The COPD-X Plan: Australian and New Zealand Guidelines for the management of Chronic Obstructive Pulmonary Disease 2006

These guidelines have been developed and revised by the Australian Lung Foundation and the Thoracic Society of Australia and New Zealand as part of a national COPD program.

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## Contents

Authors and contributors to the original guidelines (March 2003) ........................................... 6  
Writing Group and Editorial Committee .................................................................................. 6  
Original COPD Guidelines Steering Committee ..................................................................... 6  
Other Contributors .................................................................................................................. 7  
COPD Guidelines Evaluation Committee .................................................................................. 7  

Foreword ...................................................................................................................................... 8  
The COPD-X guidelines .............................................................................................................. 9  
Levels of evidence ...................................................................................................................... 10  
Box 1: Levels of evidence ............................................................................................................ 10  

Summary of the COPD-X guidelines .......................................................................................... 11  
C: Confirm diagnosis and assess severity .................................................................................. 11  
Evidence level ............................................................................................................................. 11  
O: Optimise function .................................................................................................................. 11  
Evidence level ............................................................................................................................. 11  
P: Prevent deterioration .............................................................................................................. 11  
Evidence level ............................................................................................................................. 11  
D: Develop support network and self-management plan .......................................................... 12  
Evidence level ............................................................................................................................. 12  
X: Manage eXacerbations ......................................................................................................... 12  
Evidence level ............................................................................................................................. 12  

Box 2: Overlap of bronchitis, emphysema and asthma within chronic obstructive pulmonary disease (COPD) ........................................................................................................... 13  

Aetiology and natural history ..................................................................................................... 13  
Box 3: Time-course of chronic obstructive pulmonary disease (COPD) .................................... 14  

Diagnosis ...................................................................................................................................... 15  
History ......................................................................................................................................... 15  
Box 4: Medical Research Council grading of functional limitation due to dyspnoea 17 ............ 15  

Physical examination .................................................................................................................. 15  

Spirometry ................................................................................................................................... 16  
Box 5: Maximal expiratory flow-volume curves in severe chronic obstructive pulmonary disease (COPD) and chronic asthma ................................................................. 16  

Flow volume tests ....................................................................................................................... 17  

Assessing the severity of COPD ................................................................................................ 17  
Assessing acute response to bronchodilators .......................................................................... 18  
Box 7: Assessment of acute response to inhaled beta-agonist at diagnosis ............................... 18  
Confirm or exclude asthma ........................................................................................................ 18  

Specialist referral ....................................................................................................................... 19  
Box 8: Referral to respiratory medicine specialist ........................................................................ 19  
Complex lung function tests ..................................................................................................... 19  
Exercise testing ........................................................................................................................... 19  
Sleep studies ............................................................................................................................... 19
The COPD-X Plan: Australian and New Zealand Guidelines for the management of Chronic Obstructive Pulmonary Disease

Chest x-rays ................................................................................................................................. 20
High resolution computed tomography ...................................................................................... 20
Ventilation and perfusion scans .................................................................................................... 20
Transcutaneous oxygen saturation .................................................................................................. 20
Arterial blood gas measurement .................................................................................................... 20
Sputum examination ........................................................................................................................ 20
Haematology and biochemistry ...................................................................................................... 20
Electrocardiography and echocardiography .................................................................................. 20
O: Optimise function ..................................................................................................................... 21
Summary ....................................................................................................................................... 21
Symptom relief ............................................................................................................................... 21
Inhaled bronchodilators .................................................................................................................... 21
   Box 9: Initial treatment with short-acting bronchodilators* ....................................................... 22
Long-acting bronchodilators ........................................................................................................... 22
Theophyllines ................................................................................................................................. 22
Assessment of response and continuation of bronchodilator therapy ............................................. 23
   Box 10: Assessing long term medication response .................................................................. 23
Short-course oral glucocorticoids ................................................................................................. 23
Combination inhaled glucocorticoid/long-acting bronchodilator therapy ................................... 24
Optimise inhaler technique ............................................................................................................ 24
Surgery .......................................................................................................................................... 24
   Bullectomy ................................................................................................................................. 24
   Lung volume reduction surgery .............................................................................................. 24
   Lung transplantation ............................................................................................................... 24
Identify and treat aggravating factors ............................................................................................ 25
   Sleep apnoea, hypoventilation and hypoxaemia .................................................................... 25
   Gastro-oesophageal reflux ...................................................................................................... 25
   Aspiration ................................................................................................................................. 25
   Alcohol and sedatives ............................................................................................................. 26
Hypoxaemia and pulmonary hypertension .................................................................................... 26
   Treatment ............................................................................................................................... 26
Osteoporosis ................................................................................................................................. 27
Improve function ............................................................................................................................ 28
   Pulmonary rehabilitation ......................................................................................................... 28
   Exercise training ..................................................................................................................... 28
   Patient education ................................................................................................................... 28
   Psychosocial support ............................................................................................................. 28
   Comprehensive integrated rehabilitation .............................................................................. 29
   Chest physiotherapy ............................................................................................................. 29
   Weight management and nutrition ........................................................................................ 29
   Opioids .................................................................................................................................. 29
The COPD-X Plan: Australian and New Zealand Guidelines for the management of Chronic Obstructive Pulmonary Disease

P: Prevent deterioration

Summary............................................................................................................................................. 30
Evidence level................................................................................................................................... 30
Risk factor reduction............................................................................................................................. 30
Smoking cessation.................................................................................................................................. 30
Nicotine replacement therapy .............................................................................................................. 31
Bupropion ............................................................................................................................................. 32
Box 11. Advantages and disadvantages of pharmacological treatments for smoking cessation6,121-132
Prevent smoking relapse ..................................................................................................................... 32
Quit Line.............................................................................................................................................. 33
Prevent infection and exacerbation ...................................................................................................... 33
Influenza vaccination ............................................................................................................................. 33
Pneumococcal vaccination .................................................................................................................... 33
Haemophilus influenzae vaccination ...................................................................................................... 33
Antibiotics ............................................................................................................................................. 33
Glucocorticoids ..................................................................................................................................... 34
Mucolytic agents .................................................................................................................................... 34
Regular review ...................................................................................................................................... 34
Oxygen therapy ...................................................................................................................................... 34
Fitness to fly.......................................................................................................................................... 35
D: Develop support network and self-management plan ...................................................................... 35
Pulmonary rehabilitation ....................................................................................................................... 36
Support team ...................................................................................................................................... 36
General practitioner ............................................................................................................................... 36
Nurse/respiratory educator .................................................................................................................... 37
Physiotherapist .................................................................................................................................... 37
Occupational therapist .......................................................................................................................... 37
Social worker ........................................................................................................................................ 37
Clinical psychologist ............................................................................................................................. 37
Speech pathologist/therapist ................................................................................................................. 37
Pharmacist .......................................................................................................................................... 37
Dietitian ................................................................................................................................................ 38
Non-medical care agencies .................................................................................................................. 38
Multidisciplinary care plans .................................................................................................................. 39
Self-management plans ....................................................................................................................... 39
Maintenance therapy ........................................................................................................................... 39
Exacerbations and crises ...................................................................................................................... 40
Treat anxiety and depression ................................................................................................................ 40
Referral to a support group .................................................................................................................. 40
Box 12: Patient support groups ......................................................................................................... 41
End-of-life issues ................................................................................................................................. 41
X: Manage eXacerbations ............................................................................................................................... 42
  Summary.......................................................................................................................................................... 42
  Evidence level............................................................................................................................................... 42
Home management ........................................................................................................................................ 42
COPD acute exacerbation plan ....................................................................................................................... 43
  Initial assessment of severity.......................................................................................................................... 43
  Optimise treatment ....................................................................................................................................... 43
Refer appropriately .......................................................................................................................................... 45
  Box 13 Indications for hospitalisation of patients with chronic obstructive pulmonary disease .......... 45
  Box 14: Indications for increased respiratory support or intensive care unit admission ..................... 45
Controlled oxygen delivery .......................................................................................................................... 45
Non-invasive positive pressure ventilation .................................................................................................. 46
Invasive ventilation (intubation) .................................................................................................................... 46
Clearance of secretions..................................................................................................................................... 46
Monitor and review ......................................................................................................................................... 46
Discharge planning ......................................................................................................................................... 47
  Box 15: Criteria for discharge .................................................................................................................... 47
Support after discharge .................................................................................................................................. 47
Clinical review and follow-up ........................................................................................................................ 47
  Box 16: Follow-up – initial and subsequent .............................................................................................. 48
Appendix 1....................................................................................................................................................... 49
  Box 17: Use and doses of long-term inhaled bronchodilator and glucocorticoids determined in response trials .................................................................................................................................. 49
Appendix 2....................................................................................................................................................... 50
  Box 18: Explanation of inhaler devices* ................................................................................................. 50
Appendix 3....................................................................................................................................................... 53
Initiating oxygen therapy............................................................................................................................... 53
  What the patient needs to know .................................................................................................................. 53
Review ............................................................................................................................................................ 53
Dangers ........................................................................................................................................................... 53
Choosing the right method ............................................................................................................................ 53
Appendix 4....................................................................................................................................................... 54
Vaccination ...................................................................................................................................................... 54
References ....................................................................................................................................................... 55
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Foreword

Chronic obstructive pulmonary disease (COPD) is a major cause of disability, hospital admission and premature death. More than half a million Australians are estimated to have moderate to severe disease, and, as the population ages, the burden of COPD is likely to increase. In Australia, only heart disease and stroke contribute more to the overall burden of disease, while, in New Zealand, COPD is second only to stroke. COPD ranks fourth among the common causes of death in Australian men and sixth in women. In New Zealand, it ranks third in men and fourth in women.

Smoking is the most important risk factor for COPD. Further, smoking-related diseases are increasing substantially in women, and death rates from COPD in women are expected to overtake those in men. The death rate from COPD among Indigenous Australians is five times that for non-Indigenous Australians, and smoking is a leading cause of healthy years lost by indigenous people both in Australia and New Zealand.

COPD costs the Australian community an estimated $818–$898 million annually. This is a conservative estimate, based on 1993–1994 figures extrapolated to the year 2001. The addition of hidden costs, such as those related to carer burden, loss of productivity from absenteeism and early retirement, could increase the estimate to more than $1 billion per annum.

Because it is considered incurable, self-inflicted and relatively resistant to treatment, a sense of nihilism about COPD prevails. However, much can be done to improve quality of life, increase exercise capacity, and reduce morbidity and mortality in affected individuals. This guideline was developed according to the principles of the National Health and Medical Research Council, but differs from previous guidelines on COPD in that it draws from the recently published international Guideline for the Management of Obstructive Lung Disease as the primary evidence base. These Australian and New Zealand guidelines have a strong emphasis on the use of objective measures of function, the role of non-pharmacological interventions and promotion of self-management.

The key recommendations are summarised in the "COPDX Plan":

- Confirm diagnosis,
- Optimise function,
- Prevent deterioration,
- Develop a self-management plan and manage exacerbations.

Dr Robert L Edwards
National Chairman, Australian Lung Foundation
March 2003
The COPD-X guidelines

These guidelines are the outcome of a joint project of the Thoracic Society of Australia and New Zealand and the Australian Lung Foundation. The guidelines aim to:

- effect changes in clinical practice based on sound evidence; and
- shift the emphasis from a predominant reliance on pharmacological treatment of COPD to a range of interventions which include patient education, self-management of exacerbations and pulmonary rehabilitation.

These guidelines deal mainly with the management of established disease and exacerbations. However, this is only one element of the COPD Strategy of the Australian Lung Foundation, which has the long-term goals of:

- primary prevention of smoking;
- improving rates of smoking cessation;
- early detection of airflow limitation in smokers before disablement; and
- improved management of stable disease and prevention of exacerbations.

In May 2001 a multidisciplinary steering committee was convened by the Thoracic Society of Australia and New Zealand (TSANZ) and the Australian Lung Foundation in accordance with the National Health and Medical Research Council recommendations for guideline development. The Committee agreed to use the Global Initiative for Chronic Obstructive Lung Disease (GOLD) Workshop Report as the prime evidence base, together with systematic reviews and meta-analyses from the Cochrane Database. The GOLD Report, released in April 2001, was produced by an international panel of experts in collaboration with the United States National Heart, Lung, and Blood Institute (NHLBI) and the World Health Organization (WHO). The levels of evidence in the current guidelines were assigned according to the system developed by the NHLBI (Box 1). Any changes to the guidelines have been based on subsequent versions of the GOLD report and on the results of systematic reviews or consistent evidence from well conducted randomised controlled trials.

The Guidelines Steering Committee supervised the development of specific items such as the COPDX Plan and a management handbook for primary care clinicians. Drafts of these documents were widely circulated to key stakeholder groups and professional organisations. In addition, the draft guidelines were published on the Internet (http://www.lungnet.com.au/copd.html), and access to them was advertised in a national newspaper. The draft guidelines were circulated to all members of the TSANZ and Australian Divisions of General Practice. All comments received were reviewed by the Steering Committee. The Guidelines were then published as a supplement to The Medical Journal of Australia in March 2003.

The Steering Committee then resolved to establish a COPD Guidelines Implementation Committee and a Guidelines Evaluation Committee. The terms of reference of the Evaluation Committee included scientific assessment of the impact of the guidelines on clinical practice and rigorous examination of the relevant medical literature to ensure the guidelines remain up to date. Any suggested modifications have been circulated to members of the COPD Coordinating Committee and other key stakeholders prior to ratification. This version of the guidelines has been submitted to the COPD Special Interest Group of the Thoracic Society of Australia and New Zealand for endorsement.

