burden of care and expense is considerably greater in TIPPV as a consequence of prolonged survival in the patients receiving long term TIPPV.

### Special Circumstances

The role of NIV/TIPPV in the setting of PEG insertion and/or acute non respiratory illness is very poorly determined. There is a single uncontrolled, retrospective experience with 33 consecutive patients described for PEG tube insertion using non-invasive positive pressure ventilation and oxygen support [150]. Patients with %FVC < 50% are at increased risk for morbidity from the procedure although, mean survival was 211 days. Sixty seven percent survived more than 180 days. Forced vital capacity at the time of PEG placement did not predict survival.

There are currently no data to describe the role of peri-operative or post operative NIV in MND patients presenting with non-respiratory disease requiring emergent surgery (e.g. Cholelithiasis, appendicitis etc). A case by case determination is required to ascertain the relative risk of death from sepsis or painful co-morbidity for conditions left unattended versus the risk of remaining intubated permanently post procedure. The decision should be explained fully to the patient and carers and will invariably require ICU post anaesthetic.

### Role of the Multidisciplinary Clinic

Concentrating large numbers of patients in MND clinics allows the accumulation of resources and clinical expertise in the management of this disorder. The team usually involves a neurologist, specialist nurse, physiotherapist, occupational and speech therapist, social worker, respiratory physician and dietitian. The effectiveness of Multidisciplinary clinics versus General Neurology clinics has been shown to improve survival MND patients. MND patients in Specialised Clinics live an average of 7.5 months longer and 1 year mortality can be reduced by nearly 30% [151]. This benefit is more pronounced in the bulbar onset group of patients. MND patients attending general neurology clinics were reviewed less frequently, and consequently it was found that less attention was given to the early introduction of NIV and percutaneous gastrostomy feeding.

### Referral to Palliative Care

All patients with MND should be referred to palliative care services to ensure a whole-person approach to care that is local and supplements primary care with expertise in symptom control and (later on) end of life care [29]. Depending on the resources available, referral should be made to a specialist palliative care team before reaching the advanced stages of MND [29] (i.e. prior to the development of respiratory muscle weakness [146]). (Refer to Chapter 9, for further information on palliative care and end-of-life issues for patients on domiciliary NIV).

### End of Life Determination

Several studies of multidisciplinary referral patterns and Clinic processes have been published across different cultures [152, 153]. Clearly, there is significant variability in the determination of criteria for establishing the onset of respiratory failure as well as differences between Clinics as to the most appropriate modality of therapy and the way in which choices are given to prospective ventilation subjects. Those who had complete advance care directives are more likely to have communicated their preference to stop LTMV to family and physician than those who have not (76% versus 29%; p=0.05) [154]. An advanced care directive should be sought from **ALL** patients attending a MND Clinic to be considered for contingencies which also include the non-respiratory life-threatening but reversible conditions for which NIV may serve a role.

The clear distinction in terms of the burden to carers between long-term NIV and TIPPV should be clearly explained at the outset to both patient and carers. The financial cost should also be explained for consideration given the high likelihood of institutionalisation and the obvious level of dissatisfaction and depression evident in those who cannot be cared for at home. NIV, in this setting, should be considered for those patients deemed suitable and should be considered both as a long term proposition for survival advantage as well as a palliative tool to relieve symptomatic dyspnoea.

**Key points:**

- Due to rapid disease progression, regular monitoring should occur. Clinicians, patients and carers should remain vigilant to any potential changes in symptoms and either initiate pre-determined care plans or seek further assessment / referral.
- There should be regular assessment of cough and swallowing, and training of carers regarding secretion clearance techniques.
- Hours of ventilator usage should be carefully monitored and recorded. When ventilator usage begins to approach 18 hours a day, the patient is classified as being continuously ventilator dependent.
- Multidisciplinary review and management is required.
- Initial and ongoing discussions regarding the patient's wishes with respect to medical management in case of acute deterioration, need for tracheostomy and end-of-life care issues, need to be established.
- Whilst tracheostomy offers longer survival, it is associated with significantly greater burden of care and cost to the patient, carer and / or community.

| RECOMMENDATIONS FOR RAPIDLY PROGRESSIVE NEUROMUSCULAR DISEASE | Grade |
|---|---|
| Patients with MND are recommended to have 3 monthly clinical evaluation to monitor for symptoms and signs of respiratory and sleep complications. | D |
| All symptomatic patients should have evaluation of respiratory muscle strength with complex lung function tests and screening nocturnal pulse oximetry. | D |
| Sniff nasal inspiratory pressure and overnight oximetry are the initial investigations of choice for the assessment of early respiratory muscle compromise and nocturnal hypoventilation. | D |
| A diagnostic polysomnogram should be reserved for patients in whom co-existent upper airway obstruction is suspected on clinical grounds with inconclusive nocturnal oximetry. | D |
| The institution of NIV is recommended in patients with respiratory muscle weakness associated with orthopnoea, hypercapnia or symptomatic sleep hypoventilation (sleep fragmentation/ daytime hypersomnolence/ morning headaches and cognitive dysfunction). | B |
| While MND patients with significant bulbar dysfunction should still have the option to trial NIV, it should be recognised that this group of patients may have reduced tolerance to and derive less benefit from NIV. | B |
| The progression to tracheostomy intermittent positive pressure ventilation (TIPPV) should be made on an individual basis, weighing the longer survival advantage with a significantly greater burden of care and cost to the patient, carer and/or community and recognising that HRQoL improvements associated with the use of NIV may not be seen with TIPPV to an equivalent degree. | D |
| The elective commencement of NIV is preferred over non-elective TIPPV despite the improved survival advantage. | D |
| The use of NIV during, and/or after, the elective insertion of PEG feeding tubes in patients with demonstrable respiratory compromise should be considered. | D |
| Patients with MND should be managed in a multidisciplinary clinic as this improves survival and HRQoL, and facilitates earlier uptake of interventions including NIV and PEG insertion. | D |
| An advanced care directive should be sought from **ALL** patients. | D |

# CHAPTER 2.4 CHEST WALL DISORDERS

MARY DUNFORD, ANDREW NG & DANIEL FLUNT

## 2.4.1 BACKGROUND

Chest wall disorders include kyphoscoliosis, post-tuberculous sequelae, ankylosing spondylitis, previous major chest wall surgery and limitation of chest expansion related to trauma. These disorders produce abnormal configurations of the thoracic cage and, if severe, can significantly decrease chest wall compliance as well as lung compliance, primarily due to the reduced lung volumes [155]. Severe thoracic wall deformities cause a restrictive defect resulting in a reduction in TLC, FRC, residual volume and vital capacity [155]. These changes lead to a pattern of rapid shallow breathing which minimises the work of breathing, but increases dead space ventilation and reduces alveolar ventilation. In addition to this, deformities of the rib cage may also lead to changes in the length and orientation of the inspiratory and expiratory muscles resulting in impairment of diaphragmatic function [156] and pressure generating capacity of the other respiratory system muscles, particularly in scoliosis and after thoracoplasty [155]. Of note, if the thoracic wall deformity develops before the age of 4 to 5 years, the formation of the normal number of alveoli will be impaired [157], which may predispose the individual to the development of earlier respiratory failure.

Whilst respiratory drive is intrinsically normal in these conditions, hypercapnia develops when the muscles of respiration cannot provide adequate alveolar ventilation. This occurs when the force that can be exerted by the respiratory muscles is outweighed by the demands of the extra load of the poorly compliant respiratory system [75]. In these patients, significant hypoventilation initially occurs in REM sleep where there is reduced muscle activity to support their high work of breathing, before progressing to non-REM and ultimately diurnal respiratory failure [75]. In addition, patients may also develop atelectasis, further worsening hypoxaemia as their chest wall volume and compliance worsens with age. This chronic respiratory failure puts the patient at risk of premature death [158].

Many studies have combined the diagnostic groups of mechanical chest wall disorders and neuromuscular disorders which fall under the umbrella term of chest wall restriction. In this section we will be concentrating on the chest wall restriction based on mechanical syndromes [159] such as kyphoscoliosis, thoracoplasty and ankylosing spondylitis, as shown in Table 5. The majority of the studies in this category have focused on kyphoscoliosis, post-tuberculosis or post-poliomyelitis sequelae, most likely due to the fact that some other chest wall deformities in isolation do not appear to have important effects on ventilatory apparatus (e.g. pectus excavatum and pectus carinatum) and that ankylosing spondylitis rarely causes severe respiratory failure [75], as TLC and FRC are not reduced [160]. Chest wall restriction secondary to neuromuscular disease has been covered in an earlier section and obesity related respiratory failure (a reversible chest wall restriction) is also covered separately.

**Table 5: Risk of developing ventilatory failure in chest wall disorders secondary to mechanical syndromes** (adapted from [155])

| Low Risk | High Risk |
|---|---|
| Pectus Carinatum | Thoracoplasty |
| Pectus Excavatum | Scoliosis |
| Ankylosing Spondylitis | Post - Poliomyelitis |

**Key points:**

- Mechanical chest wall disorders result in significant alterations in chest wall mechanics, leading to hypoventilation in REM sleep initially, progressing to non-REM sleep and eventually causing diurnal hypoventilation.
- There is a wide variety of mechanical chest wall disorders and their impact on ensuing respiratory failure being dependent on degree of deformity and age of onset.
- Chronic respiratory failure puts patients with chest wall disorders at risk of premature death.

### 2.4.2 BASIC INVESTIGATIONS & MEASUREMENTS PREDICTING RESPIRATORY FAILURE

Basic information, investigations and measurements required when assessing for respiratory failure in mechanical chest wall disorders [106]:

i) A physician with skills and experience in NIV must establish and document an appropriate diagnosis on the basis of history, physical examination, diagnostic tests and assure optimal treatment of other underlying disorders

ii) Full lung function tests, with high index of suspicion when:

1. Vital capacity < 45 - 50% predicted [106, 161, 162] or < 1.0 to 1.5 L [75] *or*
2. MIP < 60 $cmH_2O$ [106, 162]

iii) Room air oximetry at rest and functional exercise. Baseline $SpO_2$<94% or significant desaturation and/or dyspnoea on exercise should be investigated.

iv) Arterial blood gases (ABGs) looking for evidence of chronic respiratory failure (hypercapnia with bicarbonate retention). However, evidence of nocturnal hypoventilation preceding day time blood gas derangements is adequate to commence positive pressure treatment [75].

v) Full diagnostic polysomnography including carbon dioxide monitoring and comparison of afternoon and morning ABGs. Also to assure optimal treatment of other underlying disorders such as excluding and/or treating associated obstructive sleep apnoea if clinically indicated [106].

vi) Evidence of right heart failure or polycythaemia, secondary to recurrent nocturnal hypoxaemia [155].

vii) Moderate (or greater) pulmonary hypertension

The severity of pulmonary impairment cannot be inferred to a clinically useful extent from the angle of scoliosis alone [163]. However, assessment of the development, extent and location of the curvature can provide some information:

i) Magnitude of the restrictive disorder seems to be related to the severity of the deformity but in some circumstances reduced VC has been found in patients with mild scoliosis. Onset of respiratory complications have been noted at spinal curvatures of less than or equal to 30 degrees, where it was concluded that it was respiratory muscle strength which is the more important determining factor [164]. However, as spinal angles < 50 to 70 degrees are generally associated with normal lung volumes [162], angles greater than this should increase the clinician's suspicion. Serial simple lung function testing (including respiratory muscle testing) should be performed to track baseline pulmonary function in these individuals.

ii) High thoracic scoliosis or involvement of the uppermost vertebrae [165] and scoliosis developing before the age of 5 years are at risk of developing respiratory failure, usually in their fourth or fifth decade [157].

iii) Thoracic kyphosis (anterior-posterior deformity), only leads to respiratory abnormalities during sleep if its onset is before 4 years of age, is severe, and when it occurs in the middle or upper thoracic spine [166].

**Key points:**

- Indications for further assessment for NIV in chest wall disorders includes VC < 45 to 50% (or VC < 1.0 to 1.5L), MIP < 60 $cmH_2O$, resting $SpO_2$ <94%, or evidence of signs or symptoms of sleep disordered breathing, hypercapnia, nocturnal desaturation, right heart failure, polycythaemia or pulmonary hypertension.
- Whilst larger spinal angle deviations, earlier age of onset (< 4-5 years) and high thoracic involvement are associated with the potential for the development of respiratory failure, respiratory compromise can occur at much milder curvatures.

### 2.4.3 TREATMENT OPTIONS

Although oxygen therapy may be required either nocturnally or on a continuous basis during the initial stages of home mechanical ventilation therapy, oxygen therapy alone is usually ineffective in relieving symptoms which are caused from nocturnal hypoventilation [167]. NIV in patients with kyphoscoliotic ventilatory insufficiency improves daytime and night-time oxygen saturation, respiratory muscle performance, symptoms of hypoventilation, and quality of life [162]. The combination of NIV plus oxygen results in greater improvement and survival than oxygen alone [5]. It has been recommended that home mechanical ventilation is the first choice of treatment when there is evidence of respiratory failure or nocturnal hypoventilation in chest wall deformity [167, 168].

### 2.4.4 OUTCOMES OF NIV

**Survival**

In prospective studies, survival of patients with chest wall disorders (kyphoscoliosis and post-tuberculosis patients) and respiratory failure receiving domiciliary ventilation has been shown to be approximately three-fold better than in those treated with long term oxygen therapy alone (with adjustments for age, gender, concomitant respiratory disease and blood gas levels) [168, 169]. Many other studies, including large cohort analyses, have also reported a significant increase in survival when NIV has been used to treat respiratory failure secondary to chest wall disorders [5, 6, 170].

The association of obstructive lung disease or concomitant respiratory disease worsens the prognosis of patients with kyphoscoliosis [169, 170]. Despite there being a trend in one prospective study for more patients with concomitant respiratory disease being treated with oxygen alone, it was shown that home mechanical ventilation was still far more beneficial for this sub-group with regard to survival when

compared to oxygen alone (ten year cumulative proportion surviving, approximately 50% versus 0%, respectively) [169].

### Symptoms and Quality of Life

As symptoms of dyspnoea, morning headache, morning confusion or grogginess, impaired sleep quality and drowsiness are common symptoms of hypoventilation, improvements are seen only with the use of mechanical ventilation and not oxygen therapy alone [162, 167].

Using the SF-36 questionnaire to monitor quality of life, significant improvements in the domains of physical function, physical capacity, vitality, emotional capacity and health transition were reported in 27 patients with thoracic wall disorders (kyphoscoliosis, fibrothorax and thoracoplasty) after commencing NIV [171], and these differences were maintained over the 18 months of treatment. Whilst social function and mental capacity significantly improved at the 6 month mark, it began to diminish from about one year of treatment, but did not return to baseline values. Similar changes in SF-36 domains were also noted in patients with kyphoscoliosis in another study, along with dyspnoea significantly decreasing after 6 months of NIV therapy and remaining that way for the duration of the 18 month study [172].

Non-invasive ventilation has also been described as being less burdensome than long term oxygen therapy in patients with kyphoscoliosis, especially when long term oxygen therapy can be prescribed for 16 to 24 hours per day (and usually provided by an oxygen concentrator connected to mains power), whereas in the majority of patients on domiciliary ventilation it is generally only prescribed for nocturnal use [169], leaving them free from equipment during the day if their $PaO_2$ allows. In addition to this, the personal financial cost of portable oxygen is prohibitive to the majority of patients.

### Physiological improvements

*Arterial blood gases*

A universal finding of all reports to date is the improvement in diurnal blood gas levels in patients with chest wall disorders commenced on non-invasive ventilation in pressure or volume preset modes [5, 12, 162, 167, 172]. In these studies, there has been a general shift from using volume ventilation to more simplistic pressure preset devices in the category of chest wall disorders. This is most likely a reflection that pressure preset devices: improve arterial blood gases in the majority of cases; are significantly cheaper; have improved technologically to provide greater inspiratory pressures; and are generally adequate for patients with chest wall deformity who are not ventilator dependent. However, it has been noted that arterial blood gas improvements may only occur with volume ventilation in a subset of patients [21].

In a study comparing LTOT with ventilation in kyphoscoliosis (with re-evaluation periods approximately averaging at 10 months) when breathing room air there was no significant increase in $PaO_2$ (50 ± 8 to 56 ± 9 mmHg) in the LTOT group whereas there was a significant increase in $PaO_2$ (44 ± 8 to 66 ± 9 mmHg) in the ventilation group [5]. These significant improvements in $PaO_2$ on room air ABGs have also been demonstrated in patients with restrictive thoracic disease within 2 weeks of commencing NIV treatment, but again not in the oxygen group [167].

*Respiratory muscle strength and lung function*

After commencing NIV, many authors have reported significant improvements in inspiratory muscle strength in patients with mechanical chest wall disorders. In patients with kyphoscoliosis, ranges of absolute mean MIP improvements have been reported as 44 to 57 cm $H_2O$ (33% increase) [5], 55.8 to 78.5 $cmH_2O$ (41% increase) [162] and 42 to 72 $cmH_2O$ (83% increase) [12]. A significant 16% increase in percent predicted MEP has also been shown in patients with kyphoscoliosis [162].

A handful of studies have shown a significant increase in vital capacity after the use of NIV, with one study significantly correlating an increase in MIP with increases in vital capacity [5]. Small but significant increases in vital capacity have been reported such as 645 ± 244 mL to 830 ± 292 mL [5] and increased percent predicted from 37.9 ± 7.2 % to 47.5 ± 11.9 % [162]. However, other studies have not demonstrated any significant improvements in lung function [12, 172].

### Decrease in hospitalisation

Commencing patients on domiciliary ventilation for chest wall disorders significantly reduces annual rates of hospitalisation. In patients with restrictive chest wall disorders (majority with mechanical chest wall disorders), number of days spent in hospitals decreased significantly between the year before NIV therapy had begun (mean ± SEM, median) from 22 ± 2, 17 days to 17 ± 4, 6 days at year one, 6 ± 3, 0 days at year two and mean range of 6 to 10 days for the next three years [6]. It has also been shown that in other groups of patients with mechanical chest wall disorders, the mean annual rate of hospitalisations significantly decreased from 1.2 - 1.52 per year, before NIV therapy to 0.8 - 0.89 per year, after commencing treatment [171, 172]. An absolute risk reduction rate to avoid hospitalisation in these patients has been calculated to be 63%, with 2 patients needing treatment to prevent one hospitalisation per year [171]. One study showed that in patients with kyphoscoliosis and ventilatory insufficiency, the number of hospitalisation days actually decreased to zero (from 10.9 ± 13.3 days per patient per year) after 6 months of NIV and remained at this level throughout the three year follow-up [162].

### Compliance

Compliance with NIV in patients with mechanical chest wall disorders appears to be very good, with daily usage generally being greater than other diagnostic groups [6]. Mean daily use (hours per day) was significantly higher in tuberculosis (TB) (9.1 ± 4.8) and post-poliomyelitis (8.6 ± 2.8) groups when compared the kyphoscoliosis (6.2 ± 3.0), COPD (6.6 ± 3.9) and OHS (6.2 ± 2.5) groups. Non-compliance was set at a usage of less than 3.5 hours per day and was not a major issue with patients with chest wall disease. All patients in the TB group were compliant whereas non-compliance in the polio and kyphoscoliosis was only 10% and 17% respectively. In this study, amongst all groups, compliant patients were differentiated from non-compliant patients by having statistically significant lower MIP and MEP values. High continuation rates were also shown in another study, where only 9% of patients commenced on NIV for chest wall deformity secondary to TB, interrupted therapy for reasons other than death [168].

**Key points:**

- Prospective studies show significant and substantial increases in survival when patients with chest wall disorders use NIV over oxygen alone.
- NIV in chest wall disorders provides significant improvements in the domains of physical function, physical capacity, vitality, emotional capacity and health transition.
- NIV in chest wall disorders universally improves diurnal blood gas levels and has also been shown to improve maximal inspiratory pressure measurements.
- NIV in chest wall disorders significantly reduces annual rates of hospitalisation and number of hospitalisation days.
- Due to the profound symptomatic improvements with the use of NIV in appropriately selected patients with chest wall disorders, compliance rates are greater than most other diagnostic groups.

### 2.4.5 INDICATIONS FOR NIV

Indications for usage include nocturnal hypercapnic symptoms with/without daytime hypercapnic symptoms generally with physiologic criteria [16, 106]:

i) symptoms & signs (shortness of breath during activities of daily living; orthopnoea in patients with disordered diaphragmatic dysfunction; poor sleep quality: insomnia, nightmares and frequent arousals; nocturnal or early morning headaches; daytime fatigue, drowsiness & sleepiness, loss of energy; decrease in intellectual performance; loss of appetite & weight loss; appearance of complications: e.g. respiratory infections; clinical signs of cor pulmonale)

***AND***

ii) Clinical diagnosis which involves significant chest wall abnormality and reduced lung volumes or inspiratory muscle pressures

***AND***

iii) Awake $PaCO_2 \geq 45$ mmHg

***OR***

Evidence of nocturnal hypoventilation on PSG with repetitive or sustained falls in $SpO_2$, rises in transcutaneous carbon dioxide or evening to morning $PaCO_2$ increase ≥ 8 mmHg or overnight $TcCO_2$ / $ETCO_2$ > 50mmHg for more than 50% of TST.

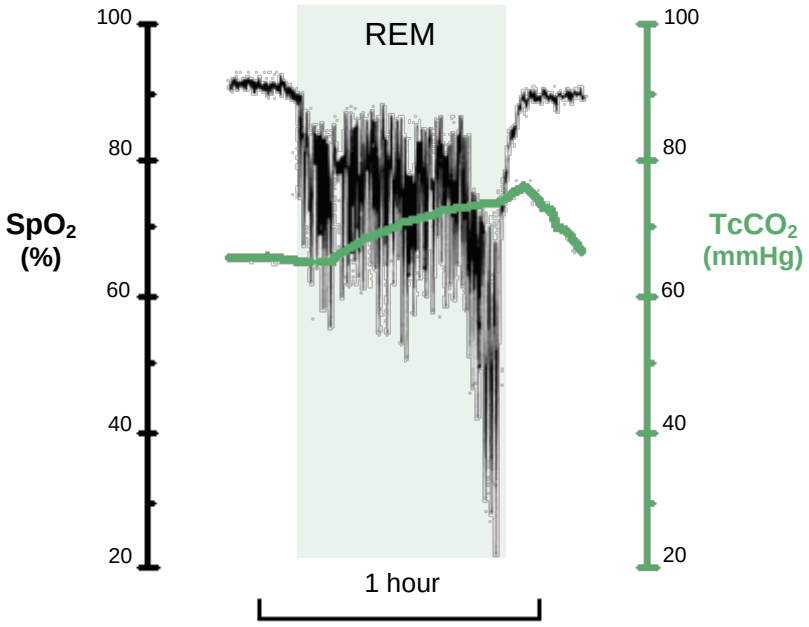



**Figure 2: Slow recording of $SpO_2$ and $TcCO_2$ on a diagnostic sleep study in a patient with kyphoscoliosis.** Modified from [12].

***OR***

Nocturnal oximetry demonstrating oxygen saturation ≤ 88% for 5 consecutive minutes

iv) Exclusion of OSA alone (i.e. patient has no evidence of hypoventilation). If significant OSA is present, a CPAP titration should be undertaken to determine if this therapy is appropriate to normalise breathing and gas exchange.

### 2.4.6 IMPLEMENTATION

In clinical practice, NIV is initiated either electively or in the context of acute ventilatory failure. In the latter circumstance, long-term necessity of NIV should be re-evaluated after weeks/months of commencement since the indications for NIV may change as the clinical conditions improve or not [16]. In the case of highly selected stable patients with chronic nocturnal hypoventilation and modest daytime hypercapnia ($PaCO_2$ ≤ 49 mmHg), comparable results have been seen for inpatient and outpatient acclimatisation of NIV [84, 86]. In other cases, initiation should take place where clinical expertise is available for monitoring and support (e.g. in-patient acclimatisation).

Mask choice primarily relies on what is effective, comfortable, safe and, ease of removal and application. However, due to the relatively high peak pressures that are usually delivered, careful attention needs to be paid to mask and mouth leak, especially when a nasal mask is used [19], and acclimatisation to optimal pressures may take some time.

Either pressure or volume-preset ventilation is likely to be effective [21, 173], with a randomised crossover study comparing pressure and volume non-invasive ventilation in chest wall disorders showing no significant difference in sleep quality, daytime arterial blood gases, lung mechanics, ventilatory drive, health status or daytime functioning [18]. However, in an open non-randomised study which compared volume versus pressure controlled ventilation in a heterogeneous group of patients with respiratory failure, Schonhofer and colleagues [21] identified a subgroup of patients (33%) that failed pressure ventilation after a one month trial after being successfully established on volume ventilation. These patients were only effectively treated and demonstrated arterial blood gas and symptom improvement when placed back on volume ventilation. Whilst the group was heterogeneous, the majority had respiratory failure secondary to chest wall restriction.

Whilst volume and pressure limited NIV have been shown to have similar effects on gas and exchange and sleep quality in patients with hypercapnic chronic respiratory failure, due to positive pressure devices being significantly cheaper [6] and associated with less gastrointestinal side effects than volume ventilators [19], current practice dictates that pressure preset devices are usually trialled first when acclimatising patients who are in respiratory failure secondary to mechanical chest wall disorders.

**Key points:**

- Long term necessity of NIV in chest wall disorders should be evaluated in a clinically stable state and initiation should occur with intensive monitoring and support (e.g. inpatient acclimatisation).
- Both pressure and volume preset NIV are likely to be as equally effective in chest wall disease, but there is a subset of patients which may demonstrate the need for volume ventilation if adequately titrated pressure-preset fails to significantly improve diurnal hypercapnia.

### 2.4.7 TITRATION OF NIV

i) Establish that the problem is not one of upper airway obstruction alone that would respond effectively to CPAP. This could be determined from the diagnostic sleep study by the pattern of desaturation and recovery, especially in REM sleep. Likewise, as part of the pressure titration, the titration could commence in CPAP mode to abolish frank apnoeas. Where hypopnoeas or sustained falls in $SpO_2$ persist, or a rise in $CO_2$ occurs, a switch to bi-level support should occur.

ii) Titrate EPAP to prevent UAO. Inspiratory pressures up to 25 cm $H_2O$ may be required to prevent hypoventilation [75, 162]. Some patients, independent of BMI, may have upper airway obstruction due to torsional influences of their scoliotic chest wall on their upper airway [174].

iii) If the patient is unable to trigger the device consistently, especially in REM sleep, despite efforts to minimise leak, and optimise trigger sensitivity where available, the mode should be changed from spontaneous to spontaneous-timed. The initial rate may be based around

quiet and relaxed wakefulness when on the spontaneous mode. If required, a set rate between 15 to 25 has been suggested [162].

iv) If the mean oxygen saturations remain ≤88% for >30% total sleep time [175], supplemental oxygen should be added. Long term supplemental oxygen is rarely required unless $PaO_2$ cannot be normalised [75].

v) Post 3 month review, if REM hypoventilation cannot be controlled with a pressure preset machine at best settings, a trial of volume ventilation needs to be undertaken. This should occur at a centre which has experience and expertise with volume preset ventilation.

**Key points:**

- Ensure IPAP-EPAP difference is adequate enough to move the stiff chest wall
- In the absence of leak, if patient flows are insufficient to trigger in the spontaneous mode during sleep, trial a spontaneous-timed mode.
- If sleep disordered breathing is predominately related to upper airway obstruction alone, a treatment trial with CPAP is indicated.

### 2.4.8 FOLLOW UP CARE AND ANCILLARY CARE

After successful initiation of NIV a home trial of therapy should be arranged. Monitoring should take place within weeks/months if commenced acutely. Otherwise a review in the sleep laboratory should occur at three months measuring: compliance (> 4 hours per night); awake arterial blood gases; symptoms and problems with therapy. The full PSG or nocturnal respiratory monitoring (including $SpO_2$ and leak) is performed to check the appropriateness of the settings and the continued need for long term oxygen therapy.

After this initial review, further clinical reviews should be performed by a Sleep Physician / Respiratory Physician or Respiratory Failure clinic every 6 to 12 months [16] depending on patients primary condition and response to therapy. At any time, when there are indications of unsatisfactory results like the recurrence of clinical symptoms or awake blood gases deteriorate despite clinical stability (e.g. absence of recent pulmonary infection) and adequate compliance, then inadequate ventilation must be suspected and objective evaluation during sleep must be undertaken [16].

The role of pulmonary rehabilitation to improve exercise tolerance should also be addressed. Non-invasive ventilation may also be used during rehabilitation where it has been shown that pressure support ("IPAP-EPAP difference") of ≥19 $cmH_2O$ can significantly ameliorate breathlessness [176, 177], increase alveolar ventilation [176] and consequently improve exercise endurance in patients with severe mechanical restrictive thoracic diseases [176, 177].

Referral to a home respiratory program where available is suggested. Depending on clinical circumstances and progression, further referrals to allied health and palliative physicians are suggested.

**Key points:**

- After initiation of NIV, a review sleep study should occur at three months, followed by reviews every 6 to 12 months.
- Compliance is deemed adequate at > 4 hours per night
- Patients should attend pulmonary rehabilitation and use NIV during training periods which can consequently improve exercise endurance.

| RECOMMENDATIONS FOR CHEST WALL DISORDERS | Grade |
|---|---|
| Individuals with vital capacity < 50% predicted (or 1.0 to 0.5L), MIP < 60 $cmH_2O$, or awake baseline $SpO_2$ < 94% are at risk of nocturnal desaturation. Overnight oximetry should be undertaken in these individuals. Polysomnography should be performed where there are concomitant signs and symptoms of sleep disordered breathing. | C |
| Where there is no overt sign of respiratory compromise, serial VC and respiratory muscle testing should be performed to track baseline pulmonary function in these individuals. | D |
| NIV in patients with respiratory insufficiency from chest wall disease provides greater physiological and symptomatic relief over oxygen alone. NIV should be trialled in all patients with chest wall disorders with evidence of nocturnal hypoventilation. | C |
| NIV is indicated if daytime $PaCO_2$ ≥ 45 mmHg, there is a rise in a carbon dioxide measure of ≥ 8mmHg between evening and morning, or if nocturnal oximetry demonstrates oxygen saturation ≤ 88% for 5 consecutive minutes. | D |
| Initiation should occur where clinical expertise is available for monitoring and support (preferably inpatient acclimatisation). | D |
| In the absence of leak, if patient flows are insufficient to trigger in the spontaneous mode during sleep, trial a spontaneous-timed mode. | D |
| If mean oxygen saturations remain ≤ 88% for >30% total sleep time, supplemental oxygen should be added. | D |
| Both pressure and volume preset ventilation is likely to be equally effective in chest wall disease, but there is a subset of patients which may demonstrate the need for volume ventilation if adequately titrated pressure-preset fails to significantly improve diurnal hypercapnia. | C |
| Compliance is deemed adequate at > 4 hours per night. | D |
| Monitoring should take place within weeks/months if commenced acutely, otherwise a review in the sleep laboratory should occur in three months. After this initial review, further clinical reviews should be performed by a Sleep Physician / Respiratory Physician or Respiratory Failure clinic every 6 to 12 months. | D |
| At any time, when there are indications of unsatisfactory results like the recurrence of clinical symptoms or awake blood gases deteriorate despite clinical stability (e.g. absence of recent pulmonary infection) and adequate compliance, then inadequate ventilation must be suspected and objective evaluation during sleep must be undertaken. | D |

# CHAPTER 2.5 OBESITY HYPOVENTILATION SYNDROME

**AMANDA PIPER**

## 2.5.1 BACKGROUND

Obesity hypoventilation syndrome is characterised by a body mass index (BMI) >30kg/m$^2$, raised daytime carbon dioxide ($PaCO_2$>45mmHg) and an absence of other causes to explain awake hypercapnia. In severe cases, polycythaemia, pulmonary hypertension and cor pulmonale are also present. While obesity levels are increasing generally, it appears that the prevalence of individuals in the heaviest BMI groups (>40kg/m$^2$) is increasing at levels 2 to 3 times faster than the growth of moderate obesity (BMI>30kg/m$^2$) [178]. This degree of obesity is associated with significant health burdens including compromise of the respiratory system. It is unclear how common daytime hypoventilation is amongst those with morbid obesity in the general community. However, current evidence suggests that around 10-15% of individuals presenting to sleep laboratories will have awake hypercapnia [179], with the incidence increasing as BMI increases [180]. In a study of morbidly obese patients (BMI >40kg/m$^2$) recruited consecutively from an obesity clinic, 23% were found to be hypercapnic [181]. The prevalence of OHS amongst hospitalised patients with a BMI>35kg/m$^2$ has been reported to be as high as 31% [182].

The limited work that has been done to date in this area suggests that untreated OHS is associated with significant comorbidities [180], increased health care expenses [183], high hospital admission rates [183] and reduced survival [182, 184]. In a study of morbidly obese individuals requiring hospitalisation, the mortality of those with awake hypercapnia was 23% compared to 9% for equally obese, eucapnic individuals, with the majority of the deaths occurring within 3 months of hospital discharge [182]. However, it appears the disorder is poorly recognised by clinicians, with 70% of patients with OHS being admitted to hospital at least once in the year prior to their diagnosis [183]. Despite the problem being under recognised, non-invasive ventilation (NIV) for these patients is becoming more common, with OHS now a major indication for home ventilatory support [6, 8]. Therefore, with an increasingly obese population, and improving recognition of OHS as a significant health problem, demand for therapy to manage the respiratory aspects of the disorder will escalate over the coming years.

## 2.5.2 SCREENING OF PATIENTS TO IDENTIFY OHS

Generally, patients with OHS are morbidly obese (i.e. BMI>40kg/m$^2$) and present with complaints of hypersomnolence, morning headaches, snoring and/or witnessed apnoeas [180, 185]. Although these symptoms overlap with those of simple obstructive sleep apnoea (OSA), patients with OHS are more likely to also complain of dyspnoea [185], have lower extremity oedema and low pulse oxygen saturation [180]. In addition, pulmonary hypertension occurs more frequently than in OSA (58% vs. 9%) [186].

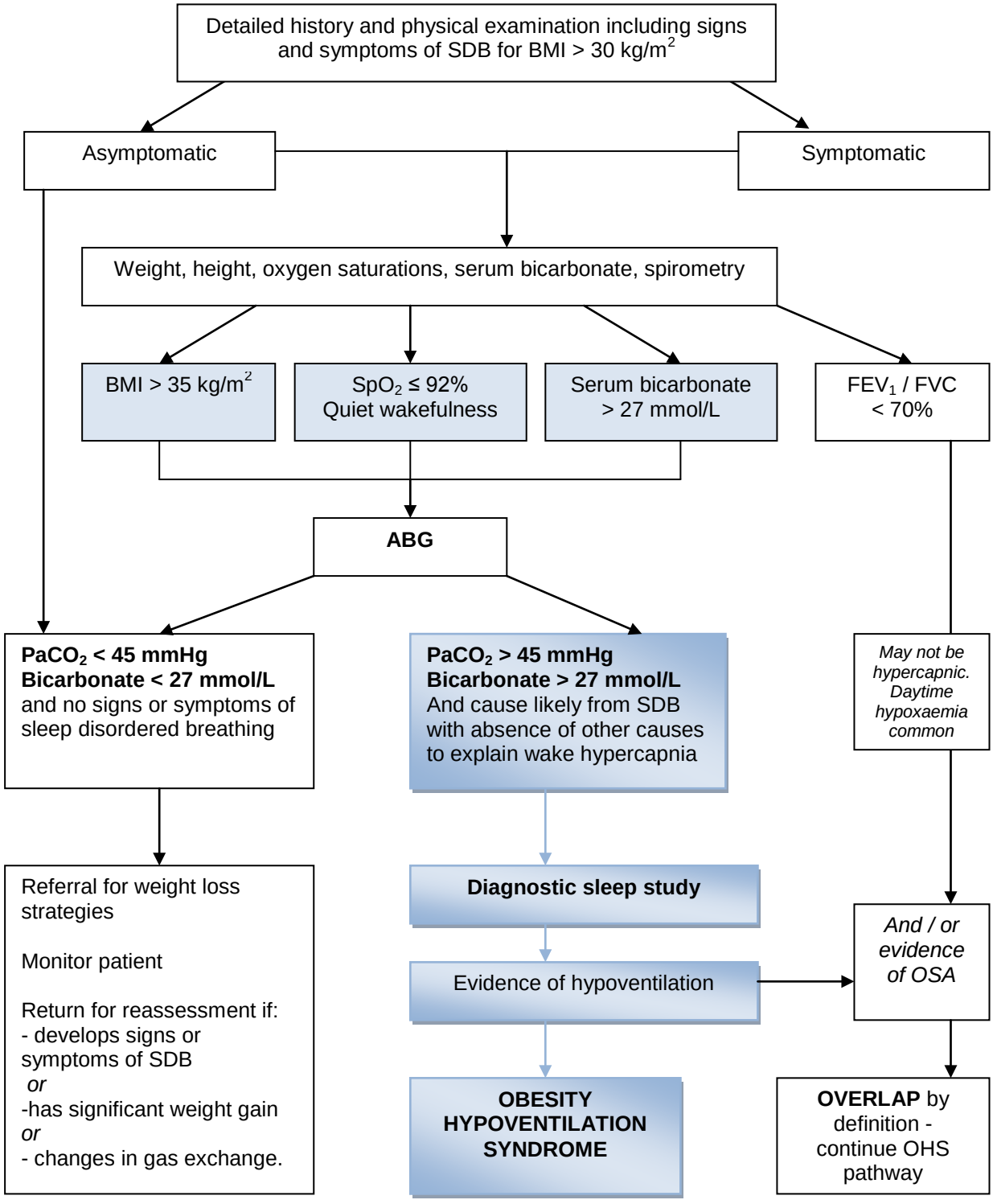
While there are several laboratory findings that are supportive of OHS, the definitive test for alveolar hypoventilation is an arterial blood gas (ABGs) [180, 187]. Elevated serum bicarbonate is common and reflects the metabolic compensation for chronic hypoventilation. In a large prospective study, only 3% of patients with a serum bicarbonate level <27 mmol/L were hypercapnic compared to 50% with a level >27mmol/L [187]. It has been suggested that serum bicarbonate could be used as a sensitive test to screen for hypercapnia [188]. Likewise, hypoxemia detected on pulse oximetry during quiet wakefulness should be a prompt the clinician to perform a blood gas to exclude hypercapnia [188]. Any abnormalities in thyroid function should be treated [189]. (See Figure 3 for protocol for functional evaluation of patients with obesity hypoventilation syndrome).

Overlap syndrome is defined as the combination of chronic obstructive pulmonary disease (FEV1/FVC ratio <70%) and sleep apnoea syndrome [190]. Hypercapnia is not necessarily seen in overlap syndrome, whereas daytime hypoxemia is common and more pronounced than in patients with OSA alone [191]. While BMI does not form part of the definition, patients with this disorder are generally overweight or obese [186]. Like OHS patients, those with overlap are at increased risk of developing pulmonary hypertension despite only mild to moderate daytime hypoxemia. Where an obstructive pattern is seen on spirometry, appropriate treatment for airways disease should be commenced [189]. There are no specific studies looking at therapy or outcomes in the subpopulation of hypercapnic overlap individuals. From a clinical perspective obese individuals with overlap and daytime hypercapnia are managed in a similar manner to those with OHS. Two studies evaluating therapy for OHS have included patients with an obstructive component and neither found a strong relationship between pulmonary function and change in diurnal blood gases [192, 193]. Therefore, in the remainder of this section hypercapnic overlap patients should be considered as part of the OHS grouping.