**Associate Professor David K McKenzie** and **Professor Peter Frith**
Principal authors and members of the COPD Implementation Committee.
July 2005

Logistical and financial support for the development of these guidelines was provided by the Australian Lung Foundation as part of its COPD program. This program is funded by grants from Boehringer Ingelheim Pty Ltd (North Ryde, NSW), GlaxoSmithKline Australia Pty Ltd (Boronia, VIC), Pfizer Australia (West Ryde, NSW), and Air Liquide Healthcare Pty Ltd (Alexandria, NSW).

**Associate Professor David K McKenzie**
Chair, COPD Guidelines Steering Committee
Levels of evidence
The key recommendations and levels of evidence incorporated in the COPDX guidelines are based largely on the Global Initiative for Chronic Obstructive Lung Disease (GOLD), which used the evidence ranking system of the US National Heart, Lung and Blood Institute (NHLBI). The NHLBI scheme is shown in Box 1. For comparison, the National Health and Medical Research Council (NHMRC) levels of evidence are also shown, along with the equivalent NHLBI categories.

Box 1: Levels of evidence  
A) National Heart, Lung, and Blood Institute (NHLBI) categories

<table>
<thead>
<tr>
<th>NHLBI category</th>
<th>Sources of evidence</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Randomised controlled trials (RCTs). Rich body of data.</td>
<td>Evidence is from endpoints of well-designed RCTs that provide a consistent pattern of findings in the population for which the recommendation is made. Category A requires substantial numbers of studies involving substantial numbers of participants.</td>
</tr>
<tr>
<td>B</td>
<td>Randomised controlled trials (RCTs). Limited body of data.</td>
<td>Evidence is from endpoints of intervention studies that include only a limited number of patients, postop or sub-group analysis of RCTs, or meta-analysis of RCTs. In general, Category B pertains when few randomised trials exist, they are small in size, they were undertaken in a population that differs from the target population of the recommendation, or the results are somewhat inconsistent.</td>
</tr>
<tr>
<td>C</td>
<td>Non randomised trials. Observational studies.</td>
<td>Evidence is from outcomes of uncontrolled or non randomised trials or from observational studies.</td>
</tr>
<tr>
<td>D</td>
<td>Panel consensus Judgment.</td>
<td>This category is used only in cases where the provision of some guidance was deemed valuable but the clinical literature addressing the subject was deemed insufficient to justify placement in one of the other categories. The Panel Consensus is based on clinical experience or knowledge that does not meet the above-listed criteria.</td>
</tr>
</tbody>
</table>

B) National Health and Medical Research Council (NHMRC) levels of evidence and corresponding National Heart, Lung, and Blood Institute categories

<table>
<thead>
<tr>
<th>NHLBI category</th>
<th>NHMRC level</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>I</td>
<td>Evidence obtained from a systematic review of all relevant randomised controlled trials</td>
</tr>
<tr>
<td>B</td>
<td>II</td>
<td>Evidence obtained from at least one properly designed randomised controlled trial</td>
</tr>
<tr>
<td>C</td>
<td>III - 1</td>
<td>Evidence obtained from well-designed pseudorandomised controlled trials (alternate allocation or some other method)</td>
</tr>
<tr>
<td>C</td>
<td>III - 2</td>
<td>Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case-control studies, or interrupted time series with a control group</td>
</tr>
<tr>
<td>C</td>
<td>III - 3</td>
<td>Evidence obtained from comparative studies with historical control, two or more single arm studies, or interrupted time series without a parallel group</td>
</tr>
<tr>
<td>C</td>
<td>IV</td>
<td>Evidence obtained from case series, either post-test or pretest/post-test</td>
</tr>
<tr>
<td>A</td>
<td>I</td>
<td>Evidence obtained from a systematic review of all relevant randomised controlled trials</td>
</tr>
</tbody>
</table>
### Summary of the COPD-X guidelines

**C: Confirm diagnosis and assess severity**

<table>
<thead>
<tr>
<th>Evidence level</th>
<th>Item</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>- Smoking is the most important risk factor for COPD</td>
</tr>
<tr>
<td>A</td>
<td>- Consider COPD in patients with other smoking-related diseases</td>
</tr>
<tr>
<td>B</td>
<td>- Consider COPD in all smokers and ex-smokers older than 35 years</td>
</tr>
<tr>
<td>B</td>
<td>- The diagnosis of COPD rests on the demonstration of airflow limitation which is not fully reversible</td>
</tr>
<tr>
<td>D</td>
<td>- If airflow limitation is fully or substantially reversible, the patient should be treated as for asthma</td>
</tr>
</tbody>
</table>

**O: Optimise function**

<table>
<thead>
<tr>
<th>Evidence level</th>
<th>Item</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>- Inhaled bronchodilators provide symptom relief in patients with COPD and may increase exercise capacity</td>
</tr>
<tr>
<td>A</td>
<td>- Long-acting bronchodilators provide sustained relief of symptoms in moderate to severe COPD</td>
</tr>
<tr>
<td>A</td>
<td>- Long term use of systemic glucocorticoids is not recommended</td>
</tr>
<tr>
<td>B</td>
<td>- Inhaled glucocorticoids should be considered in patients with a documented response or those who have severe COPD with frequent exacerbations</td>
</tr>
<tr>
<td>A</td>
<td>- Identify and treat hypoxaemia and pulmonary hypertension</td>
</tr>
<tr>
<td>A</td>
<td>- Prevent or treat osteoporosis</td>
</tr>
<tr>
<td>A</td>
<td>- Pulmonary rehabilitation reduces dyspnoea, anxiety and depression, improves exercise capacity and quality of life and may reduce hospitalisation</td>
</tr>
<tr>
<td>C</td>
<td>- In selected patients, a surgical approach may be considered for symptom relief.</td>
</tr>
</tbody>
</table>

**P: Prevent deterioration**

<table>
<thead>
<tr>
<th>Evidence level</th>
<th>Item</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>- Smoking cessation reduces the rate of decline of lung function</td>
</tr>
<tr>
<td>A</td>
<td>- General practitioners and pharmacists can help smokers quit</td>
</tr>
<tr>
<td>A</td>
<td>- Treatment of nicotine dependence is effective and should be offered to smokers</td>
</tr>
<tr>
<td>A</td>
<td>- Pharmacotherapies double the success of quit attempts; behavioural techniques further increase the quit rate by up to 50%</td>
</tr>
<tr>
<td>A</td>
<td>- Influenza vaccination reduces the risk of exacerbations, hospitalisation and death</td>
</tr>
<tr>
<td>A</td>
<td>- Long-term oxygen therapy (&gt; 15 h/day) prolongs life in hypoxaemic patients (PaO₂ &lt; 55 mmHg, or 7.3 kPa)</td>
</tr>
<tr>
<td>B</td>
<td>- Inhaled glucocorticoids are indicated for patients with a documented response or who have severe COPD with frequent exacerbations</td>
</tr>
<tr>
<td>A</td>
<td>- Mucolytics may reduce the frequency and duration of exacerbations</td>
</tr>
</tbody>
</table>
D: Develop support network and self-management plan

- Pulmonary rehabilitation increases patient/carer knowledge base, reduces carer strain and develops positive attitudes towards self-management and exercise  
  Evidence level A

- COPD imposes handicaps which affect both patients and carers  
  Evidence level B

- Multidisciplinary care plans and individual self-management plans may help to prevent or manage crises  
  Evidence level B

- Enhancing quality of life and reducing handicap requires a support team  
  Evidence level C

- Patients and their family/friends should be actively involved in a therapeutic partnership with a range of professional disciplines  
  Evidence level C

- Patients should be encouraged to take appropriate responsibility for their own management  
  Evidence level C

X: Manage eXacerbations

- Inhaled bronchodilators are effective treatments for acute exacerbations  
  Evidence level A

- Systemic glucocorticoids reduce the severity of and shorten recovery from acute exacerbations  
  Evidence level A

- Non-invasive positive pressure ventilation is effective for acute hypercapnic ventilatory failure  
  Evidence level A

- Exacerbations with clinical signs of infection (increased volume and change in colour of sputum and/or fever, leukocytosis) benefit from antibiotic therapy  
  Evidence level B

- Multidisciplinary care may assist home management  
  Evidence level B

- Early diagnosis and treatment may prevent admission  
  Evidence level C

- Controlled oxygen delivery (28% or 0.5–2 L/min) is indicated for hypoxaemia  
  Evidence level C

- Involving the patient's general practitioner in a case conference and developing a care plan may facilitate early discharge  
  Evidence level C

Chronic obstructive pulmonary disease (COPD) is characterised by airway inflammation and airflow limitation that is not fully reversible. It is a progressive, disabling disease with serious complications and exacerbations that are major burdens for healthcare systems.

Small-airway narrowing (with or without chronic bronchitis) and emphysema caused by smoking are the common conditions resulting in COPD. Chronic bronchitis is daily sputum production for at least three months of two or more consecutive years. Emphysema is a pathological diagnosis, and consists of alveolar dilatation and destruction. Breathlessness with exertion, chest tightness and wheeze are the results of airway wall collapse during expiration, leading to dynamic hyperinflation and consequent increased work of breathing.

The irreversible component of airflow limitation is the end result of inflammation, fibrosis and remodelling of peripheral airways. Airflow limitation leads to non-homogeneous ventilation, while alveolar wall destruction and changes in pulmonary vessels reduce the surface area available for gas exchange. In advanced COPD there is a severe mismatching of ventilation and perfusion leading to hypoxaemia. Hypercapnia is a late manifestation and is caused by a reduction in ventilatory drive. Pulmonary hypertension and cor pulmonale are also late manifestations, and reflect pulmonary vasoconstriction due to hypoxia in poorly ventilated lung, vasoconstrictor peptides produced by inflammatory cells and vascular remodelling. The clinical features and pathophysiology of COPD can overlap with asthma, as most COPD patients have some reversibility of airflow limitation with bronchodilators. By contrast, some non-smokers with chronic asthma develop irreversible airway narrowing. The overlap between chronic bronchitis, emphysema and asthma and their relationship to airflow obstruction and COPD are illustrated in Box 2. Patients with chronic bronchiolitis,
bronchiectasis and cystic fibrosis may also present with similar symptoms and partially reversible airflow limitation.

**Box 2: Overlap of bronchitis, emphysema and asthma within chronic obstructive pulmonary disease (COPD)**

This non-proportional Venn diagram shows the overlap of chronic bronchitis, emphysema and asthma within COPD. Chronic bronchitis, airway narrowing and emphysema are independent effects of cigarette smoking, and may occur in various combinations. Asthma is, by definition, associated with reversible airflow obstruction. Patients with asthma whose airflow obstruction is completely reversible do not have COPD. In many cases it is impossible to differentiate patients with asthma whose airflow obstruction does not remit completely from persons with chronic bronchitis and emphysema who have partially reversible airflow obstruction with airway hyperreactivity.

**Aetiology and natural history**

Smoking is the most important risk factor in the development of COPD. There is a close relationship between the amount of tobacco smoked and the rate of decline in forced expiratory flow in one second (FEV₁), although individuals vary greatly in susceptibility. Around half of all smokers develop some airflow limitation, and 15%–20% will develop clinically significant disability. Smokers are also at risk of developing lung cancer, and cardiovascular disease such as ischaemic heart disease and peripheral vascular disease.

In susceptible smokers cigarette smoking results in a steady decline in lung function, with a decrease in FEV₁ of 25–100 mL/year. While smoking cessation may lead to minimal improvements in lung function, more importantly it will slow the rate of decline in lung function and delay the onset of disablement. At all times smoking cessation is important to preserve remaining lung function.

Impairment increases as the disease progresses, but may not be recognised because of the slow pace of the disease. The time course of development of COPD and disability and the influence of smoking cessation are illustrated in Box 3.
Box 3: Time-course of chronic obstructive pulmonary disease (COPD)7

The figure (adapted from Fletcher and Peto7) shows the rate of loss of forced expiratory flow in one second (FEV1) for a hypothetical, susceptible smoker, and the potential effect of stopping smoking early or late in the course of COPD. Other susceptible smokers will have different rates of loss, thus reaching “disability” at different ages. The normal FEV1 ranges from below 80% to above 120%, so this will affect the starting point for the individual’s data (not shown).

Other factors that can contribute to the development of COPD9 include:
- occupational dust and fume exposure;
- outdoor and indoor air pollution (including environmental tobacco smoke);
- alpha-1-antitrypsin deficiency;
- genetic predisposition;
- recurrent respiratory infections in childhood; and
- bronchial hyperresponsiveness.

The single best predictor of mortality in COPD is FEV1.7,10 In one study the five-year survival rate was only about 10% for those with an FEV1 < 20% predicted, 30% for those with FEV1 of 20%–29% predicted and about 50% for those with an FEV1 of 30%–39% predicted.10 Continued smoking and airway hyperresponsiveness are associated with accelerated loss of lung function.11 However, even if substantial airflow limitation is present, cessation of smoking may result in some improvement in lung function and will slow progression of disease.