**Key points:**

- Need for greater clinician awareness of this problem in order to identify and treat OHS individuals at an earlier stage before presentation with acute respiratory compromise.
- Simple spirometry, $SpO_2$ and serum bicarbonate should be performed in all patients referred for SDB assessment when BMI is greater than 35kg/$m^2$.
- Thyroid function should also be assessed and any airflow limitation treated appropriately.
- Where bicarbonate is > 27mmol/L or $SpO_2 \leq 92\%$, an arterial blood gas should be taken.

**Figure 3: Protocol for Functional Evaluation of Patients with Obesity Hypoventilation Syndrome**



## 2.5.3 TREATMENT OPTIONS

Despite the high incidence of significant morbidity and increased mortality in patients with OHS and the well-documented improvement in daytime respiratory failure and symptoms achieved with reversal of abnormal sleep breathing events, there is scant data about optimal therapy modes in this population. In a retrospective study, Berger et al [192] identified a spectrum of respiratory disturbances during sleep in patients with OHS ranging from frank obstructive events, obstructive hypoventilation (i.e. hypoventilation with evidence of flow limitation) through to central hypoventilation. In that study, treatment aimed at correcting the specific ventilatory abnormalities resulted in improved daytime blood gases when patients were compliant with therapy [192].

### Oxygen therapy

Supplemental oxygen alone is not appropriate therapy in these individuals as it does not improve nocturnal hypoventilation, and may increase symptoms related to hypercapnia such as morning headaches and confusion [167]. However, daytime and/or nocturnal oxygen therapy may be needed initially in many individuals, as well as longer term especially in those with significant coexistent lung disease.

### Positive airway pressure

Most studies have reported the use of nocturnal NIV (either using a volume ventilator or bilevel support) in the management of OHS [184, 194-196]. However, ventilation is not needed in all patients to reverse daytime respiratory failure, and CPAP can be effective therapy for many [180, 197-200]. At present, short of titrating positive airway pressure and monitoring response, there are no clinical indicators available to predict those individuals in whom CPAP will be effective and those who will need NIV. In addition, no long-term follow up studies (i.e. >6 months) of those OHS patients managed with CPAP either as de novo treatment [197, 198] or following a period on bilevel support [184, 195], have been reported, so it remains unclear whether there are important clinical differences in outcomes with the two different forms of therapy over time [201]. To date, only three randomised trials of PAP therapy have been reported in this population [200, 202, 203]. In the first, patients were allocated to either CPAP or NIV set in the spontaneous mode. Both therapies were equally effective in correcting daytime respiratory failure and subjective daytime sleepiness, although there appeared to be a suggestion of better subjective sleep quality and greater improvements in some aspects of daytime function in those allocated to NIV [200]. In the second study, a randomised, cross over trial, two forms of NIV were compared in OHS patients failing CPAP [202]. While slight differences in nocturnal carbon dioxide levels were noted between the two modes, these differences did not affect daytime clinical outcomes. In the third study, standard bilevel pressure NIV in an S/T mode was compared to volume targeted bilevel pressure NIV in a single night randomised crossover study [203]. Although volume targeting improved control of nocturnal $CO_2$ and increased average nocturnal tidal volume and minute ventilation, this was at the expense of sleep quality and patient comfort. All studies have enrolled only small numbers of patients who were followed for 3 months or less. In addition, those individuals with a poor first night response to CPAP were excluded from the first two studies, limiting the extension of findings to the wider OHS population. Larger randomised trials over longer treatment periods are required to determine if important differences not just in daytime blood gases but other clinically relevant outcomes exist between the various modes of positive pressure therapy.

In patients with morbid obesity and coexisting conditions such as COPD or hemi-diaphragm weakness, exhalation out against CPAP at levels sufficient to control upper airway obstruction may be difficult or uncomfortable for the patient. In these circumstances, the expiratory pressure relief or C-Flex feature found on some CPAP devices may be advantageous and should be trialled. However, as inspiratory efforts are not supported by these devices, hypoventilation may persist. Such patients need to be carefully monitored during pressure titration [126].

**Key points:**

- Positive airway pressure should be first line therapy in OHS, although adjunctive oxygen therapy is likely to be required, at least initially, for a significant number of patients
- CPAP therapy is frequently effective in controlling sleep disordered breathing and improving daytime blood gases and symptoms

## 2.5.4 OUTCOMES

### Physiological

Unloading of the respiratory muscles has been proposed as one mechanism by which positive pressure therapy may confer clinical benefits in patients with chest wall restriction including those with OHS. Pankow et al [204] studied diaphragmatic pressure time product (PTPdi) as an indicator of energy expenditure during the application of NIV in 18 subjects with morbid obesity (BMI>40kg/$m^2$), six of whom had OHS, 7 OSA and 5 simple obesity. During baseline spontaneous breathing, PTPdi was similar in the simple obesity and OSA groups, but significantly higher in the OHS group. With the application of bilevel support, PTPdi was reduced by around 46% in all three groups, demonstrating that partial respiratory muscle unloading using bilevel support is possible even in the presence of severe obesity.

### Clinical

*Arterial blood gases*

A universal finding of all reports to date is the improvement in diurnal blood gases in OHS patients commenced on positive pressure therapy, with most patients being treated with bilevel support [184, 192-194, 200, 205]. To date, only one randomised trial has compared CPAP to bilevel support in OHS [200]. A significant improvement in awake $PaCO_2$ occurred with both therapies, with no significant difference in the change in $PaCO_2$ found between the two therapies over a 3-month treatment period. In a randomised crossover trial comparing the impact of 6 weeks bilevel support in a spontaneous/timed mode to bilevel support in a spontaneous/timed mode with average volume assured pressure support (AVAPS) in OHS patients failing initial CPAP therapy, both forms of bilevel therapy improved nocturnal oxygenation [202]. Although the bilevel mode with AVAPS provided a more efficient reduction in overnight $TcCO_2$ than standard bilevel support in a spontaneous/timed mode, the lower carbon dioxide during sleep did not translate into further clinical benefits with regards to sleep quality or health related quality of life (HRQoL).

*Lung function*

Individuals with OHS have a marked restrictive ventilatory pattern, with reductions in total lung capacity (TLC), vital capacity (VC) and expiratory reserve volume (ERV), while $FEV_1$/FVC remains >70%. There are few reports on changes in pulmonary function following PAP therapy, and all relate to the use of bilevel ventilatory support [184, 185, 194, 206]. While some studies found no change in pulmonary function [184, 185, 195], in a large prospective study of 35 patients, significant improvements in TLC, VC and ERV were seen following 12 months of therapy without a significant change in BMI [206].

*Symptoms and daytime function*

Symptoms such as sleepiness, morning headache, dyspnoea and morning confusion are common in OHS and improve significantly with therapy [184, 185]. Both CPAP and NIV therapy provide significant improvements in subjective daytime sleepiness as measured by the ESS [184, 198, 200, 205], with no differences between therapies [200]. One study has suggested that patients with more marked REM hypoventilation at baseline are the sleepiest and demonstrate more significant improvement is objective daytime sleepiness after receiving short-term NIV [205].

Polycythaemia, a common finding in severe OHS, is also improved with NIV therapy [206], although this has not be studied in patients managed with CPAP.

*Sleep Quality*

Few studies have systematically reported on the changes in objective sleep quality that occur with PAP therapy in this population. Generally, baseline sleep efficiency is around 70-75%, with a high proportion of Stage I sleep and reduced REM sleep [186, 197, 200, 205]. With CPAP or NIV, sleep efficiency is not significantly different, but the amount of Stage I sleep [202, 205] is reduced while the proportion of REM sleep increases [197, 200, 205]. Using the PSQI, patients reported improvements in subjective sleep quality if allocated to NIV compared to CPAP, but this did not result in differences in other clinical outcomes or compliance with therapy [200].

### Quality of life

Patients with OHS have significantly impaired health related quality of life (HRQoL) compared to the general population [198, 200], and to patients with OSA with respect to social functioning [198]. This latter finding has been attributed to the more severe degree of daytime sleepiness seen in patients with OHS [198]. Significant improvements in HRQoL occurs once therapy is commenced either with CPAP [198, 200] or NIV [198, 200] as measured by the SF-36, with significant within group improvements in vitality scores occurring with both forms of short-term PAP therapy [200]. However, significant within group improvements in other health dimensions were seen only in patients randomised to NIV (Physical Functioning, Role-Physical and Social Functioning). Between group differences in the two forms of PAP therapy could not be demonstrated, probably due to the wide variability in responses and small number of patients studied [200]. In comparing two modes of NIV support, Storre et al [202] used a disease specific scale, the Severe Respiratory Insufficiency questionnaire (SRI). Although they identified one form of NIV was more efficient in reducing nocturnal and daytime carbon dioxide than another, this did not translate into further benefits with regard to sleep quality and health related quality of life, with both therapies providing substantial benefits. Future studies should more fully address quality of life issues in this population and the impact of different PAP therapies on health outcomes over the longer term.

### Hospitalisation and health care utilisation

Compared to individuals with similar degrees of obesity and the general population, patients with OHS are higher uses of health care resources [183] and are more likely to require hospitalisation [6, 183]. In one study, 70% of individuals with OHS had been hospitalised at least once in the 12 months prior to being diagnosed and treated [183]. Once hospitalised, patients with OHS have higher rates of intensive care admission and are more likely to require invasive ventilation than patients with equal degrees of obesity but who maintain eucapnia [182]. Several studies have shown that the use of NIV in the form of bilevel ventilatory support can significantly reduce the need for hospitalisation once NIV is commenced [6, 183]. In a prospective study, the number of days spent in hospital decreased significantly between the year before commencing NIV and the following 3 years [6].

### Mortality

If these patients are left untreated, they are at markedly increased risk of death. In a prospective study, 23% of hospitalised patients with morbid obesity and hypercapnia followed after discharge died within an 18 month period. This compares to a 9% death rate for equally obese eucapnic individuals [182]. A retrospective study reported 7 of 15 patients with OHS refusing therapy died over a 4-year period [184]. In contrast, of the 54 patients compliant with therapy, 3 died within the same time period. Longitudinal studies suggest a 2 and 5 year survival rate of around 92 and 88% in patients using bilevel support [6, 207]. Although a significant number of patients with OHS may be initially managed with CPAP or transferred to this therapy following acute bilevel use, long-term data regarding survival outcomes in this group have not been reported. Most deaths in OHS appear to be due to cardio-pulmonary disease [207].

### Compliance

In patients willing to use NIV, compliance with therapy appears to be good with a mean nightly use of 6.2 hrs at 12 months and 6.8 hrs at 24 months reported [206]. In the short-term trial comparing CPAP to NIV, no difference in compliance was found, again with a mean nightly use of around 6 hours found [200]. Irrespective of the mode of PAP therapy used, improvement in daytime blood gases appears to be directly related to the daily dose of PAP used [193], with those using PAP for >4.5hrs/day experiencing larger improvements in $PaCO_2$ and $PaO_2$ compared to less adherent patients. In addition, improvements occur and plateau at around 1 month after the commencement of treatment. One prospective study following 71 patients over a 7 year period found 11% used therapy less than 3.5 hrs/day, while non-compliance was around 10% [6].

### 2.5.5 INDICATIONS FOR NIV

i) Presence of daytime hypercapnia with an arterial blood gas of ≥45mmHg

***OR***

ii) Failure to respond to a trial of CPAP as evidenced by

- Persisting sustained oxygen desaturation during sleep in the absence of upper airway obstruction

***OR***

- An increase in nocturnal or daytime $CO_2$ ≥8mmHg despite elimination of obstructive events on CPAP

***OR***

iii) Persisting significant daytime hypercapnia despite adequate compliance with CPAP therapy (>4hrs/day)

### 2.5.6 IMPLEMENTATION AND TITRATION

Although autoadjusting devices (APAP) may be used to titrate CPAP in OSA, this approach is not recommended in individuals with OHS [180, 208], as the algorithms identifying abnormal respiratory events cannot recognise hypoxemia or hypoventilation. In addition, up to 50% of patients with OHS may require initial oxygen therapy in addition to PAP therapy, and this will need to be added appropriately. With the increasing number of morbidly obese individuals in the community and an increasing trend towards use of simplified screening and home treatment of sleep apnoea, the importance of clinicians recognising this disorder and referring patients for supervised titration needs to be highlighted.

In stable patients a full polysomnogram (PSG) should be undertaken to identify the underlying sleep disorder and to individualise treatment to correct the primary breathing abnormality [184, 192, 193]. Although no standard protocol for PAP titration currently exists, most reports in the literature suggest commencing in a CPAP mode, increasing the pressure to abolish apnoeas, hypopnoeas and flow limitation [180, 192, 199]. If oxygen saturation remains low, IPAP is added to improve oxygenation above 90%, using the lowest CPAP pressure that eliminated obstructive apnoeas and hypopnoeas (i.e. EPAP) and increasing IPAP above this level until $SpO_2$ is above 90% or high pressures (20-22cm$H_2O$) are reached [199]. Oxygen therapy is then added if significant oxygen desaturation persists [193, 199]. However, it should be noted that in individuals with only moderate daytime respiratory failure ($PaCO_2$<55mmHg), complete resolution of abnormal nocturnal events on the initial titration night does not appear to be essential for longer-term improvements in the clinical status of the patient to occur [200, 202]. Therefore, until larger studies are available, a reasonable approach would be to commence CPAP as initial therapy in those patients with only moderate awake respiratory failure ($PaCO_2$<55mmHg), or where rises in nocturnal $TcCO_2$ on CPAP <10mmHg occur [200]. In these individuals, a clinical review at one month should be undertaken to monitor blood gases, compliance and clinical response [180, 193]. In those with more severe daytime or nocturnal respiratory failure ($SpO_2$<80% or rise in $CO_2$>8mmHg despite CPAP), bilevel ventilatory support should be used initially, with a CPAP re-titration after a 12-week period to determine whether an adequate response to CPAP is achievable [184, 196, 200, 201, 209]. (See Figure 4 for overview of titration and review in OHS).

In up to 30% of cases, commencement of therapy occurs during an acute episode of decompensation [8]. Although both CPAP [184, 210] and NIV [184] have been used successfully in decompensated patients with OHS in these individuals, NIV has been recommended first line therapy in this group [211]. Once stable, diagnostic and titration studies can be scheduled, following the same management algorithm as outlined above.

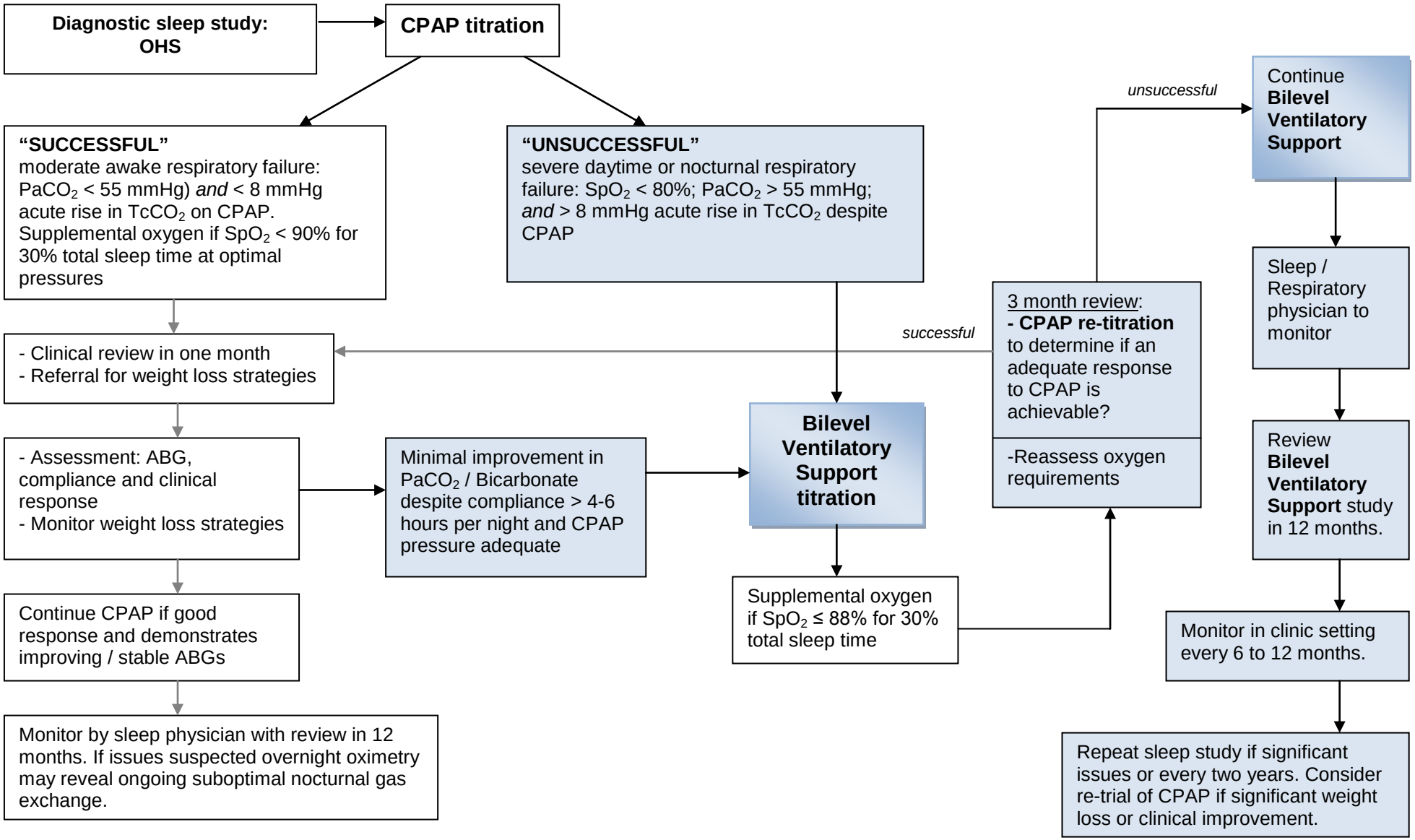
Around 40-60% of individuals are likely to require oxygen in addition to their PAP therapy, at least initially [184, 193]. However, this can be removed in a significant number of patients once daytime respiratory failure resolves [184, 193, 200]. At this time it remains unclear what the clinical implications of isolated nocturnal desaturation are and what level/dose of persisting desaturation is required for clinical consequences to emerge [199]. $SpO_2$ ≤ 88% for 30% of TST has generally been used as the criteria for initiating or continuing nocturnal oxygen in Australia [175]. In patients with moderate or

severe co-existent COPD, marked daytime hypoxemia may persist despite effective nocturnal therapy [212]. If patients meet the criteria for daytime oxygen therapy [175], then this will need to be prescribed and used appropriately long term.

**Key points:**

- Autotitrating and home studies are not appropriate for this patient group.
- A full PSG should be performed during manual CPAP titration in these patients to identify the nature of the sleep disordered breathing and response to CPAP pressure.
- Many individuals will respond to initial intervention with CPAP, even in the presence of severe nocturnal desaturation. Therefore, titration should commence in CPAP mode to document the patient's response to therapy.
- When NIV is used as initial therapy, a review on CPAP 8-12 weeks later should be undertaken as many individuals are able switch to simpler therapy.
- Acutely decompensated patients should be managed initially with NIV, with a trial of CPAP once clinical stability and improved awake $CO_2$ have been achieved.
- The need for additional oxygen therapy should be assessed initially and again once established on PAP therapy.
- Ongoing compliance with therapy should be monitored regularly.

**Figure 4: Obesity hypoventilation syndrome – titration and review**



### 2.5.7 FOLLOW UP AND ANCILLARY MANAGEMENT

Once treatment is commenced, early follow up to determine adherence to therapy and to monitor ABGs is essential. The improvement in symptoms and blood gas levels appear to be related to adherence with PAP therapy [193]. Reports from both uncontrolled [184, 195, 199] and randomised trials [200] have demonstrated that once the patient is stable after initial bilevel therapy (2-3 months of treatment), a significant number of individuals may be maintained longer term on CPAP alone. Substantial cost savings may be achieved by changing from bilevel to CPAP therapy and discontinuing oxygen therapy if it is no longer indicated [201]. However, ongoing suboptimal nocturnal gas exchange on therapy cannot be identified from daytime or evening blood gases alone [199], and direct assessment of nocturnal oximetry has been recommended [199].

**Weight loss**

In the long term, weight reduction is the preferred solution to OHS, resulting in improved lung function [213], sleep disordered breathing and awake ventilation [214]. In addition, surgical intervention has also been associated with improvements in a number of comorbidities related to morbid obesity such as pulmonary hypertension [215], diabetes and hyperlipidemia [216]. However, data from the Swedish Obesity Subjects trial suggests that some of these improvements are less marked at 10 years compared to 2 years, although they remain significant [217].

However, patients with OHS are at increased risk of death primarily from post operative respiratory failure and pulmonary embolism [218]. Consequently, assessment and management of these individuals with PAP therapy in the post operative period has been recommended to avoid respiratory failure [188]. There is no evidence that PAP therapy postoperatively increases the risk of anastomotic breakdown [219].

Currently, the lack of publicly funded services for bariatric surgery means that most individuals with OHS will not be able to access this form of therapy. Therefore, weight loss efforts need to be directed towards dietary advice, exercise and lifestyle changes, with referral of the patient to available hospital or community based programs. Long lasting weight reduction in severely obese individuals is associated with a positive improvement in HRQoL, with a maintained weight loss of around 10% sufficient to achieve these effects [220]. If significant weight loss occurs over time, review PAP studies should be undertaken to determine whether a switch to CPAP or no therapy is possible [184].

**Key points:**

- Dietary advice and life style modification should be encouraged to promote weight loss and improve markers of cardiovascular disease
- Referral to other health providers may be needed to supervise weight loss and exercise programs

| RECOMMENDATIONS FOR OBESITY HYPOVENTILATION SYNDROME | Grade |
|---|---|
| Simple spirometry, $SpO_2$ and serum bicarbonate should be performed in all patients referred for SDB assessment when BMI is greater than 35kg/$m^2$. | C |
| Arterial blood gases should be obtained in those individuals where $SpO_2$ is ≤ 92% or where the serum bicarbonate is >27mmol/L to confirm the presence and severity of hypoventilation. | C |
| Thyroid function should also be assessed and any airflow limitation treated appropriately. | D |
| Positive airway pressure is first line therapy in patients with OHS, although adjunctive oxygen therapy is likely to be required, at least initially, for a significant number of patients. | C |
| Autotitrating and home studies are not appropriate for this patient group. | D |
| A full PSG should be performed during manual titration in order to identify the nature of the sleep disordered breathing and response to CPAP pressure. | B |
| Many individuals will respond to initial intervention with CPAP. Titration should commence in CPAP mode to document the patient's response to abolition of upper airway obstruction alone. | A |
| Complete correction of sleep disordered breathing during the initial titration night is not necessary for improvement of daytime blood gases and symptoms to occur | B |
| Indications for NIV in OHS include an awake $PaCO_2$ >45mmHg and failure of CPAP therapy as evidence by either sustained oxygen desaturation during sleep or an increase in nocturnal daytime or nocturnal $CO_2$ >8mmHg. | D |
| Individuals initially using bilevel support should be reviewed again after 3 months on therapy and CPAP retried, since a significant number may be switched to CPAP without clinical deterioration. | B |
| In patients placed on CPAP in whom awake $PaCO_2$ at baseline was 45-55mmHg, a clinical review at one month with repeat blood gases should be performed. | D |
| Continued oxygen therapy during PAP is not required by all patients and this should be reviewed. | B |
| Bilevel support should be used as initial therapy in patients presenting with acute decompensated respiratory failure. After 3 months, a CPAP titration should be undertaken to determine long term therapy. | D |
| Outcome measures should include awake ABGs, nocturnal $SpO_2$ and assessment of daytime sleepiness, breathlessness and health related quality of life. | C |
| Once established on therapy, regular monitoring of compliance data should be performed. | C |
| All patients should be advised on appropriate dietary and lifestyle changes to promote weight loss and referred to appropriate programs where possible. | D |
| The need for and type of nocturnal PAP therapy should be reassessed if significant weight loss occurs. | D |

# CHAPTER 2.6 CHRONIC OBSTRUCTIVE PULMONARY DISORDER

**DANIEL FLUNT**

## 2.6.1 BACKGROUND

COPD is a very common respiratory disorder, with the majority of patients presenting with hypoxemic respiratory failure requiring oxygen therapy. However, a small proportion will develop awake hypercapnia. While there is a substantial body of evidence to support the use of NIV for acute exacerbations of COPD in the hospital setting, the evidence for domiciliary use is less convincing. Although the role of home NIV in chronic hypercapnic COPD still a topic of debate [221], the technique is widely used, with 38% of patients prescribed home NIV in Europe having COPD as the primary reason for therapy [2].

A Cochrane meta-analysis [222] concluded that nocturnal NIV for at least 3 months in hypercapnic patients with stable COPD had no consistent clinically or statistically significant effect on lung function, gas exchange, respiratory muscle strength, sleep efficiency or exercise tolerance. However, a systematic review suggested that there may be a supportive role of NIV in a selective subset of severe stable COPD patients [223].

One study demonstrated significant improvements in awake blood gases and quality of life using NIV plus oxygen compared to oxygen therapy alone [224] over a 3-month period. In contrast, a later trial found that over a 12-month period, NIV did not affect the natural course of the disease and was of marginal benefit only [225]. However, this study enrolled patients based on lung function ($FEV_1$ < 45% predicted) rather than the presence of hypercapnia or nocturnal hypoventilation. In a larger Italian trial, 90 stable hypercapnic patients were randomised to NIV and LTOT or LTOT alone and followed over a 2-year period [226]. These investigators found a small improvement in awake blood gases, and significant improvements in dyspnoea and health-related quality of life in the NIV treated group compared to those on LTOT alone. In addition, although hospital admissions were not different between the groups during the follow up period, overall hospital admissions decreased by 45% in the NIV group and rose by 27% in the LTOT group when compared to the 3-year period preceding the study. In a quasi-experimental study comparing patients tolerant or declining/intolerant of NIV, improvements in dyspnoea and daytime sleepiness [227] following the use of NIV were reported. Likewise, significant improvements in HRQoL as measured by the SF-36 occurred with NIV, with improvements apparent in most domains, except for bodily pain [227]. In this study, days in hospital were also significantly reduced, although no effect on the number of exacerbations were found. In a cost and consequences analysis of patients with recurrent acidotic exacerbations of COPD who tolerated and responded well to NIV in hospital, it was shown that domiciliary NIV was effective in reducing admissions and minimising acute care costs [33]. One randomised controlled trial has demonstrated that nocturnal NIV may improve survival in oxygen dependent hypercapnic COPD patients, but in contrast to other findings, appears to be at the cost of worsening quality of life [228].

A key point from the GOLD 2007 executive summary [229] regarding the management of stable COPD is that the “overall approach to managing stable COPD should be individualised to address symptoms and improve quality of life”. The document also recommends that the selection of therapies, whilst being guided be the degree of airflow limitation, should be predominantly based on symptoms, clinical presentation and willingness to apply the recommended management. Specifically with regard to NIV therapy in severe stable COPD, health related outcomes to date have been the least studied outcomes in the literature [223]. However, for these patients, improvements in the severity of their disability may be more important than improving physiological outcomes or prolonging life [230].

A recent overview of the literature [231] concluded that in patients with COPD and hypercapnic respiratory failure using NIV, when sufficient pressure support and adequate compliance was achieved, beneficial effects with regard to physiological measures and some health-related outcomes can be realised. It may be inappropriate to base the decision to undertake domiciliary NIV on $PaCO_2$

alone and that patients requiring recurrent admissions for hypercapnic decompensations, life-threatening events or high risk for death should also be considered for long-term NIV [231].

Until more controlled trials are performed to define the role of NIV in stable hypercapnic COPD, it generally appears that the use of NIV is indicated in a small number of patients with stable COPD who are hypercapnic and demonstrate nocturnal hypoventilation unresponsive or made worse by oxygen therapy.

**Key points:**

- Whilst there is strong evidence for the use of NIV in acute exacerbations of COPD, the use of NIV as routine care in chronic hypercapnic COPD remains equivocal.
- Positive studies using NIV in chronic stable COPD have attributed success to higher inspiratory pressures, adequate compliance, higher baseline $PaCO_2$ and patient selection including recurrent admissions for hypercapnic compensations or life threatening events.
- Improvements in HRQoL may be more important than improving physiological outcomes.
- NIV is indicated in stable COPD where nocturnal hypoventilation is unresponsive or made worse by oxygen therapy.

## 2.6.2 TREATMENT OPTIONS FOR THE MANAGEMENT OF STABLE COPD

### Oxygen therapy

Long term oxygen therapy (LTOT) or the use of oxygen for >15 hours a day has been shown to increase the survival in patients with chronic hypoxaemia and COPD [232]. Maintaining $PaO_2$ within a more desirable range at rest (to at least 60 mmHg) can prevent end organ damage and LTOT may also be beneficial by dampening exercise induced oxidative stress [233]. However, oxygen alone is not appropriate when hypoxaemia is primarily caused by hypoventilation. In this case adding further oxygen can permit hypoventilation to continue, resulting in a worsening of carbon dioxide retention.

### Smoking cessation

Smoking cessation is the most effective way to reduce exposure to COPD risk factors and to stop its progression [229]. It is also very cost effective and randomised controlled trials have shown that both health education and pharmacotherapies can assist smoking cessation [229].

### Pharmacologic treatments

None of the current medications prevent the long-term decline in lung function and ultimately survival in COPD [229, 234]. The main role of drug therapy is symptomatic prevention and control, reducing the severity and frequency of exacerbations and improving exercise tolerance [229]. It has been recommended that all patients are pharmacologically optimised prior to commencing NIV [106].

### Pulmonary Rehabilitation

In a recent evidence based guidelines [235] the panel concluded that there was high-grade evidence (including randomised controlled trials) that pulmonary rehabilitation improves dyspnoea and health related quality of life in patients with COPD. They also provided a weak recommendation that pulmonary rehabilitation reduces the number of hospital days. Whilst a population cohort study demonstrated that patients with COPD engaging in low to high levels of physical activity have a lower risk of hospitalisations and mortality compared to the very low physical activity group [236], there is generally insufficient evidence to determine if pulmonary rehabilitation improves survival in COPD [235].

**Surgery**

*Lung volume reduction surgery*

A large multi centre trial (1218 patients) comparing LVRS with medical treatment showed that after 4.3 years, patients with upper lobe involvement and worse pre-surgery exercise capacity had a greater survival rate when compared to COPD patients who only received standard medical therapy (54% versus 39.7%) [237]. However, patients with better pre-surgery exercise tolerance demonstrated no survival advantage. Consequently, LVRS is regarded as an expensive palliative procedure and is only suitable for carefully selected patients with COPD [229].

*Lung transplantation*

Non-randomised trials and observational studies have shown that lung transplant in appropriately selected patients with advanced COPD can improve quality of life and functional capacity [229]. Significant complications after lung transplant impairs survival, with survival being reported as approximately 80% at 1 year, 50% at 5 years and 35% at 10 years [238]. Clinically, domiciliary NIV has been indicated in patients with severe lung disease, as a bridge to transplant.

**Key points:**

- Oxygen therapy when used for >15 hours a day has been shown to increase survival.
- Smoking cessation is the most effective way to reduce exposure to COPD risk factors and to stop its progression.
- The main role of pharmacotherapy in stable COPD is for symptomatic prevention and control. However, it has not been shown to improve survival.
- Pulmonary rehabilitation is important in improving dyspnoea and HRQoL.
- Lung volume reduction surgery has mixed impact on survival depending on location of lobar involvement and pre-surgery exercise capacity.
- Lung transplant in appropriately selected patients with COPD can improve quality of life. However, significant complications can arise which will impair survival.

## 2.6.3 OUTCOMES OF NIV

**Survival**

Only one randomised controlled trial has demonstrated that nocturnal NIV in stable, oxygen dependent, hypercapnic COPD patients improves survival [228]. These findings were based on a Cox model which was adjusted for baseline $PaO_2$, $PaCO_2$ and respiratory quality of life measurements. With respect to other prospective controlled trials, no survival benefit has been found with the use of NIV in COPD, compared to LTOT alone [225, 226, 239-241]. However, these trials have been critiqued as having small groups of patients, inadequate patient selection, ineffective ventilation efficacy, poor compliance or short-term follow-up [230, 242].

Observational studies with adequate pressures and compliance in patients with significant airways obstruction and hypercapnia have demonstrated a survival benefit [242] or increased survival when compared against historical survival data from previous LTOT trials [243]. One study which compared 140 patients with severe persistent hypercapnic COPD ($FEV_1$ = 28.7 ± 8.7 % predicted, $PaCO_2$ = 60.1 ± 9.2 mmHg) which used NIV versus 41 which did not, demonstrated one and two year survival rates of 87.7% and 71.8% in the NIV group respectively, versus 56.7 and 42.0% in the non-users group, respectively [242]. Survival rates remained significantly higher in the NIV group even after adjusting for BMI, haemoglobin levels, LTOT and age. The findings of this study may have been attributed to the ventilator parameters used (IPAP=21.0 ± 4.0 cm $H_2O$, EPAP= 4.5 ± 1.4 cm$H_2O$ and back-up rate = 17.3 ± 2.5 breaths/min) and compliance (6.4 ± 2.6 hours/day). In addition, further stratification revealed that greater benefits in survival were seen in those patients where physiological measures

showed a base excess > 8.9 mmol/L, pH < 7.41, $FEV_1$ < 27.5% predicted, RV/TLC 73% or haemoglobin < 13.8 g/dL [242, 244].

Long term NIV has also been associated with a survival advantage in COPD patients which have been discharged home post successful tracheostomy decannulation after a prolonged period of invasive ventilation [245]. After correcting for age and length of stay, survival advantage has been calculated at 0.48 and median survival for patients receiving NIV was 3.3 years compared to 1.6 years for those discharged without it. This suggests that long term NIV using reasonable pressures (mean inspiratory pressure = 28 cm $H_2O$) could protect the patient during subsequent exacerbations.

**Physiological**

*Arterial Blood Gases*

In a Cochrane meta-analysis [222] only one [224] of the four [224, 225, 240, 241] randomised controlled trials included showed improvements in daytime arterial blood gases. A recently published randomised controlled trial involving 144 patients also demonstrated no significant differences in arterial blood gases between the LTOT and LTOT + NIV group at 12 months [228]. However, as discussed in previous sections potential confounders included lower levels of hypercapnia (including patients with normocapnia [225]), lower pressure trials with IPAP-EPAP differences between 8 -13 $cmH_2O$ [225, 228, 240, 241] and short duration trials [240, 241]. In trials where improvements in daytime arterial blood gases occurred, there were higher baseline $PaCO_2$ levels (>54 mmHg), higher pressures used and compliance was greater than 6 hours per day [224, 226, 246].

Higher mean inspiratory pressures have been successful in reducing hypercapnia, even to levels of normocapnia. One study which used a mean inspiratory pressure of 28 $cmH_2O$ showed a reduction in $PaCO_2$ from 53.3 ± 4.8 to 46.4 ± 7.0 mmHg [247] and another study aiming for normocapnia (40 mmHg) demonstrated that mean pressures of 30.4 $cmH_2O$ achieved normocapnia within 8.8 days from a baseline of 59.5 mmHg [248]. The COPD patients in these studies had mean $FEV_1$ values of 1.03 [247] and 0.97 L [248]. However, it is possible that these studies were looking at patients with an element of obesity related sleep disordered breathing, as the mean body mass indices were 28.3 and 29.4 $kg/m^2$, respectively. Interestingly, the pressures were well tolerated and compliance remained excellent at 6 months [247] and over a 2 year period [248].

Reductions in bicarbonate, a marker of chronic hypercapnia have also been shown. After a month of therapy at IPAP= 15.3 and EPAP= 5.4 $cmH_2O$ with compliance at 9 hours, in comparison to a control group, a group of COPD patients demonstrated significant reductions in $PaCO_2$ (54.1 ± 4.5 to 44.6 ± 5.6 mmHg, p <0.0001) with a corresponding reduction in bicarbonate (35.3 ± 3.7 to 29.2 ± 3 mmol/L, p< 0.0001) were demonstrated in the first month [227]. These findings remained until the twelfth month.

*Lung function*

Most studies report no significant improvements in spirometric values or lung volumes with the long term use of NIV in COPD [227, 228, 249-251]. Small but significant increases in MIP have been recorded [246, 251] and reductions in measures of dynamic hyperinflation have been noted [252-254].

*Dynamic Hyperinflation*

The use of NIV in COPD has also been beneficial in significantly reducing measures of dynamic hyperinflation and inspiratory mechanical workload. A randomised controlled trial comparing NIV (3 hours a day, 5 days a week for 3 weeks), to sham bi-level found statistically significant reductions in dynamic hyperinflation with reductions in total lung capacity, functional residual capacity (FRC) and residual volume by 10, 25, and 36% of their predicted value respectively [252]. The changes in $PaCO_2$ were most strongly correlated to changes in dynamic intrinsic positive end-expiratory pressure ($r=0.72$; $p < 0.0001$). Another study had similar findings with reductions in $PaCO_2$ not being related to increase muscle strength but was significantly correlated with a decrease in gas trapping [253].

In a study looking at the long term application of nocturnal NIV, a decrease in hyperinflation in terms of RV:TLC ratio has also been observed with the reduction in hyperinflation being accompanied by significant improvements in arterial blood gases [254]. Interestingly no significant correlation was found between changes in $PaCO_2$ and IPAP for all patients, however, for patients with the most severe

hyperinflation (RV/TLC >75%), changes in $PaCO_2$ were significantly correlated to inspiratory pressure. These findings suggest that stable COPD patients with higher levels of dynamic intrinsic PEEP may be part of the subset which may benefit from NIV from a reduction in dynamic hyperinflation by producing a slower more effectual breathing pattern [223, 252].

**Quality of life measures**

The importance of evaluating health related quality of life in patients with chronic and non-curable disorders, such as COPD, has been highlighted as being essential in evaluating the human and financial costs and benefits of modern modalities in health care practice [255]. A recent systematic review shows that whilst health related quality of life is one of the least studied outcomes, it shows consistent evidence of improvement with NIV in severe stable COPD [223]. In contrast to this, the largest randomised controlled trial which post dates this review showed that the addition of NIV to usual care in COPD patients resulted in deterioration in general and mental health and some aspects of mood [228].

*Sleep parameters*

Significant increases in sleep efficiency and total sleep time have been observed in patients with COPD after commencing NIV. With regard to short term effects, one study comparing two nights of either NIV (IPAP = 22 ± 0.3 cmH2O, EPAP= 3 ± 1 $cmH_2O$) or CPAP (5 $cmH_2O$) demonstrated that sleep efficiency improved from 63 ± 7 to 81 ± 4% and total sleep time significantly improved from 205 ± 33 to 262 ± 28 minutes in the NIV group [256]. Significant increases in these measures have also been recorded after 3 months [224] and after 6 months use where sleep efficiency increased by 5% (range -3 to +30%) and total sleep time increased by 72.5 minutes (range +21 to +204 minutes) [257].

Contrary to the above findings, a RCT noted a decrease in sleep efficiency in their seven patients after 3 months of NIV [241]. However, baseline $PaCO_2$ was only 46 mmHg in this series, suggesting that sleep quality was worse due to the burden or disruption of nocturnal NIV outweighing any potential benefits of therapy.

*Health related quality of life questionnaires*

The Medical Outcome Trust 36-item short form health survey status (SF-36) is a well validated questionnaire [258, 259] and to date has been the most commonly used English language multipurpose survey of general health status in COPD receiving long-term NIV [227, 243, 260, 261]. A recent study which used SF-36 to compare compliant NIV to a control group to assess quality of life showed that NIV provided significant improvements in physical and mental component summary scores [227]. These authors also noted that it was the improvements in dyspnoea that was the major determinant of the improvements in the quality of life and that total hours spent on the ventilator per day was an independent predictor of dyspnoea. Another randomised controlled trial also found that NIV significantly improves dyspnoea over LTOT alone [226]. Contrary to these findings, one randomised controlled trial suggested that patients treated with NIV had poorer SF-36 general and mental health component summary scores, and reported less vigour, more confusion and bewilderment as assessed by a Profile of Mood State questionnaire [228]. Whilst changes in SF-36 have been noted after the initiation of NIV, at times these changes have been small [243]. This could be due to the scale not specifically covering the impact of chronic hypercapnic respiratory failure on COPD [255].