The development of hypoxaemic respiratory failure is an independent predictor of mortality, with a three-year survival of about 40%.12 Long term administration of oxygen increases survival to about 50% with nocturnal oxygen12 and to about 60% with oxygen administration for more than 15 hours a day13 (see also section P). Admission to hospital with an infective exacerbation of COPD complicated by hypercapnic respiratory failure is associated with a poor prognosis. A mortality of 11% during admission and 49% at two years has been reported in patients with a partial pressure of carbon dioxide (PCO2) > 50 mmHg.14 For those with chronic carbon dioxide retention (about 25% of those admitted with hypercapnic exacerbations), the five-year survival was only 11%.14

Patients with an FEV1 <20% predicted and either homogeneous emphysema on HRCT or a DLCO <20% predicted are at high risk for death after LVRS and unlikely to benefit from the intervention.212
Diagnosis

**History**

Consider COPD in all smokers and ex-smokers over the age of 35 years\(^7\) [evidence level B]

The main symptoms of COPD are breathlessness, cough and sputum production.\(^{15}\) Patients often attribute breathlessness to ageing or lack of fitness. A persistent cough, typically worse in the mornings with mucoid sputum, is common in smokers. Other symptoms such as chest tightness, wheezing and airway irritability are common.\(^{16}\) Acute exacerbations, usually infective, occur from time to time and may lead to a sharp deterioration in coping ability. Fatigue, poor appetite and weight loss are more common in advanced disease.

The functional limitation from breathlessness due to COPD can be quantified easily in clinical practice\(^{17}\) (see Box 4).

<table>
<thead>
<tr>
<th>Grade</th>
<th>Symptom complex</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&quot;I only get breathless with strenuous exercise&quot;.</td>
</tr>
<tr>
<td>2</td>
<td>&quot;I get short of breath when hurrying on the level or walking up a slight hill&quot;.</td>
</tr>
<tr>
<td>3</td>
<td>&quot;I walk slower than most people of the same age on the level because of breathlessness or have to stop for breath when walking at my own pace on the level&quot;.</td>
</tr>
<tr>
<td>4</td>
<td>&quot;I stop for breath after walking about 100 yards or after a few minutes on the level&quot;.</td>
</tr>
<tr>
<td>5</td>
<td>&quot;I am too breathless to leave the house&quot; or &quot;I am breathless when dressing&quot;.</td>
</tr>
</tbody>
</table>

**Physical examination**

The sensitivity of physical examination for detecting mild to moderate COPD is poor.\(^{16}\) Wheezing is not an indicator of severity of disease and is often absent in stable, severe COPD. In more advanced disease, physical features commonly found are hyperinflation of the chest, reduced chest expansion, hyperresonance to percussion, soft breath sounds and a prolonged expiratory phase. Right heart failure may complicate severe disease. During an acute exacerbation, tachypnoea, tachycardia, use of accessory muscles, tracheal tug and cyanosis are common. The presence and severity of airflow limitation are impossible to determine by clinical signs.\(^{18}\) Objective measurements such as spirometry are strongly recommended. Peak expiratory flow (PEF) is not a sensitive measure of airway function in COPD patients, as it is effort dependent and has a wide range of normal values.\(^{19}\)
 Spirometry

The diagnosis of COPD rests on the demonstration of airflow limitation which is not fully reversible [evidence level B]

Spirometry is the gold standard for diagnosing, assessing and monitoring COPD (see Box 5). Most spirometers provide predicted ("normal") values obtained from healthy population studies, and derived from formulas based on height, age, sex and ethnicity.

Airflow limitation is non-reversible when, after administration of bronchodilator medication, the ratio of FEV$_1$ to forced vital capacity (FVC) is $< 70\%$ and the FEV$_1$ is $< 80\%$ of the predicted value. The ratio of FEV$_1$ to vital capacity (VC) is a sensitive indicator for mild COPD.

---

Box 5: Maximal expiratory flow-volume curves in severe chronic obstructive pulmonary disease (COPD) and chronic asthma

The patient with COPD has reduced peak expiratory flow, and severely decreased flows at 25%, 50% and 75% of vital capacity compared with the normal range (vertical bars), and shows minimal response to bronchodilator (BD). By comparison, the patient with chronic asthma shows incomplete, but substantial, reversibility of expiratory flow limitation across the range of vital capacity. After BD the forced expiratory volume in one second (FEV$_1$) was within the normal range (82% predicted). Absolute and per cent predicted values for FEV$_1$ and forced vital capacity (FVC) before and after BD are shown for each patient.
Indications for spirometry include:

- breathlessness that seems inappropriate;
- chronic (daily for two months) or intermittent, unusual cough;
- frequent or unusual sputum production;
- relapsing acute infective bronchitis; and
- risk factors such as exposure to tobacco smoke, occupational dusts and chemicals, and a strong family history of COPD.

**Flow volume tests**

Electronic spirometers allow for the simultaneous measurement of flow and volume during maximal expiration. Reduced expiratory flows at mid and low lung volumes are the earliest indicators of airflow limitation in COPD and may be abnormal even when FEV\(_1\) is within the normal range (> 80%).

**Assessing the severity of COPD**

Spirometry is the most reproducible, standardised and objective way of measuring airflow limitation, and FEV\(_1\) is the variable most closely associated with prognosis. The grades of severity according to FEV\(_1\) and the likely symptoms and complications are shown in Box 6. However, it should be noted that patients with an FEV\(_1\) > 80% predicted, although within the normal range, may have airflow limitation (FEV\(_1\)/FVC ratio < 70%).

**Box 6. Classification of severity (Airflow limitation is indicated by FEV\(_1\)/FVC <0.7)**

<table>
<thead>
<tr>
<th>Factor</th>
<th>COPD Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spirometry findings -</td>
<td></td>
</tr>
<tr>
<td>postbronchodilator FEV(_1)%</td>
<td>Mild</td>
</tr>
<tr>
<td></td>
<td>60-80% predicted</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td>40-59% predicted</td>
</tr>
<tr>
<td></td>
<td>Severe</td>
</tr>
<tr>
<td></td>
<td>&lt;40% predicted</td>
</tr>
<tr>
<td>Functional assessment</td>
<td></td>
</tr>
<tr>
<td>(Activities of daily living)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Few symptoms</td>
</tr>
<tr>
<td></td>
<td>No effect on daily activities</td>
</tr>
<tr>
<td></td>
<td>Breathless on moderate exertion</td>
</tr>
<tr>
<td></td>
<td>Increasing dyspnoea</td>
</tr>
<tr>
<td></td>
<td>Breathless on the flat</td>
</tr>
<tr>
<td></td>
<td>Increasing limitation of daily activities</td>
</tr>
<tr>
<td></td>
<td>Dyspnoea on minimal exertion</td>
</tr>
<tr>
<td></td>
<td>Daily activities severely curtailed</td>
</tr>
<tr>
<td>Complications</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Exclude complications; consider</td>
</tr>
<tr>
<td></td>
<td>sleep apnoea if there is pulmonary</td>
</tr>
<tr>
<td></td>
<td>hypertension</td>
</tr>
<tr>
<td></td>
<td>Severe hypoxaemia (PaO(_2) &lt;60mm Hg or 8kPa)</td>
</tr>
<tr>
<td></td>
<td>Hypercapnia (PaCO(_2) &gt;45mm Hg or 6kPa)</td>
</tr>
<tr>
<td></td>
<td>Pulmonary hypertension</td>
</tr>
<tr>
<td></td>
<td>Heart Failure</td>
</tr>
<tr>
<td></td>
<td>Polycythaemia</td>
</tr>
</tbody>
</table>

FEV\(_1\) = forced expiratory volume in one second. PaO\(_2\) = partial pressure of oxygen, arterial. PaCO\(_2\) = partial pressure of carbon dioxide, arterial.
Assessing acute response to bronchodilators
The response to bronchodilators is determined to:

- assign a level of severity of airflow obstruction (post-bronchodilator); and
- help confirm or exclude asthma.

The details for this assessment are outlined in Box 7.

The change in FEV₁ after an acute bronchodilator reversibility test indicates the degree of reversibility of airflow limitation. This is often expressed as a percentage of the baseline measurement (eg, 12% increase). An increase in FEV₁ of more than 12% and 200 mL is greater than average day-to-day variability and is unlikely to occur by chance. However, this degree of reversibility is not diagnostic of asthma and is frequently seen in patients with COPD (eg, the FEV₁ increases from 0.8 L to 1.0 L when the predicted value is, say, 3.5 L). The diagnosis of asthma relies on an appropriate history and complete, or at least substantial, reversibility of airflow limitation (see also below).

**Box 7: Assessment of acute response to inhaled beta-agonist at diagnosis**

**Preparation**

- Patients should be clinically stable and free of respiratory infection.
- Withhold inhaled short-acting bronchodilators in the previous six hours, long-acting beta-agonists in the previous 12 hours, or sustained-release theophyllines in the previous 24 hours.

**Spirometry**

- Measure baseline spirometry (pre-bronchodilator). An FEV₁ < 80% predicted and FEV₁/FVC ratio < 0.70 shows airflow limitation.
- Give the bronchodilator by metered dose inhaler (MDI) through a spacer device or by nebuliser.
- Give short-acting beta-agonist, at a dose selected to be high on the dose–response curve (eg, 200–400 mcg salbutamol from MDI and spacer).

Repeat spirometry 15–30 minutes after bronchodilator is given and measure degree of reversibility.

FEV₁ = forced expiratory flow in one second.
FVC = forced vital capacity.

**Confirm or exclude asthma**

If airflow limitation is fully or substantially reversible, the patient should be treated as for asthma [evidence level D]

Asthma and COPD are usually easy to differentiate. Asthma usually runs a more variable course and dates back to a younger age. Atopy is more common and the smoking history is often relatively light (eg, less than 15 pack-years). Airflow limitation in asthma is substantially, if not completely, reversible, either spontaneously or in response to treatment. By contrast, COPD tends to be progressive, with a late onset of symptoms and a moderately heavy smoking history (usually > 15 pack-years) and the airflow obstruction is not completely reversible.

However, there are some patients in whom it is difficult to distinguish between asthma and COPD as the primary cause of their chronic airflow limitation. Long-standing or poorly controlled asthma can lead to chronic, irreversible airway narrowing even in non-smokers.
### Specialist referral

Confirmation of the diagnosis of COPD and differentiation from chronic asthma, other airway diseases or occupational exposures that may cause airway narrowing or hyper-responsiveness, or both, often requires specialised knowledge and investigations. Indications for which consultation with a respiratory medicine specialist is recommended are shown in Box 8.

#### Box 8: Referral to respiratory medicine specialist

<table>
<thead>
<tr>
<th>Circumstances possibly requiring specialist review</th>
<th>Role of respiratory specialist</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Moderate or severe chronic obstructive pulmonary disease (COPD)</td>
<td>Confirm diagnosis and optimise therapy. Cease inappropriate or ineffective therapies. Assess side effects. Determine need for nebulised therapy. Assess complications.</td>
</tr>
<tr>
<td>2. Uncertain diagnosis (&lt; 10 pack-year smoking history or &lt; 40 years of age or rapid decline in FEV1)</td>
<td>Confirm diagnosis and exclude other diagnoses (eg, asthma, bronchiolitis obliterans, pulmonary embolism, cancer, heart failure, pneumothorax, anaemia). Determine other aetiological factors. Determine if the patient is predisposed (eg, alpha-1-antitrypsin deficiency).</td>
</tr>
<tr>
<td>3. Recurrent infections, exacerbations</td>
<td>Exclude other conditions (eg, bronchiectasis, cystic fibrosis, immunological abnormality, aspiration).</td>
</tr>
<tr>
<td>4. Symptoms out of proportion to lung function impairment</td>
<td>Exclude complications of COPD or comorbidities (eg, pulmonary hypertension, cardiac disease). Consider sleep study.</td>
</tr>
<tr>
<td>5. Cor pulmonale</td>
<td>Confirm diagnosis and optimise treatment, including assessment for oxygen or other ventilatory support.</td>
</tr>
<tr>
<td>7. Bullous lung disease or severe emphysema</td>
<td>Determine suitability for bullectomy or lung volume reduction surgery.</td>
</tr>
<tr>
<td>8. Severe disability or respiratory failure</td>
<td>Determine suitability for lung volume reduction surgery or lung transplantation or home ventilation.</td>
</tr>
</tbody>
</table>

COPD = chronic obstructive pulmonary disease. FEV$_1$ = forced expiratory volume in one second.

### Complex lung function tests

Measurement of airways resistance, static lung volumes and diffusing capacity of lungs for carbon monoxide assists in the assessment of patients with more complex respiratory disorders.

### Exercise testing

Cardiopulmonary exercise tests may be useful to differentiate between breathlessness resulting from cardiac or respiratory disease, and may help to identify other causes of exercise limitation (eg, hyperventilation, musculoskeletal disorder).

### Sleep studies

Specialist referral is recommended for COPD patients suspected of having a coexistent sleep disorder or with hypercapnia or pulmonary hypertension in the absence of daytime hypoxaemia, right heart failure or polycythaemia. Overnight pulse oximetry may be indicated in patients receiving long-term domiciliary oxygen therapy to assess its efficacy.
Chest x-rays
A plain posteroanterior and lateral chest x-ray helps to exclude other conditions such as lung cancer. The chest x-ray is not sensitive in the diagnosis of COPD, and will not exclude a small carcinoma (≤ 1cm).

High resolution computed tomography
High resolution computed tomography (HRCT) scanning gives precise images of the lung parenchyma and mediastinal structures. The presence of emphysema and the size and number of bullae can be determined. This is necessary if bullectomy or lung reduction surgery is being contemplated. HRCT is also appropriate for detecting bronchiectasis. Vertical reconstructions can provide a virtual bronchogram. Spiral computed tomography (CT) scans with intravenous contrast should be used in other circumstances, such as for investigating and staging lung cancer. CT pulmonary angiograms are useful for investigating possible pulmonary embolism, especially when the chest x-ray is abnormal.

Ventilation and perfusion scans
The ventilation and perfusion (V/Q) scan may be difficult to interpret in COPD patients, because regional lung ventilation may be compromised leading to matched defects. If pulmonary emboli are suspected, a CT pulmonary angiogram may be more useful. Quantitative regional V/Q scans are helpful in assessing whether patients are suitable for lung resection and lung volume reduction surgery.