Other health related quality of life questionnaires have also been used in the assessment of NIV in COPD. The St George respiratory questionnaire revealed no improvements in HRQL after the initiation of NIV [226] and this was most likely due to the scale not being sensitive enough for patients with more severe COPD [228, 255]. On the other hand, the Maugeri Foundation Respiratory item set (MRF-28), a scale which has been designed for patients with chronic respiratory failure secondary to pulmonary and chest wall disorders, showed some improvements in the same study [226], possibly because it covers a broader scale range in these patients [255].

The Severe Respiratory Insufficiency Questionnaire (SRI), a multidimensional and highly specific tool with high psychometric properties for HRQoL assessments in respiratory failure patients, has recently been validated for COPD patients with severe chronic respiratory failure on home ventilation [255, 262]. Whilst it appears to be a suitable instrument that reliably allows for longitudinal assessment of

HRQoL in COPD on domiciliary ventilation, researchers and clinicians are awaiting a validated English version. Until then, the SF-36 and possibly the MRF-28 appear to be the most suitable choice for monitoring HRQoL changes in patients with COPD on long term ventilation.

### Hospitalisation

A reduction in hospital admissions after the commencement of NIV has been shown in retrospective audits and controlled trials. Studies have shown significant reductions in hospital admissions from 5 ± 3 to 2 ± 2 per patient per year [33], a halving of two (range 0-5) admissions per year after one year [249] and a RCT showed that in comparison to the period before the start of the study, hospital admissions decreased by 45% in the NIV group whereas they increased by 27% in the LTOT group [226]. However, no significant differences in hospital admissions [228], exacerbation rates or need for endotracheal intubation with the use of NIV have been shown [225] in other studies.

### Compliance

Many COPD patients tolerate NIV poorly, and adherence to NIV is lower than in patients with restrictive disorders [124, 260]. Drop-out rates of 23 to 63% been reported in controlled trials [226, 239-241].

Some investigators report using lower pressures to increase patient tolerance and in turn compliance. Whilst lower pressures are usually trialled in the initial acclimatisation phase they have not always been associated with improved compliance. After a three month trial at pressures of IPAP=10 and EPAP=2, only 4/7 patients completed one trial [240]. Conversely, excellent compliance rates have been documented at much higher inspiratory pressures [224, 247, 248].

Currently there are no randomised controlled trials comparing inpatient versus outpatient NIV acclimatisation which include COPD patients. With respect to other studies, compliance has been generally been more successful when an intensive inpatient acclimatisation to NIV has occurred [124, 224, 226, 247, 249]. In a study where acclimatisation to NIV was carried out over thirteen days a follow up visit at 2 months showed that only one of 37 patients dropped out due to noncompliance [247]. In another study inpatient acclimatisation led to only 11.1% rejecting NIV and only 6% using NIV for less than 3 hours /day [242]. In a study by Jones and colleagues [249], median stay in hospital was three days, but four patients were discharged on the same day. Three of these patients who received less intensive training, chose to discontinue therapy or were removed from NIV secondary to poor compliance.

In contrast, another study found that only 50% of COPD patients continued to use NIV during a follow up period of approximately 6 months, despite enrolment in a comprehensive inpatient and outpatient programme [124]. Outpatient acclimatisation has demonstrated poorer compliance rates in COPD [230]. Closer supervision combined with greater time spent practicing in the inpatient environment appears to be the reason why NIV compliance is greater in the more structured in hospital setting [263].

Excellent compliance has also been shown when patients experience relief of their daytime symptoms such as morning headache, daytime somnolence or improved sleep quality. In 11 patients with COPD and BMI mean 33.3 $kg/m^2$ (with 6 experiencing significant sleep hypoventilation), there were no withdrawals from the study and usage averaged 6.5 hours of NIV per night [249]. This was attributed to all patients experiencing relief of their symptoms. Similarly, Elliott et al [257] reported that 7 out of 12 patients who continued with NIV after 12 months (one died) had greater symptoms at baseline and therefore wanted to continue to experience the perceived benefit.

**Key points:**

- Only one randomised controlled trial has demonstrated a survival benefit with the routine use of NIV, although this was at the expense of quality of life.
- Observational studies have shown increased survival compared to historical controls, especially when significant pressures are used in compliant patients with significant lower airway flow limitation, dynamic hyperinflation or higher $PaCO_2$ and base excess levels.
- Higher pressures are associated with reductions in $PaCO_2$ and bicarbonate.
- Apart from reductions in dynamic lung hyperinflation, generally there are no significant improvements in spirometric values or lung volumes with the long term use of NIV.
- Where improvements in HRQoL have been shown these appear to be related to improvements in dyspnoea.
- The SF-36 is the most commonly used English language multipurpose survey of general health status in COPD patients receiving long term NIV.
- Reductions in hospital admissions and total days spent in hospital has been shown post NIV commencement in appropriate COPD patients.
- Improved compliance is related to patients receiving a more intensive education programme and to the severity of their sleep disordered breathing at baseline.
- Constant checks on compliance should be performed to ensure that patients with COPD are using their NIV adequately.

### 2.6.4 INDICATIONS FOR NIV

**Level of Hypercapnia and arterial blood gas findings**

Chronic hypercapnic respiratory failure by definition includes elevated daytime $PaCO_2$ as a result of chronic alveolar hypoventilation, in the absence of an acute exacerbation [264]. While in other disorders it appears that NIV is indicated at the first sign of nocturnal hypoventilation or daytime hypercapnia, in COPD, the level of stable daytime hypercapnia required before the need for commencing NIV is indicated is less clear cut. Systematic reviews have demonstrated that combined analyses of randomised controlled trials have found no improvement in $PaO_2$ and $PaCO_2$ level [222, 223], whereas with regards to meta analyses of non-randomised controlled trials [223], significant improvement in $PaO_2$ (seven studies) and $PaCO_2$ (8 studies) have been shown. Whilst the majority of the above studies included patients with a $PaCO_2$ of greater than 50 mmHg, it appeared that when the studies are viewed individually, patients who received the greatest physiological benefit included those with higher baseline $PaCO_2$ levels, received more substantial pressure support or were more compliant. The Global Initiative for Chronic Obstructive Lung Disease, executive summary (updated 2007) [229] supports this by recommending that long term NIV may be of some benefit in a subset of patients, particularly in those with “pronounced daytime hypercapnia”. One study demonstrated that the degree of improvement in daytime $PaCO_2$ was correlated with changes in mean overnight values, suggesting that control of nocturnal hypoventilation was the main factor for the success of ventilatory support [224].

In comparison to $PaCO_2$, base excess has been shown in a prospective observational study to be a more reliable and consistent predictor of survival in patients with chronic hypercapnic respiratory failure receiving non-invasive home ventilation [244]. In a multivariate analyses, patients with a base excess ≥ 9 mmol/L at baseline and who demonstrated a ≥ 42% decrease after 6 months on NIV therapy, demonstrated improved survival. These findings suggest that the degree of metabolic compensation of chronic hypercapnia, expressed as base excess, is an independent predictor of mortality that is not accounted for by $PaCO_2$.

### Recurrent admissions

Hospitalisations resulting from severe acute exacerbations of COPD have a substantial negative impact on HRQoL (based on The Saint George Respiratory Questionnaire and SF-36) among patients who survive for at least 5 years, independent of their baseline $FEV_1$ and HRQoL [265]. It has been proposed that establishing measures to prevent exacerbations or treating patients early to avoid hospitalisations, may slow or prevent this loss of HRQoL [265].

Recurrent acute on chronic hypercapnic hospital presentations or life threatening events, should form a large part of the consideration for initiating a trial of NIV [231]. Two or more hospitalisations for episodes of hypercapnic respiratory failure, in a 12 month period, may be an indication for NIV commencement [106]. This has been based on the reported reductions in hospitalisations after commencing home NIV in appropriate patients with COPD, diffuse bronchiectasis and CF [34, 249, 266, 267].

Longer term follow up of 110 COPD patients who survived acute hypercapnic respiratory failure after NIV, but not sent home on domiciliary NIV, showed that one year after discharge: 79.9% had been readmitted; 63.3% had another life threatening event and 49.1% had died [268]. Survivors spent a median of 12% of the subsequent year in hospital and a significant proportion required NIV for recurrent acute hypercapnic respiratory failure. These results suggest that a significant proportion of patients requiring NIV for acute hypercapnic respiratory failure, will likely suffer from a life threatening event in the following year and that these patients could form the basis for future randomised trials of home NIV [268]. It has also been suggested that maintenance NIV has a role in the management of a subgroup of patients with severe COPD with a history of difficulty in weaning from invasive ventilation [245].

### Presence of sleep related breathing events

Some studies which have demonstrated improvements also appeared to have higher sleep related apnoea/hypopnoea index at baseline. In a study which demonstrated benefits of NIV, the average AHI was 10 per hour [224], whereas in another trial which demonstrated no additional benefit of NIV over standard medical care, AHI was 3.5 episode per hour [225]. Whilst a direct comparison is difficult, as the positive trial used higher pressure support and baseline $PaCO_2$ were higher, it does appear intuitive that patients with more sleep disordered breathing have more to gain from a therapy which is designed to ameliorate this abnormality. Similarly, other studies have demonstrated positive results with NIV treatment for nocturnal hypoventilation in those patients where BMI is greater than $30kg/m^2$ [249], AHI is higher [240] or where complaints of disturbed sleep are present [257].

Worsening hypoventilation with supplemental oxygen, especially nocturnally, has been used by many clinicians as a reason to commence NIV. Some researchers have included patients into their long term NIV trials if supplemental oxygen therapy failed either to raise the daytime $PaO_2$ to > 55 mmHg without a rise in the awake $PaCO_2$ to > 60 mmHg or failed to rise nocturnal $SpO_2$ >90% without a rise in the transcutaneous $CO_2$ tension to > 68 mmHg [243].

**INDICATIONS FOR A TRIAL OF HOME VENTILATION IN PATIENTS WITH COPD INCLUDE:**

i) clinical review to ensure all other appropriate therapies / treatments have been commenced

ii) awake stable $PaCO_2$ levels ≥ 50 mm Hg

***AND***

iii) symptoms consistent with a sleep breathing problem that is impacting adversely on quality of life

***OR***

comorbidities secondary to hypoxemia such as pulmonary hypertension or heart failure

***AND***

iv) demonstration of nocturnal hypoventilation / desaturation on full PSG that is not corrected or made worse by LTOT alone (based on a measure of carbon dioxide)

**OR**

v) recurrent admissions for acute exacerbations of COPD with respiratory acidosis where the patient has tolerated NIV and responded well to it.

vi) willingness to undergo a trial of therapy

**Key points:**

- COPD patients with stable $PaCO_2$ > 50 mmHg appear to receive more benefit from NIV.
- Reductions in base excess has been shown to be a predictor of survival in COPD patients with chronic hypercapnic respiratory failure receiving NIV.
- Two or more hospitalisations for acute hypercapnic respiratory failure per year (especially life threatening events) or difficulty weaning from invasive ventilation appear to be an indicator for domiciliary NIV commencement.
- Patients with more significant dynamic hyperinflation appear to get greater reductions in $PaCO_2$ when treated with NIV.
- COPD patients with greater baseline sleep disordered breathing (apnoea-hypopnoea index or severe nocturnal hypoventilation), demonstrate greater symptomatic relief and compliance from nocturnal ventilation.

## 2.6.5 IMPLEMENTATION

A systematic review of NIV in severe stable COPD summarised that comfort and compliance issues were generally recorded in shorter trials with brief acclimatisation attempts and in the presence of patient-ventilator dysynchrony which can occur either from excessive mask leaks (which can occur at higher pressures) or from increased inspiratory efforts (which may result from inadequate pressures or inappropriate settings) [223]. Acclimatising to NIV as an inpatient appears to be successful, especially if the education process is intensive and of adequate duration to ensure that discharge only occurs when patients are fully adjusted to using NIV [243] and when beneficial effects on excessive diurnal somnolence and intellectual function can be ultimately demonstrated [224, 249].

Whilst the concept of non-invasive ventilation may be initially trialled during an acute exacerbation of COPD, it is important to ascertain the patient's respiratory status once they are chronically stable to see if they are a suitable candidate for long term domiciliary NIV. The majority of studies define chronically stable as pH>7.35 [226, 247, 269] and free of signs of acute exacerbation at the time of [247] or up to 1 month [226, 269] preceding the investigations into the appropriateness of long term ventilation and settings.

When commencing NIV, settings can be made initially for patient comfort then adjusted for diurnal $PaCO_2$ values as tolerance allows [249]. A study which compared the titration of NIV in COPD using an invasive method (oesophageal and gastric pressure balloon monitoring) to a method based on tolerance, comfort, arterial blood gases and nocturnal oxygen saturations showed that both methods were effective in improving arterial blood gases and unloading inspiratory muscles [269]. The only difference was that the invasive titration resulted in a reduction in ineffective triggering of the ventilator by 70% in 36% of patients.

For ongoing compliance, regular reviews including outpatient clinics and the use of diary cards to document ventilator related issues have also been suggested and have excellent compliance rates (~95%) [224]. Frequency of visits after initial hospital acclimatisation in trials have been as regular as every month for 3 months [224] to 6 months [250], to being reviewed at 1 month, 6 months, 12 months and 2 years [243] after initiation of a NIV trial. Patients may also increase their knowledge or exposure to the concept of NIV within education sessions in pulmonary rehabilitation.

### Interfaces

In chronic COPD, a variety of masks have been used, with one study showing 58% of COPD patients using a nasal mask and 42% requiring or preferring an oronasal mask [243]. As COPD patients who have suffered a life threatening event are predisposed to further acute events [268], it may be beneficial to acclimatise or introduce an oronasal mask to patients with COPD for the purpose of use during acute exacerbations [15, 26]. Overall, long term mask choice should be based primarily on patient comfort and acceptance, whilst ensuring that it is both safe and effective [26].

### Spontaneous versus spontaneous / timed mode

Both spontaneous and spontaneous-timed have been utilised in the NIV management of chronic stable COPD. The spontaneous-timed approach attempts to override the patient's ventilation, allowing them to be passively ventilated by the machine, whereas the spontaneous approach is designed to offset the work of breathing by assisting the patient's spontaneous effort.

In a study aiming for normocapnia in COPD (baseline $PaCO_2$ = 59.5 ± 8.4 mmHg), passive ventilation was achieved by providing inspiratory pressures with a mean of 30.4 ± 3.9 $cmH_2O$ and respiratory rates of 22.9 ± 1.9 breaths/min [248]. These authors have suggested that a high back-up rate (and inspiratory pressure) is required to reverse hypercapnia and stated that the use of spontaneous mode in some studies was the reason why there was no change in hypercapnia in patients with stable COPD [241, 270].

In contrast to the above, other researchers have chosen a spontaneous mode as they have observed that excessively increasing the respiratory rate can lead to greater patient-ventilator dysynchrony and may be poorly tolerated by patients without apnoea [240]. One study which compared one night spent on spontaneous versus one night spent on spontaneous-timed mode against a control night, included 5 patients with COPD (baseline $FEV_1$ = 0.6 L and $PaCO_2$ = 59 mmHg) [271]. Here it was demonstrated that the time spent below $SpO_2$ < 90% was significantly reduced in both modes of ventilation compared to the control night with no statistical difference between the two modes. A

similar finding was also found for overnight transcutaneous carbon dioxide improvements. Whilst visual analogue scales showed no significant difference in ventilatory modes with respect to comfort and sleep quality, PSG was not performed to objectively assess sleep consolidation, arousals or sleep stage proportions. These authors suggested that spontaneous is as effective as spontaneous-timed mode in patients who can adequately trigger the machine (including patients with COPD who are unable to tolerate oxygen therapy alone through worsening hypercapnia) and it has the benefits of substantial cost savings in these patients.

**Key points:**

- Intensive inpatient acclimatisation to NIV has been shown to improve compliance.
- Education should be long enough for the patient or carer to achieve mastery over NIV application.
- Either nasal or oronasal masks may be used. However, patients should be exposed to an oronasal mask, which are predominantly used during exacerbations.
- Spontaneous mode appears to be as effective as spontaneous/timed mode with respect to gas exchange in patients who can adequately trigger the machine.

### 2.6.6 TITRATION OF NIV

The use of pressure devices appears adequate especially as the majority of patients with stable COPD requiring NIV are not ventilator dependent, believed to offer better synchronisation [16] and health-care funding constraints favour the cheaper pressure pre-set machines over volume preset devices. If there is a need for a volume preset ventilator, set up and titration should be carried out at a centre familiar with the use of such devices.

Titration principles for chronic stable COPD using bilevel devices during full polysomnography should include:

i) Commence with an EPAP that is comfortable for the patient, with an aim of offsetting intrinsic PEEP [272, 273] to reduce the work of breathing. Whilst in the typical clinical situation intrinsic PEEP is not measured, an EPAP of 4-6 $cmH_2O$ is usually appropriate unless there is evidence of marked dynamic hyperinflation [269, 274, 275].

   - Increasing EPAP over a certain level may increase lung volume and inturn worsen dynamic hyperinflation.
   - In addition, EPAP needs to be further increased where ineffective triggering (in the absence of leak) occurs due to complete or partial upper airway obstruction. Patients with COPD may also have other co-morbidities, such as OSA from obesity (overlap syndrome), and a higher EPAP may be required to treat upper airway dysfunction.

ii) Increase the IPAP – EPAP difference to resolve hypoventilation, ensuring that pressures are sufficient to ensure effective ventilation [276]. A Cochrane review [222] reported that it is questionable whether IPAP pressures below 14 $cmH_2O$ is enough to improve ventilation in stable COPD, as the only included RCT which demonstrated positive results was above 14 $cmH_2O$ with mean IPAP pressures of 18 $cmH_2O$ [224].

iii) Triggering from EPAP to IPAP should be consistent if adequate EPAP is used to offset intrinsic PEEP, leaks are minimised and respiratory rate is not excessively high. If triggering remains a problem, a trial of spontaneous-timed can be initiated and captured on PSG for comparison.

iv) Entrain oxygen initially aiming for a $SpO_2$ baseline > 88%, but not excessively higher than this in order not to mask any residual hypoventilation. Optimise ventilatory settings first, prior to making any further adjustments to entrained oxygen. Supplemental oxygen has been added generally to maintain oxygen saturations between 88 to 92% [227].

### 2.6.7 FOLLOW UP CARE AND ANCILLIARY CARE

Given that there is very limited evidence to support the use of NIV for the majority of patients with COPD, the appropriateness of long-term NIV must be supported by objective evidence that the patient, in a stable state, has experienced clinical or physiological improvements. Requests for respiratory equipment should be made by representatives of a multidisciplinary team from a centre with recognised experience in the assessment and management of patients requiring home ventilatory support.

After initial acclimatisation to non-invasive ventilation the following should be performed and assessed [277]:

i) Home trial of NIV for a 2-month period completed

ii) Patient compliant with therapy >4hrs/night

iii) Documentation of improved daytime blood gases or nocturnal gas exchange

iv) Improved symptoms such as sleep quality or symptom score on quality of life questionnaires

v) Reassess the continued need for supplemental oxygen especially if recently commenced during an acute exacerbation

Once a patient with COPD has been established on treatment the following should occur:

i) Annual electrical safety checks or as per manufacturers instructions.

ii) Written client information regarding their responsibilities with respect to the care and maintenance of the equipment, and to regular clinical review to ensure benefit from therapy and identify changes to treatment that need to occur and to monitor compliance.

iii) Regular clinical review either by the service that established therapy or an appropriately trained sleep physician closer to home. This should include checking of filters and mask/tubing as well as confirming machine settings remain as documented.

iv) Arterial blood gases and weight should be measured periodically at the discretion of the treating service or physician.

v) Written information for the patient explaining hypoventilation syndromes and the implications for surgery, sedative procedures or uncontrolled oxygen therapy. Also, the patient and relatives should be instructed to bring in their NIV equipment if they are admitted for either planned or unplanned (acute exacerbation) admissions.

vi) Remaining life style issues should be addressed and appropriate referrals made to smoking cessation clinics, pulmonary rehabilitation and dietitians for nutritional deficits [229, 231].

**Key points:**

- Regularly monitor compliance, especially as compliance can be much lower in COPD diagnostic group.
- Monitor changes in appropriate HRQoL questionnaires.
- Ensure patient has been referred to a smoking cessation programme, pulmonary rehabilitation programme and to a dietitian for management nutritional deficits or calorific surpluses.

| RECOMMENDATIONS FOR CHRONIC OBSTRUCTIVE PULMONARY DISEASE | **Grade** |
|---|---|
| Nocturnal NIV is indicated in COPD with $PaCO_2$ > 50 mmHg, where there is evidence of signs and symptoms of sleep disordered breathing, and full PSG demonstrates nocturnal hypoventilation (based on a measure of $PaCO_2$) that is not corrected or made worse by LTOT alone. | D |
| Recurrent hospitalisations (2 or more in a year) for acute hypercapnic respiratory failure (especially life threatening events) or difficulty weaning from invasive ventilation are an indicator for assessment for domiciliary NIV. | C |
| Titration for long term NIV should occur when the COPD patient is chronically stable (pH>7.35) and free from exacerbation. | D |
| Bi-level ventilation should be commenced in the spontaneous mode, unless there is specific evidence that the patient is unable to trigger the machine. | D |
| Adequate IPAP-EPAP difference is required to ameliorate hypoventilation. | A |
| Compliance with NIV therapy is improved with intensive inpatient acclimatisation of adequate duration. | B |
| Initial review of patients should occur at 6 to 8 weeks following the commencement of NIV to determine the clinical response to therapy. | D |
| Compliance is deemed adequate at > 4 - 6 hours per night. | C |
| Changes in awake blood gases are not the best measure of effectiveness of NIV in chronic hypercapnic COPD. Changes in symptoms including exertional dyspnoea, control of nocturnal hypoventilation, reduction in hospital admissions and HRQoL (SF-36) are better indicators of the patient's response to therapy. | C |
| If supplemental oxygen is entrained through the bi-level machine at initial commencement, continuation of supplemental oxygen should be reviewed at the subsequent review. | D |

# CHAPTER 2.7 CYSTIC FIBROSIS

**AMANDA PIPER**

## 2.7.1 BACKGROUND

Cystic fibrosis is a common genetic disorder characterised by mucus hypersecretion, airway inflammation and chronic pulmonary infection. Airway obstruction worsens over time with ongoing parenchymal damage, affecting gas exchange. For most patients pulmonary complications are the major cause of morbidity and mortality. Lung damage creates V/Q mismatch, resulting in hypoxemia. With disease progression, alterations in lung compliance and resistance occur increasing the work of breathing. This, coupled with poor nutritional status, eventually produces a fall in tidal volume with further worsening of hypoxia and the emergence of hypercapnia. It is thought that significant nocturnal falls in $SaO_2$ can contribute to the development and progression of pulmonary hypertension in patients with CF [278]. The appearance of pulmonary hypertension even at a subclinical degree has been found to be associated with increased mortality [279] and the development of hypercapnia has been linked to poorer survival [280, 281]. Therefore, identifying at risk patients and intervening to correct gas exchange abnormalities early before irreversible changes to the cardiovascular system develop are considered important therapeutic goals [282, 283].

Additionally, the progressive decline in lung function and frequent exacerbations that characterise this disorder results in impaired quality of life [284]. From cross sectional studies, it appears that pulmonary exacerbations of CF have a profound impact on physical and psychosocial aspects of quality of life, more so than other traditional severity measures such as $FEV_1$ percent predicted and nutritional indices [285]. Therefore, the introduction of any intervention that is able to reduce the frequency or severity of exacerbations could have a significant impact on health outcomes for these patients.

### Sleep, breathing and gas exchange

Sleep acts as a further load on breathing, and it is during this period that hypoventilation first appears [286, 287]. Nocturnal respiratory events are usually confined to REM sleep initially and are characterised by increased respiratory variability together with reduced chest wall movement and inspiratory flow [282]. Minute ventilation is reduced resulting in poorer oxygenation during REM compared to non-REM sleep with a concurrent rise in transcutaneous carbon dioxide [288].

Polysomnographic data regarding objective sleep quality in this population is contradictory with some studies reporting sleep architecture and efficiency as similar to that seen in normal controls [278, 289], while in other studies sleep is markedly abnormal [290-292]. These differences are likely due to variations in disease severity of the patients studied, as a number of studies have shown a relationship between changes in sleep quality and lung function [292, 293]. Actigraphy studies performed over several nights have demonstrated significantly more disrupted sleep in CF patients compared to age matched controls, with more fragmented sleep seen in those with more severe lung disease [294, 295]. These objective findings are supported by subjective ratings of patients who perceive their sleep quality as poor [293-295]. This increased sleep fragmentation or loss appears to have consequences for daytime functioning. CF patients have been shown to have objective evidence of daytime sleepiness, while neurocognitive performance is only around 60% of that seen in healthy age-matched controls [290]. Although the data is limited, it is generally thought poor quality sleep has a significant impact on quality of life and clinical outcomes in this population, and is most marked in those individuals with more severe lung disease.

**Key points:**

- Since pulmonary hypertension and hypercapnia are linked to poorer survival in CF, identifying at risk individuals and correcting abnormalities in gas exchange is important.
- Sleep, especially rapid eye movement sleep, is a time of vulnerability for gas exchange abnormalities, and is most marked in those individuals with more severe lung disease.

## 2.7.2 TREATMENT OPTIONS

**Oxygen therapy for nocturnal hypoxemia**

Oxygen therapy for hypoxemia has been the standard of care for patients with chronic lung disease including those with CF for decades. Supplemental oxygen is usually introduced when $PaO_2$ falls below 55mmHg (or $SpO_2$<88%) based on two large long-term trials in people with chronic obstructive pulmonary disease [296, 297]. The development of pulmonary hypertension and cor pulmonale are associated with higher mortality rates [279]. Pulmonary artery systolic pressure correlates with awake, post exercise and sleep $SpO_2$ in CF [279], and pulmonary hypertension in CF can be reduced with oxygen supplementation [298]. Therefore, identifying and preventing oxygen desaturation including during the sleep period has become standard care, with the aim of preventing the development and/or progression of pulmonary hypertension [299].

There is a paucity of data confirming the benefits of oxygen therapy in CF and its effect on quality of life, morbidity or mortality [300]. Supplemental oxygen sufficient to raise awake SpO2 level above 92% in patients with moderate-to-severe CF lung disease has been shown to prevent desaturation during sleep [301]. There appears to be no significant change in sleep architecture with the introduction of oxygen therapy despite improved $SpO_2$ [288, 301, 302], although a small but probably clinically significant rise in $CO_2$ during REM can occur [288, 301-303]. Only one trial has reported the long term effects of nocturnal oxygen therapy in CF, evaluating its impact on mortality, frequency of hospitalisation, lung and right heart function, nutritional status, psychosocial and cognitive aspects of daily living over a 2 year period [304]. These authors were unable to detect any benefit of nocturnal oxygen therapy, although there was a trend towards improved right ventricular ejection fraction and cardiac output in those receiving oxygen. However, study numbers were small (14 in each group), and subjects were enrolled based on a daytime $PaO_2$ $\leq$65mmHg, without measurement of sleep oxygenation either on or off supplemental oxygen.

A major problem in this area is that a threshold of nocturnal desaturation that is physiologically significant in CF patients has not been established. Investigators have used $SpO_2$ values of <90% for >5% of the night [302, 305] or mean minimum average $SpO_2$ < 90% [291] to classify CF patients as experiencing nocturnal hypoxemia, while a Consensus Report regarding Cystic Fibrosis Adult Care have suggested $\geq$10% of the total sleep time below 88-90% [299]. These criteria for oxygen therapy are more liberal than current TSANZ guidelines for nocturnal oxygen therapy that state "nocturnal oxygen therapy may be indicated in patients whose nocturnal arterial oxygen saturation falls below 88% and who have evidence of hypoxia-related sequelae" or where "$SpO_2$ $\leq$88% for more than a third of the night" [175].

**Key points:**

- Criteria for introducing oxygen therapy in CF is based on long-term trials in patients with COPD
- The threshold of nocturnal desaturation that is physiologically significant in CF has not been established.
- Since the development of pulmonary hypertension is associated with higher mortality rates, and pulmonary artery systolic pressure correlates with sleep $SpO_2$, the identification and prevention of oxygen desaturation has become a standard of care.
- There is limited data regarding the benefits of oxygen therapy in CF with regard to its effects on HRQoL, morbidity or mortality.

## 2.7.3 SCREENING FOR SLEEP DISORDERED BREATHING

Since the development of hypoxia and hypercapnia are considered to have significant clinical consequences in CF, identifying daytime measurements that predict abnormal gas exchange during sleep has been the focus of some attention. Significant oxygen desaturation can be missed in these patients unless it is specifically sought. Unfortunately, although resting awake $SpO_2$ and $FEV_1$ have been shown to be associated with nocturnal oxygenation [305], there are no thresholds of these measurements that reliably exclude those who do not desaturate. While patients with significant nocturnal desaturation tend to have more advanced pulmonary disease [305, 306], use of basic lung

function variables such as $FEV_1$ does not add significantly to the discriminatory power of $SpO_2$ [307]. Evening $PaO_2$ and morning $PaCO_2$ have been found to be the most predictive of sleep-related oxygenation in patients with moderate-to-severe lung disease, accounting for 74% of the variability in $SpO_2$av percentage [291]. However, for most centres obtaining arterial blood gases at these two time points while the patient is in a stable state will be logistically difficult. Therefore, nocturnal $SpO_2$ monitoring should be performed in all individuals thought to be at risk.

**Key points:**

- Individuals with awake resting $SpO_2$ <94% and/or $FEV_1$ <65% predicted are considered to be most at risk of developing nocturnal desaturation.
- Nocturnal $SpO_2$ monitoring is the only method to accurately detect individuals who desaturate during sleep.

## 2.7.4 OUTCOMES

Currently only one longer term randomised trial of nocturnal ventilatory support has been conducted, and this was a crossover 18 week trial, comparing nocturnal air, nocturnal oxygen and NIV in stable subjects with daytime hypercapnia [302]. Two earlier studies compared NIV to oxygen [303] or to air and oxygen [288] in a randomised fashion. However, these latter studies were conducted over a single night only. Most data dealing with the long-term use of NIV in patients with CF arise from case series or case control studies. When interpreting outcomes in this population it should be borne in mind that, although improvements in management have significantly improved survival, lung disease remains progressive and patients will eventually succumb to respiratory failure. Consequently, the ultimate aim of NIV for these individuals is to improve symptoms and survival until transplantation is possible [308]. In those deemed unsuitable for transplant or in whom suitable organs will not be found in time, NIV may reduce the burden of disease and improve the quality of the life they have left. However, alternative measures to ease breathlessness and promote comfort in the end stages of the disease will need to be implemented.

### Physiological

*Arterial blood gases*

Although initial improvements in $PaCO_2$ can be achieved [267, 309-311], in contrast to other disorders where NIV is commonly used, reduction in $PaCO_2$ is not necessarily achieved in CF [302, 308], especially over the longer term. However, significant improvements in dyspnoea, quality of life and exercise tolerance can be achieved following NIV without changes in awake blood gases [302].

*Work of breathing*

Short term physiological studies during wakefulness have demonstrated that NIV can significantly reduce diaphragmatic pressure time product and the work of breathing in both children [312] and adults [313, 314] with severe CF lung disease. In addition to unloading inspiratory muscle activity, NIV also increases tidal volume and reduces respiratory rate, thereby improving alveolar ventilation [312, 313]. This has also been shown in sleep [288].

### Clinical

*Lung function*

In CF, lung disease is characterised by an irreversible decline in lung function over time. Therefore, demonstrating a slowing in the decline of lung function with NIV represents a strong argument favouring this technique. Over a 6-week period, NIV had no impact on lung function [302]. However, in a case control study of patients with advanced disease, 12 months of NIV was associated with a stabilisation of the decrease in lung function [315]. Improvements in respiratory muscle have also been

reported following use of NIV during chest physiotherapy [316, 317] and after longer term nocturnal ventilatory support [267].

*Sleep quality and gas exchange*

In several uncontrolled early studies, improved sleep quality on NIV was reported [267, 318]. However, objective findings from overnight randomised trials have been conflicting, with no changes in sleep macrostructure found [288, 302] or an increase in REM compared to room air [303]. Oxygen therapy and NIV appear to be equally effective in improving mean nocturnal $SpO_2$ in NREM and REM sleep [288, 303]. In contrast to oxygen therapy, which induces increases in nocturnal carbon dioxide, NIV has consistently been shown to significantly reduce nocturnal carbon dioxide [288, 302, 303]. Nocturnal ventilatory support at appropriate pressures is able to improve minute ventilation by ameliorating the significant fall in tidal volume, which is frequently seen in patients with severe lung disease [288].

*Daytime symptoms and performance*

In a number of case series reports, meaningful subjective improvements in dyspnoea have been reported following the introduction of NIV [310, 313]. In a randomised trial, an increase in Transitional Dyspnoea Index of 3.1 units was seen with NIV compared to placebo [302]. While adult patients with cystic fibrosis and severe lung disease have impaired neurocognitive function and daytime sleepiness [290], these parameters did not improve with the use of nocturnal bilevel support, at least over a 6-week treatment period [302].

*Acute exacerbations*

No randomised studies have yet evaluated the impact of NIV used long term on the rate of acute exacerbations. However, data from case series have reported reductions in the number of hospital days following the commencement of NIV compared to the period prior to using NIV [310]. Single intervention studies using NIV as a method of airways clearance in patients with moderate to severe lung disease have demonstrated improvements in respiratory muscle function and oxygen saturation, while reducing dyspnoea and perceived effort during therapy were lower when NIV was used compared to standard therapy alone [316, 317, 319].

Bilevel ventilatory support has emerged as a useful therapeutic alternative to invasive ventilation in patients presenting with severe exacerbations of their lung disease and respiratory failure [320, 321]. However, the clinical deterioration that can accompany such episodes may necessitate the introduction of NIV on an ongoing basis to maintain clinical stability. NIV may be used as bridge to transplant [322] or to improve survival to hospital discharge [321] and beyond [323]. In one study, the need for ICU admission led to a change in chronic management in many survivors, with the implementation of home NIV in 28% of individuals [320].

**Exercise tolerance**

This has been reported in only one study. In a randomised trial comparing air, nocturnal oxygen and nocturnal NIV, NIV produced a significant increase in shuttle distance compared to room air [302].

**Quality of life**

While a number of uncontrolled trials have suggested that the implementation of NIV can improve quality of life in individuals with CF, only one randomised trial to date has addressed this issue. Young et al [302] found that NIV significantly improved the chest symptom score of the CF Quality of Life questionnaire, with no change during the periods on nocturnal air or oxygen therapy. However, they were unable to show changes in any other HRQoL measure including the ESS or the PSQI.

**Survival**

There have been no long-term studies specifically addressing this issue.

**Compliance**

NIV is not tolerated by all patients [302, 303], and insufficient inspiratory support may limit the degree to which nocturnal hypoventilation is attenuated [288, 302]. When asked, patients generally prefer oxygen therapy to NIV, at least initially [302, 303]. In the longer term randomised trial, a mean nightly use of 4.3 hrs was sufficient to induce significant improvements in exercise tolerance, reduce breathlessness and improve the chest symptom score of the CF HRQoL questionnaire [302].

**Adverse effects**

Aerophagia [302, 318] and skin breakdown [324] have occasionally been reported. Worsening of mucus plugging or drying of secretions has not been found to be a problem [302, 318], although humidification may be required in some patients [302, 318]. Spontaneous pneumothorax is also a common complication of CF lung disease, characterised as it is by apical subpleural cysts that often rupture. Despite this, pneumothorax occurrence during NIV appears to be a rare occurrence [325].

**Key points:**

- NIV may be introduced for chronic stable hypercapnic disease or following an acute exacerbation where NIV has been used but the patient's clinical condition remains impaired relevant to their baseline state despite prolonged hospitalisation.
- Significant physiologic and clinical benefits can be achieved with the use of NIV in patients with daytime hypercapnia and/or nocturnal hypoventilation.
- Exercise tolerance and quality of life can also be improved.
- The impact of therapy on the incidence of acute exacerbations and survival has not been studied.
- No major adverse effects have been reported. In particular, worsening of mucus plugging or increased incidence of pneumothorax has not been seen.

## 2.7.5 INDICATIONS FOR NIV

There is presently no data available to guide when is the most appropriate time to commence nocturnal ventilatory support in this population. It is also important to remember that the clinical course with CF may be one of slow deterioration over months or conversely, a rapid, dramatic step change following an acute exacerbation. In the first situation, NIV may be introduced with the aim of improving quality of life, symptoms and slowing the development of pulmonary hypertension. In the second situation, the aim of therapy is primarily to "bridge" the patient to transplant or transplant evaluation, permitting them the opportunity to return home in the interim. In the latter case only limited benefits of therapy can be expected [312].

**In patients in a stable clinical condition:**

- Daytime blood gases showing a $PaCO_2$ >45mmHg [302]
- Nocturnal gas exchange demonstrating $SpO_2$<90% for >5% of TST and/or a rise in transcutaneous $CO_2$ from NREM to REM >5mmHg performed during room air breathing [302]

**In patients experiencing an acute deterioration:**

- Awake $PaCO_2$ remains > 45mmHg despite maximal medical therapy including inpatient NIV therapy
- The patient remains clinically impaired compared to their normal stable state (e.g. loss of lung function, increased breathlessness, increased oxygen need) despite a prolonged period of hospitalisation (>2 weeks).
- The patient has been tolerant of NIV and is willing to continue a trial of NIV at home

## 2.7.6 IMPLEMENTATION AND TITRATION OF NON-INVASIVE VENTILATION

### Baseline measurements

Awake spontaneous blood gas measurements should be obtained. To assess the benefits of introducing NIV in patients with stable disease, lung function, quality of sleep and quality of life are important parameters and should be documented, where possible, prior to commencing therapy. In addition, a chest X-Ray should be assessed to ensure no pneumothoraces are present [308].

Increasingly, NIV may be used during acute deterioration of patients to avoid intubation [320, 323], as acute on chronic respiratory failure is a significant predictor of mortality in those receiving invasive ventilation [326]. In addition to the risk of death during these episodes, there may also be considerable physiologic deterioration with irreversible worsening of the individual's pulmonary status. As a consequence, a significant proportion of patients hospitalised with initial severe respiratory deterioration may require NIV as home therapy at hospital discharge [320, 323]. In these individuals, stable baseline measurements from prior to their deterioration may not reflect their current clinical state.

Comfort on ventilatory support is a major consideration when using NIV in CF. A thorough explanation of the principles of therapy, progressive stepwise increments in ventilatory assistance and ongoing training is required to fully acclimatise the patient to treatment [312]. This means time needs to be taken to optimise not only IPAP and EPAP settings, but also to determine appropriate triggering and pressure delivery slopes to maximise patients' comfort. Although NIV for home use is usually introduced when evidence of sleep hypoventilation or daytime respiratory failure becomes apparent, it has been suggested that familiarising the patients with the technique beforehand may be advantageous [308].

### Mode and settings

Volume preset devices were initially used in these patients, mostly under circumstances of acute on chronic respiratory failure where the aim of therapy was to bridge the patient to transplant [267, 322]. In these reports, patients were considered end stage and $PaCO_2$ ranged for 59-87mmHg prior to commencing NIV. In later case series, pressure preset devices primarily in the form of bilevel machines have been used [309, 310, 318]. In an experimental protocol, the pressure preset and volume targeted modes were compared during daytime breathing in eight children with CF and chronic respiratory failure. Both modes were equally effective in unloading the respiratory muscles and improving gas exchange, although the majority of patients preferred the pressure preset mode [312]. As bilevel devices are easier to set-up and better tolerated, it has been recommended that this mode should be the first option in this patient group [327]. In the longer-term randomised trial comparing NIV with oxygen and a placebo, a bilevel device was used, with a mean IPAP of $12cmH_2O$ and EPAP of $5cmH_2O$. Other studies have used higher inspiratory pressures [311, 328]. Although increasing the level of ventilator assistance should produce progressive decreases in inspiratory muscle effort and dyspnoea, it may also be accompanied by increases in the rate of ineffective triggering [329].

### Monitoring

Initial settings are usually clinician driven, with machine variables adjusted according to pulse oximetry, respiratory rate on the device, minute ventilation and comfort [311, 328]. In a study evaluating setting up NIV for patients with stable NIV using clinical monitoring versus a more invasive approach (oesophageal and gastric catheters), both approaches were found to be equally effective in unloading the respiratory muscles and improving gas exchange [328]. However, a small comfort benefit with the invasive method was seen, which was thought to be due to improved patient-ventilator synchronisation obtained by the invasive method. A recommendation arising from this data suggests a standard clinical method to set up NIV in most patients but that more detailed investigation is warranted in those patients experiencing difficulty tolerating therapy [328].

### Particular precautions/issues

Although there is no current evidence to suggest that there is a higher incidence of pneumothorax in CF patients managed with NIV compared to CF patients receiving standard therapy [325], careful

surveillance is recommended. Patients should be alerted to the symptoms suggestive of pneumothorax and be instructed to seek immediate medical attention should these symptoms occur.

### 2.7.7 ONGOING FOLLOW UP AND ANCILLARY CARE

Cystic fibrosis is a progressive disorder, characterised by ongoing parenchymal damage. Consequently, periodic review of the patient's response to therapy and adjustment of settings is required. In addition, the aims and limitations of therapy need to be clearly outlined and discussed with the patient. While NIV can provide an additional period of clinical stability with symptom relief, this extra time is limited. In patients in whom transplantation is contraindicated or declined, alternative methods of symptom relief and management will need to be introduced at the appropriate time.

As improvements in exercise tolerance, symptoms and breathlessness can be achieved by six weeks of therapy [302], patients should be reviewed following 6-8 weeks on therapy to determine their clinical response and compliance with therapy. Although a reduction in $CO_2$ may be achieved with NIV, this does not need to occur for other clinical benefits to be realised [302]. Therefore, a fall in $PaCO_2$ should not be the only criteria by which the appropriateness of continuing NIV should be judged.

Tolerance of NIV can be problematic in this population [302, 303] and not all patients will accept pressures that are therapeutically effective [288]. Therefore, regular review of compliance data should be undertaken to check whether the patient is achieving sufficient time on therapy for benefit. Current data suggests that at least 4 hrs/night of therapy is required for clinical benefit [302].

If the patient is not tolerant of therapy or is failing to respond as expected, a trial of different settings or mode of support should be undertaken [328]. Although bilevel support is most commonly used and best tolerated when NIV is initially introduced, there is evidence that a volume preset mode may offer additional benefits in some individuals, through further reductions in the work of breathing [312]. Therefore, a trial of this mode should be considered where there is a poor response to bilevel support, blood gases are deteriorating and the patient is actively listed for transplant [308].

The need for humidification during NIV in this population has not been specifically studied. However, NIV is known to deliver air with a low relative humidity, especially with high inspiratory pressures. Reduced inspired humidity may have adverse effects on mucociliary function including decreased ciliary function, increased mucus viscosity, and inflammation of the airway mucosa. As CF is characterised by problems with tenacious secretions, the risk of adding to this problem should be minimised. The addition of a heated humidifier increases the relative and absolute humidity to levels acceptable for non-intubated patients [330]. Therefore, consideration should be given to using heated humidification during NIV.

The role of polysomnography in CF patients for NIV titration and follow up remains unknown. Daytime determination of settings using a clinical response and comfort approach has been shown to be as effective as more invasive techniques aimed at reducing the work of breathing, in improving patient-ventilator synchronisation [328]. However, it is unknown if these findings extend to optimal synchronisation during sleep. Polysomnography was used to titrate pressures and minimise leaks in the single longer-term randomised trial performed to date [302].

**Key points:**

- Bilevel support is as effective as volume ventilation, at least initially, and is preferred by the majority of individuals.
- Basic clinical monitoring such as $SpO_2$, $TcCO_2$ / $ETCO_2$, respiratory rate and comfort is sufficient in most cases to set up NIV initially.
- Daytime blood gases may not alter with NIV even though significant improvements in other clinical parameters are achieved.
- Compliance with therapy should be regularly checked.
- Poor tolerance or failure to respond as expected to therapy should trigger a trial of different settings or a different mode of support.
- Polysomnography is useful to trouble shoot problems with therapy such as poor synchronisation, leak or persisting hypoventilation.

| RECOMMENDATIONS FOR CYSTIC FIBROSIS | **Grade** |
|---|---|
| Individuals with awake $SpO_2$<94% or spirometry ($FEV_1$<65% predicted) are at risk of nocturnal oxygen desaturation. Overnight oximetry should be undertaken in individuals meeting these criteria. | C |
| Hypoxia, hypercapnia, or an elevation in serum bicarbonate indicate the need for additional respiratory assessments and interventions. | D |
| Non-invasive ventilation is indicated if daytime $CO_2$>45mmHg and nocturnal gas exchange shows $SpO_2$<90% for >5% of TST and/or a rise in $TcCO_2$ from NREM to REM >5mmHg during room air breathing occurs. | B |
| Nocturnal NIV is more effective than oxygen therapy in controlling nocturnal hypoventilation in patients with hypercapnic CF lung disease. | A |
| Bilevel ventilation should be trialled initially. Volume ventilation may offer additional benefits in some individuals especially if work of breathing is high. | B |
| NIV does not appear to increase the incidence of pneumothorax, but this is a relatively common occurrence in this population. Therefore, patients need to be educated regarding the symptoms of pneumothorax and should seek immediate medical attention should these symptoms arise. | D |
| Changes in awake blood gases are not the best measure of the effectiveness of NIV. Changes in symptoms, exertional dyspnoea and exercise tolerance, and control of nocturnal hypoventilation are better indicators of the patient's response to therapy. | B |
| NIV may be used in patients unsuitable for transplant to relieve symptoms and improve sleep quality. However, alternative methods of symptom relief need to be introduced at the appropriate time. | D |
| Initial review of patients should occur at 6-8 weeks following commencement of NIV to determine clinical response to therapy. | B |
| Consider the use of heated humidification in all patients to minimise the risk of secretion drying and retention. | D |

# CHAPTER 2.8 HYPERCAPNIC CENTRAL SLEEP APNOEA / CENTRAL ALVEOLAR HYPOVENTILATION

**DANIEL FLUNT**

## 2.8.1 BACKGROUND

This is a group of disorders characterised by primary abnormalities in ventilatory control leading to central apnoea and ultimately hypoventilation during sleep (see Table 6).

The congenital form of the disorder is known as congenital central hypoventilation syndrome (CCHS) or “Ondine’s Curse” and produces severe sleep hypoventilation although adequate ventilation during wakefulness is usually maintained. In addition to the respiratory manifestations of this disorder, CCHS is also associated with a more global autonomic nervous system dysfunction. The disorder is diagnosed in the absence of primary neuromuscular, lung or cardiac disease, or the presence of an identifiable brainstem lesion [331]. The abnormality arises from mutations of the PHOX2B gene [332]. During sleep, these children have little or no ventilatory sensitivity to $CO_2$, and a variable or absent sensitivity to hypoxia. Ventilatory responsiveness to chemical stimuli is also abnormal during wakefulness. Consequently, severe alveolar hypoventilation during sleep develops during spontaneous breathing, necessitating long term nocturnal ventilation. However, CCHS differs from other respiratory disorders causing hypoventilation during sleep in that the level of ventilation, though abnormal, is better in REM than non-REM sleep [333]. With improved care, patients with CCHS are surviving into their adulthood with 13 of 196 patients surveyed (including countries from North America, European Union and Australia) aged over 20 years [334]. Although generally thought of as a paediatric disorder, a recent case series identified 5 adults presenting after the age of 21 with respiratory failure without early overt manifestations of CCHS yet heterozygous for a polyalanine expansion mutation in the PHOX2B gene [335].

Central hypoventilation may also be *acquired* following neurologic disorders that affect the brainstem, such as stroke, vascular malformations, infections and brainstem tumours. If no cause for the hypoventilation can be found the disorder is labelled *idiopathic*. However, it is possible that many of these individuals have milder forms of disorders known to cause hypoventilation. Opioid-induced central apnoea and hypoventilation may be another cause of abnormal sleep gas exchange and daytime respiratory failure. Central sleep apnoea is common in this population [336] along with prolonged periods of hypoventilation. In stable methadone managed patients, central chemosensitivity is reduced while peripheral chemosensitivity is increased. Although the exact mechanisms underlying the development of sleep disordered breathing in this population remains unclear, the interplay between depressed respiratory drive and abnormalities in chemoreceptor sensitivity undoubtedly plays an important role [337].

**Table 6: Manifestations of hypercapnic CSA secondary to impaired central drive, especially with brainstem involvement** [338-340]

| | |
|---|---|
| **Congenital** | Congenital Central Hypoventilation Syndrome (CCHS) |
| **Neurologic conditions** | Tumours / Space occupying lesions |
| | Vascular malformations |
| | CNS infection / Encephalitis |
| | Bulbar polio-myelitis |
| | Stroke / Infarction / Near drowning |
| | Neurosurgical procedures |
| | Cervical cordotomy |
| | Arnold-Chiari malformation |
| | Shy-Drager syndrome |
| **Pharmacological** | μ-Opioid / Methadone induced SDB |
| **Radiotherapy** | Radiation necrosis |
| **Idiopathic** | Alveolar hypoventilation in patients in the absence of:<br>- lung and chest wall abnormalities or<br>- skeletal malformations or<br>- neuromuscular disorders |

**Key points:**

- Hypercapnic central sleep apnoea occurs when abnormalities in primary ventilatory control causes a lack of respiratory effort resulting in awake $PaCO_2$ > 45 mmHg.
- There are multiple aetiologies of hypercapnic central sleep apnoea, and whilst some arise from genetic mutations (e.g. PHOX2B in CCHS), the remainder are usually caused from a disruption to the normal function of respiratory centres in the brainstem.

### 2.8.2 SCREENING & INVESTIGATIONS

Investigations in this category are two-fold. Firstly it is to exclude lung and chest wall abnormalities, skeletal malformations and neuromuscular disorders. In this instance full lung function (including respiratory muscle testing) [16], neurological examination, fluoroscopy of the diaphragm and muscle biopsies should be essentially normal [335]. In the absence of the above, screening for central alveolar abnormalities could be assisted by the presence of: reduced or absent ventilatory responses (including observations such as extreme amounts of time spent underwater without perceiving physiological compromise) [341]; radiographic abnormalities in the brainstem region; evidence of specific gene mutations (e.g. PHOX2B) [335]; observed long periods of absent breathing when asleep with signs of central cyanosis or if sleep disordered breathing shows improvement in REM sleep compared to non-REM sleep on a diagnostic sleep study as seen in CCHS and opioid induced centrals [333, 342]. Holter monitoring has also revealed decreased heart rate beat to beat variability and increased arrhythmias, predominantly sinus bradycardia or transient asystole in conditions of autonomic dysfunction [341].

### 2.8.3 TREATMENT OPTIONS

When nocturnal hypoventilation is caused by a lack of respiratory muscle activity from an absence of central input during sleep, only treatments which maintain effective minute ventilation during sleep will be successful. The need to mechanically ventilate patients with severe hypercapnic CSA is clear [338, 339], with the majority of evidence coming from infants with severe CCHS [334, 343]. Non-invasive ventilation is becoming the preferred mode of ventilation delivery if there is no need for invasive

ventilation, especially when patients require ventilation during sleep only [334, 340, 344]. Whilst CCHS have altered ventilatory responses, the majority of patients do not require supplemental ventilation when awake (81.6% of surveyed patients) [334]. When awake alveolar hypoventilation persists, ventilation needs to be utilised either for parts of the day (7.7% of surveyed) or for the entire 24 hour period (10.2% of surveyed). In infants, this usually necessitates the need for a tracheostomy, although decannulation and transference to NIV by the ages of 6-11 years, is feasible. While there are wide variations between US and European practices [334], there appears to be an increasing trend for using NIV over tracheostomy. Total ventilator dependence requires the continuation of life long tracheostomy. With increasing survival into adulthood, specialised adult sleep centres are likely to be treating more of these patients in the future, although still infrequently. In other hypercapnic CSA conditions there is limited literature, and consequently NIV is commenced in response to the level of hypoventilation induced from their pathology.

Whilst diaphragmatic pacing is used in select individuals, predominantly for residual daytime hypoventilation [334], it has the disadvantages of expense and potential problems of upper airway obstruction unless a tracheostomy is already in situ.

In the case of high dose narcotic induced CSA, a gradual reduction of opioid medication may improve the central events and stabilise oxygen saturations on polysomnography [338]. With regards to methadone, a study has shown using multiple linear regression that the logarithmic methadone blood concentration was the only statistical significant variable associated with the logarithmic central apnoea index. However, it still only explained 12% of the variance [336].

**Key points:**

- Further screening should occur when alveolar hypoventilation is present in the absence of lung and chest wall abnormalities, skeletal malformations and neuromuscular disorders.
- Central sleep disordered breathing is usually worse in non-REM in comparison to REM sleep (e.g. CCHS and opioid induced centrals).
- Only treatments which maintain effective minute ventilation (i.e. domiciliary ventilation) will be successful.
- Especially with regard to CCHS, there is an increasing trend globally (where appropriate) to use NIV over tracheostomised invasive ventilation.
- Reduction in opioid medication may improve central events and stabilise oxygen saturation.

### 2.8.4 OUTCOMES OF NIV IN HYPERCAPNIC CSA

Outcomes of survival or quality of life are scarce and rely on retrospective observations, predominantly in children with CCHS. A summary in 1999 speculated that CCHS not treated with ventilation causes death within one to two months from birth [341]. However this does not include the less severe forms of the disease which may not overtly present until later in life [335]. Early diagnosis and careful ventilatory management of patients with CCHS can minimise the sequelae of hypoxaemia, reduce morbidity and improve long-term outcome (including physical and mental outcome) [343, 345].

Other patients who present with acute or acute on chronic respiratory failure secondary to pathologies of the brainstem may demonstrate a failure to wean from nocturnal or 24 hour-dependent ventilation in high care environments. As the acute needs of these patients decrease, it becomes obvious in certain patients that ventilation needs to be continued in the chronic setting in order to improve daytime function and ultimately survival.

Whilst the conclusion of these findings lack randomised trials, medical communities accept the findings in retrospective or observational studies as they provide enough logical justification for the continuation of ventilation in this group of patients. Future randomised controlled trials would now be viewed as unethical.

**Key point:**

- Early diagnosis and careful ventilatory management of patients with hypercapnic CSA minimises the sequelae of hypoxaemia, which should lead to improvements to long term physical and mental outcomes, as well as survival

## 2.8.5 INDICATIONS FOR NIV

Patients with severe central alveolar hypoventilation are noted to have marked nocturnal hypoxaemia and hypercapnia, significant enough to cause daytime hypercapnic respiratory failure [338, 340, 346], as well as impacting on daytime function [339, 340]. Nocturnal ventilation should be commenced as soon as possible to prevent the patient from experiencing dangerously low levels of hypoxaemia. This is especially important in disorders with associated dysautonomia, as sudden death arising from cardiac arrhythmias may occur [347].

Indications for the initiation of NIV in hypercapnic CSA include:

i) Clinical diagnosis of a disorder associated with hypercapnic CSA (see Table 6) or if offspring have been diagnosed with congenital hypoventilation syndromes [335]

ii) clinical review to ensure all other appropriate therapies / treatments have been commenced

iii) awake $PaCO_2$ > 45 mmHg [348] ***OR***

evidence of hypoventilation in non-REM and/or REM sleep (e.g. sustained falls in $SpO_2$ such as $SpO_2$ ≤ 88% for > 5 consecutive minutes [106] *or* increase of peak $TcCO_2$ / $ETCO_2$ ≥ 8 mmHg above awake resting values *or* peak carbon dioxide being > 50mmHg for more than 50% or more of sleep time [79])

***AND***

iv) symptoms consistent with sleep disordered breathing problem that impacting adversely on the patients quality of life [338, 340]

***OR***

co-morbidities secondary to hypoxaemia such as pulmonary hypertension or heart failure or polycythaemia [335, 340]

v) demonstration of central events (loss of thoracic and abdominal band movement [338] or diaphragmatic EMG with associated cessation of airflow) significant enough to cause nocturnal hypoventilation on PSG

## 2.8.6 TITRATION

As acute or acute on chronic presentations of hypercapnic central sleep apnoea are managed in a hospital situation, acclimatisation to NIV (or weaning from invasive ventilation to NIV if appropriate) generally occurs in the inpatient setting. Before a treatment sleep study can be organised, clinicians should be guided by oximetry and afternoon and early morning arterial blood gases to monitor $PaCO_2$ acutely and bicarbonate over the longer term. Attempts to correct transient periods of hypoxaemia should be initially made by optimising the amount of pressure support and back up rate, prior to increasing inspired oxygen, especially if baseline hypoxaemia is not an issue.

After a period of acclimatisation to the sensation of non-invasive positive pressure ventilation in a back up mode, a formal titration should be performed in conjunction with full polysomnogram in order to assess the effect of non invasive ventilation across the various sleep stages. In the scenario where a patient remains fully ventilator dependent, a tracheostomy would remain in situ and a ventilator approved for life support should be arranged and set up based on nocturnal and awake requirements.

Titration during PSG in hypercapnic CSA should consider the following:

i) In isolated sleep hypoventilation – commence using a bi-level pressure preset machine.

ii) Due to lack of respiratory effort, it is important to set inspiratory times correctly and adequately (i.e. pressure control mode or near pressure control mode) as to prevent short ineffectual timed breaths. In the presence of normal lung function and mechanics an I:E ratio of approximately 1:2 can be assumed as a starting point.

iii) Titrate IPAP-EPAP difference which in combination with the chosen back up rate is sufficient to ameliorate hypoventilation.

iv) Set a pressurisation rate which is comfortable for the patient and is effective enough to provide the inflationary pressure within enough time.

v) Absent ventilatory responses when awake and potential inability to arouse to abnormal gas exchange can produce significant hypoventilation if an interruption to ventilation were to occur. This could include dislodgement of the mask during sleep or a power failure. Consequently, machines with “mask off” or “low pressure” and “power failure” alarms are recommended.

vi) Supplemental oxygen should only be used if there is residual hypoxemia from parenchymal lung disease or baseline hypoxaemia cannot be corrected by ventilation alone.

vii) In the scenario where pressure support ventilation is not sufficient to stabilise ventilation overnight or if ventilator dependence persists, a volume ventilator or more sophisticated “hybrid” ventilator with alarms and internal batteries should be initiated.

### 2.8.7 FOLLOW-UP AND ANCILLARY CARE

In the case of CCHS, where diagnosis and treatment has predominantly occurred before being transferred to adult facilities, a full handover including patient and ventilator history and requirements should be obtained. Status of ventilator equipment ownership and age should be obtained and acted on accordingly. The continued need for auxiliary physiological monitoring (e.g. oximeters / end tidal carbon dioxide monitoring) can be assessed and reduced if no longer required.

Where NIV is commenced for the first time, once nocturnal ventilation appears more stable after initial inpatient trials, a review sleep study should be performed within 3 months to ensure that ventilator settings are effective, that there are no significant equipment related issues and that compliance with therapy is recorded. Due to the rareness of such disorders, it has been proposed that these patients should be continued to be managed by specialised teams [349].

Once the patient has demonstrated stability on their current settings, they should be monitored regularly either by the service that established therapy or an appropriately trained sleep physician closer to home. This should include:

- checking the filters, mask and tubing
- confirming machine settings remain as documented.
- arterial blood gases and weight should be measured periodically at the discretion of the treating service or physician
- any signs of chest infection should be reviewed and managed promptly, especially in the case of CCHS where a lack of dyspnoea in response to pneumonia may mask severe respiratory compromise [341]

Review polysomnographic studies should be performed periodically at the discretion of the treating service or physician (generally every 1 to 2 years). However, an earlier review should occur if there is deterioration in blood gases, sustained periods of desaturations on overnight oximetry, increases in BMI which may precipitate upper airway obstruction or return of daytime symptoms.

Written information for the patient explaining hypoventilation and the implications this will have for surgery, sedative procedures and uncontrolled oxygen therapy. They should also be explicitly told that they need to tell all medical staff, especially anaesthetists and surgeons, about the implications of their condition and further clarification about fitness for surgery or sedative procedures, or peri and post operative management plan should be sought from the patient’s sleep physician or treating service.

Copies of this information sheet should be made by the patient and given to the appropriate health professionals. The patient should always bring their ventilator and associated equipment when admitted to hospital or when they undergo any sedating procedures. Ideally, these procedures should be performed at a hospital where expertise in the treatment of hypercapnic CSA with NIV has been established.

### Re-assessment of ventilatory response to exercise

Ventilatory responses to exercise can also be re-assessed. Whilst the majority of patients with CCHS can increase their ventilation appropriately during exercise [350], those with insufficient ventilatory response to meet their metabolic demand at a particular workload can be prompted by adding volitional breaths or by consciously increasing their depth of tidal volume to provide sufficient minute ventilation, or given feedback regarding what safe workloads can be achieved and how to pace themselves.

### Alcohol and recreational drug use

A case series of 3 adolescents with CCHS (ages 18-22), reported severe adverse effects of alcohol abuse including coma and death [351]. These authors speculated that adults with CCHS may be less able to perceive the risks of substance abuse and may have impulsive behaviours. The realistic risks of social drug and alcoholic use as respiratory depressants and inadvertently sleeping without their ventilator should be carefully discussed with the patient and associated networks (including trusted peers) [351].

**Key points:**

- Review should occur initially at 3 months, then at the discretion of the service that established therapy or an appropriate trained sleep physician.
- Due to the rareness of some disorders, patients should be continued to be managed by specialised teams.
- In scenarios where there are absent ventilatory responses (e.g. CCHS), chest infections need to be reviewed and managed promptly.
- Written information and education for the patient explaining hypoventilation and the implications this will have for surgery, sedative procedures, uncontrolled oxygen therapy, exercise workload, and alcohol and recreational drug use, needs to be provided.

| RECOMMENDATIONS FOR HYPERCAPNIC CENTRAL SLEEP APNOEA | **Grade** |
|---|---|
| Awake $PaCO_2$ > 45 mmHg in the absence of lung and chest wall abnormalities, skeletal malformations and neuromuscular disorders, in combination with symptoms consistent with sleep disordered breathing warrant a full polysomnogram. | D |
| Long term ventilation is appropriate when central events on the polysomnogram are significant enough to cause nocturnal hypoventilation. | D |
| In patients with isolated sleep hypoventilation, titrate NIV settings in a spontaneous-timed mode, during a full polysomnogram. | D |
| Due to lack of respiratory effort ensure that back up breaths are set to an adequate duration. | D |
| Machines with “mask off” or “low pressure” and “power failure” alarms are recommended especially in disorders where there is a potential inability to arouse from an interruption to ventilation and when there is an absence of ventilatory responses when awake (e.g. CCHS). This alarms are also required if the patient is ventilator dependent. | D |
| Ventilator dependent individuals should be titrated on and use ventilators which have been approved for life support and have an alternative battery source to mains power. This may include using a volume or hybrid dual mode (volume and pressure) ventilator. | D |
| Where hypercapnic central apnoea is caused from pharmacological intake (e.g. opioid based derivatives), referrals to chronic pain team or relevant prescribing body should be made with the aim of reducing medication intake in order to improve central events and stabilise oxygen saturations. | D |
| Overall patient management should be performed by specialised teams. | D |
| Any signs of chest infection should be reviewed and managed promptly, especially in the case of CCHS where a lack of dyspnoea in response to pneumonia may mask severe respiratory compromise. | D |

# CHAPTER 2.9 NON-HYPERCAPNIC CENTRAL SLEEP APNOEA

**RUBY BRILLANTE & LEON LAKS**

## 2.9.1 BACKGROUND

Central sleep apnoea (CSA) is characterised by unstable ventilatory control in sleep, with a lack of drive to breathe, resulting in repetitive episodes of insufficient ventilation and compromised gas exchange. It is variably associated with complications such as frequent night-time awakenings, excessive daytime sleepiness and increased risk of adverse cardiovascular outcomes [352]. There is an overlap between CSA and obstructive sleep apnoea (OSA) and it has been observed that in the majority of sleep apnoea patients, central respiratory events lead to obstructive respiratory events in patients with vulnerable pharyngeal anatomy, and vice versa [353]. A characteristic feature of CSA is an improvement in breathing in REM sleep, in contrast to that generally seen in predominantly obstructive disease. Oxygen desaturation is generally less severe than in obstructive disease, and is associated with mild sleep hypocapnia. While there are different PSG definitions for CSA, single centre trials and a post-hoc analysis of a multicentre trial have defined CSA as an AHI $\geq$15 per hour, with >50% of apnoeas and hypopnoeas being central in nature [354].

CSA is commonly observed in patients with heart failure (HF), in whom it appears to have adverse prognostic implications [355]. It is thought that stimulation by pulmonary congestion of pulmonary vagal irritant receptors [356], and an increase in peripheral and central chemosensitivity [357], lead to chronic hyperventilation. A central apnoea results when the $PaCO_2$ falls below the apnoeic threshold during sleep. In a model based analysis of sleep disordered breathing in congestive heart failure, it was postulated that the development of CSR is the result of a complex interaction between both central and peripheral receptor loops, which may in turn interact with decreased cardiac output and cardiomegaly [358]. Its significance in heart failure remains to be determined but a review of the literature found an independently increased risk of mortality and/or cardiac transplantation in association with the presence of CSA in patients with heart failure [359].

Cheyne-Stokes respiration (CSR) is a periodic breathing pattern with alternating apnoea and hyperpnoea with a waxing-waning pattern of tidal volume. Currently there is no uniformity in the criteria to describe clinically significant CSR. Over half of patients with a left ventricular ejection fraction < 35% display CSR during sleep [360]. It is associated with HF, cerebrovascular accidents (CVA) and ascent to high altitude. It is postulated that CSR in CVA arises from the increased respiratory drive due to reduced cortical inhibition of the central respiratory centre [361], whilst high altitude increases respiratory drive due to hypoxia [362]. An overwhelming majority of the studies on the treatment of CSR and CSA relate to that found in association with heart failure.

Complex sleep apnoea syndrome (CompSAS) is a term used to describe a complex pattern of breathing which was acknowledged by a task force sponsored by the American Academy of Sleep Medicine, the European Respiratory Society, the Australasian Sleep Association and the American Thoracic Society as a “common clinical experience that some patients exhibit predominantly mixed apnoeas, while other patients exhibit obstructive apnoeas that seem to change to central events by alterations in body position or application of positive airway pressure [363].” Time series analysis of sleep stability state has been proposed as a tool in recognising “complexity” but this is currently not clinically available, and such complexity may not be unmasked until application of CPAP [364].

Using a definition of CompSAS as “a syndrome whereby CPAP titration eliminated events defining OSAHS, but the residual central apnoea index was $\geq$5 per hour, or CSR became prominent and disruptive”, a retrospective study of 223 patients with suspected sleep-related breathing disorders over 1 month, reported a prevalence of 15%, whereas that of CSA was only 1% [365]. Further, clinical characteristics of patients with CompSAS were more similar to patients with OSAHS than CSA, until CPAP was applied. A retrospective case control study which included 34 patients with CompSAS, using the above definition, found that these patients experience more interface problems, required more follow up, and CPAP levels were prescribed at similar rates to OSAHS patients. In both of the

above studies, no truly optimal CPAP setting was found that abolished all respiratory sleep disturbances. The addition of supplemental oxygen to CPAP therapy may stabilise breathing in sleep [366, 367], but there is a paucity of data in this regard.

**Key points:**

- Non-hypercapnic central sleep apnoea is defined by unstable ventilatory control in sleep, with a lack of drive to breathe, resulting in repetitive episodes of insufficient ventilation and compromised gas exchange.
- Characteristically, oxygen desaturation is generally less severe than in obstructive disease and there is mild sleep hypocapnia. Also there is usually an absence of central events in REM sleep.
- The presence of CSA in patients with heart failure is associated with increased mortality and cardiac transplantation rate.
- A subgroup of patients with OSAHS develop a prominent CSA pattern on application of CPAP. Treatment with CPAP may be suboptimal and other options for therapy may need to be considered.

## 2.9.2 BASIC INVESTIGATIONS & MEASUREMENTS

The diagnostic criteria for CSA are not well defined, but the majority of evidence shows that in patients with HF, those with CSA and CSR have worse survival than patients with AHI below these threshold levels after controlling for confounding factors [368]. An echocardiogram or gated heart pool scan will document left and right ventricular function to establish the presence of HF, or in the setting of pre-existing HF, provide a baseline with which subsequent tests can be compared. $PaCO_2$ has been found to be inversely proportional to pulmonary capillary wedge pressure [369] and lowering wedge pressure is associated with a rise in $PaCO_2$ and alleviation of CSA [356].

**Key point:**

- Initial assessment should include full diagnostic polysomnography, echocardiogram or gated heart pool scan for patients with overt or suspected HF, and ABG to establish the baseline $PaCO_2$.

## 2.9.3 TREATMENT OPTIONS AND OUTCOMES

In those with HF, first-line therapy should be optimisation of HF treatment. A few small non randomised studies have found attenuation of CSA with intensification of pharmacologic therapy [370-372]. Furthermore, cardiac resynchronisation pacemaker therapy [373, 374] and heart transplantation [375] had similar effects, again in nonrandomised trials, with a resultant improvement in cardiac function.

### Oxygen Therapy

Nocturnal supplemental oxygen blunts the hypoxic respiratory drive and hyperventilation. Over a period of 1 week to 1 month, its administration has been shown to reduce CSA, abolish the apnoea- related hypoxia and decrease urinary norepinephrine, as well as improve maximum oxygen uptake during graded exercise [376-378]. Although no improvement in left ventricular ejection fraction, patient symptoms (based on Epworth sleepiness scale, visual analogue and quality of life scores) or cognitive function (by neuropsychometric testing) was shown over a period of one month [376], a more recent randomised control trial of 56 patients [379] showed that following 12 weeks of treatment, nocturnal oxygen significantly improved New York Heart Association (NYHA) functional class, Specific Activity Scale scores, and LVEF, in conjunction with an improvement in sleep disordered breathing. However, there is concern that hyperoxia from supplemental oxygen use may result in the production of free oxygen radicals thus causing cardiovascular damage [380]. These findings highlight the need for large

scale, longer term trials to determine the effect of oxygen on clinical outcomes, and which patients are most likely to benefit from this therapeutic intervention.

### CPAP Therapy

The effects of CPAP on cardiovascular outcomes have been evaluated extensively. It has been shown to reduce left ventricular transmural pressure and afterload by increasing intrathoracic pressure [381], reduce sympathetic activity [382], and augment stroke volume [383]. It also reduces LV preload by reducing end-diastolic volume and pressure [356]. In a review of the literature by Arzt and Bradley in 2006 [384], it was noted that when patients were acclimatised to CPAP during a gradual 2 to 7 day titration to higher pressures of 8 to 12.5 cmH2O, the frequency of central apnoeas and hypopnoeas fell by 50-67% after 2 to 12 weeks, whereas in randomised trials of nocturnal CPAP use for 1-14 nights at low pressures (5-7.5 cmH2O), CSA was not alleviated.

A large, long-term, randomised multicenter trial, the Canadian Positive Airway Pressure trial involving subjects with congestive heart failure, demonstrated that CPAP attenuates CSA, improves nocturnal oxygenation and LVEF, lowers plasma norepinephrine concentrations, and increases 6-minute walking distance [385]. There were, however, no significant differences in transplant-free survival, rate of hospitalisations or quality of life between the 2 groups. However, using a definition of CSA of AHI ≥ 15/hour with >50% of apnoeas and hypopnoeas being central in nature, a post-hoc analysis of the CANPAP database showed that suppression of CSA to an AHI below the threshold of 15/hour might improve both left ventricular function and heart transplant-free survival [354].

In a recent observational study it was shown that in HF patients with CSA, CPAP causes a progressive significant alleviation of CSA between the second night of its application (AHI = 22.2 ± 12.6) and 12 weeks later (12.8 ± 11.0) on the same pressure level [386]. It was concluded that CPAP therapy leads to a time dependent alleviation of CSA in some HF patients, indicating that in such patients neither clinical nor scientific decisions should be based on a short term trial of CPAP. It was recommended that the most appropriate means to judge the efficacy of CPAP on CSA would be a follow-up sleep study after a 2 to 4 week trial on CPAP [386].

### Bilevel pressure pre-set ventilation (BVS) in CSA

Studies have investigated the effect of NIV on CSA with the use of bilevel pressure pre-set machines. BVS in the spontaneous/timed mode with a back up rate has been shown to reduce arousals and improves sleep quality in patients with Cheyne-Stokes respiration in sleep [387]. Its administration for one hour was found to reduce systemic vascular resistance, systolic blood pressure and heart rate in patients with HF [388]. In a randomised controlled trial of 52 patients with idiopathic dilated cardiomyopathy and central sleep apnoea syndrome, treatment with BVS over 3 months resulted in a significant improvement in NYHA functional class score, LVEF, heart rate, systolic and diastolic blood pressures, plasma brain natriuretic peptide (BNP) and quality of life (specific activity scale) [389]. Similarly, in 14 patients with CSR-CSA treated with 3 months of NIV, there was a significant improvement in LVEF, NYHA functional class and plasma BNP [390].

Patients commenced on NIV need careful monitoring, selection, and titration as highlighted by a retrospective study of a diverse group of patients (including OSA, MND, PLMs with OSA, and primary CSR) [391], most of whom had Cheyne-Stokes respiration. There was an increase in central apnoeas from baseline and as compared with CPAP therapy when NIV was applied, especially when using higher pressure support (mean for the study was 5.9 ± 3.1 cmH2O). Interestingly only 11 of the 95 patients treated with NIV in this study also had HF as a co-morbidity. Further investigation is needed to determine longer term effects of NIV.

A randomised cross-over study of 16 patients with CSA showed equal improvements in sleep quality, daytime fatigue, circulation time and NYHA class in those on CPAP versus NIV [392]. Teschler et al compared a single night each of oxygen (2L/min), CPAP, NIV and adaptive servoventilation (ASV) administered in random order in 14 subjects with CSA [23]. NIV was superior to CPAP and oxygen alone in abolishing central sleep apnoea, but inferior to ASV. It was equal to oxygen and ASV in reducing oxygen desaturation, and superior to CPAP.

**Adaptive Servo-ventilation (ASV)**

Adaptive servo-ventilation is an emerging mode of therapy for CSA/CSR in which a varying amount of ventilatory support is provided, based on breath-by-breath analysis. Although results are promising, there is a lack of large scale, long term randomised studies to assess its efficacy and beneficial effects over the longer term.

Over a single night, ASV was shown to be superior to NIV (mean IPAP 13.5 $cmH_2O$, EPAP 5.2 $cmH_2O$), CPAP (mean 9.3 $cmH_2O$) and oxygen (2L/min), in reducing central apnoeas and in improving sleep architecture [23]. One month of ASV resulted in a reduction in excessive daytime somnolence (Osler test), BNP and urinary metadrenaline excretion [393]. Over 6 months, ASV produced complete correction of CSA/CSR, a greater reduction in daytime symptoms (ESS), better compliance, better improvement in quality of life, and a significant increase in LVEF, compared to CPAP therapy [24].

The promising efficacy of ASV has also been investigated in complex sleep apnoea syndrome, during a single night of treatment. In a randomised cross-over trial of ASV versus BVS in 21 patients with mixed, central and complex sleep apnoea, Morgenthaler et al demonstrated ASV was effective in normalising AHI in all 3 groups (residual AHI < 1.6 ± 3.6), whereas BVS was less effective in CompSAS (residual AHI 6.8 ± 6.8) than in CSA/CSR (residual AHI 1.5 ± 1.5) and ineffective when there was predominantly mixed apnoeas (residual AHI 10.2 ± 10.6) [394].

In a more recent retrospective review of 100 patients, of whom 63 had CompSAS, and 37 with CSA ± CSR, ASV was superior to BVS and CPAP in normalising AHI on the first treatment night in the sleep laboratory in CompSAS. In addition, ASV was well tolerated and resulted in symptomatic improvement on follow up [366]. However, the impact of ASV compared to other therapies on longer term outcomes such as quality of life and mortality have not been investigated.

**Key points:**

- In those with HF, optimisation of HF treatment should be first-line therapy.
- Over a period of 1 week to 1 month, nocturnal oxygen therapy abolishes CSA, and abolishes apnoea-related hypoxia.
- Oxygen therapy improves NYHA functional class, quality of life and LVEF, after 12 weeks of treatment.
- CPAP is best instituted by prior pressure titration, and if necessary, a period of acclimatisation. In comparison to lower pressures, pressures of 8 to 12.5 $cmH_2O$ have been shown to be more successful in reducing the frequency of central apnoeas and hypopnoeas.
- CPAP therapy leads to a time dependent alleviation of CSA in some HF patients, indicating that in such patients neither clinical nor scientific decisions should be based on a short term trial of CPAP.
- In the long term, CPAP attenuates CSA, improves nocturnal oxygenation and LVEF, and increases 6-minute walking distance, but it did not appear to improve quality of life, rate of hospitalisation or transplant-free survival.
- Patients with suboptimal control of CSA on CPAP alone may benefit from the addition of nocturnal oxygen.
- 3 months of BVS in CSA and HF resulted in significant improvements in LVEF, NYHA functional class, systolic and diastolic blood pressures and quality of life.
- Patients commenced on NIV need to have a full PSG/pressure titration to ensure that this treatment does not result in an increase in central apnoeas.
- ASV is effective in attenuation of CSA in HF, reducing daytime somnolence, improving quality of life, and increasing LVEF. ASV has been shown to be superior to BVS, CPAP and oxygen over 1 night to 6 months, in terms of reducing central apnoeas, patient compliance, and LVEF improvement.
- ASV is superior to CPAP and BVS in attenuating complex sleep apnoea on the first titration night.
- There is a need for long term and large scale studies in the use of oxygen, BVS and ASV in CSA.

### 2.9.4 INDICATIONS FOR NIV

A trial of home ventilation in patients with non-hypercapnic CSA should include the consideration of the following:

i) An echocardiogram or gated heart pool scan to document left and right ventricular function to establish the presence of, or provide a baseline measure of, heart failure. An arterial blood gas should be performed to document $PaCO_2$.

ii) In patients with CSA in heart failure, optimisation of heart failure should be first line treatment.

iii) Symptoms of sleep disordered breathing (such as frequent awakening, snoring, choking, gasping, waking dry mouth, waking dyspnoea or witnessed apnoeas).

***OR***

Symptoms of impaired sleep quality (such as daytime somnolence, waking headache or grogginess, fatigue, impaired cognition, impaired short-term memory, irritability, anxiety and depression).

***AND***

iv) Full diagnostic sleep study which demonstrates CSA or CSR.