Transcutaneous oxygen saturation
Oximeters have an accuracy of plus or minus 2%, which is satisfactory for routine clinical purposes. Oximetry does not provide any information about carbon dioxide status and is inaccurate in the presence of poor peripheral circulation (eg, cold extremities, cardiac failure).

Arterial blood gas measurement
Arterial blood gas analysis should be considered in all patients with severe disease, those being considered for domiciliary oxygen therapy (eg, whose FEV₁ is < 40% predicted or < 1 L, whose oxygen saturation as measured by pulse oximetry [SpO₂] is < 92%), those with pulmonary hypertension, and those with breathlessness out of proportion to their clinical status). Respiratory failure is defined as a PaO₂ < 60 mmHg (8 kPa) or PaCO₂ > 50 mmHg (6.7 kPa).

Sputum examination
Routine sputum culture in clinically stable patients with COPD is unhelpful and unnecessary. Sputum culture is recommended when an infection is not responding to antibiotic therapy or when a resistant organism is suspected.

Haematology and biochemistry
Polycythaemia should be confirmed as being secondary to COPD by blood gas measurement confirming the presence of hypoxaemia. The possibility of sleep apnoea or hypoventilation should be considered if polycythaemia is present, but the oxygen saturation is normal when the patient is awake. Hyperthyroidism and acidosis are associated with breathlessness. Hyperventilation states are associated with respiratory alkalosis. Hypothyroidism aggravates obstructive sleep apnoea.

Electrocardiography and echocardiography
Multifocal atrial tachycardia is a frequent finding. Atrial fibrillation commonly develops when pulmonary artery pressure rises, leading to increased right atrial pressure. Echocardiography is useful if cor pulmonale is suspected, when breathlessness is out of proportion to the degree of respiratory impairment or when ischaemic heart disease, pulmonary embolus and left heart failure are suspected.

Consider COPD in patients with other smoking-related diseases²² [evidence level A]
Patients with COPD are prone to other conditions associated with cigarette smoking, including accelerated cardiovascular, cerebrovascular and peripheral vascular disease, and oropharyngeal, laryngeal and lung carcinoma. Conversely, there is a high prevalence of COPD among patients with ischaemic heart disease, peripheral vascular disease and cerebrovascular disease and smoking-related carcinomas. ²² These patients should be screened for symptoms of COPD, and spirometry should be performed.
**O: Optimise function**

<table>
<thead>
<tr>
<th>Summary</th>
<th>Evidence level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhaled bronchodilators provide symptom relief in patients with COPD and may increase exercise capacity</td>
<td>A</td>
</tr>
<tr>
<td>Long-acting bronchodilators provide sustained relief of symptoms in moderate to severe COPD</td>
<td>A</td>
</tr>
<tr>
<td>Long term use of systemic glucocorticoids is not recommended</td>
<td>A</td>
</tr>
<tr>
<td>Inhaled glucocorticoids should be considered in patients with a documented response or those who have severe COPD with frequent exacerbations</td>
<td>B</td>
</tr>
<tr>
<td>Identify and treat hypoxaemia and pulmonary hypertension</td>
<td>A</td>
</tr>
<tr>
<td>Prevent or treat osteoporosis</td>
<td>A</td>
</tr>
<tr>
<td>Pulmonary rehabilitation reduces dyspnoea, anxiety and depression, improves exercise capacity and quality of life and may reduce hospitalisation</td>
<td>A</td>
</tr>
<tr>
<td>In selected patients, a surgical approach may be considered for symptom relief</td>
<td>C</td>
</tr>
</tbody>
</table>

The principal goals of therapy are to stop smoking, to optimise function through symptom relief with medications and pulmonary rehabilitation, and to prevent or treat aggravating factors and complications.

**Symptom relief**

**Inhaled bronchodilators**

Inhaled bronchodilators provide symptom relief and may increase exercise capacity\(^{23-30}\) [evidence level A]

The two classes of inhaled bronchodilators - selective beta-adrenoceptor agonists and anticholinergic agents - target airway smooth muscle contraction, which is one cause of the physiological and functional deficits in COPD.\(^{23-25}\)

All bronchodilators have been shown to variably improve exercise capacity.\(^{26-29}\) One Randomised Controlled Trial of short-acting beta-2 agonists found a significant improvement in quality of life\(^{227}\) [evidence level B]. However, changes in simple measurements of airway function (FEV\(_1\), FVC) are not closely correlated with symptomatic improvement or changes in measures of quality of life.\(^{30,31}\) The failure to achieve a large therapeutic response should not necessarily trigger the use of higher doses.\(^{23,24}\) Nebulisers are not recommended for routine use in stable disease\(^{32}\) [evidence level C].

The duration of action of short-acting inhaled anticholinergic agents is greater than that of short-acting beta-agonists\(^{32}\) [evidence level A]. The combination of beta-agonists and anticholinergics may be more effective and better tolerated than higher doses of either agent used alone\(^{32-37}\) [evidence level A].

The use of bronchodilators according to the severity of COPD\(^6\) is shown in Box 9. Appendices 1 and 2 list available products, formulations and delivery devices. Patients must be asked to show that they have effective inhaler technique. Efforts to maintain or regain physical fitness may match or exceed the benefits of bronchodilator use (see the discussion of pulmonary rehabilitation on page S19).\(^6\) Use of a short-acting bronchodilator before an exercise session may reduce dynamic hyperinflation and allow better training effects to be achieved.\(^56\) Regular treatment with short-acting bronchodilators should be reserved for those patients who report symptomatic and clinical benefit from their use.\(^228\)
Box 9: Initial treatment with short-acting bronchodilators*

<table>
<thead>
<tr>
<th>Severity</th>
<th>FEV₁</th>
<th>Suggested treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild COPD</td>
<td>60%–80%</td>
<td>Intermittent bronchodilator - salbutamol (200 mcg) or ipratropium bromide (40 mcg) as needed before exercise</td>
</tr>
<tr>
<td>Moderate COPD</td>
<td>40%–59%</td>
<td>Intermittent or regular bronchodilator — salbutamol (200–400 mcg four times daily) or ipratropium bromide (40 mcg four times daily). Combination bronchodilators may be considered</td>
</tr>
<tr>
<td>Severe COPD</td>
<td>&lt; 40%</td>
<td>Regular combination bronchodilator — salbutamol (200–400 mcg four times daily) and ipratropium bromide (40–80 mcg four times daily)</td>
</tr>
</tbody>
</table>

* Modified from GOLD* [evidence level D].

FEV₁ = forced expiratory volume in one second.
COPD = chronic obstructive pulmonary disease.

Long-acting bronchodilators

Long-acting bronchodilators provide sustained relief of symptoms in moderate to severe COPD38-44 [evidence level A]

Long-acting beta-agonists (eg, salmeterol and eformoterol) provide bronchodilation for 12 hours38-41 and are widely used for asthma. They are not currently subsidised under the Pharmaceutical Benefits Scheme for patients with COPD, although they improve exercise endurance, improve health-related quality of life and reduce both the exacerbation rate and number of hospitalisations. Regular treatment with long-acting bronchodilators is more effective and convenient than treatment with short-acting bronchodilators, but more expensive [evidence level A]. Regular use of a long-acting beta-agonist or long-acting anticholinergic improves health status.202,203

Salmeterol (50 mcg twice daily) has a favourable effect on measures of health-related quality of life.41 The dose–response relationship is low, so, compared with the standard dose, the higher dose of 100 mcg twice daily does not further improve quality of life41 [evidence level B].

Eformoterol (12 mcg twice daily) improves lung function and symptoms.40,201

Tiotropium (18 mcg daily), a new inhaled anticholinergic agent, has a duration of effect of over 24 hours and is used once daily.198-200 It is subsidised under the Pharmaceutical Benefits Scheme for use in patients with COPD. Compared with placebo and regular ipratropium, it reduces dyspnoea and exacerbation rate and improves health status.42-44 A systematic review of RCTs found that the number of patients needed to treat with tiotropium for one year were 14 (95% CI 11 to 22) to prevent one exacerbation and 30 (95% CI 22 to 61) to prevent one hospitalisation compared to placebo and ipratropium237 [evidence level A]. Tiotropium also improves exertional dyspnoea and exercise endurance by reducing hyperinflation [evidence level B].218 (see Appendix 1).

Theophyllines

Theophylline has a modest effect on FEV1 and FVC and slightly improves arterial blood gas tensions in moderate to severe COPD. However, theophyllines are rarely used because of their narrow therapeutic index and potential for significant side effects45,217 [evidence level A]. Some patients with disabling breathlessness may derive benefit from their use.46-48 Theophyllines may have an anti-inflammatory effect or reduce muscle fatigue.49,50 Evidence supports only the slow-release formulation. Dosage should be adjusted according to trough serum levels.51
Assessment of response and continuation of bronchodilator therapy

In some patients a response to bronchodilator therapy may require treatment for up to two months. Parameters for assessing long term responsiveness are outlined in Box 10. Symptomatic and functional benefits can often be demonstrated in the absence of an increase in FEV₁. Other objective measurements, such as an increase in exercise capacity (e.g., six-minute walk distance) or an increased inspiratory reserve capacity, may be useful indicators of physiological improvement. Subjective measurements, such as quality of life, breathlessness and functional limitation (e.g., MRC Dyspnoea Scale, see Box 4), can determine the patient's perception of benefit.

If there is no improvement:

- check inhaler technique;
- consider psychosocial issues and deconditioning; and
- exclude other causes of exercise impairment (consider specialist referral or a cardiopulmonary exercise test).

**Box 10: Assessing long term medication response**

**At diagnosis**
- Measure and record FEV₁ and FVC after administration of beta-agonist
- Record MRC Dyspnoea Scale score
- Prescribe trial medications as per dosage protocols

**At next visit**
- Remeasure spirometry and MRC Dyspnoea Scale score to determine response to medications
- If FEV₁ and/or FVC increases more than 15% and more than 300 mL after a treatment trial, and/or MRC Dyspnoea Scale score improves more than 1 unit, the tested medication should be included as ongoing treatment
- If FEV₁ and/or FVC reverse completely or substantially with inhaled or oral glucocorticoids, consider asthma
- If there is no significant response to the medication being tested, it could be ruled out for ongoing treatment

MRC = Medical Research Council. FEV₁ = forced expiratory volume in one second. FVC = forced vital capacity.

**Short-course oral glucocorticoids**

Long term use of systemic glucocorticoids is not recommended⁵²-⁵⁶ [evidence level A]

Indeed, caution in the long term use of systemic glucocorticoids is necessary because of limited efficacy and potential toxicity in elderly patients.

Some patients with stable COPD show a significant response to oral glucocorticoids (on spirometry or functional assessment). Therefore, a short course (two weeks) of prednisolone (20–50 mg daily) may be tried with appropriate monitoring. A negative bronchodilator response does not predict a negative steroid response.⁶,⁵¹ If there is a response to oral steroids, continued treatment with inhaled glucocorticoids is indicated, but these may fail to maintain the response.⁵⁷,⁵⁸ Patients who have a negligible response to glucocorticoids should not use them.

Inhaled glucocorticoids should be considered in patients with a documented response or those who have severe COPD with frequent exacerbations ⁵⁷-⁶¹ [evidence level B]

Inhaled glucocorticoids do not influence the rate of decline in FEV₁ in patients with no significant acute reversibility.⁵⁷-⁶¹ Smoking cessation remains the only effective means to affect the decline in lung function for these patients (see Section P). Patients with clinically significant acute bronchodilator reversibility may benefit from long-term inhaled glucocorticoid therapy. Long term inhaled therapy with glucocorticoids is also
indicated in patients with COPD who have significant reversibility of airway function after a more prolonged trial of bronchodilators or glucocorticoids. 57-59

In one large RCT of patients with severe non-reversible COPD (mean FEV₁ about 40% predicted), high-dose inhaled glucocorticoid (fluticasone, 1000 mcg daily) slowed the rate of decline in quality of life over three years and the rate of acute exacerbations without affecting overall decline in lung function.60 Similar results may be expected from high doses of other inhaled glucocorticoids, but are yet to be documented in RCTs. In another large RCT in patients with milder COPD, medium-dose budesonide had no significant impact. 59 Some systemic absorption may occur, so the modest benefits of inhaled glucocorticoids must be weighed against the potential risks of easy bruising, cataract formation and possible contribution to osteoporosis.

The response should be assessed with spirometry and measures of performance status, quality of life or both. They should be trialled for three to six months in patients with moderate to severe COPD, and continued if there is objective benefit.

**Combination inhaled glucocorticoid/long-acting bronchodilator therapy**

A systematic review of six randomised controlled trials of combined glucocorticoid steroids and long-acting beta₂-agonists in one inhaler214 for COPD reached the following conclusion:

Compared with placebo, combination therapy led to clinically meaningful differences in quality of life, symptoms and exacerbations. However, there were conflicting results when the different combination therapies were compared with the mono-components alone. One possible explanation for conflicting results is differential drop-out rates during the original studies. In order to draw firmer conclusions about the effects of combination therapy in a single inhaler more data are necessary, including the assessment of the comparative effects with separate administration of the two drugs in double-dummy trials. [evidence level A]

**Optimise inhaler technique**

Inhaler devices must be explained and demonstrated for patients to achieve optimal benefit. It is necessary to check regularly that the patient has the correct inhaler technique. Elderly and frail patients, especially those with cognitive deficits, may have difficulty with some devices. The range of devices currently available, the products and dosage, as well as their advantages or disadvantages, are listed in Appendix 2.