The diagnostic criteria for CSA are not well defined but patients with HF (LVEF<45%) with an AHI of $\geq$ 15 on full nocturnal diagnostic polysomnography, in which at least 50% of events are central, should be considered for treatment [354].

***AND***

v) Where the initial trial of CPAP (with or without supplemental oxygen) fails to adequately improve symptoms, CSA or LVEF, after a period of acclimatisation or if the patient is intolerant of this treatment.

vi) Adaptive servo-ventilation (ASV) should be considered. Patients with a persistence of CSA upon the application of CPAP after a period of time ("complex sleep apnoea") may be considered for ASV if adjunctive oxygen can be shown to be ineffective. Objectively, it should be shown that ASV is able to better control CSA than CPAP therapy, either on overnight polysomnography or after a period of inpatient acclimatisation with high resolution nocturnal oximetry.

### 2.9.5 TITRATION

A pressure titration study showing improvements in desaturation and central apnoeic events at the prescribed pressure, must be undertaken prior to instituting the positive pressure trials. This includes the initial CPAP (± oxygen) trial and where relevant, subsequent ASV trials. Gradual CPAP acclimatisation with the aim of achieving pressures of 10-12cm$H_2O$ should be undertaken in patients with CSR-CSA and heart failure, rather than a single night titration with the expectation of abolishing central events [354]. In patients who are hypocapnic, BVS is not recommended, as the pressure support can create greater fluctuations to $PaCO_2$ which can destabilise their ventilation even further.

### 2.9.6 FOLLOW UP AND ANCILLARY CARE

The patient and/or carer should be educated on machine and mask use prior to a home trial. There should be a review within 1 month with a sleep physician, to assess compliance with and response to treatment. Further reviews at 3-6 monthly intervals should aim to assess improvements in symptoms of CSA, as well as those of the underlying disease. Once the patient has acclimatised to the treatment, patients may be reviewed at least annually. There may be a need to trial more than one mode of therapy, depending on its effect on the sleep breathing disorder, as well as patient's tolerance of the treatment.

There should also be ongoing specialist reviews, such as cardiologist, neurologist, to optimise medical therapy, as well as to monitor the progress of any underlying pathology.

| RECOMMENDATIONS FOR NON-HYPERCAPNIC CENTRAL SLEEP APNOEA | **Grade** |
|---|---|
| In patients with CSA in HF, optimisation of HF treatment should be first-line therapy. | D |
| Prior to commencing treatment, patients should have full PSG demonstrating benefit from the chosen treatment. | B |
| If patients are unable to have full PSG then a period of inpatient acclimatisation/titration and overnight oximetry showing attenuation of apnoea-related hypoxia should be performed. | D |
| CPAP therapy should be trialled as a first line ventilatory assistance treatment, with or without oxygen, to attenuate CSA, improve nocturnal oxygenation, exercise capacity and LVEF. | B |
| The most appropriate means to judge the efficacy of CPAP on CSA would be a follow-up sleep study after a trial of 2 to 4 weeks on CPAP. | B |
| ASV should be considered in patients who have not had a resolution of CSA on CPAP and/or oxygen, or have been shown to have better compliance with this mode of therapy. However, it needs to be shown that ASV is able to better control CSA, either on overnight polysomnography or after a period of inpatient acclimatisation with nocturnal oximetry. | B |
| Patients with a persistence of CSA upon the application of CPAP after a period of time (“complex sleep apnoea”) may be considered for ASV if adjunctive oxygen can be shown to be ineffective. | C |
| In those with CSA in HF, at least 6 monthly echocardiogram and NYHA class score assessment should be performed to establish response to therapy. Once stable and a plateau is reached at least annual reviews may be undertaken, with interval tests when symptoms recur or worsen. | C |

# CHAPTER 2.10 RESPIRATORY INSUFFICIENCY FOLLOWING CATASTROPHIC MEDICAL ILLNESS

**AMANDA PIPER**

## 2.10.1 BACKGROUND

Most patients admitted to intensive care units (ICU) requiring mechanical ventilation are usually weaned completely within a few days or weeks following stabilisation of the primary presenting problem. However, the need for more prolonged weaning occurs in around 15% of critically ill patients [395], with 3-6% of patients requiring ongoing long-term ventilatory support [396]. In the majority of cases, these patients will have a background of underlying respiratory, cardiac or neuromuscular disease.

A significant advance in the area of weaning has been the use of non-invasive ventilatory support (NIV). Recognising patients at high risk of extubation failure and introducing NIV in the immediate post extubation period has been shown to reduce the need for re-intubation and mortality in two randomised trials [397, 398]. In a significant number of these patients there will be a history of chronic hypercapnic respiratory failure prior to their presentation with acute decompensation, and NIV will be required on a long-term basis to maintain stability and achieve successful discharge home [399]. Consequently, ongoing nocturnal non-invasive ventilatory support may be required in a minority of patients presenting with acute on chronic respiratory failure managed in intensive care units. As ventilatory support is required during sleep periods only, these individuals may be managed as any other patient presenting with nocturnal hypoventilation. In some, following a period of bilevel support a switch to long term CPAP may be possible [200].

In a small number of individuals ongoing total ventilatory support will be needed over a prolonged period of time. An appropriate weaning program may achieve a gradual improvement in respiratory function such that some of these individuals may be liberated from ventilation entirely or may eventually require nocturnal ventilation only [400, 401]. In the remainder however, continuous ventilation, usually invasively, will be required on an ongoing basis. Although the number of individuals requiring long-term continuous ventilation is small their care can consume a considerable amount of health resources and tie up ICU beds for prolonged periods. Once medical stability is achieved, the ICU environment is not the most appropriate location for ongoing management of these individuals. However, a lack of facilities to care for these patients and insufficient access to funding for equipment means that many patients remain in ICU type areas, even though this is inappropriate from an institutional resource/financial standpoint as well as from a patient psychological/well being perspective [402].

Ideally, the preferred location for long-term mechanical ventilation, regardless of whether it is delivered invasively or non-invasive is usually the home or community care facility. This is because costs are reduced, quality of life is enhanced and integration into the community is maximised [402]. However, in order to achieve this, the patient and carer need access to considerable technical and financial resources as well as family and social supports. Even if home discharge is not feasible, a transfer of the patient out of ICU to a low care environment is important to improve the efficient use of ICU beds.

In addition, the ICU setting focuses on patient stabilisation and recovery from the acute insult. For patients who are medically stable but are experiencing difficulty weaning from ventilation, this is not the most appropriate environment for ongoing weaning to occur. Overseas data have shown that a transfer to another setting where the emphasis is on continued weaning and rehabilitation increases weaning success [400, 401, 403]. Weaning in this context can refer to the complete removal of ventilatory support, as well as to a reduction in the time of support or its invasiveness.

In the past, ventilatory support via tracheostomy has been considered the more appropriate and effective approach of managing patients requiring continuous or near continuous ventilatory support [404]. Tracheostomy provides direct access to the airways for clearing secretions and provides some degree of airway protection. However, placement of a tube also increases the risk of erosion,

granulation tissue formation and haemorrhage as well as mucus hypersecretion [405]. Speech and swallowing may also be affected in some individuals. Importantly, the presence of a tracheostomy tube, whether for partial or continuous ventilation, significantly increases patient care needs, which may or may not be able to be managed in the home by the family [75, 406]. In a prospective study of consecutive patients using tracheal ventilation, 38% of carers reported that having a person at home receiving mechanical ventilation was a major burden because it affected their entire lifestyle and was very stressful [407]. Forty three per cent of respondents reported night-time was especially burdensome and stressful because of the patient's anxiety and chronic insomnia.

Overseas data suggests an increasing use of non-invasive techniques for ventilatory support in patients requiring continuous or near continuous long-term ventilation [408, 409]. However, for this to be effective and safe, an appropriate level of equipment and caregiver training is crucial. Whether the patient is best served using invasive or non-invasive techniques for long term ventilatory support is a clinical decision based on medical considerations, local resources and staff experience.

With advances in medical practices and technology, more patients are surviving catastrophic illness and living longer. As a consequence, the problem of how to manage ongoing ventilation, especially when it is required on a near continuous basis has arisen and needs to be properly addressed and adequately funded. Overseas experience suggests this can be done, but an established process which includes proper training of staff to handle these cases, an appropriately funded care package to provide equipment and care, and mechanisms whereby these individuals can be properly monitored in the community is needed. The development of appropriately staffed and resourced weaning units to maximise the likelihood of reducing the time and/or invasiveness of ventilatory support is also required.

### 2.10.2 INDICATIONS

Patients who:

i) have been managed in an ICU/HDU area for more than two weeks for medical stabilisation of an acute or acute on chronic event

ii) continue to require invasive ventilation

iii) where a tracheostomy tube has been placed due to length of ventilation requirements or an inability to protect their own airway

iv) where attempts to liberate the patient completely from ventilatory support have been unsuccessful due to rising daytime or nocturnal $CO_2$ levels

Following appropriately initiated weaning strategies, two groups of patients will emerge following catastrophic medical illness: those requiring ongoing nocturnal support only, and those in whom continuous or near continuous mechanical ventilation is required. Equipment needs, level of carer training, costs and level of community support will vary depending on the interface by which ventilatory support is delivered and the proportion of the 24 hour period over which NIV is required.

### 2.10.3 ESTABLISHING THE NEED FOR AND TYPE OF ONGOING VENTILATORY SUPPORT

Once the acute process has been managed and the patient is stable, the aim of the weaning process is to determine the medically appropriate level of ventilatory support that allows ventilator-independence without causing a physiologic deterioration [402]. While initial weaning attempts will be made in the ICU setting, this is not an appropriate environment for long-term management from either the hospital or patient perspective. The majority of long-term ventilator patients require significant rehabilitation, which is difficult to implement in ICU [402].

The appropriateness of efforts to reduce or remove ventilatory support during wakefulness can be monitored by continuous non-invasive methods such as oximetry. This should be followed up by blood gas measurements to check for changes in carbon dioxide and bicarbonate levels. Arterial access may be limited in some individuals, making venous or arterialised venous sampling a more appropriate approach than repeated arterial sampling.

In conjunction with reductions in daytime ventilatory support, trials of cuff deflation and swallow practice should be undertaken. The use of a speaking valve, once cuff deflation is tolerated, will help promote a more normal breathing route and encourage communication by the patient. Progression to capping of the tube for more extended periods is then the next step, where trials of non-invasive support during sleep and oral intake can be undertaken. If it is found that the patient is able to swallow effectively, and non-invasive ventilatory support is effective, then the tube may be removed.

If continuous spontaneous breathing during wakefulness is achieved, attention should then be directed towards the need for nocturnal ventilatory support. Withdrawal of ventilation during sleep may result in emergence of abnormal gas exchange and symptoms within days [410-412] in patients in whom ongoing ventilatory support is required. If the patient's clinical condition and daytime blood gases have improved to the point where withdrawal of ventilatory support is thought appropriate, close monitoring of daytime blood gases and nocturnal saturation needs to be undertaken until the adequacy of spontaneous nocturnal ventilation over a prolonged period has been established. Studying the patient during the first night off ventilatory support is not appropriate, as arousal from sleep and restricted REM may limit the degree of abnormality seen [411].

Volume preset devices are preferable for those individuals who require daytime ventilatory assistance in addition to nocturnal use [409, 413], as both mouthpiece support and breath stacking to aid secretion removal is possible. Many patients using NIV find pressure preset ventilation a more comfortable option for sleep. Devices that are able to provide both volume or pressure modes of ventilatory support are ideally suited for these individuals.

In patients unable to cough effectively, methods of assisted secretion clearance such as manually assisted cough, maximal insufflation and cough in-exsufflation techniques should be introduced and are especially important in patients where decannulation of the tracheostomy tube is planned. The aim is to achieve assisted cough flows above 160L/min [414]. Techniques to achieve this need to be taught to the patient and caregivers, with encouragement to continue practising with supervision. Mechanical insufflation-exsufflation is generally used when manually assisted coughing is inadequate.

### Discharge Planning

Discharge planning is crucial in achieving an effective and safe transfer of the patient out of ICU and to a setting with lower monitoring that enhances the individual's potential. Discharge planning is not only needed for patients returning home, but is also necessary to successfully transfer the patient to a ward area or nursing home facility.

For individuals where ventilatory support has been successfully reduced to nocturnal non-invasive ventilation, discharge home is usually straightforward following the same procedure as for any patient newly established on NIV. Additional follow up services such as general rehabilitation, community health support or home nursing may be appropriate if the patient's discharge status remains below their normal level.

Discharge of the ventilator dependent or tracheostomy ventilated individual, whether home or to some assisted care facility, is a more complex process and requires a multidisciplinary and integrated management approach. Identifying these individuals early and establishing likely placement possibilities is important in planning their ongoing management. As part of the plan to discharge the patient from ICU, the objectives of long-term ventilation need to be determined and barriers to transfer home including financial, social and environmental factors identified. In order for this to be done properly, an experienced multidisciplinary team of health-professionals is needed.

Possible avenues for funding of equipment, and where needed, attendant care, need to be explored and established to facilitate discharge planning into the community without affecting patient safety or placing too great a burden on family members. Once available resources are identified these can be compared to the resources needed to safely discharge the patient. Unless there are indications that ventilatory support parameters during sleep are inadequate or excessive, there is no evidence that routine full sleep studies add to patient management.

### Equipment

Equipment chosen for home care needs to be portable, user friendly and durable. The patient should be well established on the equipment prior to discharge. In selecting ventilator equipment, maintenance and replacement during servicing by the equipment supply company should be clarified.

Arrangements to deal with equipment breakdown and the time frame for replacement and repair need to be established. Identification of the type of consumables that will be needed at discharge and an estimate of quantities also needs to be made.

- Patients requiring ventilatory support > 18 hrs/day should have a back up ventilator available for emergency use in case of machine breakdown. This is also true for patients who are geographically isolated where more than 16hr/day ventilatory support is required and where a replacement ventilator cannot be provided within 4 hours.
- In such cases, only devices designated as suitable for life support should be used
- For those meeting the above requirements an alternate power source in case of mains power failure should be provided.
- Standard equipment supply should also include a manual AMBU type bagging system, adapted for mask, mouthpiece or tracheostomy use as appropriate.
- Where ventilatory support is via tracheostomy, a humidification system must be provided
- Suction equipment should also be provided
- A replacement tracheostomy tube of appropriate size plus a tube one size smaller should be sent home with the patient.
- If the patient is being managed with non-invasive support and requires more than 12hrs / day of therapy or has a disorder where increasing ventilation time is likely to occur, a range of interfaces and ventilatory strategies need to be trialled. Close monitoring to identify the need for extended periods of daytime support and the provision of a back up device is necessary.
- A risk minimisation strategy and emergency action plan should be developed and provided for each individual.

**Carers and personnel**

There is no evidence that trained nurses are needed for continuous long-term care needs in the home, and in many countries family members supported by personal attendant caregivers provide effective home care [415], even in continuously invasively ventilated patients. Family caregivers also need to be willing and capable of taking on the physical care of a person requiring ventilatory support particularly if this is through a tracheostomy. Initially, caregivers are likely to be intimidated by the ventilatory and accessory equipment required, and may find procedures such as suctioning unacceptable or frightening. For these reasons, the medical and respiratory management of the patient needs to be simplified as much as possible, suited to a home environment rather than relying on “ICU” style protocols. Caregivers should be trained on the actual brands of equipment that are to be used in the facility/location the patient is to be transferred to in order to maximise familiarity with it [402]. Training of the patient and family should include the use of the ventilator, tracheostomy care, bagging techniques and CPR. The carer/s need to develop confidence in handling equipment, identifying problems and responding to them. In those patients using NIV, assisted cough techniques also should be taught to carers.

Coordination of efforts and communication between disciplines and between sites will be essential if successful discharge of the patient is to be achieved. A comprehensive written management plan covering all aspects of the patient’s care will facilitate this and should be developed for discharge. This needs to include the goals of therapy as discussed with the patient and family, as well as clearly documented advanced care directives.

**Key points:**

- A multidisciplinary approach to the assessment, management and discharge planning of patients with high level ventilation needs is central to effective and safe discharge. A respiratory physician should be involved in ongoing patient management.
- Ongoing management in an ICU area is not medically or socially appropriate for a patient requiring long term continuous ventilatory support.
- In order to safely discharge a patient home with high-level ventilatory support needs, extensive support and planning needs to be undertaken with access to funding for equipment and additional carers, as well as access to suitable placement sites in addition to the patient's home.
- The development of specialised 'weaning units' to facilitate the liberation of the patient from ventilatory support.
- Simple bilevel devices are suitable for individuals requiring nocturnal and limited daytime ventilatory support only. However, more sophisticated volume or hybrid devices are indicated for patients requiring more than 18hrs/day or where bilevel devices have proven to be inadequate.
- The same type of ventilator equipment which is to be used at home or other long term facility should be introduced as early as possible in the care of the patient while still in the acute care facility.

## 2.10.4 ONGOING FOLLOW UP AND ANCILLARY CARE

Follow up after discharge can be difficult for the ventilator dependent patient to arrange due to transportation issues to and from outpatient clinics. In this situation, home visits by staff to monitor the patient and check equipment may be necessary. However, the small number of patients, the large geographical area over which they are living, and the limited expertise of community based staff in this area, often renders this option impractical. For each patient a process needs to be established where the patient is regularly reviewed and any change in their ventilator or general medical needs attended to.

*Equipment*

- Preventative maintenance should be provided at the frequency recommended by the manufacturer.
- The need to replace equipment which is outdated or beyond economical repair must be identified and carried out in a timely fashion to ensure the patient who is ventilator dependent is not left with inappropriate ventilatory support

*Carer training and support*

- Ongoing education of the patient and carer/s with monitoring of skills
- Periodic checking of the family/carers to ensure they are coping with the burdens of care
- Access to community packages to assist in equipment for daily care and for respite of carers is essential

*Emergency action plan*

- An action place for managing changes in medical status or emergency situations should be established and provided to the patient and carer.
- The patient/carer must have functioning phone lines for contact

| RECOMMENDATIONS FOR RESPIRATORY INSUFFICIENCY FOLLOWING CATASTROPHIC MEDICAL ILLNESS | **Grade** |
|---|---|
| A multidisciplinary approach to the assessment, management and discharge planning of patients with high level ventilation needs is central to effective and safe discharge. | D |
| The development of specialised 'weaning units' to facilitate the liberation of the patient from ventilatory support. | D |
| Ongoing management in an ICU area is not medically or socially appropriate for a patient requiring long term continuous ventilatory support. | D |
| Simple bilevel devices are suitable for individuals requiring nocturnal and limited daytime ventilatory support only. However, more sophisticated volume or hybrid devices are indicated for patients requiring more than 18 hours/day or where bilevel devices have proven to be inadequate. | D |
| Facilities for respite care should be available for ventilator dependent patients as well as for those patients requiring nocturnal ventilatory support only but with high level physical care needs. | D |

# CHAPTER 3 NOCTURNAL MONITORING IN THE DIAGNOSIS AND MANAGEMENT OF SLEEP HYPOVENTILATION SYNDROMES

**AMANDA PIPER**

## 3.1 DIAGNOSIS OF RESPIRATORY FAILURE

The indications for full polysomnography (PSG) in establishing the need for nocturnal ventilatory support remains controversial. A PSG can be a major organisational undertaking for patients with high level care needs and limited mobility. With the long waiting times in many centres for sleep studies, organising a diagnostic PSG for a patient with obvious daytime indicators for commencement of NIV may delay the institution of appropriate therapy putting the patient at risk of deteriorating during this waiting period. There is currently little evidence to support the need to document sleep quality in determining the need for NIV in patients with an appropriate diagnosis who have already developed daytime hypercapnia. Previous consensus regarding initiation of NIV has cited daytime hypercapnia as a primary indicator for the introduction of NIV [106]. On the other hand, the role of limited nocturnal monitoring involving $SpO_2$ and other respiratory parameters in screening patients with few sleep symptoms and normal daytime $CO_2$ levels has yet to be fully defined. However, it is recommended that at least a multichannel sleep study is performed to exclude sleep apnoea [106].

Recent evidence has demonstrated the benefits of commencing NIV at the first appearance of nocturnal hypoventilation and sleep breathing abnormalities [79, 136, 416] in patients with neuromuscular and chest wall disorders. In some cases this can be identified by cardiorespiratory measurements alone during sleep with an emphasis on oximetry and carbon dioxide monitoring [79, 136, 416-419]. Consequently, for patients without daytime hypercapnia or symptoms, limited monitoring which includes at least oximetry and $TcCO_2$ / $ETCO_2$ could be used to screen for sleep hypoventilation when access to full PSG is unavailable. In addition, documenting arterial blood gases prior to sleep and again on awakening can provide useful information regarding overnight $CO_2$ retention [291, 420].

It should be borne in mind however, that while a positive finding on a limited study is informative, a negative study can not rule out the possibility of sleep hypoventilation since the presence of REM sleep cannot be confirmed from limited monitoring. Consequently, sleep hypoventilation may be underestimated if the patient has poor sleep efficiency, a low proportion of REM sleep or a high REM arousal index [421, 422]. A lack of REM sleep in itself is diagnostically important [422], and in patients with MND, reduced or absent REM sleep has been shown to be associated with reduced survival [423]. Overnight oximetry alone may also be relatively insensitive to changes in oxygenation in patients in whom resting $PaO_2$ is above 70mmHg [424], as is commonly seen in patients with neuromuscular disorders. Therefore, to identify sleep hypoventilation, some measure of carbon dioxide in addition to oximetry is recommended.

## 3.2 MONITORING DURING TITRATION AND FOLLOW UP OF NIV

The PSG is often used to titrate pressures in patients with hypoventilation, especially when upper airway obstruction is present [126], or if the patient experiences a poor response to therapy [16, 126]. Periodic sleep study reviews on therapy after treatment initiation has also been recommended to evaluate response to therapy and to correct any unexpected problems [16, 424]. In children, international guidelines recommend review studies every 6-12 months based on expert opinion [425]. However, in adults there is currently no consensus on the frequency of reviews or the type of review that should be undertaken. However, periodic nocturnal studies appear justified. Although there is no literature available in adults, a recent study of children using nocturnal respiratory support demonstrated that two-thirds of sleep studies resulted in a change in respiratory support settings [426].

Most newer style bilevel machines have the capability of downloading information regarding recent machine output including leak and residual AHI. However, there is no available data independently confirming the accuracy of this information or how abnormalities identified in this manner relate to clinical status and subjective reports from the patient. Nevertheless, downloadable information from these devices could be used as a screening tool to identify the need for further investigation, especially where oximetry is included in this monitoring information.

**Key points:**

- When daytime indicators for NIV have already been met, a full diagnostic PSG measuring sleep quality is not an essential element in determining the need for NIV.
- The minimum requirement for identifying sleep hypoventilation is overnight monitoring of oxygen saturation and, where possible, carbon dioxide along with evening to morning arterial blood gases.
- In restrictive thoracic and neuromuscular disorders, NIV should be initiated once nocturnal hypoventilation is identified.
- Periodic nocturnal studies to identify unexpected problems or correct identified ones is indicated, with the frequency influenced by current response to therapy and the nature of the patient's underlying disorder.

## 3.3 THE ROLE OF CARBON DIOXIDE MONITORING

$PCO_2$ is inversely proportional to alveolar ventilation and consequently is measured extensively in patients with both acute and chronic respiratory failure to identify the degree of hypoventilation present and to monitor the impact of intervention. Although $PaCO_2$ is regarded as the "gold standard" technique for $PCO_2$ assessment [20], frequent punctures for blood gas analysis or the insertion of an arterial line are not suitable for the patient with chronic respiratory failure being assessed as an outpatient or in the sleep laboratory. In addition, arterial blood gases reflect breathing at only one point in time and may miss significant changes in $CO_2$ between measurements. Consequently, other approaches to monitoring $CO_2$ are required during the diagnostic and treatment phases in patients with hypercapnic respiratory failure.

Arterial blood gases obtained prior to sleep and again at awakening next morning can provide valuable information regarding sleep hypoventilation, with the change in value highly correlated with the severity of sleep hypoventilation present [420].

If arterial blood gases are unable to be performed, capillary blood gases taken from the fingertip or earlobe will closely reflect arterial $PCO_2$ and pH over a wide range of values [427]. However, adequate vasodilation needs to be achieved by either applying a topical vasodilatory substance to the skin and/or warming of the area. Like arterial blood gases, capillary blood values reflect only a single point in time.

Transcutaneous carbon dioxide ($TcCO_2$) measurements allow real time estimation of $CO_2$ levels over a prolonged period. There are a number of recognised limitations associated with TcCO2 monitoring, including drift [420], and the need for further technical improvements in providing for real-time drift correction is recognised [428]. There is also a lag time of approximately 2 minutes between $TcCO_2$ and $PaCO_2$ [429, 430]. Despite these limitations, most recent studies suggest that $TcCO_2$ measurements are appropriate for clinical monitoring of patients with respiratory failure both for diagnostic and treatment purposes [428-432]. As sleep hypoventilation is most likely to occur during REM sleep, the change in $TcCO_2$ from NREM to REM sleep can be a useful indicator especially when an overall drift in the signal is present. This measurement is taken as the average $TcCO_2$ in the preceding 5 minutes of NREM to the maximum value seen in REM ($\Delta$NREM-REM) [288, 420].

End tidal carbon dioxide has been widely used in intubated patients undergoing anaesthesia and during mechanical ventilation to monitor the adequacy of alveolar ventilation [433]. Although the difference between $PaCO_2$ and $ETCO_2$ is often only a few mmHg in healthy adult subjects with normal lungs [434], the gradient increases substantially and variably in the presence of V/Q mismatch or high dead space to tidal volume ratio [435]. Such circumstances occur in the presence of lung disease, poor cardiac output as well as during sleep. Sanders et al [436] evaluated the accuracy of $ETCO_2$ during sleep in a group of patients with either OSA or nocturnal hypoventilation. Even during spontaneous

room air breathing, $ETCO_2$ did not accurately reflect $PaCO_2$ during sleep with only 23% of the variation in $PaCO_2$ predicted by the variation in $ETCO_2$ [436]. $ETCO_2$ was particularly inaccurate in the setting of supplemental oxygen and PAP therapy. In the literature and in clinical practice, $TcCO_2$ is more likely to be used than $ETCO_2$ in adult patients. When $ETCO_2$ is used, even in the spontaneously room air breathing patient, attention to factors that may influence exhaled carbon dioxide levels need to be taken into account. Arterial blood gases are still required to identify the $PaCO_2$-$ETCO_2$ difference.

## 3.4 DEFINING SLEEP HYPOVENTILATION

Currently, there is no commonly accepted definition of sleep hypoventilation. In the most liberal definitions of the disorder, oxygen desaturation below 88% for more than 5 consecutive minutes [106] or a total sleep time $SpO_2$ <90% of >2% [70] have been used as indicators of clinically significant sleep hypoventilation. However, using $SpO_2$ alone to reflect hypoventilation is problematic. If the patient is using oxygen therapy, this will mask any falls in $SpO_2$. Furthermore, time spent below a threshold level of $SpO_2$ is difficult to interpret when patients begin at different points on the oxygen dissociation curve. Finally, oxygen desaturation is a non-specific finding, and may be caused not only by hypoventilation but also by deteriorating ventilation-perfusion matching.

Therefore, incorporating measures of carbon dioxide should improve the ability to identify clinically significant nocturnal hypoventilation. This approach is supported by studies in patients with restrictive chest wall disorders [79, 437] and in cystic fibrosis [302] where nocturnal $TcCO_2$ has been monitored and used to identify sleep hypoventilation and institute therapy successfully. It has been suggested that nocturnal hypoventilation be defined as a rise in overnight $PaCO_2$ > 8 to 10mmHg or a $TcCO_2$ of >50mmHg for more than 50% of sleep time (continuous hypoventilation) or >50% of REM sleep time (REM hypoventilation) [437]. While some centres may use nocturnal $ETCO_2$ in adults, the accuracy of this even in spontaneously room air breathing individuals has been questioned [436], and the literature in the area consistently reports measurements obtained from transcutaneous measurements [79, 302, 437].

| RECOMMENDATIONS FOR NOCTURNAL MONITORING IN THE DIAGNOSIS AND MANAGEMENT OF SLEEP HYPOVENTILATION SYNDROMES | **Grade** |
|---|---|
| The minimum requirement for identifying sleep hypoventilation is overnight monitoring of oxygen saturation and transcutaneous carbon dioxide along with evening to morning arterial blood gases. | B |
| When daytime indicators for NIV have already been met, a full diagnostic PSG measuring sleep quality is not an essential element in determining the need for NIV. | D |
| Periodic nocturnal studies to identify unexpected problems or correct identified ones is indicated, with the frequency influenced by current response to therapy and the nature of the patient's underlying disorder. | D |

# CHAPTER 4 SECRETION MANAGEMENT

**DANIEL FLUNT**

## 4.1 USE OF NON-INVASIVE RESPIRATORY AIDS IN NEUROMUSCULAR RESPIRATORY WEAKNESS

### Components of cough and the implications of respiratory muscle weakness

A normal cough requires a pre-cough inspiration to about 85 to 90% of total lung capacity [438]. With adequate glottic and abdominal muscle strength, peak cough flows (PCF), depending on sex, height and age are normally 360 L/min to 1200 L/min [439]. A cough is deemed effective when it is able to clear the airways of secretions or foreign bodies. For patients with neuromuscular conditions, peak cough flows can be reduced either from the inability to adequately inflate their lungs (reduced inspiratory capacity due to inspiratory muscle weakness), abdominal (expiratory) muscle weakness, or the inability to adduct or control their vocal cords and close their glottis to retain the volume of air in the lungs prior to cough initiation [414, 440]. The inability to effectively cough out secretions is the main cause of morbidity and hospital admissions for patients with neuromuscular disease [441, 442], and may underlie the need for endotracheal intubation and tracheostomy, and ultimately an earlier death [443]. The use of non-invasive respiratory aids can prolong survival and permit extubation or tracheostomy decannulation of patients with neuromuscular disease (e.g. DMD) with no off-ventilator breathing tolerance [408].

### Expiratory threshold values for effective removal of secretions

It has been shown that the ability to generate PCF of at least 160 L/min is necessary for the successful extubation or tracheostomy tube decannulation of patients with neuromuscular disease, irrespective of independent ability to breathe [414]. In addition to this, patients with maximal assisted peak cough flows of <270 L/min, whether unassisted or manually assisted, under normal conditions usually have difficulty maintaining the minimum assisted PCF value required for removal of secretion under conditions of respiratory infection or general anaesthesia [441, 444]. It has been reported that when routinely measured assisted PCF are <270 L/min, a further decrease to <160 L/min during chest infections is likely, and the likelihood of pneumonia and respiratory failure increases greatly [443].

Whilst it appears that assisted PCF (using manual assisted cough with insufflation or mechanical cough in-exsufflation) can be improved in the majority of patients with neuromuscular disease to a level >160L/min, the presence of bulbar weakness can significantly hamper the success of these non-invasive methods of secretion removal [445]. Failure of non-invasive secretion removal will require invasive suctioning, a technique which is uncomfortable, can cause trauma and may directly introduce pathogens to the airways [446]. If the patient becomes reliant on this method of secretion removal, it will most likely result in a requirement for long term tracheostomy.

Where possible, tracheostomy should be avoided if the patient has adequate bulbar function, not ventilator dependent and if secretions can be managed non-invasively. This is because ventilator users who have been converted from tracheostomy to NIV for long term ventilatory support, prefer NIV over tracheostomy for safety, convenience, comfort, speech, swallowing, sleep and appearance [447]. Tracheostomy intermittent positive pressure ventilation has also been associated with increased carer burden [407] and maintenance of a tracheostomy is associated with expensive equipment and ongoing consumables.

### Importance of glottic control for peak cough flow generation

The importance of glottic control for peak cough flow generation is demonstrated in a study of 50 MND ventilator users, where patients with a PCF greater than 180L/min (275 ± 65 L/min) were successful in being managed non-invasively, whereas patients with peak cough flows of 150 ± 80L/min could not be treated with non-invasive support [448]. Interestingly, the group which was not successful with non-invasive management had a significantly higher mean VC (934 mL) compared to the group which was

successful with non-invasive management (VC = 580mL). The authors suggested that the patients who were not successful had greater glottic impairment and that the ability to generate PCF in excess of 180L/min was more important than the ability to breathe-in independently.

**Measuring peak cough flows**

As peak cough flows are very important measures in determining a patient's ability to clear secretions and providing evidence for non-invasive expiratory aid provision, they should be performed regularly. Peak cough flows can be most simply measured using a peak cough meter and instructing the patient to cough as forcibly as possible through the device [440, 445]. It should also be used to compare peak expiratory flow rates which can be generated using insufflation and manual assist techniques. If the patient has adequate lip control a mouth-piece can be used, otherwise a non-vented face mask can be used. Authors have suggested that using a face mask provided less air leaks and was an easier way to measure changes in peak cough flows post insufflation techniques [440].

Clinicians should have access to low-flow, low resistance peak flow meters or digital peak flow meters which are capable of measuring flow rates at the lower end of the spectrum. In research environments, pneumotachographs can be used as it has been suggested that they provide a more accurate measure of peak cough flow than a standard peak flow meter [442, 449]. However, one study which compared peak cough flows obtained with a pneumotachograph with those measured using a portable peak flow meter in a healthy subjects and patients with neuromuscular disease found no statistically significant differences [450]. Furthermore, when stratified over three ranges of flows (<270 L/min, 270-480 L/min, and >480 L/min), no statistically significant differences were obtained for the population as a whole in any range, however, in the lower flow range (<270 L/min), the portable peak flow device significantly overestimated PCF in 14 patients.

**Key points:**

- For patients with neuromuscular conditions, peak cough flows can be reduced either from the inability to adequately inflate their lungs, expiratory muscle weakness, or the inability to close the glottis to retain the volume of air in the lungs prior to cough initiation.
- The inability to effectively cough out secretions is the main cause of morbidity and hospital admissions for patients with neuromuscular disease. If an effective cough cannot be generated with the use of non-invasive respiratory aids, this can ultimately lead to tracheostomy and earlier death.
- Ability to generate PCF of at least 160 L/min is necessary for the successful extubation or tracheostomy tube decannulation of patients with neuromuscular disease.
- Baseline assisted PCF <270 L/min are likely to decrease to <160 L/min during chest infections, increasing the likelihood of pneumonia and respiratory failure.
- Poor glottic control greatly impairs the ability to generate sufficient PCF.
- Clinicians should have access to low-flow, low resistance peak flow meters to routinely measure PCF.

### 4.1.1 NON-INVASIVE METHODS TO AUGMENT PEAK EXPIRATORY COUGH FLOWS

The aim of increasing insufflation capacity is to maintain the patient's chest wall range of motion as best as possible. In addition to this, it has also been shown to enhance peak expiratory cough flows, with stepwise correlation showing that inspiratory capacity contributes to 44% of the variance of peak cough flow in patients with neuromuscular disease [440]. Adding manually assisted coughing [439, 440, 451] and mechanical in-exsufflation [439, 442] further enhance peak cough flows with the latter providing the most superior cough assistance. In one study, the addition of insufflation capacity to unassisted inspiration in neuromuscular patients increased peak cough flows from 109 L/min to 202 L/min. Furthermore, adding manual abdominal assistance resulted in peak cough flows of 256 L/min, and mechanical in-exsufflation increased peak cough flows to 448 L/s [439].

All of these techniques are very important for all patients with reduced peak cough flows. However, practise and routine use of these techniques should commence well before they are to be needed in an acute setting. This is because these techniques require substantial acclimatisation and practise for both the patient and their carers. Also, in order for the techniques of insufflation, manual assisted coughing and mechanical in-exsufflation to be effective, the pressures and force used need to be adequate and therefore need to be built up over time. The patient and their carers should be well versed in these techniques prior to any acute presentations or chest infections, a time where it can be very difficult to learn or accept these important life saving skills if they have not been practised earlier.

### 4.1.2 MANUAL INSUFFLATION

Normal breathing consists of varying tidal volumes with intermittent deep breaths or sighs which assist with the prevention of the closure of lung units and maintains adequate lung and chest wall range of movement [445, 452]. In neuromuscular disease, when there is significant inspiratory and expiratory muscle weakness, loss of this normal chest wall and lung tissue expansion occurs along with a reduction in tidal breathing and a loss of intermittent stretches. This leads to a stiffening of the joints in the rib cage and muscle shortening, producing a reduction in chest wall compliance, micro-atelectasis and alterations in the elastic properties of the lungs which can further worsen compliance [452]. The aim of insufflation is to promote chest wall range of motion and to increase lung volumes or intrathoracic pressure to the extent that it significantly increases peak cough flows on expiration.

The training of insufflation has been commenced by some authors when vital capacity has been noted to be < 2 L or 50% normal [443, 445]. The air can be delivered via the assistance of a volume-ventilator or a manual resuscitator with a one way valve in situ (see Figure 5) [87, 445]. The technique is achieved by the patient taking a deep breath, holding it, and then stacking consecutively delivered volumes of air to the maximum volume that could be held with a closed glottis [452].

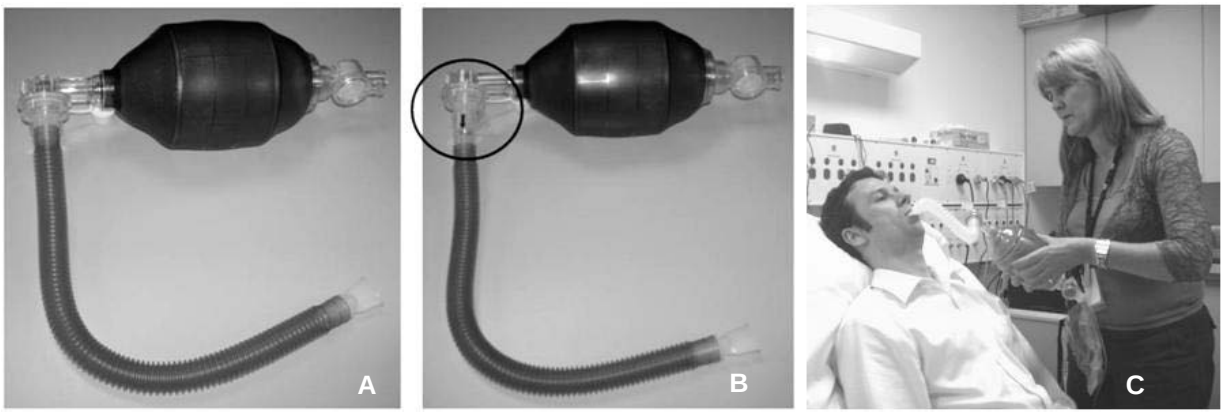



**Figure 5: Using a manual resuscitation bag for insufflation**

**A)** Bag-valve resuscitator configured for mouthpiece ventilation [87].*

**B)** Bag-valve resuscitator with one-way valve to allow breath-stacking [87].*

**C)** Demonstration of manual insufflation using a mouthpiece

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With training, the capacity to stack air to deep insufflation can improve despite neuromuscular weakness and can result in increased cough effectiveness. In a regime of 10 to 15 breath holds, performed thrice daily, the maximum insufflation capacity increased in 70% (30 out of 43) of patients with neuromuscular disease, which resulted in significantly increased assisted PCF [452].

### 4.1.3 MANUALLY ASSISTED COUGHING

After instructing the patient to take a deep breath, the patient is asked to cough as forcefully as possible whilst the carer performs an abdominal thrust. Other techniques to manually assist with expiratory flow rates include anterior chest wall compression, lateral chest wall compression or ptussive squeeze [439, 440, 442, 443, 449, 452, 453]. To maximise the efficiency of this technique, the patient is usually insufflated to maximal capacity via a manual resuscitator bag or volume ventilator prior to performing this abdominal thrust [439, 451] (see Figure 6). For patients with VC less than 1L to 1.5 L, deep ventilator insufflations or air-stacking should precede manually assisted coughing [439]. For a schematic representation of how theses techniques can affect lung volumes in a patient with inspiratory and expiratory muscle weakness, see Figure 7.

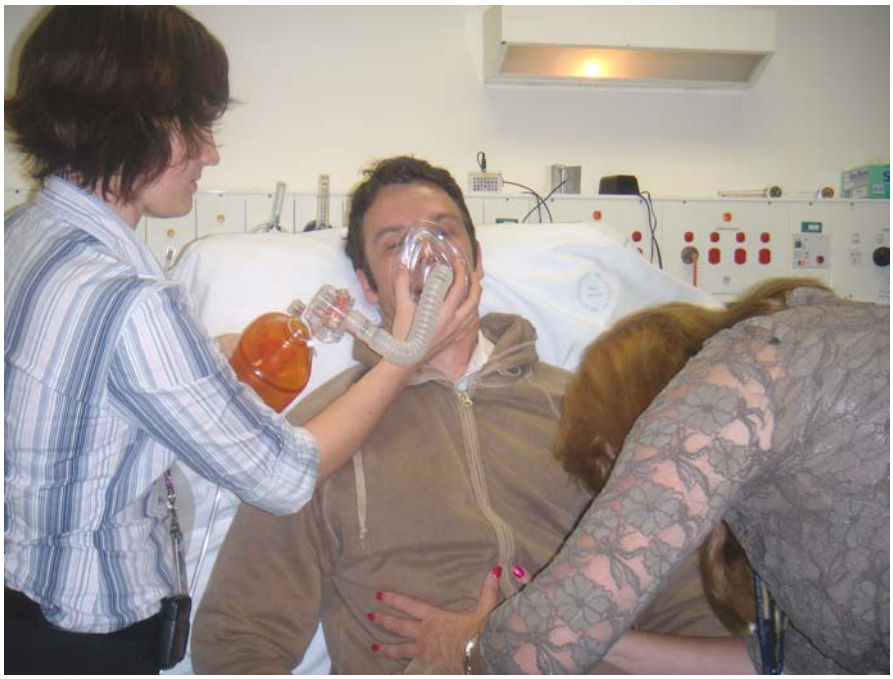
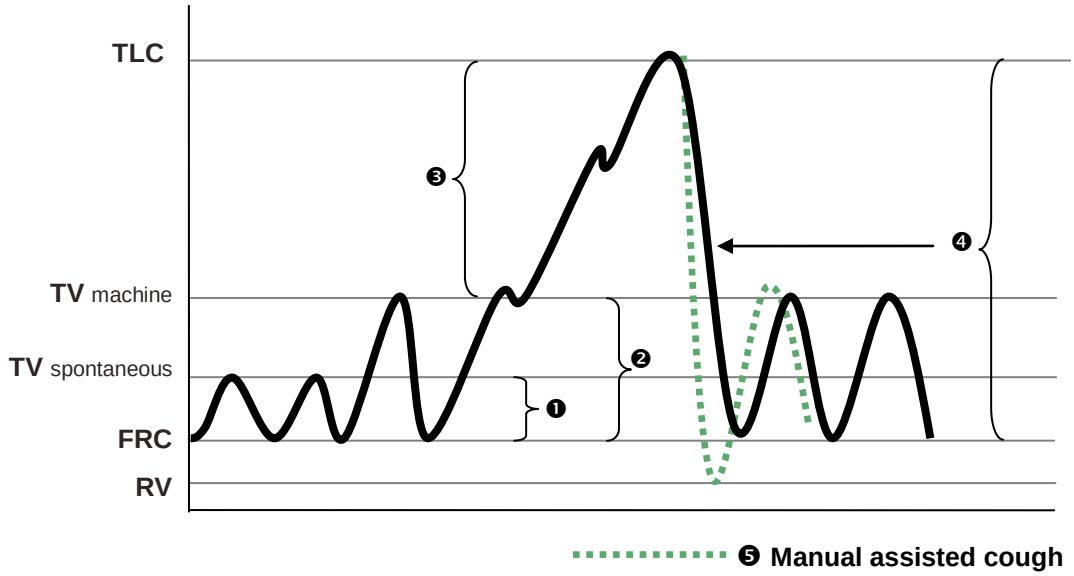


**Figure 6:** Using an abdominal thrust (manual assisted cough) which will further enhance expiratory flows if appropriately timed to glottic opening. Insufflation has been achieved using a resuscitation bag (with one-way valve) attached to a facemask.




❶ Normal tidal breathing (TV spontaneous) from functional residual capacity (FRC).

❷ Augmented tidal volume with the assistance of mechanical ventilation or a manual resuscitation bag (TV machine).

❸ Increasing tidal volume to total lung capacity (TLC) by stacking successive breaths on top of one another (insufflation).

❹ Cough in the absence of expiratory muscle strength. Passive recoil of chest wall after insufflation will decrease to FRC only.

❺ The dotted line represents external manual cough assistance (e.g. abdominal thrust) after insufflation. This will produce a faster expiratory flow rate and potentially allow a greater volume of air to be expelled by providing external compression to approximate residual volume (RV).

**Figure 7:** Representation of lung volumes in a patient with inspiratory and expiratory muscle weakness using mechanical ventilation, insufflation and manual cough assistance.

This technique requires a co-operative patient, good co-ordination between the patient and caregiver, and adequate physical effort and endurance of the care giver providing the thrust or overpressure [414]. During times of secretion retention, this technique may require frequent application and it is important to remind carers to monitor their technique and position as not to put undue stress and strain on their musculoskeletal system, especially their spine. Conditions that interfere with the application of effective manual assisted coughing techniques such as thoracic cage deformities, scoliosis, abdominal distension, abdominal surgery, full stomach and weight extremes will diminish the effectiveness of assisted peak cough flow [414]. When assisted coughing in addition to insufflation is not able to generate adequate peak cough flows, mechanical in-exsufflation can be particularly useful.

### 4.1.4 MECHANICAL IN-EXSUFFLATION

Mechanical insufflation-exsufflation (in-exsufflation) consists of insufflation of the lungs using positive pressure followed by negative (or sucking) pressure during exsufflation. This creates a peak and sustained expiratory flow which, when great enough, can provide shear forces and velocity that is adequate to loosen secretions and move them towards the mouth for expectoration or oral suctioning [454]. This technique can also be used attached to a tracheostomy or endotracheal tube, in which peripheral secretions are mobilised centrally and removed by the mechanical in-exsufflator. Once again this technique is indicated when PCF is reduced below 270L/min, the level necessary to clear bronchial secretions during a chest infection.

The most common commercially available mechanical in-exsufflator in Australia at present is the CoughAssist® In-Exsufflator (Respironics-Philips) (see Figure 8). This device gradually applies a positive pressure to the airway and then rapidly shifts to negative pressure that produces high expiratory flow rates from the lungs, which simulates a cough [454]. Depending on the degree of insufflation (maximum +60 $cmH_2O$) and level of negative pressure applied (maximum -60 $cmH_2O$), and degree of airway resistance, the manufacturers report that a maximum exhalation flow capacity of 600 L/min can be obtained [455].

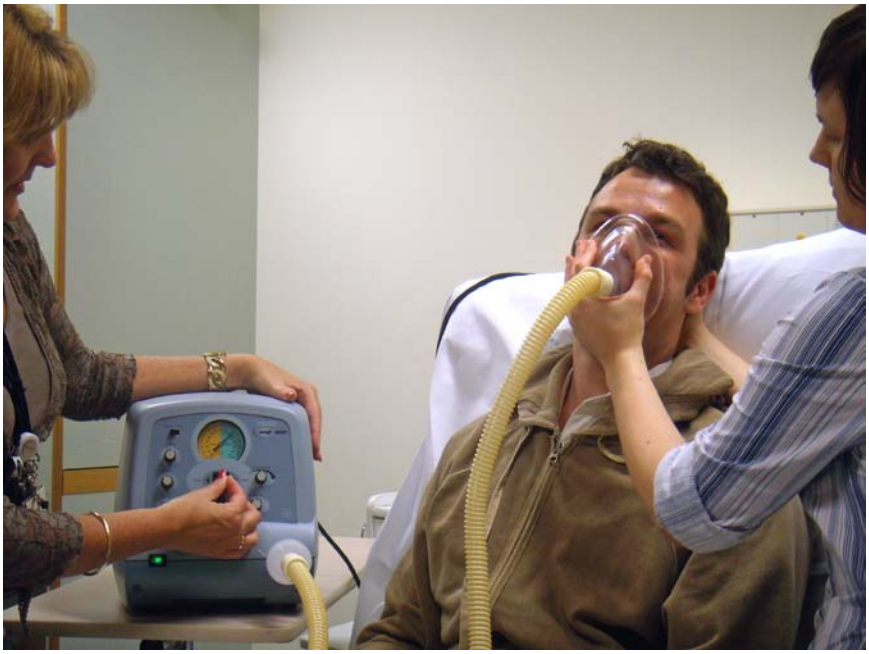


**Figure 8: Mechanical in-exsufflation using a firm fitting face mask.** Instructions of “breathe in”, “cough” and “rest” are given by the carer who is manually operating the machine. Whilst not shown here, a manual cough assist (e.g. abdominal thrust) can also be utilised during the expiratory cough phase of the technique.

In order to determine insufflation and exsufflation pressures that are required to effectively achieve sufficient peak expiratory flows, the mechanics of the CoughAssist in-exsufflator have been studied in artificial lung models. At a resistance of 6 $cmH_2O/L/s$ and static compliance of 50mL/$cmH_2O$, for a minimum clinically effective flow of 160 L/min, a preset insufflation and exsufflation pressures of +30/-30 $cmH_2O$ was required [456]. For a given insufflation and exsufflation pressure, peak expiratory flow decreased by increasing resistance and decreasing compliance (see Figure 9). The majority of clinical studies report that insufflation and exsufflation pressures of +40 $cmH_2O$/-40$cmH_2O$ to be optimal in adults. However, higher pressures of up to +60 $cmH_2O$/-60$cmH_2O$ may be required in conditions of significantly increased resistance or reduced lung or chest wall compliance [454].

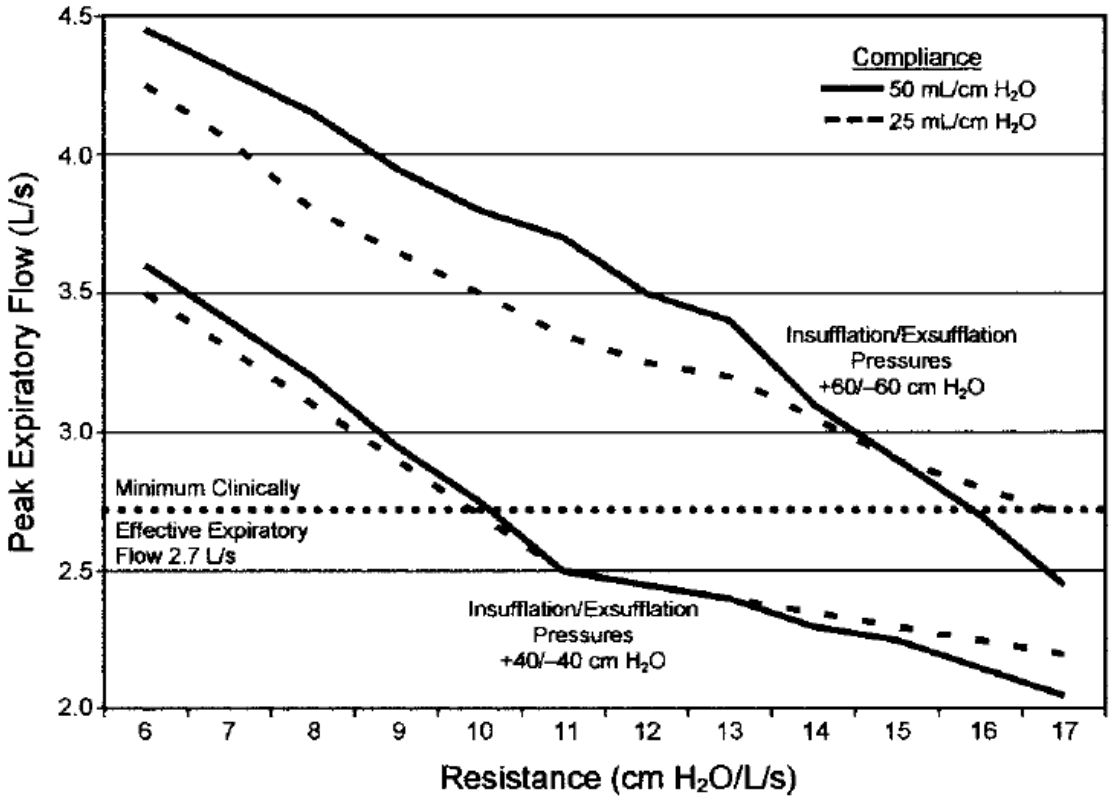



**Figure 9: Relationship between expiratory flow rate and airway resistance with two different insufflation-exsufflation pressures.** The upper two curves represent +60/-60 $cmH_2O$ and the lower two curves represent +40/-40 $cmH_2O$. The sold line is when compliance is set at 50 ml/$cmH_2O$ and the dashed line is when compliance is set at 25 mL/$cmH_2O$. The minimal clinical effective flow rate threshold of 2.7 L/s (or 160 L/s) is highlighted. From [454] which used data from [457]. *– Reproduced with permission from RESPIRATORY CARE and The American Association for Respiratory Care.*

### Clinical Studies in Neuromuscular Disease

Observational studies and retrospective studies have been used to review the effectiveness of cough in-exsufflation (CoughAssist) in various neuromuscular diseases, including DMD, MND, SMA Type 1 and 2, spinal cord injury, myopathies and myasthenia gravis [454]. In patients with neuromuscular disease, the use of mechanical in-exsufflation has been shown to produce superior peak cough flow rates over insufflation and manual cough assist, whether used separately or in combination [439, 442].

Patients with DMD, treated with mechanical in-exsufflation as part of an oximetry driven protocol (i.e. used when $SpO_2$ <95%), had significantly fewer hospitalisations over a three year period when compared to patients who did not use the protocol [441]. Others have shown that this protocol (using volume ventilation and cough inexsufflation in response to $SpO_2$ <95%) also avoids tracheostomy and improves survival in DMD [408].

Mechanical in-exsufflation has also been shown to be successful in scenarios where manual insufflation and manual cough assistance are not effective due to lack of cooperation, age, or reduced bulbar function. In children with SMA Type 1, mechanical in-exsufflation had only 5 extubation failures from 28 attempts, whereas the conventional treatment had 18 extubation failures from 20 attempts [458]. It has also been shown that the use of mechanical in-exsufflation prolongs survival without the need for tracheostomy in this patient population [459].

Cough in-exsufflation has also been successfully used in spinal cord injury. In a prospective study of sputum clearance techniques patients with C1 to C7 spinal cord injuries, adding mechanical cough in-exsufflation (pressure range 15-45 $cmH_2O$) to a treatment arm significantly increased vital capacity and peak expiratory flow, without complication [460].

One study demonstrated that manual assisted coughing and manual insufflation at ±20 $cmH_2O$ were ineffective in patients with neuromuscular disorders with significant scoliosis [449]. It was hypothesised that greater pressures would be required in this group. However, this was not the case in another series which included adult and paediatric patients, where mechanical in-exsufflation was titrated for comfort and insufflation pressures of +15±3 $cmH_2O$ and exsufflation pressures of -15± 9 $cmH_2O$, showed significant benefit in patients with scoliosis [442]. Other insufflation pressures of +35 to +60 $cmH_2O$ and exsufflation pressures of -35 to -60 $cmH_2O$ have been routinely used in adults [443]. A study which compared cough in-exsufflation at pressures of ±15$cmH_2O$, ±30 $cmH_2O$ and ±40 $cmH_2O$, demonstrated that it was safe, well tolerated and it significantly improved PCF and $SpO_2$ for patients with neuromuscular disease, especially when used at pressures of ±40 $cmH_2O$ [461].

### Poor bulbar function and Mechanical In-Exsufflation

In order for cough in-exsufflation to be effective for airway clearance the patient needs to have at least some intact bulbar function and control. When there is severe loss of pharyngeal and laryngeal muscle function, the upper airway can collapse during inspiration and expiration [462]. The collapse of the upper airway on expiration, whilst allowing the negative pressure to be generated, will not translate into effective expiratory flow rates for secretion removal. Although cough in-exsufflation has been effectively used in patients with MND and some bulbar dysfunction [414, 463], in those with very poor bulbar dysfunction and insufflation capacity of >1 L, in-exsufflation peak cough flows of < 160 L/min only could be generated, indicating severe upper airway dynamic collapse during exsufflation [463]. Mechanical in-exsufflation is often ineffective via the upper airway when there is poor glottic stability during exsufflation such as patients with bulbar-onset MND [414].

### Complications of Mechanical In-Exsufflation

Whilst it is known that mechanical positive pressure can produce complications such as abdominal distension, aggravation of oesophageal reflux, haemoptysis, chest and abdominal discomfort, acute cardiovascular effects and pneumothorax, there is little in the literature to suggest that mechanical in-exsufflation regularly causes these problems [454]. In 1994, a clinician with over 650 patient years and hundreds of applications of in-exsufflation in ventilated patients with neuromuscular disease, had noted no episodes of pneumothorax, aspiration of gastric contents or haemoptysis [464]. Other authors also support the claim of the safety of mechanical in-exsufflation in neuromuscular disease [465]. A case study published in 2008, reports being the first to describe two cases (one with C4 Tetraplegia and one with DMD) of pneumothorax occurring with the daily use of mechanical in-exsufflation (and positive pressure ventilation) [466]. Whilst still appearing to be a rare complication, the use of mechanical in-exsufflation is contraindicated in any patient with a history of bullous emphysema, susceptibility to pneumothorax or pneumo-mediastinum, or recent barotrauma.

**Key points:**

- Increasing insufflation capacity using a manual resuscitation bag with a one-way valve or volume ventilator aims to maintain the patient's chest wall and enhance PCF. Adding manually assisted coughing and mechanical in-exsufflation further enhance PCF, with the latter providing the most superior cough assistance.
- Training of insufflation should commence when VC < 2L or 50% predicted.
- Non-invasive expiratory respiratory aids are recommended for PCF < 270 L/min.
- All techniques require substantial acclimatisation and should be introduced when the patient is well.
- For patients with VC < 1 to 1.5L, insufflations should precede manual assisted coughing techniques (e.g. abdominal thrusts).
- In adults, mechanical in-exsufflation settings of +40 $cmH_2O$ and – 40 $cmH_2O$ appear to safely provide adequate PCF for the majority of patients with neuromuscular disease.
- Mechanical in-exsufflation can be ineffective in patients with very poor bulbar dysfunction with insufflation capacity >1L, where dynamic airway collapse occurs.
- Mechanical in-exsufflation is contraindicated in any patient with bullous emphysema, susceptibility to pneumothorax, pneumo-mediastinum, or recent barotrauma.

### 4.1.5 OPTIMISING HOME CARE IN THE CASE OF RESPIRATORY TRACT INFECTION IN PATIENTS WITH NEUROMUSCULAR DISEASE

The following is recommended to optimise home care in the case of a respiratory tract infection:

i) Regular vaccination against influenza and pneumococcus [62, 467, 468].

ii) Early antibiotic treatment to reduce the risk of bacterial superinfection [468]. In recurrent infections the source of the pathogen should be sought and treated appropriately [62].

- Whilst ideally the commencement of antibiotics should occur after medical assessment, in certain circumstances, a script for antibiotics can be kept at home and filled when indicated. Patients who are geographically isolated from medical attention or where carers do not have appropriate access to a pharmacy, may benefit from keeping prescribed antibiotics at home. If this is to be the scenario, the prescribing physician should carefully educate the patient about the use of antibiotics in this way (including monitoring date of expiration) and should not substitute the need for medical assessment which should occur as soon as able.

iii) Frequent use of non-invasive inspiratory and expiratory respiratory aids (such as insufflation, manual assist and cough in-exsufflation) in order to promote chest wall range of motion and for the patient and the carer to maintain proficiency in these techniques.

iv) In the absence of significant ventilation-perfusion mismatch and if home oximetry is available, assisted coughing manoeuvres should be performed continuously to resolve falls in oxygen saturations below 95% This is using the assumption that these desaturations would most likely to be a result of secretion accumulation and that if they are not attended to, atelectasis and pneumonia would result. This protocol has been shown to significantly decrease hospitalisation rates for respiratory complications of neuromuscular disease [443].

v) Admission should be arranged if domiciliary insufflation and non-invasive secretion removal techniques are not able to reverse $SpO_2$ < 95% in the presence of continual ventilator use, persisting dyspnoea, suspected dehydration, fever, lethargy or possibility of fatigue [443]. Once again this value is based on the absence of significant ventilation-perfusion mismatch and the respiratory physician may set an alternative $SpO_2$ limit depending on the patient's baseline $SpO_2$ characteristics. In children, one study gave a time limit on these recommendations to suggest that if the oxygen saturations cannot be increased > 95% for more than half an hour that the patients' physician should be contacted immediately [468].

**Key points:**

- Regular vaccination against influenza and pneumococcus.
- Early antibiotic treatment to reduce the risk of bacterial superinfection and recurrent infections should be investigated for the source of the pathogen.
- Frequent use of non-invasive inspiratory and expiratory respiratory aids (such as insufflation, manual assist and cough in-exsufflation) in order to promote chest wall range of motion and for the patient and the carer to maintain proficiency in these techniques.
- Admission should be arranged if domiciliary insufflation and non-invasive secretion removal techniques are not able to reverse $SpO_2$ < 95% in the presence of continual ventilator use, persisting dyspnoea, suspected dehydration, fever, lethargy or possibility of fatigue. This $SpO_2$ value is based on the absence of ventilation-perfusion mismatch and can be altered by the treating team accordingly.

| RECOMMENDATIONS FOR SECRETION MANAGEMENT IN NEUROMUSCULAR DISEASE | **Grade** |
|---|---|
| Clinicians should have access to low-flow, low resistance peak flow meters to routinely measure PCF. | D |
| Ability to generate PCF of at least 160 L/min is necessary for non-invasive management of pulmonary secretions. Baseline assisted PCF <270 L/min are likely to decrease to <160 L/min during chest infections, increasing the likelihood of pneumonia and respiratory failure. Patients with a baseline PCF < 270 L/min should have access to equipment which can provide insufflation and a mechanical cough in-exsufflation. | C |
| Training of insufflation should commence when VC < 2L or 50% predicted. | D |
| If a resuscitation bag with a one-way valve in situ is to be used for insufflation, the patient and their carers need to be reminded of the function of the one-way valve and that it is to be used for insufflation purposes only. The one-way valve must be removed to provide bag-valve ventilation via a mouthpiece or mask, for example, in the event of ventilator failure in ventilator dependent individuals. | D |
| As manual assisted coughing techniques (e.g. abdominal thrust) further enhance PCF, they should be incorporated with insufflation or mechanical in-exsufflation techniques, where possible. | B |
| For patients with VC < 1 to 1.5L, insufflations should precede manual assisted coughing techniques (e.g. abdominal thrusts). | C |
| In adults, mechanical in-exsufflation settings of +40 $cmH_2O$ and – 40 $cmH_2O$ appear to safely provide adequate PCF for the majority of patients with neuromuscular disease. | B |
| Mechanical in-exsufflation can be ineffective in patients with very poor bulbar dysfunction with insufflation capacity >1L, where dynamic airway collapse occurs. | C |
| In order for the techniques of insufflation, manual assisted coughing and mechanical in-exsufflation to be effective, the pressures and force used need to be adequate and therefore need to be built up over time. All techniques require substantial acclimatisation and should be trained when the patient is well and ideally prior to an acute infective requirement. | D |
| Patients should receive regular vaccination against influenza and pneumococcus. | D |
| Early antibiotic treatment to reduce the risk of bacterial super-infection and recurrent infections should be investigated for the source of the pathogen. | D |
| Admission should be arranged if domiciliary insufflation and non-invasive secretion removal techniques are not able to reverse $SpO_2$ < 95% in the presence of continual ventilator use, persisting dyspnoea, suspected dehydration, fever, lethargy or possibility of fatigue. This $SpO_2$ value is based on the absence of ventilation-perfusion mismatch and can be altered by the treating team accordingly. | C |

## 4.2 USE OF NON-INVASIVE RESPIRATORY AIDS FOR SPUTUM CLEARANCE TECHNIQUES IN CHRONIC OBSTRUCTIVE LUNG DISEASES

### 4.2.1 MECHANICAL IN-EXSUFFLATION IN CHRONIC OBSTRUCTIVE LUNG DISEASE

Trials with mechanical cough in-exsufflation in patients with COPD have produced mixed results. One study which compared mechanical in-exsufflation pressures in patients with COPD, demonstrated that ± 40 $cmH_2O$ significantly improved dyspnoea and $SpO_2$, but did not significantly increase PCF [461]. Another study with COPD patients subjected to mechanical in-exsufflation at pressures of ± 20$cmH_2O$ and manually assisted cough showed a significant deleterious effect in both peak cough flow and cough expiratory volume, whereas the neuromuscular patients in the same series showed a significant improvement [449]. Whilst it was expected that manual assisted cough would show no improvement in patients with no sign of expiratory muscle weakness (i.e. stable COPD), the decrease in PCF was unexpected. The decrease in PCF was suggested to be caused by premature peripheral airway closure, exacerbation of hyperinflation or induced bronchoconstriction from using mechanical in-exsufflation or manual cough assistance.

### 4.2.2 NON-INVASIVE VENTILATION FOR CHEST-PHYSIOTHERAPY IN CYSTIC FIBROSIS

Chest physiotherapy for secretion removal in cystic fibrosis can include techniques such as the forced expiratory technique (FET) or active cycle of breathing technique (ACBT) [469, 470]. The ACBT, for example incorporates cycles of thoracic expansion exercises (deep breathing), controlled or relaxed breathing and finally huffing from mid to low lung volumes to assist with sputum mobilisation to the central airways to which it can be expectorated. Whilst it has been shown to be effective in secretion removal [470], ACBT can cause significant $SpO_2$ falls and reductions in inspiratory muscle strength in CF patients with $FEV_1$ of 34% predicted [317]. The FET has also been associated with significant falls in $SpO_2$ and reductions in inspiratory and expiratory muscle strength after the manoeuvre [316]. When NIV is used along side these secretion removal techniques in patients with reduced $FEV_1$, it prevents a fall in inspiratory muscle function [317] or improves it [316], improves minimum and mean oxygen saturation [316, 317], improves expiratory muscle strength [316, 317] and improves small airway function, and reduces dyspnoea [317]. One study which randomly compared mask PEP, CPAP and NIV and control (directed cough) in patients with $FEV_1$ 25% predicted, showed that although there were no differences in sputum clearance or pulmonary function measures, there was less fatigue with CPAP and NIV compared to PEP [319]. These trials are single session treatments and the long-term effect of NIV for airway clearance has not yet been established [471].

**Environmental set-up for using NIV in lung disease**

Postural drainage may not be possible in the spontaneous breathing breathless patient, but the use of NIV can allow for this to occur if it can adequately reduce the patient's work of breathing and settle their dyspnoea [267]. A mouthpiece attached to an exhalation valve and nose clip rather than a mask interface may be more suitable for the airway clearance technique (see Figure 10). Using ACBT as an example of secretion removal technique, non-invasive ventilation can be used during the thoracic expansion exercises at the same or higher IPAP pressures and during breathing control at baseline pressures to promote adequate rest and recovery (see Figure 11). In order to maximise airway clearance therapy, optimal bronchodilator management that may be administered through the NIV is advisable during treatment. Humidification can also be added [472]. Heated humidifiers are preferred to the use of heat moisture exchangers, as the latter may increase dead-space, increase the work of breathing and reduce the efficacy of NIV [473].

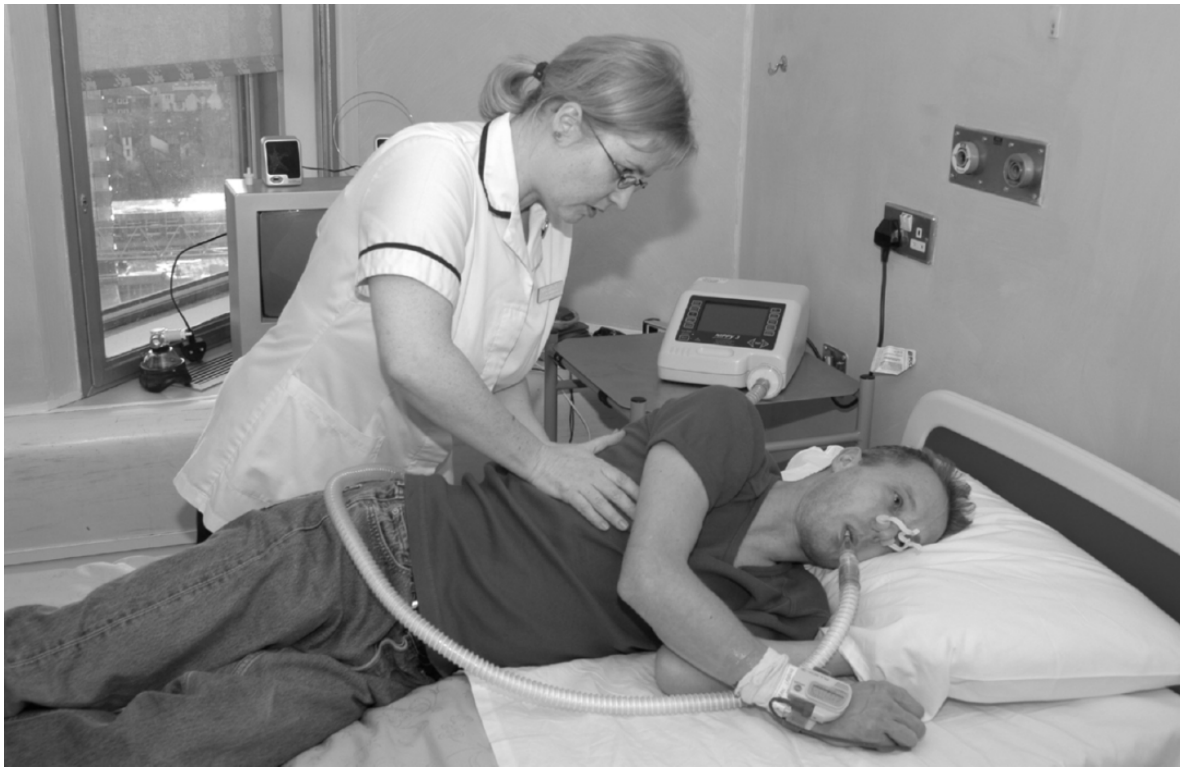


**Figure 10: Using NIV with a mouthpiece and nose clip during ACBT** [472] *– Reproduced with permission from Physical Therapy Reviews, Maney Publishing (http://maney.co.uk/index.php/journals/ptr/).*

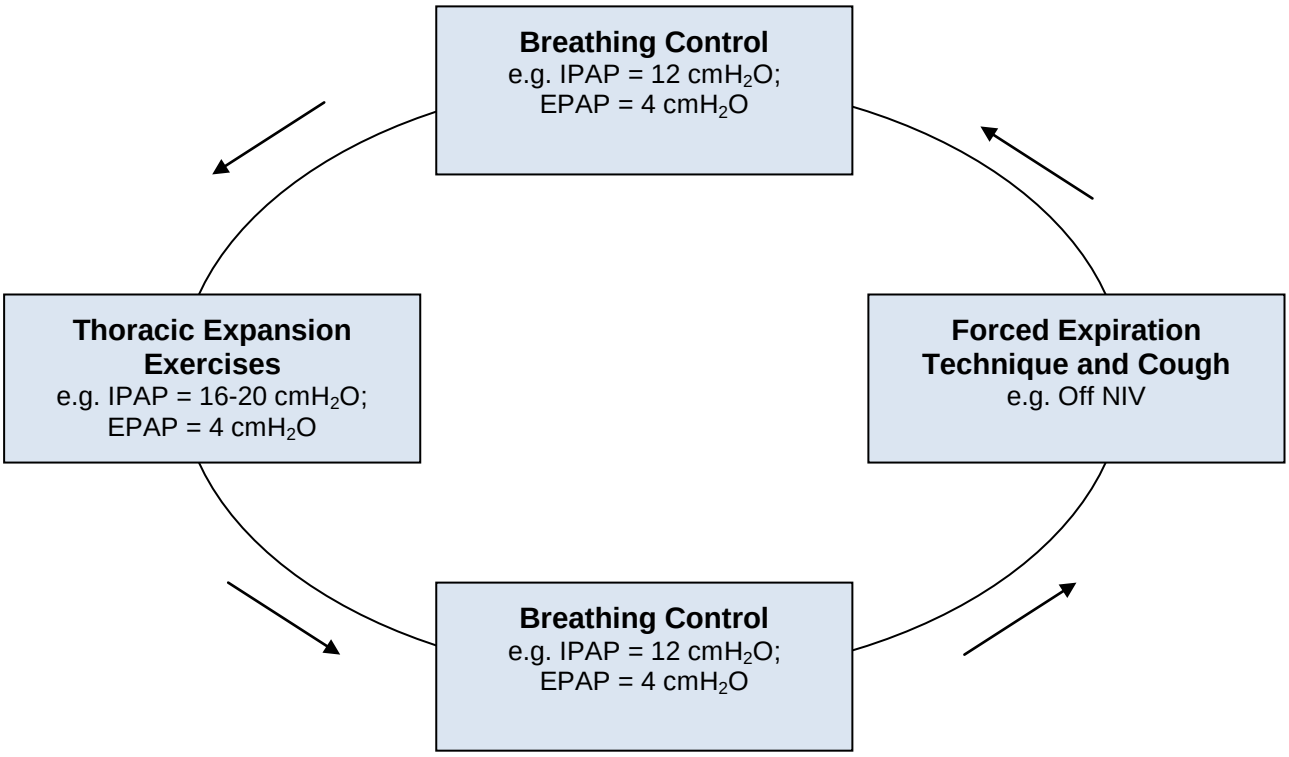



**Figure 11: Replication of ACBT during NIV in patients with cystic fibrosis**

(From [472] using evidence-based parameters from [471]).

**Key points:**

- In COPD, trials of mechanical in-exsufflation have shown no improvement or deleterious effects on PCF.
- When NIV is used along side secretion removal techniques, such as ACBT or FET in CF patients with reduced $FEV_1$, it prevents a fall in inspiratory muscle function or improves it, improves minimum and mean oxygen saturations, improves expiratory muscle strength and improves small airway function, and reduces dyspnoea.
- To maximise the airway clearance therapy, optimal bronchodilator management that may be administered through the NIV is advisable during treatment and humidification can also be added.
- The long-term effect of NIV for airway clearance in CF has not yet been established.

| RECOMMENDATIONS FOR NON-INVASIVE RESPIRATORY AIDS IN OBSTRUCTIVE LUNG DISEASES | **Grade** |
|---|---|
| Further investigation of mechanical in-exsufflation in obstructive lung disease is needed before recommendations can be made about this device for this diagnostic category. Currently there appears to be little recommendation for its use in stable COPD. | D |
| NIV may be a useful adjunct to other airway clearance techniques, particularly in people with CF who have difficulty expectorating sputum or have stable moderate to severe disease ($FEV_1$ approx < 40 – 60 % predicted). | C |
| In an attempt to optimise airway clearance, optimal bronchodilator management that may be administered through the NIV can be used and humidification via a heated humidifier can be added. | D |

# CHAPTER 5 PATIENT / CARER EDUCATION & TRAINING

**DANIEL FLUNT**

## 5.1 BACKGROUND & MINIMUM SKILLS TO BE ACQUIRED

In order for a patient to be successful with NIV in their home environment they must feel comfortable with the concept of NIV, their equipment, ventilator settings and have enough knowledge to be able to problem solve or know who to contact when required. As patients will have different levels of cognition, physical abilities, treatment tolerance and treatment acceptance, the time course of acclimatisation can vary significantly between individuals.

A common method of acclimatisation includes initial daytime ventilator sessions of 30-45 min [84] to 2 to 4 hours [85, 86, 474], in order to increase tolerance of NIV and to train the patients or their carers in the basic handling of the equipment [84, 85]. When the patient is able to tolerate daytime trials, nocturnal ventilation trials are commenced [85, 86, 474]. During this period when ventilation settings are further optimised by polysomnogram, overnight oximetry or patient tolerance, further skills and knowledge about NIV are consolidated. Where possible this should include the patient's family, carers or friends to assist with information processing. In cases where it is not possible for the patient to be able to independently manage NIV, carers should be present for all active processes of NIV acclimatisation. For a list of the minimum skills and level of knowledge to be acquired by patients or their carers during the process of acclimatisation to NIV, see Table 7.

**Table 7: Minimum skills and level of knowledge to be acquired by patients or their carers during acclimatisation of NIV**

| **Ventilator** | |
|---|---|
| 1 | Familiarity with the most important parts of the ventilator and how to operate it [84, 85]. |
| 2 | Familiarity with the main alarms on the ventilator [85]. |
| 3 | Ability to react to problems related to ventilation [85]. |
| 4 | If possible know the ventilator settings or know where a copy of their most recent ventilator settings can be obtained. |
| 5 | Know how the ventilator acts in the event of a loss of mains power. |
| 6 | Know how to change or clean the filter. |
| 7 | Depending on the patient's level of ventilator dependence, understand how a disruption to ventilation could affect them. The level of urgency to seek a response for medical attention or equipment replacement should be discussed. |
| 8 | Understand that if the ventilator is locked that they will not accidentally alter the settings of the machine. |

(table continued over)

**Table 7 (contd): Minimum skills and level of knowledge to be acquired by patients or their carers during acclimatisation of NIV**

| | |
|---|---|
| **Mask and Tubing** | |
| 1 | Competent with placement and adjustment of the mask and headgear, without significant leakage [84, 85]. |
| 2 | Know the different parts of the mask – how to dismantle and put back together, and the implications of a broken mask or a mask that has a missing piece. |
| 3 | Adequate handling, placement and importance of the expiratory valve [85]. |
| 4 | Adequate cleaning of the parts such as the masks and tubings [85]. |
| 5 | Understand the implications of excessive face-mask leakage or mouth leakage on patient-ventilator synchrony, patient tolerance and patient comfort. |
| 6 | Check the equipment regularly for wear and tear (especially mask and tubing). |
| 7 | Know how to rapidly remove the mask in the case of nausea or vomiting. |
| 8 | If supplemental oxygen is required, know how to safely entrain it into the system. |
| **Humidifiers and Nebulisers** | |
| 1 | Know how to attach, clean and fill the heated humidifiers. |
| 2 | Know to empty humidifiers for transport, especially if they are integrated units. |
| 3 | If nebulisers are to be frequently entrained through mouth pieces or oro-nasal masks, extra attention should be paid to cleaning the expiratory ports and anti-asphyxial valves (where present). |
| **Contact Information** | |
| 1 | Name and telephone number of the service to contact during work hours for standard problem solving or advice. |
| 2 | During an emergency situation, the patient should be transported to an emergency department, via emergency services. |
| 3 | Have an itemised list of the names and manufacturers of all of the equipment required. |
| 4 | Have the contact names, phone numbers and addresses of the retailers which are supplying their masks, tubing, filters and other ancillary equipment. |
| 5 | Know who is responsible for the maintenance of their ventilator and that they need to contact that department should there be an issue. |
| 6 | Speak with the supplier of their ventilator and understand the process should there be an issue with their ventilator. |
| **Other Information** | |
| 1 | Understand the importance of compliance and the implications of poor compliance. |
| 2 | Information / guidance of travelling with NIV (land based / sea travel). |
| 3 | May need to obtain clearance for air travel from a Respiratory / Sleep Physician. |
| 4 | Should bring in the ventilator equipment for unplanned hospital admissions and for outpatient appointments. |
| 5 | Understand the importance of regular follow-up and have a follow-up appointment organised. |

## 5.2 INPATIENT VERSUS OUTPATIENT ACCLIMATISATION

In the vast majority of centres where domiciliary ventilation is prescribed, the acclimatisation process is often started in a hospital inpatient setting, either during a planned admission or after an exacerbation of the underlying pathology [2, 85]. At other times, patients have been acclimatised in the outpatient setting [84, 85], or even in their own home [86]. The advantages and disadvantages of acclimatising NIV in the inpatient versus the outpatient setting are highlighted in Table 8.