**Surgery**

In selected patients, a surgical approach may be considered for symptom relief 62-72  
[evidence level C].

None of the current surgical approaches in patients with COPD provides a survival advantage. 6,62 In view of the potential for serious morbidity and mortality, all surgical treatments require careful assessment by an experienced thoracic medical and surgical team.

**Bullectomy**

This operation involves resection of large bullae (larger than 5 cm). The procedure is most successful where there are very large cysts compressing adjacent apparently normal lung. 63-65

**Lung volume reduction surgery**

Lung volume reduction surgery (LVRS) involves resection of the most severely affected areas of emphysematous, non-bullous lung. 66 This can improve lung elastic recoil and diaphragmatic function. 67 LVRS is still an experimental, palliative, surgical procedure. Several large randomised multicentre studies are under way to investigate the effectiveness and cost–benefit of this procedure. 68

Surgery is performed electively after a pulmonary rehabilitation program, to remove about 25% of each lung. Physiological improvement (eg, a 40% improvement in FEV₁ from about 25% predicted to 35% predicted, and six-minute walk from about 300 to 420 metres) takes weeks to months. The duration of the improvement is 2–4 years. These gains should be weighed against risks of operative and postoperative mortality (around 5%–15%), morbidity and cost. 68 However, the natural history of patients with COPD of this severity is a progressive decline in function and early mortality.

**Lung transplantation**

In patients with COPD, this procedure usually involves replacement of one diseased lung with a normal lung from an organ donor. 69,70 Detailed medical and psychological assessment and counselling are required to
avoid excessive morbidity and mortality. Malnutrition, severe weakness and steroid and ventilator
dependence predict a poor outcome. The procedure is most successful when lung disease is the
recipient's only medical problem and is usually offered to younger patients (e.g., those with alpha-1-antitrypsin
deficiency).

Physiological improvement takes weeks to months, and would typically translate to a large improvement in
FEV₁ (from about 20% to 60% predicted for a single lung transplant), exercise performance and quality of
life.69-72

Identify and treat aggravating factors

Sleep apnoea, hypoventilation and hypoxaemia
COPD has adverse effects on sleep quality, resulting in poor sleep efficiency, delayed sleep onset, multiple
wakenings with fragmentation of sleep architecture, and a high arousal index. Arousals are caused by
hypoxia, hypercapnia, nocturnal cough and the pharmacological effects of methylxanthines and beta-
adrenergic agents. Intranasal oxygen administration has been shown to improve sleep architecture and
efficiency, as well as oxygen saturation during sleep.74

Indications for full diagnostic polysomnography in patients with COPD include persistent snoring, witnessed
apnoeas, choking episodes and excessive daytime sleepiness. In subjects with daytime hypercapnia,
monitoring of nocturnal transthoracic carbon dioxide levels should be considered to assess nocturnal
hypoventilation. Patients with COPD with a stable wakeful PaO₂ of more than 55 mmHg (7.3 kPa) who have
pulmonary hypertension, right heart failure or polycythaemia should also be studied. Overnight pulse
oximetry is also useful in patients with COPD in whom long-term domiciliary oxygen therapy is indicated
(stable PaO₂ < 55 mmHg, or 7.3 kPa) to determine an appropriate oxygen flow rate during sleep.

The overlap syndrome: The combination of COPD and obstructive sleep apnoea (OSA) is known as the
"overlap syndrome". The prevalence of COPD in unselected patients with OSA is about 10%, while about
20% of patients with COPD also have OSA. Patients with COPD who also have OSA have a higher
prevalence of pulmonary hypertension and right ventricular failure than those without OSA. There is
frequently a history of excessive alcohol intake. While oxygen administration may diminish the degree of
oxygen desaturation, it may increase the frequency and severity of hypoventilation and lead to carbon
dioxide retention.

As in other patients with OSA, weight reduction, alcohol avoidance and improvement of nasal patency are
useful in those with COPD. Nasal continuous positive airway pressure (CPAP) is the best method for
maintaining patency of the upper airway and may obviate the need for nocturnal oxygen. If nasal CPAP is
not effective, then nocturnal bilevel positive airway pressure ventilation should be considered, although the
benefits of this in chronic stable COPD remain to be established. The role of other OSA treatments, such as
mandibular advancement splinting, remains to be evaluated in the overlap syndrome.

Gastro-oesophageal reflux
In patients with COPD, hyperinflation, coughing and the increased negative intrathoracic pressures of
inspiration may predispose to reflux, especially during recumbency and sleep. Microaspiration of
oesophageal secretions (possibly including refluxed gastric content) is a risk, especially with coexistent
snoring or OSA. Reflux and microaspiration exacerbate cough, bronchial inflammation and airway narrowing.
Diagnosis may be confirmed by 24-hour monitoring of oesophageal pH, modified barium swallow or
gastroscopy. However, a therapeutic trial of therapy with H₂-receptor antagonists or a proton-pump inhibitor
may obviate the need for invasive investigations. Lifestyle changes, including stopping smoking, reduced
intake of caffeine and alcohol, weight loss and exercise, will also help. Elevation of the head of the bed is
also recommended.

Aspiration
Aspiration of food and liquid is common in COPD and may be the cause of recurrent exacerbations and
complications, such as pneumonia and patchy pulmonary fibrosis.

Diagnosis is usually easy with an adequate history from patients and their partners or carers. Dry biscuits
and thin fluids cause the most difficulty. Confirmation rests with assessment by a speech therapist and a
modified barium swallow.
Treatment involves retraining in safe swallowing techniques, which may include:

- avoiding talking when eating [evidence level D];
- sitting upright [evidence level D];
- taking small mouthfuls [evidence level D];
- chewing adequately [evidence level D];
- drinking with dry foods [evidence level D];
- using a straw [evidence level D]; and
- drinking thickened fluids [evidence level D].

### Alcohol and sedatives

Patients with COPD have impaired gas exchange and an exaggerated fall in PO₂ with recumbency and sleep onset. 74,75 Excessive use of alcohol and sedatives exacerbates this and predisposes to sleep-disordered breathing. Heavy cigarette smoking is associated with misuse of other substances in many individuals. Nicotine, caffeine and alcohol also predispose to gastro-oesophageal reflux.

### Hypoxaemia and pulmonary hypertension

**Identify and treat hypoxaemia and pulmonary hypertension** 76-85 [evidence level A]

Pulmonary hypertension in patients with COPD results mainly from vasoconstriction of pulmonary arterioles in response to local hypoxia, usually resulting from impaired ventilation, and vasoconstrictor peptides produced by inflammatory cells. 76-79 The vasoconstriction minimises blood flow through poorly ventilated lung, reducing the mismatch of ventilation and perfusion. While this compensatory mechanism initially helps to maintain blood gas levels, the price is increased pulmonary vascular resistance, ultimately leading to right ventricular strain and failure (cor pulmonale). The vasoconstriction is reversible initially, but vascular remodelling occurs eventually and the condition becomes irreversible. In pulmonary emphysema there is also an anatomical disruption of capillaries in alveolar walls.

Right ventricular hypertrophy is seen in about 40% of patients with an FEV₁ less than 1.0 L and in 70% of those with an FEV₁ less than 0.6 L. The presence of hypercapnia is strongly associated with cor pulmonale.

When pulmonary hypertension and cor pulmonale seem out of proportion with the severity of airway narrowing, the additional factors that need to be considered include:

- sleep apnoea (central and obstructive);
- polycythaemia; and
- recurrent pulmonary thromboembolism.

The development of pulmonary hypertension and peripheral oedema is a poor prognostic sign in COPD.80 If untreated, the five-year survival rate is about 30%. Pulmonary hypertension is difficult to detect on clinical evaluation in patients with COPD.

Chest x-rays may show enlargement of proximal pulmonary arteries, but right ventricular enlargement is difficult to detect because of hyperinflation. Right axis deviation and P pulmonale on ECG may be difficult to detect because of low voltage traces (also a result of hyperinflation). Multifocal atrial tachycardia and atrial fibrillation are common.

Echocardiography is the best non-invasive method of assessing pulmonary hypertension, but image quality is reduced by hyperinflation. Echocardiography is indicated in patients with severe disease, or when symptoms seem out of proportion to the severity of airflow limitation. Estimation of pressure relies on at least some tricuspid regurgitation. Other findings include mid-systolic closure of the pulmonic valve and increased right ventricular wall thickness.
Treatment

Treat underlying lung disease: The logical first step is to optimise lung function and treat all potential aggravating conditions.

Oxygen therapy: Long term, continuous (> 15 h/day) oxygen therapy to treat chronic hypoxaemia prolongs survival of patients with COPD, presumably by reducing pulmonary hypertension.12,13,80-82 (For a detailed description of oxygen therapy in COPD see Section P).

Ventilatory support: For patients with COPD who also have sleep apnoea or hypoventilation, ventilatory support with continuous positive airway pressure (CPAP) or non-invasive positive pressure ventilation (NIPPV) may be more appropriate than oxygen therapy (for more details see Section X). The efficacy of NIPPV for long-term treatment has not yet been proven. 74,83-85 Although preliminary studies have suggested that the addition of NIPPV to long-term therapy may have some beneficial effects on CO₂ retention and shortness of breath, based on a 12-month study209 and a 24-month study210 in stable COPD patients with chronic respiratory failure, its widespread use cannot be advocated as yet. 211 However, compared with long-term oxygen therapy alone, the addition of NIPPV has some beneficial effects on CO₂ retention and shortness of breath. 210

Diuretics: Diuretics may reduce right ventricular filling pressure and oedema, but excessive volume depletion must be avoided. Volume status can be monitored by measuring serum creatinine and urea levels. Diuretics may cause metabolic alkalosis resulting in suppression of ventilatory drive.

Digoxin: Digoxin is not indicated in the treatment of cor pulmonale and may increase the risk of arrhythmia when hypoxaemia is present.6 It may be used to control the rate of atrial fibrillation.

Vasodilators: Vasodilators (hydralazine, nitrates, nifedipine, verapamil, diltiazem, angiotensin-converting enzyme [ACE] inhibitors) do not produce sustained relief of pulmonary hypertension in patients with COPD.86,87 They can worsen oxygenation (by increasing blood flow through poorly ventilated lung) and result in systemic hypotension. However, a cautious trial may be used in patients with severe or persistent pulmonary hypertension not responsive to oxygen therapy. Some vasodilators (eg, calcium antagonists) have been shown to reduce right ventricular pressure with minimal side effects and increased well-being, at least in the short term. Nitric oxide worsens V/Q mismatching and is therefore contraindicated in patients with COPD. 211

Osteoporosis

Prevent or treat osteoporosis [evidence level A]

Patients with COPD have high rates of bone fracture (11%-14%) and bone mineral density (BMD) an average of 10% lower compared with control patients. 88 A 10% drop in BMD equates to a 2.6-fold increase in fracture risk.88 Greater deficits are seen in patients with more severe disease.

The risk factors for low BMD in patients with COPD include periods of immobilisation or hospitalisation, low FEV₁, use of oral corticosteroids, decreased weight-bearing activity, and smoking. Other risk factors relevant to the general population also apply. These include low calcium intake, low body mass index, alcohol abuse and hypogonadism.

All patients who take corticosteroids should be advised to undertake regular, weight-bearing exercise (eg, walking and light resistance training). There is no evidence of an effect of inhaled corticosteroid at conventional doses (<2,200 mcg/day) given for two or three years on BMD or vertebral fracture. However triamcinolone was associated with reduced BMD in the Lung Health Study239 [evidence level B]. Australian Guidelines on the prevention and treatment of osteoporosis, including glucocorticoid-induced osteoporosis have been published.240 Higher doses were associated with biochemical markers of increased bone turnover, but data on BMD and fractures at these doses are not available231 [evidence level A]. Those who have had long-term steroid therapy at lower doses and who have other risk factors should be screened.

Intervention should be targeted at men and women who are taking more than 15 mg daily of prednisolone or who have several risk factors for osteoporosis and whose BMD is < 1.5 standard deviations below the young adult mean. 58 Oral bisphosphonates, particularly risedronate, have been shown to be effective in preventing and treating bone loss in men and women taking corticosteroids.58,219 However, most patients in these studies did not have respiratory disease. The studies also showed a reduction in risk of spinal fracture, especially in postmenopausal women. Other agents that have been used with some success in patients with respiratory disease include calcium, calcitonin, vitamin D [evidence level A]220,221 and medroxyprogesterone acetate.
Selecting patients with COPD who may be at increased risk of osteoporosis is most appropriately done on the basis of conventional risk factors. Further refining of clinical predictors and more evidence for the cost-effectiveness of such programs still needs to be resolved before recommendations on a screening strategy in patients with COPD can be made. For more information on prevention and treatment of osteoporosis, see the current Australian guidelines. 88

Improve function

**Pulmonary rehabilitation**

Pulmonary rehabilitation reduces dyspnoea, anxiety and depression, improves exercise capacity and quality of life and may reduce hospitalisation86-107 [evidence level A]

Pulmonary rehabilitation is one of the most effective interventions in COPD99-93 and has been shown to reduce symptoms, disability and handicap and to improve functioning by:

- improving cardiovascular fitness, muscle function and exercise endurance;89,90,93-99
- enhancing the patient's self-confidence and coping strategies, and improving medication adherence and use of respiratory treatment devices;89-91,95,100,101-103
- improving mood by controlling anxiety and panic, decreasing depression, and reducing social impediments.89,90,104

Pulmonary rehabilitation should be offered to patients with moderate to severe COPD, but can be relevant for people with any long-term respiratory disorder characterised by dyspnoea.101,102 Exercise programs alone have clear benefits,89,100,101-107 while the benefits of education or psychosocial support without exercise training are less well documented.101,106 Comprehensive programs incorporating all three interventions have the greatest benefits (see below).

Most research has been undertaken with hospital-based programs, but there is increasing evidence of benefit from rehabilitation in the community.95,100 The minimum length of an effective rehabilitation program that includes exercise training is six weeks; the longer the program continues, the more effective the results.113,204,205 [evidence level B] However, as yet, effective structures that maintain benefit have not been subjected to robust clinical trials.206

**Exercise training**

Numerous randomised controlled trials in moderate to severe COPD have shown decreased symptoms (breathlessness and fatigue) and improved cardiovascular fitness, exercise endurance, health-related quality of life and mood following exercise conditioning alone103 [evidence level A]. Improvements in muscle strength and self-efficacy have also been reported.89-101,103

The evidence for benefit from high-intensity training of the respiratory muscles is less convincing.101,103,104 Some very disabled patients are shown how to reduce unnecessary energy expenditure for activities of daily living.101 Some patients may benefit from portable oxygen (see section P).

Maintenance of activities is essential for continuing the benefits from the initial training program. Home- or community-based exercise should be encouraged6,105 [evidence level D].

**Patient education**

There is limited evidence that education alone can improve self-management skills, mood and health-related quality of life105-107 [evidence level C]. Providing information and tools to enhance self-management in an interactive session is more effective than didactic teaching.105,108

The single most important intervention is assistance with smoking cessation.6 Good nutrition; task optimisation for more severely disabled patients; access to community resources; help with control of anxiety, panic or depression; instruction on effective use of medications and therapeutic devices (including oxygen where necessary); relationships; end-of-life issues; continence; safety for flying; and other issues may be addressed.6,101,102

**Psychosocial support**

Improved exercise tolerance, mood, self-efficacy and health-related quality of life have been reported from cognitive behavioural therapy alone82,105 [evidence level C]. Depression, anxiety and panic are frequent complications of chronic disabling breathlessness, with dependence and social isolation being common.109
General support, specific behavioural training and the use of appropriate antidepressant medications may enhance quality of life for the patient, and for the spouse or carer.

**Comprehensive integrated rehabilitation**

Comprehensive pulmonary rehabilitation, [89-100,101-103,110-116](#) which includes all the components discussed above, enhances health-related quality of life and self-efficacy, improves exercise performance, and reduces breathlessness and healthcare use [evidence level A]. It is possible to provide these comprehensive programs in the community, [95,100,101,102](#) as well as in larger hospitals. [114](#)

Lung support groups may provide patients and carers with emotional support, social interaction, and other social outlets, and help them gain new knowledge and coping strategies. More than 80 groups throughout Australia can be contacted via LungNet.

<table>
<thead>
<tr>
<th>Australia</th>
<th>New Zealand</th>
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<tbody>
<tr>
<td>LungNet</td>
<td>Asthma and Respiratory Foundation of New Zealand</td>
</tr>
<tr>
<td>toll-free phone number 1800 654 301</td>
<td>phone (04) 499 4592</td>
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</table>

**Chest physiotherapy**

A systematic review in COPD and bronchiectasis showed a significant increase in sputum clearance with no change in lung function or health status [89-100,101-107](#) [evidence level B].

The aims of chest physiotherapy are to assist sputum removal and improve ventilation without increasing the distress of the patient. [117](#) Auscultation plus chest x-ray findings help determine the regions of the lung to be treated. Bronchodilator therapy before treatment may result in a more effective treatment. If patients are hypoxaemic (Spo2 < 88%), supplemental oxygen is given during treatment.

Various techniques and devices are available to aid sputum removal. The choice of technique depends on the volume of sputum, the patient's condition (eg, extent of airflow limitation, severity of breathlessness), patient preference and the cognitive status of the patient.

**Weight management and nutrition**

In patients with COPD, both excess and low weight are associated with increased morbidity. Excessive weight increases the work of breathing and predisposes to sleep apnoea — both central hypoventilation and upper-airway obstruction. Progressive weight loss (body mass index < 20) is an important prognostic factor for poor survival [118,119,232](#) [evidence level A]. This may be the result of a relative catabolic state (related to high energy demands of increased work of breathing) added to disturbance of nutritional intake (related to breathlessness while eating). Deleterious consequences include combined protein–energy malnutrition, [119](#) and possibly mineral or essential vitamin and antioxidant deficiencies. [119](#)

Randomised controlled trials of nutritional support in COPD have not shown significant improvements in nutrition, exercise capacity or other outcomes [233](#) [evidence level A]. Patients with COPD should not eat large meals, as this can increase dyspnoea. Several small nutritious (high energy, high protein) meals are better tolerated. Snacks may provide a useful addition to energy and nutrient intake. Referral to a dietitian for individual advice may be beneficial.

Anabolic steroids in patients with COPD with weight loss increase body weight and lean body mass but have little or no effect on exercise capacity. [207-208](#)

**Opioids**

Opioids may have a role for patients with severe retractable dyspnoea [235](#) [evidence level A]. However, opioids may be associated with drowsiness, nausea, vomiting, dizziness, constipation and, in two of the four multiple dose studies, an opioid withdrawal syndrome.
P: Prevent deterioration

<table>
<thead>
<tr>
<th>Summary</th>
<th>Evidence level</th>
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<tbody>
<tr>
<td>Smoking cessation reduces the rate of decline of lung function</td>
<td>A</td>
</tr>
<tr>
<td>General practitioners and pharmacists can help smokers quit</td>
<td>A</td>
</tr>
<tr>
<td>Treatment of nicotine dependence is effective and should be offered to smokers</td>
<td>A</td>
</tr>
<tr>
<td>Pharmacotherapies double the success of quit attempts; behavioural techniques further increase the quit rate by up to 50%</td>
<td>A</td>
</tr>
<tr>
<td>Influenza vaccination reduces the risk of exacerbations, hospitalisation and death</td>
<td>A</td>
</tr>
<tr>
<td>Long-term oxygen therapy (&gt; 15 h/day) prolongs life in hypoxaemic patients (PaO2 &lt; 55 mmHg, or 7.3 kPa)</td>
<td>A</td>
</tr>
<tr>
<td>Mucolytics may reduce the frequency and duration of exacerbations</td>
<td>A</td>
</tr>
<tr>
<td>Inhaled glucocorticoids are indicated for patients with a documented response or who have severe COPD with frequent exacerbations</td>
<td>B</td>
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</tbody>
</table>

Reducing risk factors for COPD is a priority, and smoking is the most important of these. Reduction of exposure to occupational dust, fumes and gases and to indoor and outdoor air pollutants is also recommended6 [evidence level D]. Influenza vaccination reduces the risk of exacerbations and death [evidence level A], while long term oxygen therapy reduces mortality [evidence level A].

Risk factor reduction

Smoking cessation

Smoking cessation reduces the rate of decline of lung function6,7 [evidence level A]

A successful smoking cessation strategy involves integration of public policy, information dissemination programs and health education through the media and schools.6 Smoking prevention and cessation programs should be implemented and be made readily available6,120 [evidence level A].

Smoking cessation (see Box 3) has been shown to halt the accelerated decline in lung function seen with COPD6,7 [evidence level A]. People who continue to smoke despite having pulmonary disease are highly nicotine dependent and may require treatment with pharmacological agents to help them quit.121,122

Smoking cessation interventions have been shown to be effective in both sexes, in all racial and ethnic groups tested, and in pregnant women.6 International data show that smoking cessation strategies are cost effective, but with a 10-fold range in cost per life-year gained depending on the intensity of the program and the use of pharmacological therapies.6

General practitioners and pharmacists can help smokers quit.123-125 Relapse is common [evidence level A]
Brief counselling is effective [evidence level A] and every smoker should be offered at least this intervention at every visit.6 Currently accepted best practice is summarised in the 5-A strategy: 6

Ask and identify smokers.

Advise smokers about the risks of smoking and benefits of quitting and discuss options.

Assess the degree of nicotine dependence and motivation or readiness to quit.

Assist cessation — this may include specific advice about pharmacological interventions or referral to a formal cessation program if available.

Arrange follow-up to reinforce messages.

Cessation of smoking is a process rather than a single event, and smokers cycle through the stages of being not ready, unsure, ready, quitting and relapsing before achieving long-term success. The aim of initial intervention is to advance one stage in the cessation cycle. The most strenuous efforts should be made with those smokers ready to quit or quitting. Cessation rates increase with the amount of support and intervention, including practical counselling and social support arranged outside of treatment.

Treatment of nicotine dependence is effective and should be offered to smokers in addition to counselling 124-132 [evidence level A]

Pharmacotherapies for nicotine dependence, including nicotine replacement and bupropion (sustained-release), are effective [evidence level A]. 124-132 At least one of them should be added to counselling if necessary and in the absence of contraindications6 [evidence level A]. Caution is recommended in people with medical contraindications, light smokers (< 10 cigarettes a day) who may become dependent on nicotine replacement therapy, pregnant women and adolescent smokers. 6

All forms of nicotine replacement therapy (NRT) appear to be useful in aiding smoking cessation. 126 NRT is most suitable for highly dependent smokers who are motivated to quit. There is little evidence for its role in those who smoke up to 15 cigarettes daily. The choice of type of NRT depends on patient preference, needs and tolerance.

NRT is more effective when combined with counselling and behavioural therapy. 131 NRT is safe in patients with stable cardiac disease such as angina pectoris [evidence level A]. 6,122 NRT produces lower peak levels of nicotine than active smoking, so, theoretically, should be safer than smoking, even in patients with unstable disease.

**Nicotine replacement therapy**

**Nicotine transdermal patch:** A steady nicotine level (about half that of smoking) is maintained to reduce withdrawal symptoms. However, the patch does not provide the peak nicotine levels of smoking which reinforce the addiction. Addition of a self-administered form of nicotine, such as gum, inhaler or lozenge, improves abstinence rates. 126,127

The strength of patch used depends on the degree of nicotine dependence, indicated by number and strength of cigarettes smoked daily. Three strengths are available — 7 mg, 14 mg and 21 mg — and both 24-hour and 16-hour patches are available. The 24-hour patches achieve higher blood nicotine levels and provide more relief of morning cravings, but both patches have about the same efficacy. Patch use doubles the success rates of attempts to quit compared with placebo. Six to eight weeks of use are generally required, with tapering of the nicotine dose every two weeks. 128

The only significant side effect is skin irritation, which is generally mild and rarely leads to cessation of use.

**Nicotine gum:** Nicotine is rapidly absorbed through the oral mucous membrane, so gum should be chewed only two to three times per minute to avoid excessive salivation, swallowing of nicotine and gastrointestinal side effects. The blood levels achieved by nicotine chewing gum are one-third (2 mg gum) or two-thirds (4 mg gum) those of smoking. Patients should taper the dose gradually, but dependence on the gum can occur in up to 20% of users. Most patients should have stopped using the gum within three months.

**Nicotine lozenge:** Nicotine lozenges are available in 2 mg and 4 mg doses. No special technique is required — the lozenge is held in the mouth and moved around periodically until it dissolves. As the lozenge dissolves, it releases about 25% more nicotine than the equivalent dose of gum. Patients should reduce the number of lozenges they are using over 12 weeks, remaining on the same strength lozenge throughout. Lozenges may be preferable for denture wearers who wish to use oral NRT.
Nicotine inhaler: The nicotine inhaler consists of a plastic mouthpiece and cartridge containing 10 mg of nicotine. The inhaler produces nicotine concentrations that are a third those achieved with smoking. The inhaler is useful for smokers who miss the hand-to-mouth action of smoking, or who have problems with the gum. The recommended maximum period of use is 16 weeks.

Bupropion

Bupropion hydrochloride, in conjunction with counselling and support, doubles the quit rates achieved by placebo, with or without nicotine replacement therapy as an adjunct.\textsuperscript{126-132} It is recommended as first-line pharmacotherapy for smoking cessation alongside NRT [evidence level A],\textsuperscript{6} but there are currently insufficient data to recommend its use in preference to NRT, or vice versa. The recommended dose is 150 mg orally once daily for three days, then 150 mg twice daily (at least eight hours apart) for between seven and nine weeks, in combination with counselling. A quit date should be set (eg, Day 5–10). The drug works equally well in smokers with and without a past history of depression. It is also effective in people who have relapsed and are motivated to quit again.

Bupropion is contraindicated in patients with epilepsy, bulimia or a history of head trauma. It may interact with other antidepressants, especially monoamine oxidase inhibitors, which require a 14-day washout. There is a relative contraindication in other conditions that may lower the seizure threshold, such as diabetes mellitus. It should only be prescribed to patients at an advanced stage of readiness to quit. Some deaths have been reported in patients taking bupropion in routine clinical practice, but there is no evidence that bupropion was responsible for these deaths.\textsuperscript{122} The contradictions and adverse effects for bupropion hydrochloride are shown in Box 11.

<table>
<thead>
<tr>
<th>Box 11. Advantages and disadvantages of pharmacological treatments for smoking cessation\textsuperscript{6,121-132}</th>
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<tbody>
<tr>
<td><strong>Treatment</strong></td>
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<tr>
<td>Nicotine patch</td>
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<td>Nicotine gum</td>
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<td>Nicotine lozenges</td>
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<tr>
<td>Nicotine inhaler</td>
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<tr>
<td>Bupropion hydrochloride</td>
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Prevent smoking relapse

Pharmacotherapies double the success of quit attempts. Behavioural techniques further increase the quit rate\textsuperscript{121-125,132,230} [evidence level A]

Counselling sessions, possibly involving professional psychological support and use of nicotine patches and bupropion, increase the chances of successful quitting by 5%–30% compared with control groups.
Family, friends and workmates should be advised of the intention to quit and provide understanding and support. The relapse rate is increased if there are other smokers in the household. Success is more likely if all the smokers agree to quit together. Suggest the patient ring the Quit Line or other local services.