A recent RCT compared inpatient versus outpatient initiation of home mechanical ventilation in patients with nocturnal hypoventilation secondary to neuromuscular and chest wall disease [84]. This study showed that there were improvements in $SpO_2$ and $TcCO_2$ measures and that there was no significant difference between the two groups. Health professional contact time and ventilator compliance was also not significantly different between the two groups. However, it is important to note that the participants were highly selected, had a near normal daytime $PaCO_2$, and that the inpatient group were more effectively ventilated initially. It would therefore be difficult to recommend outpatient acclimatisation in patients with acute exacerbations, unstable hypercapnia or in patients with more complex medical problems.

A prospective study comparing outpatient to inpatient acclimatisation demonstrated similar findings with the effectiveness of ventilation and the number of hours of ventilation being equivalent in all groups [85]. This study also demonstrated a saving of health care costs by 50%. Another prospective study which compared inpatient acclimatisation to acclimatisation in the patient's home, showed similar improvements in quality of life measures and improvements in ABGs in both groups (with the home group recording significantly higher improvements) [86].

In the appropriate context, outpatient acclimatisation appears to be as effective as inpatient acclimatisation with the added benefit of potential patient convenience and cost saving. However, authors have stated that outpatient acclimatisation should only be seen as an alternative to inpatient acclimatisation and that when medically and logistically appropriate, both models should be offered with the patients being free to choose the most appropriate model of acclimatisation [85].

What appears to be more important is the framework and clinical expertise of the specialised NIV service offering either the inpatient or outpatient acclimatisation. This requires good infrastructure, adequate equipment, staff motivation, staff experience and dedication [86]. The initiation of patients on NIV will also be more successful if it is performed by members of an institution which has adequate through-put of patients requiring NIV from a variety of diagnostic categories [475].

**Table 8: Advantages and disadvantages of inpatient versus outpatient acclimatisation of NIV**

| | ADVANTAGES | DISADVANTAGES |
|---|---|---|
| **INPATIENT** | - Presence of a team of trained experts able to resolve any medical or technical problem that may arise [85]<br>- More appropriate for unstable patients with acute exacerbation, uncontrolled hypercapnia, multiple medical problems, cognitive impairment and severe bulbar weakness [84, 85]<br>- More appropriate for patients who are geographically isolated or if regular transport is too difficult [84]<br>- May be more appropriate if the carers have a high level of anxiety or feel like they would not be able to cope in the initial stages of acclimatisation [84]<br>- May be more appropriate for patients who live alone [84] | - Occupies hospital beds designated for acute care and its accompanying costs are high [85]<br>- Risk of nosocomial infections [84]<br>- Hospital wards may lack specific facilities for patients with physical disabilities and for their carers / family to stay [84]<br>- Patients and families inevitably lose time off work or study [84] |
| **OUTPATIENT** | - Outpatient sessions reduces days of hospitalisation and significantly cuts costs for the health care financier (bed occupancy, general care, meals and medication) [84, 85]<br>- As outpatient admissions can be more flexible, patients may be assessed and commenced on treatment earlier if inpatient beds are unavailable [84]<br>- More convenient for patients who will be able to return home to utilise their specialised equipment (e.g. hoists, wheelchairs, mattress, bed etc.) such that the NIV acclimatisation will be a more pleasant experience [84] | - Requires residence to be in the urban area or within easy reach [85]<br>- Requires adequate family support or sufficient degree of autonomy to allow daily attendance at hospital [85]<br>- Only appropriate for patients in a clinically stable condition [85], and not appropriate for patients likely to experience problems with acclimatisation (e.g. cognitive impairment, severe bulbar weakness) [84] |

## 5.3 CARER BURDEN

The major causes of burden for carers looking after patients on home mechanical include: the patient's underlying disease; level of the patient's dependency; hours spent under mechanical ventilation; presence of a tracheostomy; home distance from hospital and presence of frequent hospitalisations due to respiratory deterioration or side effects of mechanical ventilation. Carer's looking after patients with neuromuscular disorders or COPD patients are likely to contend with 2 to 3 criteria of burden in more than 50% of cases [476].

More patients with greater levels of ventilator dependency, medical complexity and physical assistance are being managed in the home. This has great implications to both families and health care services with regards to time and costs. In neuromuscular disease, especially the slowly or non-progressive disorders, the burden is highest for the family than for the health system, especially in terms of hospital admissions [476]. The time spent by care givers in providing assistance for patients with poor activities of daily living has been described as enormous and additional time required for caregivers to provide transportation for clinical visits are usually not included in cost-analyses [477]. In order, to optimise the health of patients without putting undue burden on the carers, home visits or home care (either through face to face or telemedicine) [478, 479] are most likely to enhance the situation. Planning visits for education, supervision or continued training may improve quality of life and health for patients and the security for care givers [476]. A dedicated respiratory failure service or discharge co-ordinator is important to ensure that this will occur upon discharge of the patient from hospital [480, 481].

**Key points:**

- Acclimatisation to NIV needs to ensure that the patient and their carers are competent with a basic set of skills and have sufficient knowledge of NIV to ensure safe and successful use of this treatment in the home.
- Whilst acclimatisation generally occurs as an inpatient, it can also be performed in the outpatient setting.
- Patients who have easy transport access to their health care facilities, not medically complicated and do not have unstable respiratory failure, can be successfully acclimatised in the outpatient model.
- Success for initiation and education for NIV is more likely to come from institutions where there is a sufficient through-put of patients requiring NIV acclimatisation.
- Care givers of patients with chronic respiratory failure under NIV are at high risk to develop burden, including caring for their patients during hospital admissions and transporting them for clinical appointments.
- To reduce carer burden and enhance patient health, home visits or home care (either through face to face or telemedicine) should be provided and ideally managed by a dedicated respiratory failure service or discharge co-ordinator.

| RECOMMENDATIONS FOR PATIENT / CARER EDUCATION AND TRAINING | **Grade** |
|---|---|
| Minimum skills and level of knowledge need to be acquired by patients and / or their carers during the process of acclimatisation to NIV. See Table 7. | D |
| Acclimatisation and education for domiciliary NIV should occur at institutions where there is a sufficient through-put of patients requiring long term NIV. | D |

# CHAPTER 6 NIV & RESPIRATORY MANAGEMENT OF PATIENTS ON DOMICILIARY NIV UNDERGOING ANAESTHESIA OR SEDATION

**DANIEL FLUNT**

## 6.1 BACKGROUND

NIV can play an important role during sedative procedures and surgical anaesthesia, to enhance security in high risk patients with chronic respiratory failure secondary to neuromuscular disease, obesity, chest wall disorders and lung disease [219, 482-485]. General anaesthesia and surgical interventions that affect thoracic or abdominal musculature adversely effect pulmonary mechanics, which can worsen gas exchange and cause significant respiratory complications in the post-operative period [486]. Lung volumes, like FRC can decrease by 10 to 15% after lower abdominal surgery, decrease by approximately 30% after upper abdominal surgery and decrease around 35% after a thoracotomy [487]. In patients with baseline chronic respiratory failure and altered lung mechanics (such as kyphoscoliosis, obesity and neuromuscular disease), this further decline puts these patients at high risk of developing acute on chronic respiratory failure post procedure [482]. Sedative procedures which are normally tolerated by the general population without assisted ventilation, may cause significant hypoventilation in patients and also precipitate acute on chronic respiratory failure, if ventilatory assistance is not given during and after the sedative process.

Mechanisms of post-operative ventilatory failure include: atelectasis; respiratory depressant effects of opiates and sedatives; infection; sputum retention; and pain leading to decreased chest wall movement and decreased lung compliance [484]. The consequences of these mechanisms is that it can lead to pneumonia, respiratory failure with prolonged mechanical ventilation, bronchospasm, lung collapse and exacerbation of the underlying disease [487]. As post-operative respiratory complications are an important part of the risk of surgery and prolong hospital stay by an average of one to two weeks in the general population [488], every effort should be made in patients with chronic respiratory failure to ensure adequate ventilation and secretion removal is maintained, prior, during and post procedures requiring sedation or anaesthesia.

Whilst there is a paucity of prospective randomised controlled trials establishing that NIV can prevent peri or post-operative complications across the various diagnostic groups of chronic ventilator users, there have been retrospective analyses and case studies which support its usefulness in preventing complications.

A retrospective study of 20 patients (including kyphoscoliosis, morbid obesity, thoracoplasty and neuromuscular disease) showed that use of bilevel or volume ventilation which was commenced immediately or 2 hours after extubation prevented the need for re-intubation for respiratory failure and that the mean stay in the post-operative unit was not significantly different to the general population [482]. However, hospital stays for the different pathologies were greater in the NIV patient group, except for gastroplasty where NIV produced significantly shorter hospital stays. The mean time for post intervention extubation was 3.8 ± 3.2 hours. With regards to one year follow-up, general anaesthesia and surgical interventions did not worsen lung function or gas exchange. A fundamental factor that can influence good results is the tight collaboration between the post-operative unit and the team carrying out the NIV. The existence of specialised NIV teams helps to predict the problems that may arise in the peri and post operative period for the patient with respiratory insufficiency due to chronic respiratory failure [482].

In case studies using NIV to treat ventilatory failure post corrective spinal surgery, the need to return to ICU for intubation and conventional mechanical ventilation was avoided [484]. In addition to curbing significant patient morbidity, this practise also prevented the increased cost and possible complications of intubation and conventional ventilation (including nosocomial pneumonia and ventilator dependence).

Recommendations for the evaluation and management of patients with chronic respiratory failure on NIV requiring a sedative procedure or surgical anaesthesia will be grouped as a whole at the end of this section. The following paragraphs highlight specific issues or cases for some of the diagnostic disorders.

### Neuromuscular Disorders

Whilst the risks of sedation and anaesthesia pose serious risks to all patients who have underlying chronic respiratory failure, patients with neuromuscular disease have additional and unique issues. These risks include: extubation failure due to chronic respiratory insufficiency; risk of intubation difficulty and airway instability while sedated due to macroglossia, stiff temperomandibular joint and upper airway hypotonia; secretion retention and plugging due to ineffective weak cough; poor glottic control at baseline; malnutrition at baseline; sensitivity to sedatives, with loss of spontaneous respiratory efforts; cardiovascular complications and malignant hyperthermia-like syndrome with the use of certain anaesthetics [489, 490]. Due to improvements in medical technologies and care, patients with neuromuscular disease on mechanical ventilation are now living longer and therefore it is now more common for patients with neuromuscular disorders to require procedures involving sedation or general anaesthesia [489, 491, 492]. Some examples of procedures include radiographic procedures, PEG tube insertions, endoscopies, surgery to correct scoliosis, pregnancy, caesarean sections and other incidental procedures which become more prevalent as the population ages. In addition to providing ventilatory support for these individuals, extra vigilance is required to ensure effective expectoration of secretions through manually or mechanically assisted coughing, especially when peak cough flows are < 270 L/min due to baseline or post-procedural expiratory muscle weakness [441, 489].

### Chest Wall Disorders

NIV has been used in the post-operative period of corrective spinal surgery for kyphoscoliosis after developing hypercapnic respiratory failure, thus avoiding the need for invasive mechanical ventilation [484]. Successful full term pregnancies have also been possible with the assistance of NIV in patients with kyphoscoliosis whose pre-pregnancy vital capacities ranged from 240 to 280 mL [493]. Other procedures have been performed in patients with chest wall disorders (kyphoscoliosis or thoracoplasty) requiring baseline NIV, include mastectomy, septoplasty, hip prosthesis, non-laparoscopic cholescystectomy and endoscopic retrograde cholangiopancreatography [482].

### Lung Disease

With regards to obstructive lung diseases, it has been suggested that an increased risk of pulmonary complication is associated with $FEV_1$ or FVC < 70% predicted or $FEV_1$/FVC ratio < 65% [494] or $PaCO_2$ >45 mmHg [495]. However, these measures tend to have a variable predictive value [488, 496] for post operative complications and are not designed to predict the need for NIV in peri or post operative procedures. A consult from a respiratory physician would therefore be required to identify these patients as “at risk” on clinical grounds [487] .

In order to ensure that the patient is at their optimal condition prior to a sedative procedure or surgical anaesthetic, elective surgery should be deferred if an acute exacerbation is present. Pre-operative optimisation of lung function with the use of bronchodilators, physiotherapy, smoking cessation and corticosteroids should also be arranged as necessary. Pre-operative antibiotics should be reserved for the outpatient where the presence of infection is suggested by a change in the character or amount of sputum [487].

### Obesity

Obesity increases postoperative pulmonary complication [497]. In particular central obesity is associated with decreased total lung capacity, vital capacity, functional residual capacity and chest wall compliance, and increased work of breathing and upper airway resistance [498]. Reductions in FRC, and hence propensity for small airway closure and atelectasis, on induction of anaesthesia occurs to a greater extent in normocapnic obese patients (50%), compared to non-obese patients (20%) [499].

After surgical procedures, overweight or obese patients are more likely to have clinically significant pneumonia [500], atelectasis [501] and hypoxaemia [502].

In patients undergoing gastric surgery for obesity with BMI > 40 $kg/m^2$, which were randomised to prophylactic bilevel ventilation for two out of every three hours for the first 12 to 24 hours post operation demonstrated a 24 to 30% increase in FVC compared to the post-operative values in the group treated with oxygen alone [219]. However, these improved measures of lung function did not translate into fewer hospital days or lower complication rate. However, other researchers found a significantly reduced hospitalisation rate with the use of prophylactic NIV for gastroplasty [482].

Another prospective RCT showed that bilevel at IPAP=12 $cmH_2O$ and EPAP=4 $cmH_2O$ significantly improved the falls in $FEV_1$, FVC and $SpO_2$ which occurred after gastroplasty when this group was compared to bilevel ventilation at IPAP=8 $cmH_2O$ and EPAP = 4 $cmH_2O$ or oxygen via facemask at 10L/min [483]. It appears that the use of prophylactic NIV during the first 24 hours post-operation significantly reduces pulmonary dysfunction after gastroplasty in obese patients and accelerates re-establishment of pre-operative pulmonary function.

In high risk patients, the use of spinal or epidural anaesthesia instead of general anaesthesia has been recommended as a risk reducing strategy [485, 487].

**Key points:**

- Advancements in medical technology, including NIV has meant that more patients with chronic respiratory failure are living longer, and therefore it is now becoming more common for these patients to require sedative procedures or surgical anaesthesia.
- Patients with chronic respiratory failure on domiciliary NIV require adequate ventilatory support both during and post sedative procedures or surgical anaesthesia, to ensure that they do not develop acute on chronic respiratory failure and other respiratory complications.
- As shown by retrospective analyses and case studies, NIV can prevent complications from procedures requiring sedation and surgical anaesthesia in the peri and post-operative period across the various diagnostic groups of chronic ventilator users.
- The presence of a specialised NIV team during and after the procedure helps to predict the problems that may arise in the peri and post operative period for the patient with respiratory insufficiency due to chronic respiratory failure.
- Use of NIV in the post operative period can potentially prevent re-intubation, admission to ICU and significant patient morbidity.
- Prior to the procedure, patients should be assessed by a respiratory physician, anaesthetist and the patient's NIV service.
- Procedures should be performed at a tertiary hospital where staff has experience in NIV for acute and chronic hypoventilation and that there is access high level monitoring or an ICU.
- In patients with expiratory muscle weakness causing PCF < 270 L/min, manual and mechanical non-invasive secretion removal techniques are paramount in the post-operative period.
- Patients with obesity are prone to large reductions in FRC post induction of anaesthesia. NIV used post-operatively can significantly retard this decrease.

## 6.2 EVALUATION AND MANAGEMENT OF PATIENTS WITH CHRONIC RESPIRATORY FAILURE ON NIV REQUIRING A SEDATIVE PROCEDURE OR SURGICAL ANAESTHESIA

Due to the lack of prospective randomised trials looking at the NIV and related respiratory management of patients on domiciliary NIV undergoing anaesthesia or sedation, the majority of the recommendations are based on expert consensus statements, particularly with regards to DMD [467, 489]. However, it has been made clear that the respiratory interventions can be adapted to the care of patients with other types of neuromuscular disorders [467] and logically is appropriate for other diagnostic groups.

**Evaluation and management of patients <u>before</u> general anaesthesia or procedural sedation**

1. Obtain respiratory and anaesthetics consultations [489] at least 2 months prior to intended procedure to allow for intervention if required [467]
2. Pulmonary evaluation [489]:
   i) VC: Consider pre-operative training of NIV if not already commenced
      - At risk is defined as VC < 50%
      - High risk of complication is defined as VC < 30%.
   ii) $SpO_2$ on room air for baseline.
   iii) Carbon dioxide measure via ABG or end-tidal $CO_2$ if $SpO_2$ < 95% on room air.
   iv) PCF: If PCF < 270 L/min, pre-operative training in manual and mechanically assisted cough, including mechanical in-exsufflation.
3. If not on NIV and not already performed, assess for sleep hypoventilation pre-operatively [467].
4. Cardiology and/or Nutritional assessment as required [489].
5. Optimisation of preoperative nutritional status may involve the use of NIV, as patients with untreated respiratory failure may be malnourished due to increased work of breathing or inability to eat due to dyspnoea [489].
6. Discuss the risks and benefits of the procedure and discuss resuscitation parameters and, if applicable, advanced care directives [489].
7. Procedure should be planned to be performed at an institution which has expertise in treating neuromuscular disorders, a dedicated non-invasive ventilation service and has access to an intensive care unit.
8. Information / education to patients, carers and clinicians involved in care include:
   i) Basic knowledge about their disease and how sedative procedures, respiratory depressants, surgical anaesthetics, or uncontrolled use of oxygen are likely to interact with their hypoventilation disorder.
   ii) Bring equipment to hospital including mask, ventilator tubing or any additional ancillary equipment e.g. chin straps, oxygen side-port connectors etc.
   iii) Equipment should follow the patient.
   iv) If the patient has a more basic model of NIV, the NIV service accompanying the patient should provide a model which has the capabilities of a spontaneous-timed mode and the ability to change the settings easily and without the requirements of additional equipment.
   v) NIV service should organise a method of entraining supplemental oxygen should it be required during / after the procedure.
   vi) A variety of masks (nasal, oronasal or mouthpiece) in addition to the patients usual interface should be on hand.
   vii) Where the ventilator does not have an internal battery for transport, an external battery should follow the patient.
   viii) For convenience, a longer 3m ventilator tube, mains power extension cord and frequently used connectors should be available for the procedure.

**Management of patients during general anaesthesia or procedural sedation**

1. Procedure to be performed in an appropriate high level environment and an ICU or high level monitoring unit should be available for post procedure management [489].
2. Consider spinal or epidural anaesthesia, if possible for surgical interventions [487].
3. Skilled personnel should be present, including [489]:
   i) Anaesthesiologist with experienced in the management of neuromuscular disorders.
   ii) Therapist/nurse or medical staff skilled in management of NIV.
4. Intraoperatively continuously monitor $SpO_2$ and whenever possible perform measures of $CO_2$ [489].
5. Options for providing respiratory support during general anaesthesia and sedation include [489]:
   i) Endotracheal intubation
   ii) Laryngeal mask airway
   iii) NIV delivered via a nasal or face mask
   iv) Volume ventilator using a mouth piece with leak proof seal
   v) Manual ventilation using a flow-inflated manual resuscitation bag
   vi) Use of NIV to facilitate extubation
   vii) Use of NIV during the induction of and recovery from deep sedation or anaesthesia [490]
9. Application of NIV should be considered with VC < 50% and strongly considered with VC < 30%, during induction of or recovery from general anaesthesia, and throughout procedural sedation [489].
10. Have the ventilator set in spontaneous-timed or assist control (if not already). In patients with normal baseline respiratory strength and normal control of breathing, monitoring the proportion of patient triggered to machine delivered breaths may assist with assessing the patient's level of sedation and its affect on respiration.

**Management of patients after general anaesthesia or procedural sedation**

1. Consider extubating patients with VC < 50% predicted, and those with VC <30%, directly to NIV [489].
2. Monitor $SpO_2$ post procedure carefully. If a patient is hypoxaemic, assess to see if it is due to hypoventilation, atelectasis or airway secretions and treat accordingly, prior to using supplemental oxygen [489].
3. If supplemental oxygen is indicated, use judiciously and whenever possible monitor carbon dioxide levels [489]. Always avoid routine protocol oxygen administration in these patients. Limits or aims for desired $SpO_2$ should be set by the treating clinicians if appropriate.
4. Stay in post-operative surgical unit for constant monitoring by post-operative staff and NIV team until stabilisation, extubation and spontaneous ventilation can be achieved prior to transfer to ward [482]. Otherwise patient is transferred to ICU / HDU for further monitoring.
5. Use manually assisted cough and mechanical in-exsufflation if peak cough flows are < 270 L/min [489].
6. Ensure adequate humidification of NIV post procedure, especially if the patient has a suppurative lung disease or if the anaesthetic-ventilation procedure is likely to cause a drying of the airways.
7. Optimise pain control in patients. If sedation and/or hypoventilation occurs as a result, extubate onto NIV or delay endotracheal extubation for 24 to 48 hours if required [489].
8. Post-operative pain relief via epidural anaesthesia can reduce the rate of pulmonary complication in comparison to parenteral narcotics in patients at high risk [487].
9. Patients who are sensitive to sedatives or anaesthetic agents (e.g. neuromuscular disorders) [68, 503], will be at risk of loss of spontaneous respiratory efforts. Post-operative NIV should be encouraged and patients closely monitored for an extended period to ensure that adequate spontaneous breathing has returned if it was present prior to the procedure.

| RECOMMENDATIONS FOR NIV AND RELATED RESPIRATORY MANAGEMENT OF PATIENTS ON DOMICILIARY NIV UNDERGOING ANAESTHESIA OR SEDATION | **Grade** |
|---|---|
| Prior to undergoing anaesthesia or sedation, patients on domiciliary NIV should be assessed by a respiratory physician, anaesthetist and the patient's NIV service. | D |
| Ensure that patients with chronic respiratory failure on domiciliary NIV receive adequate ventilatory support both during and post sedative procedures or surgical anaesthesia. This is to minimise the risks of the patient potentially developing acute on chronic respiratory failure or other respiratory complications. | C |
| Procedures should be performed at a tertiary hospital where staff have experience in NIV for acute and chronic hypoventilation and that there is access high level monitoring or an ICU. | D |
| A specialised NIV team should be present during and after the procedure to assist with predicting problems that may arise in the peri and post operative period for patients who are usually treated with domiciliary ventilation secondary to respiratory insufficiency. | D |
| A ventilator with the ability to set a back-up rate should be used for the procedure. | D |
| Routine administration of oxygen should be avoided. | D |
| In patients with expiratory muscle weakness causing PCF < 270 L/min, manual and mechanical non-invasive secretion removal techniques are paramount in the post-operative period | C |

# CHAPTER 7 NOCTURNAL TO CONTINUOUS NIV USE

**DANIEL FLUNT**

## 7.1 BACKGROUND

Although tracheostomy ventilation is critical in survival in patients with glottic dysfunction and respiratory failure, for those without glottic dysfunction requiring continuous ventilatory support, tracheostomy ventilation has several potential disadvantages that may be avoided by using NIV instead [504] (see Table 9).

**Table 9: Potential Disadvantages of Long-Term Tracheostomy** [504, 505]

| |
|---|
| Expense of procedure |
| Higher risk of respiratory infection |
| Formation of granulation tissue |
| Airway stenosis / malacia |
| Tracheoinnominate-artery fistula |
| Tracheoesophageal fistula |
| Impairs speech and swallowing |
| Inability to stack breaths for cough augmentation |
| May require skilled assistance for suctioning |
| Increased carer burden |
| Social issues around stoma and tracheostomy tube |

Relatively lightweight, portable ventilators and a wide variety of comfortable interfaces have become available, allowing for continuous NIV rather than tracheostomy ventilation in selected patients [504]. In neuromuscular disorders (and to a lesser degree in end stage lung diseases), ventilator dependency may be continuous when commencing NIV, or may increase with time, depending on the progression of disease aetiology [277]. Patients with a variety of neuromuscular diseases including quadriplegia due to high spinal cord lesions [115], post-poliomyelitis [506], SMA [458], DMD [408, 409, 507, 508], and other non-bulbar neuromuscular disorders [507] can be managed with continuous NIV instead of invasive tracheostomy ventilation [509].

Continuous NIV can be possible in carefully selected motivated individuals with intact upper airway function [3, 507, 509] who have access to centres with expertise in nocturnal and diurnal ventilation [504], and have access to adequate levels of carers who are skilled in NIV and assisted coughing techniques [3]. Centres delivering the training and support for continuous ventilation need to have significant expertise. They and the patients they manage need to be completely informed and conscious of the constraints and dangers involved in undertaking such an approach [277].

To be successful with continuous NIV, the ventilator user must realise three goals [277, 509]:

1. Optimise and maintain respiratory system compliance by frequent full insufflations delivered by breath stacking, using a resuscitation bag with a one way valve, volume ventilator or insufflating using adequate pressures with a mechanical in-exsufflator.
2. Normal or adequate levels of alveolar ventilation are sustained using a variety of interfaces and approaches including nasal, oronasal, or mouthpiece interfaces which are alternated night and day.
3. Patient must be taught and practice techniques to enhance their peak cough flows. This includes insufflation, manual cough assist techniques and mechanical in-exsufflation (see Chapter 4, Secretion Management).

## 7.2 INDICATIONS FOR TRACHEOSTOMY VENTILATION OVER NIV

As with nocturnal NIV for neuromuscular disease, there have been no randomised controlled trials of continuous ventilation [504] and there is no clear answer as to whether, and beyond what duration, a totally ventilator-dependent patient is better or more safely ventilated with NIV or tracheostomy [277]. The final decision to continue to use NIV or to convert to tracheostomy is therefore highly dependent on the philosophy, preferences and capabilities of the clinical team, the patient and the patient's family and resources available [277]. However, in some circumstances it can be clear when invasive ventilation is indicated over NIV [504] (see Table 10).

**Table 10: Indications for Tracheostomy in Neuromuscular Disease** [504]

| |
|---|
| Substantial glottic dysfunction |
| Increased risk of aspiration |
| Inability to clear secretions, despite cough augmentation |
| Inability to generate adequate cough flow, despite aggressive cough assistance |
| Recurrent pneumonia on full-time NIV with adequate cough assist |
| Substantially elevated $PaCO_2$, despite optimal full-time NIV |
| Patient preference |
| Lack of experienced health-care providers in continuous NIV |

## 7.3 RELATIVE CONTRAINDICATIONS TO CONTINUOUS DOMICILIARY VENTILATION

At other times clinical decision making regarding the choice of using continuous domiciliary ventilation can be guided by the following relative contraindications:

i) $FiO_2 > 0.4$ [510] or where it is impractical to deliver required $FiO_2$

ii) Patients choice not to opt for continuous NIV [510]

iii) Inadequate resources for home care including [510]

- personnel
- financial

iv) Inadequate respite for care givers [510]

v) Inadequate numbers of competent caregivers. A minimum of two competent caregivers are required [510].

## 7.4 PROGRESSION OF NIV FROM NOCTURNAL TO CONTINUOUS VENTILATORY SUPPORT

Patients with progressive neuromuscular disease usually require gradual increases in inspiratory pressure and longer periods of assisted ventilation per 24 hour (until continuously) to avoid the sequelae of hypoventilation, including excessive increases in $PaCO_2$ and worsening of symptoms such as dyspnoea [20, 511]. The actual extension from nocturnal to daytime use is empirically driven [511]. What constitutes the definition of continuous ventilatory support remains arbitrary and is generally based on what clinicians feel is a safe margin. Various types of mechanical ventilation (including NIV) have been reported to be naturally extended to 18 ± 2 hours and 24 hours in patients with VC≤400mL [512] and VC < 300mL [507], respectively. For this document, the working party classifies a ventilator dependent patient as one who requires ventilation for≥ 18 hours in a 24 hour period or is unable to sustain independent, spontaneous ventilation for > 4 hours [402, 510].

## 7.5 OUTCOME OF PATIENTS ON CONTINUOUS NIV

There is little information on the outcome of 24 hour NIV [511]. In one of the larger observational studies, out of 257 patients with chronic respiratory failure (predominantly with neuromuscular disorders), 144 required 20 to 24 hour of ventilatory support daily and 67 were successfully switched from tracheostomy ventilation to NIV, predominantly through the assistance of mouthpiece ventilation. It was concluded that the addition of mouthpiece NIV prolonged survival and enhanced convenience and communication in these patients. Other studies have also reported prolonged survival in DMD patients with combination of daytime mouthpiece and nocturnal nasal NIV [409, 508] with one study demonstrating stabilisation in vital capacity over 5 years [409]. While mouthpiece ventilation can be very successful in providing daytime ventilation, the challenge of breathing via the mouthpiece and eating can be too difficult for some patients, resulting in the need for the placement of an enteral feeding tube [513].

## 7.6 TYPE OF VENTILATOR FOR CONTINUOUS NIV

For continuous ventilatory support more sophisticated volume-limited ventilators are recommended [402] and the currently available volume-limited ventilators are well suited for patients in need of continuous ventilatory support [20]. This is in contrast to the pressure preset bilevel devices which generally have limited pressure-generating capabilities (20 to 35 depending on the ventilator) and most lack sophisticated alarms or battery back-up systems [20]. Also these bilevel pressure machines may not have manufacturer or regulatory approval for use in continuous ventilatory support (invasive or non-invasive) or for “life support” scenarios. Therefore, they are not currently recommended for patients who require high inflation pressures, or are dependent on continuous mechanical ventilation unless appropriate alarms, monitoring systems and suitable external batteries can be added [20]. Newer generations of bi-level ventilators which contain batteries, may only be able to provide autonomy from a mains power source for a relatively short period of time [277]. This would limit security and mobility of neuromuscular patients with ventilator dependence and then shift the preference to the volume ventilator [277].

A hybrid ventilator is one which is able to provide both volume and pressure pre-set modes of ventilation. The volume mode can be used during the day when standard bi-level pressure therapy is unable to maintain adequate gas exchange or mouthpiece ventilation is used. The pressure preset mode is utilised when the patient is unable to tolerate volume ventilation when asleep.

## 7.7 QUALITY CONTROL

**Risk minimisation for patients dependent on domiciliary ventilation**

To improve safety in domiciliary ventilator users, they should be provided with telephone access to a team member, hospital ward, hospital service, or equipment provider that they can contact at all times in case of an emergency [514]. It is important for the patient who is dependent on ventilation to clearly understand the demarcation of who is responsible for their medical care and who is responsible for

their ventilator equipment provision. Clear individual action plans for medical deterioration or ventilator malfunction (including contact details) should be provided for the patient and their carers [514].

It has been recommended by American adult [402] and paediatric [515] consensus statements that the medical equipment company should have a 24 hour emergency support service for ventilator dependent patients. Such arrangements should be contractually agreed upon by the consumer and the company providing the ventilators. It is inappropriate to transfer follow up of mechanical issues to a GP or local team with no experience in ventilatory support [514].

The lack of a centralised database can make it difficult to assess the extent of ventilator related complications in the home or community and even when equipment failure is recorded the consequences of the malfunction for the patient are not clear or always acted upon accordingly [514].

### Quality control of domiciliary ventilators

A multicentre quality control study examined the performance of domiciliary ventilators in 300 patients in Barcelona [516]. In this study 4.3% required tracheostomy ventilation and 1.3% were 24 hour ventilator dependent. Ventilator care was provided by four different homecare companies. Discrepancy between the prescribed and actual measured main ventilator variable (minute ventilation or inspiratory pressure) of more than 20% and 30% was 13 and 4% respectively. In addition to this, built in alarms for power off, disconnection or obstruction did not work (where installed) in 0.9%, 18.6% and 5.1% of machines respectively. This highlights the limitations of quality control of home mechanical ventilation and that a system should be put in place to ensure accurate ventilator settings, correct ventilator performance and alarm operation. Another quality control European survey which involved 326 centres (access to >20,000 patients on home ventilation) also showed that quality control procedures vary considerably among the different providers [517].

### Frequency of causes and outcomes of ventilator failure

A U.S. study surveyed the frequency, causes and outcomes of home ventilator failure in 106 adults and 44 paediatric patients which equated to 841, 234 ventilator hours in one year [518]. Tracheostomy ventilation was provided in 76% of cases and 46% required 24 hour continuous ventilatory support. In total, 189 reports of home ventilator failures were found in 39% of these reports, which is equivalent to one home ventilator failure for every 1.25 years of continuous use. Other causes of ventilator failure included: improper care, damage, or tampering with the ventilator by caregivers (13%); functional equipment being improperly used by caregivers (30%) and equipment functional but patient's condition had altered (3%). This highlights that in addition to routine equipment maintenance and quality control, continued caregiver training and support should be provided especially in the areas of ventilator function, back-up battery systems, back-up ventilator function and ability to action skills for emergencies.

A recent U.K. study analysed all calls placed to a dedicated respiratory support telephone hotline over 6 months for 1211 adult and paediatric patients with neuromuscular disease, COPD or chest wall disease receiving home ventilation [519]. In contrast to the U.S. study above, the predominant method of providing domiciliary ventilation was non-invasive with 99% patients using NIV and only 12 patients requiring ventilation via a tracheostomy. In total, 188 home visits for "ventilator malfunction" were required. From 25 home visits which no mechanical fault was identified, 13 patients were unwell or required hospitalisation. This study highlights that in ventilator users, (especially where there is predominance in NIV), that early clinical evaluation should take place where no fault can be found during an equipment check, as patients may have mistaken clinical deterioration for an equipment problem [519].

**Key points:**

- Continuous NIV can be a suitable option over tracheostomy ventilation in selected patients with ventilatory dependency, assuming they have adequate glottic function and sufficient peak cough flows with assisted coughing techniques.
- When continuous NIV can be used, it can potentially avoid the complications associated with tracheostomy including trauma to the airway, impairing speech and swallowing, higher risk of infection and increased carer burden.
- With continuous NIV, a range of interfaces are required to alternate between night and day use (including mouthpiece ventilation) and, insufflation techniques and assisted coughing techniques must be taught to caregivers.
- Continuous NIV should only be commenced and followed by centres with expertise in nocturnal and diurnal ventilation.
- Based on consensus, a ventilator dependent patient for this document is defined as one who requires ventilation for ≥ 18 hours in a 24 hour period or is unable to sustain independent, spontaneous ventilation for > 4 hours.
- In observational studies, continuous NIV, with the assistance of mouthpiece increases survival in neuromuscular disorders.
- Volume ventilators or hybrid ventilators which are manufactured and approved for “life support” are recommended for ventilator dependent patients. These generally have more sophisticated alarms and battery systems.
- A centralised programme to ensure monitoring quality control of domiciliary ventilation should be put in place.
- Continued caregiver training and support should be provided especially in the areas of ventilator function, back-up battery systems, back-up ventilator function and ability to action skills for emergencies.
- If patients report ventilator malfunction and no mechanical fault is identified, early clinical evaluation should take place, as patients may have mistaken clinical deterioration for an equipment problem.

## 7.8 REQUIREMENTS FOR EQUIPMENT, HOME ENVIRONMENT & CARE-GIVER COMPETENCY & SUPPORT FOR PATIENTS REQUIRING CONTINUOUS NIV SUPPORT

Most non-invasive devices are not manufactured for life support and careful consideration of device specifications is required for patients requiring continuous ventilatory support. The following requirements are targeted towards maximising safety for ventilator dependent patients using continuous domiciliary NIV.

The majority of requirements presented in this section are based on formal consensus and expert opinion.

### 7.8.1 REQUIREMENTS FOR EQUIPMENT (CONTINUOUS NIV)

**Ventilator**

1. Choice should be based on patient's clinical need [510].
2. Equipment shall comply with the Therapeutic Goods Act and have a valid Australian Register of Therapeutic Goods (ARTG) number.
3. Ventilators must be dependable, and easy for the caregiver to operate [510].
4. The ventilator system chosen should allow mobility and able to operate when a patient is mobile and at different levels of incline (e.g. able to transported on the patient's wheelchair) [510].
5. Desirable for ventilators to be of a small size and lightweight [510].
6. Hybrid ventilators (volume and pressure pre-set) can be used when standard bi-level therapy is unable to maintain adequate gas exchange during the day and the patient is unable to tolerate volume ventilation when asleep.

**Back-up ventilator**

1. A second ventilator should be provided for:
   i) Patients who cannot maintain spontaneous ventilation for 4 or more consecutive hours [402, 510].
   ii) Patients who require NIV for ≥ 18 hours per 24 hours.
   iii) Patients who are geographically isolated where more than 16 hours/day ventilatory support is required and where a replacement ventilator cannot be provided within 4 hours.
   iv) Patients who require ventilation during mobility as prescribed in their care plan [510].
2. The second (back-up ventilator) should be same as the patient's primary ventilator to ensure that the patient and carers are familiar in its use.

**Power source**

An adequate and consistent power source must be available to operate the ventilator [402, 510].

i) Mains power is the primary power source for most ventilators.

ii) The ventilator must be able to run on a minimum of two independent battery sources (one source may be an internal battery).

iii) The internal battery should only be used for short-term use and should not be used as a primary source of power.

iv) External batteries providing direct current may be used to allow mobility and as an emergency power source.

v) Ventilators with in-line battery backup are preferred.

vi) External batteries need to always be appropriately charged and patients /carers need to know how to attach them to a ventilator and charge them.

vii) Charge indicators for internal and external batteries should be available where possible.

viii) A power generator may be recommended if frequent power outages occur or if the home is in a remote location.

ix) 12 Volt adapter for use with car power jacks.

x) External batteries and power generators must be rated to provide sufficient total energy requirements to run all emergency equipment. This includes emergency lighting, the ventilator, suction machine or mechanical cough in-exsufflator.

xi) Patient's electricity company is informed that they are classed as a priority in case of emergency, such as a power cut.

**Alarms**

1. A patient-disconnect (e.g. low pressure or low-exhaled volume [in dual limb circuits]) and power failure alarm are essential [402].
2. A patient-disconnect and power failure alarm should be used at all times [402].
3. If patient disconnection is likely to produce a serious adverse effect, a remote alarm and a secondary alarm may be indicated [510].
4. High pressure alarm should be available [510].
5. Audible alarms must be loud enough to be heard by caregivers in all areas of the home [510].

**Circuits and interfaces**

1. Three circuits and a minimum of two NIV interfaces which are compatible to both ventilators should be available.
2. Worn or damaged circuits or masks need to be replaced in a timely manner.
3. Patients should have contact details of their mask and circuit distributors. They should also have a written list of all of the required parts and their respective ordering numbers.

**Humidification**

1. Continuous NIV can cause drying of the patients airways, especially in the presence of leaks or when it is used in a dry climate. Heated humidification is indicated in these scenarios [510].

**Service and Maintenance of Ventilators**

1. Regular service and planned preventative maintenance should be provided at the frequency recommended under the manufacturer guidelines [510]. This should be documented. Patients should have access to an emergency contact line to report problems [514].
2. A contractual service and maintenance agreement is in place from the equipment supplier.
3. The service supplier has provided contact details that are known to the patient or carer and a 24 hour emergency contact number is clearly displayed for accessing repairs, maintenance and or replacement device with a safe turnaround time for response, including weekends. If the patient's primary ventilator fails, the backup ventilator should be used and the service supplier should provide a replacement ventilator for the primary ventilator as soon as possible and within 24 hours.
4. If equipment is to be removed for repair, maintenance or testing, an equivalent loan unit will be available to the patient

**Devices for communication**

1. The patient must have adequate means of communicating their needs/desires and have the means to summon help from their caregivers in the case of emergency. Where a patient has sufficient ability to activate a switch to attract carer attention, this should be implemented. Many light touch, mechanical, air or sensor switches are available and the most appropriate should be connected to a call system [510].
2. The system should be reliable and allow the patient to communicate regularly and at will [402].

**Self-inflating resuscitation bag**

Self-inflating resuscitation bag and a non-vented mask of an appropriate size should be issued. Bag ventilation is to be used in the absence of a functioning ventilator or for resuscitation purposes. If oxygen is usually prescribed for the patient, an oxygen side-port should be supplied with the resuscitation bag [510].

### 7.8.2 REQUIREMENTS FOR HOME ENVIRONMENT (CONTINUOUS NIV)

1. The patient and their caregivers must have functioning phone lines so that they can be contacted by clinicians in the case of emergency [510].
2. Home environment must also have safe electrical, plumbing and heating / cooling systems [515].

### 7.8.3 REQUIREMENTS FOR CAREGIVER COMPETENCY AND SUPPORT (CONTINUOUS NIV)

**Competency and monitoring**

1. All caregivers must display competency in equipment, set-up use and checking, and how to respond during power failures, equipment failures and acute life threatening events [510].
2. Ventilator settings, proper function of equipment, and the patient's physical condition should be verified with each initiation of ventilation, changing from one ventilator to another, after moving the patient, or changing the ventilator settings [510].
3. Carers and patients trained to recognise early signs of chest infection or ventilatory decompensation [514]. Care givers should demonstrate understanding and competency in patient's physical condition including [510]:
   i) respiratory rate
   ii) chest excursion (amplitude and synchrony with machine delivered breaths)
   iii) colour changes
   iv) diaphoresis and lethargy
   v) body temperature
   vi) heart rate
   vii) blood pressure (if available)
4. Care givers should demonstrate understanding and competency in ventilator settings and maintenance including [510]:
   i) Peak pressures
   ii) Pre-set tidal volume or pressure control
   iii) Frequency of ventilator delivered breaths
   iv) Verification of entrained oxygen setting or $FiO_2$, if applicable
   v) PEEP level (if applicable)
   vi) Humidification
   vii) Appropriate configuration of ventilator circuit
   viii) Alarm function
   ix) Battery power levels (internal and external) and how to attach external batteries.
   x) Condition and assembly of non-invasive ventilation interfaces

5. Care givers need to demonstrate how to use self-inflating manual resuscitation bag effectively and safely. If a one-way valve is to be used with a manual resuscitation bag for manual insufflation then the carers need to be strictly reminded that it needs to be removed when it is to be used during times of ventilator failure or resuscitation.

**Support**

1. Clinical and technical support should be available 24 hours a day. Users must be provided with relevant and up-to-date phone numbers.
2. Written plan of action for predictable problems such as power cuts, chest infection, and equipment failure.

| RECOMMENDATIONS FOR NOCTURNAL TO CONTINUOUS NIV USE | **Grade** |
|---|---|
| While continuous NIV is a therapy option for ventilator dependent patients, such therapy needs to be set up and supervised by centres with expertise in nocturnal and continuous ventilatory support modes, cough assist techniques and tracheostomy care. | D |

# CHAPTER 8 TRANSITION FROM PAEDIATRIC TO ADULT CARE

**DANIEL FLUNT**

## 8.1 TRANSITION FROM PAEDIATRIC TO ADULT CARE

Due to advances in care, including non-invasive ventilation and secretion removal techniques, technology-assisted children with neuromuscular disease now routinely live beyond the second decade of life [520]. In one ventilator assisted children's home programme in the United States, there has been a 360% increase in the number of ventilator-assisted adolescents who reached or were soon to reach adulthood in the years 2001-2006 compared to the period 1991-1996 [521]. Of this group, 50% require ventilation for disorders that cause neuromuscular weakness. Other diagnostic groups, including CCHS [522], are also surviving later into adulthood with successful use of mechanical ventilation.

As a child becomes an adult they outgrow the expertise of paediatric health services and need to find an adult health provider that is suitable and appropriate for them. A consensus statement [523] reports that the "goal of transition in health care for young adults with special health care needs is to maximise lifelong functioning and potential through the provision of high-quality, developmentally appropriate heath care services that continue uninterrupted as the individual moves from adolescence to adulthood". The main challenge that young people face when they move from a paediatric to an adult service is the need to improve their independence with regard to knowledge of their medical condition, making and keeping their own appointments and moving away from a family focused environment. As this is a learning process, it requires a well designed transition programme and time to ensure this occurs in a positive and successful manner.

In Australia, there are a few identifiable transition programmes [524] and currently there is little evidence on which to base the best transition practice [525], although consensus statements have been formulated [523, 526]. A recent study identified the five most prevalent clinical groups requiring adult specialist healthcare in NSW [524]. Whilst the neuromuscular group identified between 2-4 adolescents per annum having DMD and other muscular dystrophies requiring transition to adult care, the report did not highlight the number of paediatric patients on ventilation (invasive or NIV) requiring transition. Currently there is no published data about the number of young people undergoing transition from paediatric to adult domiciliary NIV services in the Australian literature.

The transition for young adults on NIV is a staged process which requires close collaboration between paediatric and adult specialist care teams. The choice of primary adult physician and respiratory support service for adolescents and young adults on respiratory support will depend on the underlying diagnosis of the young person, the locality of services and the wishes of the patient. The timing of transition can be especially difficult in adolescents with a progressive disorder who are nearing the terminal stages of their disease [527]. Standards of care for the transition from paediatric to adult health care [528] which have been adapted for NIV have been listed in Table 11.

**Table 11: Transition from paediatric to adult health care: best practice standards – NIV**

(Adapted and modified from [528])

| | |
|---|---|
| **Standard 1** | Transition is a process that requires close collaboration between paediatric and adult specialist care teams. |
| **Standard 2** | The process of transition should begin around the time of secondary school entry (age 12) and finish around school leaving time (18 years). |
| **Standard 3** | The transition process should engage young people and their family in a proactive and positive way. |
| **Standard 4** | Depending on the young person's abilities, they should be encouraged to learn how to maintain their ventilator equipment and mask, know how their equipment is put together and how it works, and become independent with ventilator application prior to transition to adult services. This should be promoted from an early age. |
| **Standard 5** | Paediatric and adult specialist teams should ideally develop a joint transition plan and meet to discuss individuals in transition prior to transfer to adult health services. |
| **Standard 6** | A Transition Case Manager should be designated. Opportunity should be provided for the young person and their family to meet the adult team prior to transfer. |
| **Standard 7** | Discussions about potential differences in ventilator equipment provision between paediatric and adult services should commence 24 months prior to the transition (16 years). Carers and patients need to be aware of eligibility criteria for equipment provision from the appropriate governmental bodies (e.g. EnableNSW and Centrelink). The Transition Case Manager can assist with this aspect. |
| **Standard 8** | A comprehensive summary of medical and social issues should be available to the adult team well in advance of transfer. Young people and their families should have copies of all relevant documents. |
| **Standard 9** | Young people with chronic complex conditions that might require life threatening emergency management should be flagged on adult health service emergency department databases. |
| **Standard 10** | Adult health services should provide youth friendly resources and ensure that staff members are educated in the management of young people with chronic health problems. Family focused care should be promoted. |
| **Standard 11** | The impact of alcohol, illicit drugs and other medications on hypoventilation needs to be appropriately introduced by the paediatric teams and reinforced by the adult specialist care teams. |

The method of provision of ventilator equipment, consumables, home monitoring equipment and home care, in the paediatric setting can vary widely in NSW. The patient and carer should not assume that this level of equipment provision and assistance will be given once they are transitioned into adult services. Health care providers need to discuss these potential issues with the carers and the patient at least 24 months prior to transition, or approximately at 16 years of age. This is so that the young adult and their carers can commence discussions with relevant government bodies (EnableNSW and Centrelink) such that they can become aware of eligibility requirements and the implications this will have on future provision of equipment. This should be done in an environment which fosters independence in the adolescents, and aspirations of achieving paid employment should not be discouraged for the sake of meeting financial eligibility for obtaining expensive life-sustaining equipment.

For more resources regarding transition from paediatric to adult services in NSW, we refer the reader to the following website:

http://www.health.nsw.gov.au/ACI/transition/index.asp

**Key points:**

- Due to advances in care, including non-invasive ventilation and non-invasive secretion removal techniques, more patients on mechanical ventilation are surviving childhood, requiring adult ventilation services.
- Programmes need to be implemented for young people on ventilation to ensure a smooth transition of care and equipment.
- A Transition Case Manager should be appointed to ensure adequate standards are maintained during the transition.
- Appropriate adult services should be identified locally that are appropriate for adolescents with complex health needs.
- Funding should be maintained through the transition process.

| RECOMMENDATIONS FOR TRANSITION FROM PAEDIATRIC TO ADULT CARE | **Grade** |
|---|---|
| A Transition Programme needs to be implemented for young people on ventilation to ensure a smooth transition of care and equipment. | D |
| A Transition Case Manager should be appointed to ensure adequate standards are maintained during the transition. | D |

# CHAPTER 9 PALLIATIVE CARE & END-OF-LIFE ISSUES FOR PATIENTS ON DOMICILIARY NIV

**DANIEL FLUNT**

## 9.1 BACKGROUND

Palliative care "seeks to prevent, relieve, reduce or soothe the symptoms of disease or disorder without effecting a cure" [529]. Using this description, palliative care is not restricted to patients who are dying or in hospice programmes, and suits the description of the use of NIV in certain disorders, such as rapidly progressive neuromuscular disorders and during advanced stages of other diseases where the focus is shifted from improving survival or quality of life to only being used when it is able to enhance physical, emotional or social comfort for the patient [29, 530, 531].

Respiratory failure is a common terminal event in many conditions including COPD, interstitial lung disease and neuromuscular disorders involving the respiratory muscles. Despite this, palliative and end-of life care services for these disorders are less well developed and are often *ad hoc* or fragmented compared to palliative care programmes for those with malignant disease [530, 532]. Using cancer palliative care models (which generally follow a more predictable time course) to predict the need for palliative care in non-malignant disease can be unhelpful. This is because non-malignant diseases of respiratory failure usually remain at a slowly deteriorating level of function until an unpredictable acute exacerbation may suddenly worsen their prognosis [530]. An exception to this may be MND, a rapidly progressive neuromuscular disorder where outcome is more predictable [530], and in this diagnostic group, disease specific recommendations have been made [29, 146, 533]. Irrespective of the disease process, a better outcome can be achieved in these patients by placing focus on symptom relief, patient education and by early and timely discussions involving clinicians, patients and their families to address present and future decision making [29, 530].

In examining patient attitudes to physician skills in providing end of life care, COPD patients had a strong desire for more information, specifically on the course of the disease, treatment options and how these treatment option work and their limitations [534]. There was also a need to discuss what dying might be like. Other authors have described that the components of a good death include: pain and symptom management; clear decision making; preparation for death; a sense of completion; contributing to others; and affirmation of the whole person [535]. In addition to patients with lung disease, respiratory physicians often need to advise on the end stage management of respiratory complications of neuromuscular disease with respiratory weakness [530].

Palliative and end-of-life care of patients with terminal cardiopulmonary disease [531] and neuromuscular disease [29, 146] requires a multidisciplinary approach including, respiratory physicians, consultants and services in palliative care, domiciliary non-invasive ventilation service, neurologists, cardiologists, nurses, speech pathologists physiotherapists, occupational therapists, dietitians, social workers and chaplains.

## 9.2 COMMENCING PALLIATIVE CARE AND END-OF-LIFE DISCUSSIONS

A "bad death" has been defined by Quill [536] as a medical emergency. On the other hand a "good death", has been described as "one that is free from avoidable distress and suffering for patients, families and caregivers; in general accord with patient's and families wishes; and reasonably consistent with clinical, cultural and ethical standards" [529]. In order for a "good death" to occur strong communication needs to be established between the patient, and their clinicians and carers to ensure that their goals and preferences for end-of life care are acknowledged and carefully planned for [29, 537].

Despite the importance of commencing such discussions, failure of physicians to initiate end-of-life discussions has been identified as a significant barrier to determining patient preferences for end-of life care [538]. One major reason is that clinicians find it difficult to commence such sensitive discussions with their patients and find it a source of stress [539]. Despite this it is important for the physician to discuss disease progression in the context of NIV and other forms of ventilation in a realistic, balanced and honest manner, while trying to avoid crushing all hope in relation to prognosis [29]. Physicians should also discuss symptom management and how it is going to affect the rest of their patient's life, rather than a completely focussing on how they might die [530].

Successful palliative and end-of-life care for patients with cardiopulmonary disease require the physician, palliative care and multi-disciplinary team to coordinate and maintain the following [531]:

*Support for patient and family*

- Advance care planning
- Maintaining and supporting the patient's dignity, including cultural and spiritual needs
- Support for the family, including familiarity and confidence with equipment and medication regimes, and bereavement services

*Care of the patient*

- Relief of distressing symptoms, particularly appropriate management of pain, breathlessness or pulmonary secretions
- Management of the dying process, including withdrawal of life sustaining treatment. Ideally these issues would have been previously raised, discussed and documented in an up-to-date advance care directive in the presence of the patient's physician and next-of kin who are likely to be their surrogate decision maker.
- Preferences and limits for cardiopulmonary resuscitation, surgery, non-invasive ventilation, progression to invasive mechanical ventilation, dialysis and other life-prolonging measures can be made known.
- Referral to appropriate hospital and community resources
- Quality palliative and end-of-life care in all treatment settings, including institution and home

**Commencing palliative care and end-of-life discussions - How?**

End of life decision making will only occur if opportunities for such discussions exist [540]. A protocol for establishing a framework to discussing patient preferences for withholding and/or withdrawing life support may assist providing an environment which may assist with the commencement of such discussions [531]. This includes:

i) Being familiar with national and local policies, and legal statutes concerning the withdrawal of life support measures [531].

ii) Having an appropriate setting within which to initiate the discussion [531]. Patients may prefer to have family member to be present especially if they are told and expect to ask questions [541].

iii) Asking the patient (and family) what they understand about the disease and its course [531].

iv) Having a general informational discussion about the goals of care [531].

v) Establishing the context for the discussion, *i.e.*, death is inevitable at some point [531].

vi) Discussing specific preferences for various treatment options, *e.g.*, surgery, mechanical ventilation [531].

vii) Responding sympathetically to emotions which come as a result of the discussion [531].

viii) The clinician and the patient are aware that they will establish a plan together, and that it will be implemented [531].

ix) Making it clear that their plan may change as circumstances dictate, and thus should be reviewed periodically [531].

Once the above framework has been established, more specific discussions about how NIV or invasive ventilation can be used or ceased in the context of disease progression or end-of life care can be commenced. Most importantly patient preferences and goals need to be elicited, the rationale for NIV needs to be communicated, parameters for NIV success and failure needs to be outlined, and the corresponding appropriate settings for NIV use need to be defined [537]. Essential topics of discussion to assist with planning include [146]:

i) Diagnosis and prognosis in the context of NIV [146]. Where relevant, it is important to highlight that respiratory failure is not necessarily the terminal event in patients with some forms of neuromuscular disease and that domiciliary ventilation can improve both survival and quality of life [530].

ii) Symptom development [146].

iii) Explore/discuss issues regarding use of NIV for symptom management, life prolongation and quality of life [146].

iv) If the patient elects NIV, consider appropriate timing of commencement, i.e. based on symptoms or investigation results [146].

v) Treatment options and desire for palliation or life prolongation with nutritional support [146].

vi) Encourage discussion and documentation of advanced directives [146]:

   a. resuscitation status

   b. treatment end points for NIV ( e.g. unacceptable quality of life or when unable to communicate by any means)

   c. use of antibiotics for chest infection

   d. attitude towards intubation / tracheostomy ventilation

vii) Patient and carers should feel supported all the way and contacts of local support groups should be given to patients [29, 146].

viii) Explain palliative care services and the rationale for appropriate timing of referral. Patients can be referred to palliative care before reaching the advanced stages of their disease [29, 146]. This is to ensure adequate planning, linking to services and for the patient and the palliative care clinicians to become familiar with each other and what they have to offer.

ix) End-of life planning also explores issues relating to death including preferred place of death [146].

In addition to dedicated appointments with physicians, pulmonary rehabilitation sessions as well as outpatient appointments can provide opportunities for education and the outcomes of these discussions can be recorded in medical notes [530]. Ideally any outcome of discussions should be summarised, kept up to date and placed in an accessible place so that it can be easily and quickly retrieved when required.

**Commencing palliative care and end-of-life discussions - When?**

While it is the physicians role to initiate discussion about future care directives, the ideal timing of such difficult conversations is unclear [146]. Discussing sensitive end-of-life care issues too soon to diagnosis can cause unnecessary distress and hopelessness and discussion of these issues too late can lead to poor planning and unwanted or inappropriate end-of-life management [29]. Even in a rapidly progressive neuromuscular disease like MND, clinically significant respiratory problems are not common within a year of baseline diagnosis [542]. Therefore, in this scenario such discussions could be delayed for 6 to 12 months after diagnosis [146], so long as initial clinical presentation does not involve significant respiratory or bulbar symptoms. In other, more stable conditions, such conversations could be brought up once the patient has established good rapport with their clinicians, at a time which is relevant to their current state of their disease and its likely progression. At other times, the patient or their family may independently raise concerns about the course of the disease and implications of management in weeks or months after diagnosis [29]. In disorders which have been diagnosed from an early age, issues with regards to ventilation may have not been brought up for some time. Planning and discussions should occur at the physician's discretion but ideally before significant respiratory decline or predicted respiratory crisis point [27].

A survey of UK physicians showed that >80% always or nearly always discuss NIV therapy with DMD patients and families [543]. However, in depth discussions usually only occurred at the point at which clinical signs or symptoms developed. It has been recommended that in diseases which have more predictable time courses such discussions should be commenced much earlier [27]. It is important to note that while these discussions should occur prior to significant respiratory decline in the patient, treatment options and decisions can change throughout the disease course and opportunities should be made to acknowledge these changes [146].

**Key points:**

- NIV can be used in the palliative care / end-of-life scenario when it is able to enhance physical, emotional or social comfort of the patient, without effecting a cure.
- Despite respiratory failure being a terminal event in many patients with chronic respiratory failure, palliative and end-of-life services are generally less well developed and structured in comparison to programmes for those with malignant disease.
- Respiratory physicians are frequently consulted for end stage management of respiratory complications in patients with lung disease and neuromuscular disorders.
- Palliative and end-of-life care requires a multi-disciplinary approach.
- An appropriate environment should be set up to discuss advanced care planning, which is appropriately and humanely timed, but ideally well in advance of a respiratory crisis point.
- Specific discussions of how and under what circumstances is NIV to be used as the patient's disease progresses should be documented. Directives about invasive ventilation (including long term tracheostomy) and resuscitation orders should also be discussed.
- The patients advanced care plan may change as their symptoms or circumstances change. Opportunities should arise for patients to voice these changes.

## 9.3 WHEN TO STOP NIV

While many patients remain stable for many years while receiving domiciliary NIV, increasing muscle weakness or lung disease progression can mean that the patient's reliance on NIV can increase in terms of the hours of usage and the level of support required [27]. In certain circumstances, continuous NIV can be achieved in stable respiratory failure where there is adequate rotation of effective interfaces to prevent skin breakdown and the absence of significant bulbar weakness [509]. In cases where continuous NIV cannot be tolerated such as in patients with significant bulbar weakness, where arterial blood gases can no longer be controlled or if interface difficulties arise, a transfer to invasive ventilation via tracheostomy needs to be considered if ventilation is to be continued [27]. Invasive ventilation by tracheostomy can be accepted by some patients and carers and the concept of a tracheostomy can be discussed [29]. While tracheostomy can enhance survival, it can do so at the expense of reductions in quality of life, swallow and speech impairment, bronchospasm, tracheomalacia, haemorrhage, and socioeconomic problems including lack of long-term residential facilities equipped to manage tracheostomised patients, carer burden, potential to progress to a "locked in state" and high economic costs [146]. The progression to a tracheostomy for continued ventilation should therefore be discussed on an individual basis. In particular, in some disorders such as MND, few patients would elect to have tracheostomy ventilation when their disease progressed to the point that NIV was no longer effective and in Australia and the UK, tracheostomy is rarely an option for these patients [146]. Unplanned or unwanted tracheostomy can be avoided by discussions early in the course and through advance directives [29]. Either way, if the patient remains on NIV or decides to have tracheostomy ventilation, the patient and their carers must agree under the specific circumstances under which ventilatory support should be discontinued [29]. Particularly, all involved need to be clear whether NIV will be the ceiling of treatment or if intubation and conventional ventilation are indicated should NIV fail [530].

It can be a difficult decision to ascertain the optimal time to cease NIV. The continuation or discontinuation of NIV in acute respiratory failure has been described in one model over three categories: life support without preset limits; life support with preset limits (do not intubate); and comfort measures only [537]. To assist with the placement of the patient into a certain category, both the patient and clinician need to be aware of the specific goals of care which are relevant at particular stages of their disease. In patients with chronic respiratory failure, these particular goals should be

discussed in depth with the patient and documented to reflect the patient's wishes for different scenarios. Ideally this should occur before a point of respiratory crisis. Putting the goals of care in context can practically assist with how NIV is to be used as their disease progresses or when they are faced with a potential terminal event (see Table 12 for the overview of the three-category approach to using NIV for acute respiratory failure). It is important to acknowledge that individual patients may transition from one category to another as the goals of care or the risks and benefits of NIV change [537].

**Table 12: Overview of the three-category approach to using non-invasive positive pressure ventilation (NIV) for acute respiratory failure** (From [537]).

| Approach | CATEGORY 1 | CATEGORY 2 | CATEGORY 3 |
|---|---|---|---|
| **Definition** | **Life Support Without Preset Limits** | **Life Support With Preset Limit (Do Not Intubate)** | **Comfort Measures Only** |
| **Primary goals of care** | Assist ventilation and/or oxygenation.<br>Alleviate dyspnoea.<br>Achieve comfort.<br>Reduce risk of intubation.<br>Reduce risk of mortality.<br>Avoidance of intubation. | Includes same as category 1 except intubation declined.<br>Also could include briefly prolonging life for a specific purpose (e.g. arrival of family member). | Palliation of symptoms (relief of dyspnoea). |
| **Main goals to communicate with patient and family** | Goal is to restore health and use intubation if necessary and indicated. | Goal is to restore health without using endotracheal intubation and without causing unacceptable discomfort. | Goal is to maximise comfort while minimising adverse effects of opiates. |
| **Determination of success** | Improved oxygenation and/or ventilation.<br>Tolerance of NIV or minor discomfort that is outweighed by potential benefit. | Improved oxygenation and/or<br>Ventilation.<br>Tolerance of NIV or minor discomfort that is outweighed by potential benefit. | Improved symptoms.<br>Tolerance of NIV. |
| **Endpoint for NIV** | Unassisted ventilation adequately supporting life. Intolerance of NIV. | Unassisted ventilation adequately supporting life.<br>Intolerance of NIV. | Patient is *not* more comfortable having NIV on or wants NIV stopped.<br>Patient becomes unable to communicate. |
| **Response to failure** | Intubation and mechanical ventilation<br>(if indicated). | Change to comfort measures only and palliate symptoms without NIV. | Palliate symptoms without NIV. |
| **Likely location of NIV** | ICU but may include step-down unit or acute care bed in some hospitals with appropriately monitored setting and trained personnel. | Variable but may include ICU or step-down unit or acute care bed. | Acute care bed but could be applied in hospice by appropriately trained personnel. |

ICU = intensive care unit.

With regards to protocols and guidelines for withholding and withdrawing life prolonging treatment, all emphasise that the primary goal is to restore or maintain health, but when treatment fails or it causes negative effects which outweigh benefits, then the justification for providing that treatment is lost [540]. Instead of withdrawal of treatment, a more accurate description could be "redirection of care". In the example of NIV in end-of-life scenarios, this requires the immediate institution of other interventions, such as sedation or analgesia [540].

While there has been little systematic study of the end-of-life wishes in non-malignant conditions [530], patients who receive mechanical ventilation (whether NIV or invasive ventilation) may reach a stage where their quality of life is intolerable and may request discontinuation of ventilation [533]. While this situation can be distressing for family and staff, patient autonomy and dignity should be preserved and there is no ethical reason why ventilation should not be discontinued at a time decided by the patient who has adequate capacity [533]. The management of ventilator withdrawal is controversial and where possible should be guided by patient preference. Withdrawal of ventilatory support will usually cause significant dyspnoea and the clinician has the responsibility to execute the patient's request in a compassionate and humane manner [544]. Ideally, when a patient is on domiciliary non-invasive ventilation, preferences should be documented to why and how non-invasive ventilation should be used or ceased during palliative care or end-of-life care approaches.

Ventilator withdrawal becomes more difficult when a patient is using it continuously, 24 hours a day. In a majority of such cases patients rely on their carers or clinicians to apply the NIV for them when they are incapable of applying or removing the mask. In this scenario a clinician would have to actively withdraw ventilation [146]. This is in contrast to the patient who can tolerate sufficient periods off the mask during the day, where it can be viewed that the focus is shifted from "withdrawing active treatment" to one of "not re-applying futile treatment". Such elective withdrawal is emotionally and ethically sensitive and must be carefully discussed and incorporate the patient's wishes, advance care directives or enduring guardian recommendations. A multidisciplinary approach including primary care physicians, palliative care services and NIV service should be adopted [146]. Ventilator dependent patients should be counselled against attempts to cease ventilatory support in the absence of medical support, as undesirable dyspnoea will occur without appropriate medication [146].

## 9.4 USES OF NIV IN PALLIATIVE OR END-OF-LIFE CARE

**Relief of symptoms: dyspnoea and sequelae of nocturnal hypoventilation**

The palliative use of NIV to control symptoms of dyspnoea and nocturnal hypoventilation without the goal of improving survival has been suggested to be an entirely appropriate choice for some patients with end-stage disease [27]. NIV can also be theoretically used as an adjunct to opiates for relieving breathlessness, in a way that it may decrease some side effects of opiates, such as decreased level of consciousness [537].

**For alertness and communication**

Although most patients and families are interested in ensuring comfort while dying, some are interested in maintaining a level of alertness, cognition and ability to communicate [545]. NIV is this circumstance would be considered successful if it allows this to occur without causing other consequences [537]. Others find NIV a hindrance to verbal communication and this may in itself cause distress. When the primary goal for the patient is comfort, NIV should not be encouraged if it is causing discomfort [537].

**"Buying time"**

NIV can be used to "buy time" to find out more information and allow time to clarify appropriate limits to the patient's care. It also may provide time to finalise personal affairs, allow closure for patients and relatives, and for loved-ones to arrive before the patient dies [532, 546]. Some patients who do not want prolonged life-sustaining therapy may elect to undergo a time or event limited trial of NIV. In this scenario NIV would be used actively as a ceiling treatment until the end of this trial. When appropriate, the patient's NIV management will then follow a palliative or comfort measures approach [537].

## 9.5 WHEN NIV IS USED AS A CEILING TREATMENT

Where the physician and the patient agree that invasive ventilation is inappropriate or if the patient refuses NIV, the physician can respect the patient's decision if they demonstrate adequate capacity. Otherwise they can be guided by the advance directive or enduring guardian. When a patient wishes to receive NIV as a ceiling treatment, certain parameters of continuation or discontinuation should be put in place.

NIV should be applied after careful discussion of the goals of care, with explicit parameters for success and failure, by experienced clinicians, and in the appropriate health care settings [537]. Issues and parameters to be discussed when NIV is to be used as a ceiling treatment could include:

i) If a patient is tolerating NIV, but showing no early signs of improvement, then NIV can be continued and the response can be reassessed a few hours later [532].

ii) If there remains no physiological or biochemical improvement but the patient is symptomatically improved, then it is reasonable to continue if it remains an effective palliative measure [532].

iii) Symptomatic improvements can include reducing breathlessness which can settle the patient's anxiety levels, allow them to rest, communicate, and sleep.

iv) If the patient feels no benefit from optimised NIV or if NIV is distressing the patient, then it should be stopped [532].

v) Parameters of when a patient would not want to wear NIV should be established. This may include level of ventilator dependence, discomfort, inability to return to living at home, inability to eat or drink, etc.

vi) Communication between multidisciplinary team, patient and family is crucial throughout [537].

vii) If NIV is to be ceased due to it being ineffective and causing distress, or providing negative quality of life, adequate pharmacological symptomatic relief of dyspnoea should be provided prior to removal of ventilation [537].

## 9.6 PRACTICAL ISSUES TO CONSIDER WITH VENTILATION AT END-OF-LIFE

### Pharmacological relief of dyspnoea

Many clinicians will start a low-dose subcutaneous infusion of opioid and/or benzodiazepine before removing the mask [532]. The "double effect" principle permits the relief of suffering as the primary intention but at the opportunity cost of reducing life-span. While sedating medication can worsen hypoventilation through depressing reparatory drive and potentially accelerate death, there is little evidence to suggest cautious use of opioids or benzodiazepines hastens death in this context [146, 532].

Acute and sudden dyspnoea can occur in patients with advanced MND. To relieve this acute dyspnoea in the home situation, a breathing space kit has been recommended which is filled with drugs supplied by the GP for each specific patient [533]. This pack has one section which contains diazepam suppositories which can be used by the carer and the other section has drugs such as diamorphine to be administered by health professionals.

### Home services

There has been shift from inpatient to home health care and in response to this, there has been an increase in home services [531]. It is important that the patient and the family are linked to all of the appropriate home services and that they do not feel isolated during the process.

### Appropriate adjustment of ventilator settings

Nearly all neuromuscular patients treated with NIV choose to continue it, even in the terminal phase of their disease [540]. One third of deceased MND patients were reported to die under NIV, revealing a high acceptance of this modality in the end stages of life [547]. When it has been decided to use NIV for symptomatic relief at the end of life, after appropriate medications for dyspnoea have been given, the bi-level device should be changed from a spontaneous-timed mode to a spontaneous mode. A

gradual reduction in the efficacy of the ventilator can also be attempted by reducing the pressure support to allow for a gradual development of hypercapnia and provide terminal coma [533]. The mask can be removed when the patient is not suffering from symptoms of breathlessness.

### Staff / Carer experience with NIV application and principles

Staff training and experience in NIV is very important and adequate numbers of skilled staff should be available throughout the 24 hour period [532]. Inexperienced staff in the area of NIV, can inadvertently cause distressing episodes of dyspnoea, pain from mask application or inappropriate continuation or discontinuation of NIV. If staff and family are appropriately trained in NIV, an inpatient or supported home setting can be appropriate for the end of life in chronic respiratory failure patients [537].

### Bereavement

It is important for palliative care to continue after death, through bereavement support [29]. A letter of condolence can also assist the bereavement process with the deceased family and can also place closure on the relationship between the physician and the late patient's family [548].

**Key Points:**

- Continuous NIV can be used in select patients with stable chronic respiratory failure. In other situations, where appropriate, some patients make an informed decision for continuous ventilatory support to continue via tracheostomy.
- Where continuous NIV is not tolerated and/or failing as a treatment, and invasive ventilation is deemed inappropriate by the patient or clinical context, the focus of NIV should shift to its use for comfort measures.
- Both the clinician and the patient need to be aware of the specific goals of care at particular stages of the patient's disease and adjust the use of NIV accordingly. Ideally prior to a significant event, all involved need to be clear whether NIV will be used as a ceiling treatment or palliation, or if intubation and conventional ventilation are indicated should NIV fail.
- There is no ethical reason why ventilation should not be discontinued at a time decided by the patient who has adequate capacity.
- Ventilator withdrawal should be performed in a compassionate and humane manner, with the use of pharmacotherapy which is titrated to relieve dyspnoea and distress.
- NIV can be used in the palliative care / end-of-life setting to: relieve dyspnoea and the sequelae of nocturnal hypoventilation; to allow patient alertness and communication; and to "buy time".
- When a patient wishes to receive NIV as a ceiling treatment, certain parameters of continuation or discontinuation should be put in place.
- Staff / carers skilled in NIV should be available during end-of-life care to ensure that it is used appropriately and that it does not cause undue stress for the patient.

## 9.7 ADVANCED CARE PLANNING

Advance care planning refers to the "process of preparing for likely scenarios near the end of life and usually includes assessment of, and dialogue about, a person's understanding of their medical history and condition, values, preferences, and personal and family resources" [549]. It is a document that describes a patient's future preferences for medical treatment in anticipation of a time when one is unable to express those preferences because of illness or injury. Despite the apparent importance of advance care planning, it appears that they are uncommon [550]. A European survey of end-of-life decision making in respiratory intermediate care units was made in only 22% of patients [551].

In addition to respecting patient autonomy, the process of advance care planning has the benefits of promoting the discussion of goals, values and preferences for particular medical interventions in particular situations between patients, family members, carers and clinicians [552]. It also provides the forum for family members to understand the wishes of the patient and for the patient to hear the

family's ideas regarding potential therapies [552]. By doing so, it can help to remove some of the burden of decision making for patient's next of kin and may relieve them of future thoughts of guilt or self-doubt [531].

The presence of an advance care directive can also ensure that the patient's actual preferences are more likely to be implemented [531]. This is particularly important where future problems can be anticipated as the disease progresses and the patient may not be able to effective communicate despite being fully conscious, as can occur in MND where a "locked in" state can develop [552].

The main limitation of advanced care directives is that the document is unable to encompass the entire wide range of possibilities available for health care as the end-of-life approaches [553, 554]. In diseases with more predictable end-of-life time courses, some tools to assist with writing advance care directives with regards to ventilation have been developed. For an example of one tool which focuses on respiratory failure and invasive mechanical ventilation, see Figure 12 [552]. Whilst it has been specifically written with MND in mind, it can also be used as a starting place for other respiratory failure disease processes. This tool highlights that when discussions are being held with regard to advance care directives that it should not only outline patient preferences but should be in depth enough to define the clinical situations in which these preferences hold, to attempt to avoid ambiguity which can make more general advance directives ineffectual [552].

**Figure 12: Health-care directive for the individual with amyotrophic lateral sclerosis**

(From [552], - *Reproduced with permission of John Wiley & Sons, Inc.*

**HEALTH-CARE DIRECTIVE FOR THE INDIVIDUAL WITH AMYOTROPHIC LATERAL SCLEROSIS.**

Recognising that respiratory failure is frequently the cause of death in cases of ALS, I hereby wish to state in advance my preference regarding invasive mechanical ventilation. It is my desire that these preferences guide the decision making of my family and my physician(s) in the event that I am unable to participate in a meaningful way in discussions regarding my health care. I understand that none of the choices made here will be put into effect without my agreement as long as I retain the capacity for decision making and the ability to communicate, in some form, those decisions.

**With regard to invasive mechanical ventilation requiring endotracheal intubation, it is my preference that:**

(Choose one of the following three main options):

**A.** ____ Invasive mechanical ventilation not be instituted under any circumstances. I understand that such a choice will almost certainly mean that my death will occur earlier than if such support is instituted. I also understand that some processes that might precipitate respiratory failure may be readily reversible and that, therefore, mechanical ventilation may not necessarily be long-term, yet I still do not wish to undergo mechanical ventilation even in such circumstances.

**B.** ____ Invasive mechanical ventilation be used only when, in the judgment of appropriate medical personnel, the acute cause of respiratory failure is believed to be likely reversible, for example, in the case of choking. If, on the other hand, respiratory failure is a result of the irreversible deterioration from ALS, I do not wish to undergo mechanical ventilation, knowing that such a choice will almost certainly mean that my death will occur earlier than if such support is instituted.

If invasive mechanical ventilation is used and it becomes evident that long-term mechanical ventilation is required, then (choose none, one, or more of the following):

1. ____ I wish for mechanical ventilation to be discontinued regardless of the circumstances, knowing that this will result in my death.
2. ____ I wish for mechanical ventilation to be discontinued if I should be diagnosed in writing by two physicians to be in a permanent unconscious condition.
3. ____ I wish for mechanical ventilation to be discontinued if I become permanently unable to effectively communicate (“locked-in”).
4. ____ I wish for mechanical ventilation to be discontinued if I am unable to return to living at home.
5. ____I wish for mechanical ventilation to be discontinued if my care results in major financial hardship or other burden on my family.

**C.** ____ Invasive mechanical ventilation should be instituted in all circumstances for respiratory failure not treatable by other measures, and long-term mechanical ventilation with tracheostomy should be continued with the following exceptions (choose none, one, or more of the following):

1. ____ I wish for mechanical ventilation to be discontinued if I should be diagnosed in writing by two physicians to be in a permanent unconscious condition.
2. ____ I wish for mechanical ventilation to be discontinued if I become permanently unable to effectively communicate (“locked-in”).
3. ____ I wish for mechanical ventilation to be discontinued if I am unable to return to living at home.
4. ____ I wish for mechanical ventilation to be discontinued if my care results in major financial hardship or other burden on my family.

To be more meaningful and to ensure that the likelihood of the patients wishes to be carried out, the advance care directive must be completed in consultation with a health-care provider familiar with their condition and mechanical ventilation and preferably in the presence of family members and the patient's Enduring Guardian, if one has been appointed. An Enduring Guardian is someone that a patient legally appoints to make personal and lifestyle decisions and/or decisions about medical treatment on the patient's behalf, when they are unable to make those decisions themselves. Although currently advance care directives are not legally binding in NSW, they still may be valid under common law and when the content of advance care directive is consistent, current and up-to-date, then medical professionals are encouraged to respect the wishes stipulated in the document [549].

For more information on Advance Care Directives refer to:

**The Advance Care Directive Association Inc.**

18 / 113 Johnston Street Annandale, NSW 2038

www.advancecaredirectives.org.au

**NSW Department of Health**

Author Branch: Health Research and Ethics [549]

Document Title: Advance Care Directives (NSW) - Using

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**Key points:**

- The process of advance care planning has the benefits of: respecting patient autonomy; promoting the discussion of goals, values and preferences for particular medical interventions in particular situations between patients, family members, carers and clinicians; providing the forum for family members to understand the wishes of the patient; and ensuring that patient's actual preferences are more likely to be implemented.
- To be more meaningful and to ensure that the likelihood of the patients wishes to be carried out, the advance care directive must be completed in consultation with a health-care provider familiar with their condition and mechanical ventilation and preferably in the presence of family members or the patient's Enduring Guardian.
- Advance care directives should outline patient preferences in sufficient detail to define the clinical situations in which their preferences hold.

| RECOMMENDATIONS FOR PALLIATIVE CARE AND END-OF-LIFE ISSUES FOR PATIENTS ON DOMICILIARY NIV | **Grade** |
|---|---|
| Early and timely discussions involving clinicians, patients and their families to address present and future decision with regards to the use of NIV during the progression of their disease should be held. Focus should be placed on the role of NIV in symptom relief as their disease progresses. | D |
| To ensure adequate time for planning, patients should be referred to palliative care services before they reach the advanced stages of their disease. | D |
| Encourage discussion and documentation of advanced directives:<br>• resuscitation status<br>• treatment end points for NIV (e.g. unacceptable quality of life or when unable to communicate by any means)<br>• attitude towards intubation / tracheostomy ventilation | D |
| NIV can be used in the palliative care / end-of-life setting to: relieve dyspnoea and the sequelae of nocturnal hypoventilation; to allow patient alertness and communication; and to "buy time". | D |

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