**Quit Line**

<table>
<thead>
<tr>
<th>Australia</th>
<th>New Zealand</th>
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<tbody>
<tr>
<td>131 848</td>
<td>0800 778 778</td>
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</table>

Ex-smokers who attend for follow-up are more likely to be successful in the long term. Support is most needed in the first few weeks, so regular follow-up visits then and over the first three months should be encouraged.

**Prevent infection and exacerbation**

**Influenza vaccination**

Influenza vaccination reduces the risk of exacerbations, hospitalisation and death \(^{133,134}\) [evidence level A]

Annual influenza vaccination reduces by about 50% the development of severe respiratory complications and hospitalisation or death from both respiratory disease and all causes \(^{133,134}\) [evidence level A]. The vaccine used in Australia does not contain a live virus and cannot cause an infection. Side effects include a sore arm the following day and possibly a mild fever and arthralgia at five to eight days caused by the immune response. The vaccine usually contains three strains (2A and 1B), which are adjusted annually based on epidemiological data. It should be given in early autumn to all patients with moderate to severe COPD. \(^{133,134}\) A second vaccination in winter increases antibody levels. \(^6\)

**Pneumococcal vaccination**

Pneumococcal vaccination is known to be highly effective in preventing invasive bacteraemic pneumococcal pneumonia, but may be less effective in elderly or immunosuppressed patients. \(^{135}\) There is no direct evidence of its efficacy in preventing pneumococcal exacerbations of COPD, but prevention of pneumonia in these patients with already reduced respiratory reserve is a worthy goal in its own right, \(^{135-137}\) so pneumococcal vaccination (polyvalent covering 23 virulent serotypes) is recommended in this group [evidence level B]. \(^6\) There is no evidence or rationale for vaccinating more frequently in COPD.

**Haemophilus influenzae vaccination**

Six randomised trials of oral mono-bacterial whole cell killed non-typable haemophilus influenzae vaccine \(^{216}\) found a significant reduction in the incidence of bronchitic episodes three months after vaccination, but the effect had disappeared by nine months. The severity of exacerbations in the treatment group as measured by the requirement to prescribe antibiotics was reduced by 65% at six months. However, a larger clinical trial is needed to assess longer term prognosis. [evidence level A]

**Antibiotics**

Current evidence does not support long-term antibiotic use to prevent exacerbations in patients with COPD \(^{138,139}\) [evidence level A]. However, they should be used in exacerbations with an increase in cough, dyspnoea, sputum volume or purulence (see Section X).

Prophylactic antibiotics in chronic bronchitis/ COPD have a small but statistically significant effect in reducing the days of illness due to exacerbations of chronic bronchitis. However, they do not have a place in routine treatment because of concerns about the development of antibiotic resistance and the possibility of adverse effects. The available data are over 30 years old, so the pattern of antibiotic sensitivity may have changed and there is a wider range of antibiotics in use. \(^{234}\)
Glucocorticoids

The effect of inhaled glucocorticoids on decline in lung function is controversial. Systematic reviews and meta-analyses of the available RCTs have found a small benefit of uncertain significance compared to placebo[^6^,^57^,^61^] [evidence level A]. A 2003 meta-analysis by Highland et al[^22^] found a combined difference in the rate of decline in FEV1 of 5mL/year between treatment groups (95% CI 11.2 to -1.2mL/year/year, p=0.11) while a second meta-analysis in the same year by Sutherland et al[^22^] found a combined difference of 7.7mL/year between treatment groups (95% CI 1.3 to 14.2mL/year, p=0.02). Neither systematic review addressed adverse effects of inhaled glucocorticoids. The varying conclusions of these reviews would not lead us to recommend the routine use of inhaled corticosteroids in all patients with COPD. However, inhaled glucocorticoids are indicated for patients with a documented response or those who have severe COPD with frequent exacerbations[^58^,^61^] [evidence level B].

In patients with severe COPD, high-dose inhaled corticosteroids may reduce the rate of acute exacerbations[^23^] [evidence level A] and slow the rate of decline of quality of life[^60^] [evidence level B]. Cessation of therapy is recommended if no benefit is seen. Detailed discussion appears in section O and section X.

Mucolytic agents

Mucolytics may reduce the frequency and duration of exacerbations[^14^] [evidence level A].

Drugs that decrease the viscosity of sputum (eg, bromhexine, N-acetylcysteine, ambroxol, potassium iodide and glycerol guaiacolate) may play a useful role, but criteria for predicting a response have not been established. A Cochrane Review concluded that, in patients with COPD or chronic bronchitis who have a higher than average rate of exacerbations, treatment with mucolytic agents was associated with a small, but significant, reduction in acute exacerbations and total number of days of disability[^14^].

However, a recent large RCT of N-acetylcysteine did not confirm an overall reduction in exacerbations, although a significant reduction was still seen in the subgroup who were not on concomitant treatment with inhaled steroids[^24^] [evidence level B].

Regular review

Regular review, with objective measures of function and medication review, is recommended in the hope that this may reduce complications and the frequency or the severity (or both) of exacerbations and admissions to hospital.[^6^]

Oxygen therapy

Long-term oxygen therapy (more than 15 h/day) prolongs life in hypoxaemic patients (PaO2 < 55 mmHg, or 7.3 kPa)[^12^,^13^,^80^-^82^,^14^] [evidence level A].

Long-term oxygen therapy reduces mortality in COPD.[^12^,^13^,^80^-^82^,^14^] It may also have a beneficial impact on haemodynamics, haematological status, exercise capacity, lung mechanics and mental state[^80^,^82^,^14^]. Although effective, it is a potentially expensive therapy that should only be prescribed for those in whom there is evidence of benefit (see below). Information on prescribing oxygen therapy is given in Appendix 3.

**Long-term continuous oxygen therapy**: (at least 15 hours a day) is appropriate for patients who have PaO2 consistently ≤ 55 mmHg (7.3 kPa; SpO2 88%)[^12^,^13^] when breathing air, at rest and awake [evidence level A]. If oxygen is prescribed when the patient's condition is unstable (eg, during an exacerbation), then the requirement for it should be reviewed four to eight weeks after initiation. At assessment for ongoing therapy, the patient's condition must be stable, all potentially reversible factors must have been treated and the patient must have stopped smoking at least one month previously.

Polycythaemia (haemoglobin level > 170 g/L), clinical or electrocardiographic evidence of pulmonary hypertension, as well as episodes of right heart failure, are consistent with the systemic effects of chronic hypoxaemia, and continuous oxygen should be supplied if the stable PaO2 is 55–59 mmHg (7.3–7.9 kPa; Spo2 < 90%)[^14^,^14^] [evidence level D]. Continuous oxygen therapy is of most benefit for patients with increased arterial PaCO2 (> 45 mmHg, or 6 kPa).[^15^]

Government funding is available on the basis that the prescribing doctor is an approved prescriber (usually a respiratory physician). Oxygen is usually supplied to patients meeting specific criteria and means testing by state or regional health departments in Australia and New Zealand.
Intermittent oxygen therapy: Available evidence does not allow any firm conclusions to be made about the effectiveness of intermittent ambulatory domiciliary oxygen therapy in patients with COPD. However, use of intermittent oxygen therapy may be considered for:

- People who experience oxygen desaturation on exertion [evidence level C]. Supplementary oxygen may improve exercise capacity. The benefit cannot be predicted by a resting test; acute benefit may be established by comparing exercise endurance when breathing oxygen and when breathing air, while using a treadmill, or during a six-minute walk test or shuttle walking test.

- Patients living in isolated areas or prone to sudden life-threatening episodes while they are awaiting medical attention or evacuation by ambulance.

- Patients travelling by air. Flying is generally safe for patients with chronic respiratory failure who are on long-term oxygen therapy, but the flow rate should be increased by 1–2 L/minute during the flight (see also below).

Nocturnal oxygen therapy: Patients with hypoxaemia during sleep may require nocturnal oxygen therapy. Nocturnal hypoxaemia should be considered in patients whose arterial gas tensions are satisfactory when awake, but who have daytime somnolence, polycythaemia or right heart failure. Oxygen is indicated for patients whose nocturnal arterial oxygen saturation repeatedly falls below 88% [evidence level D]. Sleep apnoea should be excluded.

Fitness to fly

Commercial aircraft operate at altitudes of up to 12 500 metres, with the plane's interior pressurised to 2100–2400 metres. At this "altitude" the alveolar PaO₂ for healthy individuals decreases from 103 mmHg (13.7 kPa) to 64 mmHg (8.5 kPa) and oxygen saturation declines from 97% to 93%.

As a general rule, supplemental oxygen is unlikely to be required if the resting oxygen saturation is 95% or higher, and likely to be required if oxygen saturation is 88% or lower. Patients with oxygen saturation values between these levels might require specialist assessment.

Before flying, patients should ideally be clinically stable. Patients recovering from an acute exacerbation are particularly at risk. Those already on long-term oxygen therapy need an increase in flow rate of 1–2 L per minute during flight. Careful consideration should be given to any comorbidity that may impair delivery of oxygen to the tissues (eg, cardiac impairment, anaemia). Exertion during flight will exacerbate hypoxaemia.

The American Thoracic Society currently recommends that PaO₂ during air travel should be maintained at more than 50 mmHg (6.7 kPa). At altitude, PaO₂ can be estimated from PaO₂ at sea level by means of published nomograms. If the PaO₂ at sea level is less than 70 mmHg (9.3 kPa), PaO₂ at 2300 metres is less than 50 mmHg (6.7 kPa). The natural conclusion is that all patients with a PaO₂ less than 70 mmHg (9.3 kPa) at rest at ground level should receive supplemental oxygen.

Many lung function laboratories perform assessments for fitness to fly. These may include measurement of arterial blood gas levels or transcutaneous oxygen saturation while breathing a mixture of 15% oxygen and 85% nitrogen, which mimics conditions at 2800 metres.

D: Develop support network and self-management plan

<table>
<thead>
<tr>
<th>Summary</th>
<th>Evidence level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary rehabilitation increases patient/carer knowledge base, reduces carer strain and develops positive attitudes towards self-management and exercise</td>
<td>A</td>
</tr>
<tr>
<td>COPD imposes handicaps which affect both patients and carers</td>
<td>B</td>
</tr>
<tr>
<td>Multidisciplinary care plans and individual self-management plans may help to prevent or manage crises</td>
<td>B</td>
</tr>
<tr>
<td>Enhancing quality of life and reducing handicap requires a support team</td>
<td>C</td>
</tr>
<tr>
<td>Patients and their family/friends should be actively involved in a therapeutic partnership with a range of professional disciplines</td>
<td>C</td>
</tr>
<tr>
<td>Patients should be encouraged to take appropriate responsibility for their own management</td>
<td>C</td>
</tr>
</tbody>
</table>
In the early stages of disease, patients with COPD will often ignore mild symptoms. As the disease progresses, impairment and disability increase. As a health state, severe COPD has the third-highest perceived "severity" rating, on a par with paraplegia and first-stage AIDS. Depression, anxiety, panic disorder, and social isolation add to the burden of disease as complications and comorbidities accumulate. Patients with COPD often have neuropsychological deficits suggestive of cerebral dysfunction. The deficits are with verbal and visual short-term memory, simple motor skills, visuomotor speed and abstract thought processing.

COPD imposes handicap which affects both patients and carers\(^{89-92,102}\) [evidence level B]

People with chronic conditions are usually cared for by partners or family members. In populations where the patient's chronic disease is non-respiratory, there is evidence that the psychological health status of carers and patients is linked. In one small population of patients with COPD, levels of loneliness, social isolation and depression were similar among carers and their patients.

The quality of care received from family carers is linked with the health of those carers, so that poor carer health status has been found to be associated with high rates of health service use, including hospitalisation, in patients with COPD.

It is not surprising that significant psychological and physical consequences occur in carers of patients with chronic diseases. One of the most effective means of improving the patient's functional and psychological state and reducing carer strain is pulmonary rehabilitation.

**Pulmonary rehabilitation**

Pulmonary rehabilitation increases patient/carer knowledge base, reduces carer strain and develops positive attitudes toward self-management and exercise\(^{89-100,101-108,111-116,141,142}\) [evidence level A]

The primary goal of pulmonary rehabilitation is to restore the patient to the highest possible level of independent functioning. Benefits are wide-ranging and there are minimal risks (see Section O).

Health education can play a role in improving skills, ability to cope with illness and health status.\(^{105-107}\)

It is aimed at improving compliance with pharmacological treatments and maintaining an exercise program after pulmonary rehabilitation, undertaking and sustaining smoking cessation, and using devices such as nebulisers, spacers and oxygen concentrators properly.

Education is most effective when it is interactive and conducted in small workshops.\(^6\) Pulmonary rehabilitation, including health education for patients, has also been shown to improve the coping ability and psychological functioning of carers.\(^{105-108}\)

**Support team**

Enhancing quality of life and reducing handicap requires a support team\(^{142}\) [evidence level C]

In advanced disease, the many comorbidities, social isolation and disability mean that a multidisciplinary approach to coordinated care may be appropriate. The multidisciplinary team, depending on local resources, may include the members listed below. The role of respiratory specialists is outlined in Section C.

**General practitioner**

As the primary healthcare provider, the GP is uniquely placed to identify smokers and help them quit, diagnose COPD in its early stages and coordinate care as the disease progresses.

**Smoking cessation:** A doctor's advice is an important motivator for smoking cessation, especially if the doctor is the family physician. The GP can help initiate the cycle of change by repeated brief interventions. There are several smoking cessation programs that have been developed for use in general practice (outlined in the RACGP "Green Book\(^{145}\)). The GP is also the appropriate health professional to recommend or prescribe nicotine replacement therapy and pharmacological treatment of nicotine addiction (for a detailed discussion of smoking cessation interventions, see Section P).

**Early diagnosis:** Most people visit a GP about once a year. Simple questions relating to smoking history, daily cough and degree of breathlessness should lead to lung function testing.
Coordinate investigation and management: GPs will manage patients with mild to moderate COPD. Referral to a respiratory physician may be indicated to confirm the diagnosis, exclude complications and aggravating factors, and to help develop a self-management plan (Section C, Box 8).

Coordinate care in advanced disease: GPs play a crucial role coordinating services provided by a range of healthcare professionals and care agencies (the "multidisciplinary team").

Patients and their family/friends should be actively involved in a therapeutic partnership with a range of professional disciplines89,96,92,105-108[evidence level C]

Nurse/respiratory educator
Specific aspects of care provided by nurses in COPD may include:
- respiratory assessment, including spirometry and pulse oximetry;
- implementation of, or referral for, interventions such as smoking cessation, sputum clearance strategies, oxygen therapy;
- skills training with inhalation devices;
- education to promote better self-management (eg, medications and response to worsening of symptoms);
- organisation of multidisciplinary case conferences and participation in care-plan development; and
- assessment of the home environment.

Physiotherapist
Physiotherapists are involved in a broad range of areas, including exercise training, sputum clearance, breathing retraining, mobility, non-invasive positive pressure ventilation, postoperative respiratory care (eg, after LVRS), and assessment and treatment of musculoskeletal disorders commonly associated with COPD.

Occupational therapist
Occupational therapists provide specific skills in task optimisation and prescription of adaptive equipment and home modifications. Some therapists also teach energy conservation for activities of daily living and can help in the set-up of home and portable oxygen.

Social worker
Social workers can provide counselling for patients and their carers, organisation of support services, respite and long-term care.

Clinical psychologist
Anxiety and depression are common comorbidities in patients with COPD. Panic disorder is also frequent, and can be disabling and out of proportion to the impairment of lung function. Clinical psychologists can use techniques such as counselling and cognitive behavioural therapy to help address anxiety and depression. They may also advise whether pharmacological treatment may be appropriate.

Speech pathologist/therapist
Speech pathologists can be involved in the assessment and management of recurrent aspiration, swallowing and eating difficulties caused by shortness of breath, and dry mouth associated with some pharmaceuticals, age and mouth breathing.

Pharmacist
Pharmacists are involved in education about medications and supply of medications. They can help smokers quit by advising about nicotine replacement and can counsel patients requesting over-the-counter salbutamol. They are well placed to monitor for medication problems and complications and suggest solutions (eg, individual dosing dispensers). 215
Dietitian
Excessive weight-loss is a common problem in patients with end-stage COPD. Conversely, obesity in patients with COPD is associated with sleep apnoea, CO₂ retention and cor pulmonale. Dietitians play a central role in managing these problems.

Non-medical care agencies
Many patients with COPD have difficulties with activities of daily living and may require a range of non-medical support services, including governmental and non-governmental organisations. Availability of services varies between states and between areas within states (eg, urban, rural, remote). Some examples include:

- financial support and organisation of oxygen, CPAP machines, nebulisers, etc;
- Homecare;
- government-supported assistance with activities of daily living (showering, cleaning, shopping, etc);
- home maintenance;
- Meals on Wheels;
- exercise programs; and
- support groups.
Multidisciplinary care plans

Multidisciplinary care plans and individual self-management plans may help to prevent or manage crises [evidence level B]

A multidisciplinary care plan involves documentation of the various medical, paramedical and non-medical services required to keep a patient functioning in the community. Various generic and disease-specific proformas are available (see http://www.lungnet.com.au/copd.html for examples). The care plan may be initiated in the context of a multidisciplinary case conference involving the GP and at least two other health professionals (one of whom is not a doctor).

GPs are remunerated for their involvement in case conferences. This is supported by Extended Primary Care (EPC) item numbers, which vary according to the level of involvement of the GP and the location of the patient. The GP may participate by telephone. A consultant physician is also entitled to claim rebates for organising or participating in case conferences. Further information about item numbers is available at http://www.health.gov.au/epc.

The multidisciplinary care plan may include a component of self-management with appropriate support.

Self-management plans

Patients should be encouraged to take appropriate responsibility for their own management [evidence level C]

Patients with chronic illness who participate in self-management have better outcomes, including reduced healthcare costs, than those who do not. This study included some people with COPD. In COPD, behavioural education alone is effective, although less effective than integrated pulmonary rehabilitation programs that include an exercise component.

In patients with COPD, most exacerbations evolve over days rather than hours, but even small changes can precipitate a major deterioration in functional status. Psychosocial factors such as depression, anxiety, panic or lack of a carer have also been shown to influence the model of care. The traditional approach to exacerbations of moderate to severe COPD has been admission to hospital. Recent work exploring the concept of hospital-at-home has shown that many patients can be managed at home by appropriately qualified staff. Whether such treatment is cost-effective remains controversial.

The concept of self-management plans for patients with COPD is derived from their success in asthma management indicating doses and medications to take for maintenance therapy and for exacerbations. Instructions for crises are often also included. A systematic review by Turnock et al found that the use of action plans results in an increased ability to recognise and react appropriately to an exacerbation by individuals. Unfortunately, there was no evidence these behavioural changes alter health-care utilisation. However, pharmacological treatment of COPD is generally less effective, as the condition is, by definition, non-reversible. Some interventions have strong support (eg, use of bronchodilators and systemic glucocorticoids for exacerbations and antibiotics if there is purulent sputum). They might be more effective if instituted early in an exacerbation, thereby preventing crisis and hospital admission. The primary care team needs to develop systems to identify those with more severe COPD who might benefit from more intensive education and training in self-management skills.

GP involvement in review of self-management plans (including medications) may be undertaken in the context of Domiciliary Medication Management/Review (DMMR), for which a Medicare Benefits Schedule fee is applicable (EPC Item 900). This requires the involvement of an accredited pharmacist and patient consent.

The plan should be reviewed after any exacerbation to make adjustments as appropriate. Patients should be encouraged to start additional treatment at the earliest sign of an impending exacerbation.

Maintenance therapy

Detailed discussion of the maintenance therapy for COPD appears in Section O. In general, the use of drugs in COPD does not involve back-titration, which is a core principle in asthma management. The exception is when oral glucocorticoids have been given for an acute exacerbation.
Exacerbations and crises
Detailed discussion of the management of exacerbations is found in Section X. For mild to moderate exacerbations, an increase in inhaled bronchodilator therapy and an increase in, or introduction of, inhaled glucocorticoid therapy may be beneficial.

For severe exacerbations there is evidence for the use of bronchodilators, antibiotics, systemic glucocorticoids and supplemental oxygen (if patients are hypoxaemic). Selected patients may benefit from early intervention with these agents according to a predetermined plan developed by a GP or respiratory specialist. Some patients can be instructed to start using a "crisis medication pack" while awaiting medical review. They may also be instructed to contact a particular member of the multidisciplinary care team as part of their overall care plan.

Controlled trials are required to document the efficacy of self-management plans in patients with stable COPD, but, drawing on the success of asthma action plans, education of patients with COPD in self-management is recommended [evidence level D]. Written plans are usually required to complement such interventions (see examples at http://www.lungnet.com.au/copd.html).

Treat anxiety and depression
The strong relationship between anxiety and COPD has long been established. Anxiety symptoms lead to repeated presentations for hospital admission for many patients, at a significant financial cost. Anxiety and mood disturbances can often be exacerbated by respiratory drugs (eg, theophylline and steroids, respectively).

Identifying individuals at risk for clinical anxiety and developing effective interventions for treating, or, ideally, preventing panic disorder in COPD should be priorities. There are many outcome trials showing the effectiveness of cognitive behavioural therapy in treating panic disorder when no respiratory disease is present. Cognitive behavioural therapy should also be an effective intervention for treating patients with COPD-related panic disorder.

Depression is common in patients with chronic illness, and COPD is no exception. Pharmacological treatment of depression in COPD may be hampered by poor tolerance of side effects such as sedation, which may cause respiratory depression and aggravate sleep disturbances. In addition to usual clinical assessment, the presence and impact of anxiety and depression may be reliably predicted with several validated questionnaires.

Referral to a support group
Patients who receive education and psychosocial support show greater improvements in more aspects of health-related quality of life than those who receive education with no ongoing support. One way to provide such education and support is through patient support groups. Support groups aim to empower patients with COPD to take a more active role in the management of their healthcare, and thus reduce the psychosocial impact of their disease. Although no direct evaluation of support groups has been published, the likely benefits are summarised in Box 12.
Box 12: Patient support groups

Typical support group activities
- Regular meetings
- Expert guest speakers on COPD topics
- Telephone calls, hospital and home visits
- Receive and distribute lung health education information
- Special seminars and patient programs
- Social outings
- Rehabilitation assistance and maintenance of exercise
- Social enjoyment

Benefits of support groups
- Reinforce and clarify information learnt from health professionals
- Provide access to new information on lung health
- Share experiences in a caring environment
- Empower patients to be more actively involved in their healthcare through self-management techniques
- Participate in social activities and exercise programs
- Encourage patients to think more positively about their lung disease
- Help carers understand lung disease

COPD = chronic obstructive pulmonary disease.

End-of-life issues

Terminally ill patients with COPD are usually elderly and have already experienced one or more decades of increasingly frustrating functional restriction. Their course is likely to have been punctuated by hospital admissions. They often have several comorbidities and are frequently dependent on the care of others.

Determining prognosis in end-stage COPD is difficult, although guides to shortened survival include an FEV₁ < 25% predicted, weight loss (body mass index below 18), respiratory failure (PaCO₂ > 50mmHg, or 6.7 kPa), and right heart failure.

The major ethical issues are deciding whether to offer invasive or non-invasive ventilatory support, or, alternatively, to withhold, limit or withdraw such support. These decisions are often complex, but, as in other areas of medicine, they are ultimately constrained by the standard ethical principles of respect for patient autonomy, and ensuring that good and not harm is achieved. Most patients with end-stage COPD wish to participate in end-of-life management decisions and would prefer to do so in a non-acute setting.

In some states the patient’s wishes can be given legal force through the use of an enduring power of attorney or advance health directive. Although difficult for the health professional and potentially distressing for the patient, a frank discussion about these often unspoken issues can be beneficial.

Opioids and many anxiolytics depress ventilatory drive and are contraindicated in most patients with COPD. When palliation is warranted, however, their use for the short term relief of dyspnoea could be considered. [evidence level B]\textsuperscript{224}
X: Manage eXacerbations

<table>
<thead>
<tr>
<th>Summary</th>
<th>Evidence level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhaled bronchodilators are effective treatments for acute exacerbations</td>
<td>A</td>
</tr>
<tr>
<td>Systemic glucocorticoids reduce the severity of and shorten recovery from acute exacerbations</td>
<td>A</td>
</tr>
<tr>
<td>Non-invasive positive pressure ventilation is effective for acute hypercapnic ventilatory failure</td>
<td>A</td>
</tr>
<tr>
<td>Exacerbations with clinical signs of infection (increased volume and change in colour of sputum and/or fever, leukocytosis) benefit from antibiotic therapy</td>
<td>B</td>
</tr>
<tr>
<td>Multidisciplinary care may assist home management</td>
<td>B</td>
</tr>
<tr>
<td>Early diagnosis and treatment may prevent admission</td>
<td>C</td>
</tr>
<tr>
<td>Controlled oxygen delivery (28% or 0.5–2 L/min) is indicated for hypoxaemia</td>
<td>C</td>
</tr>
<tr>
<td>Involving the patient's general practitioner in a case conference and developing a care plan may facilitate early discharge</td>
<td>C</td>
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</tbody>
</table>

Acute exacerbations of COPD often require hospital admission for treatment of respiratory failure. Hospital mortality for such patients is about 10%, reaching 40% at one year after discharge, and higher for patients aged over 65 years. 14,150,151

In one study of more than 1000 patients admitted to several hospitals with an acute exacerbation of severe COPD, about 50% were admitted with a respiratory infection, 25% with congestive cardiac failure, and 30% with no known cause for the exacerbation. 15 A study of 173 patients with COPD reported an average of 1.3 (range, 0–9.6) exacerbations annually. In patients with COPD the normally sterile lower airway is frequently colonised by Haemophilus influenzae, Streptococcus pneumoniae and Moraxella catarrhalis. While the number of organisms may increase during exacerbations of COPD, the role of bacterial infection is controversial. 152-160 Exacerbations can also be caused by viral infection and by non-infectious causes, such as left ventricular failure, pulmonary embolus, and possibly other factors, such as air pollution. 161 Chest trauma and inappropriate use of sedatives can lead to sputum retention and hypoventilation.

Early diagnosis and treatment may prevent admission 108,148 [evidence level C]

Early diagnosis and prompt management of exacerbations of COPD may prevent progressive functional deterioration and reduce hospital admissions. 108,148 Education of the patient, carers, other support people and family may aid in the early detection of exacerbations. A self-management plan developed in conjunction with the patient's GP and specialist to indicate how to step-up treatment may be useful (see examples at http://www.lungnet.com.au/copd.html). This plan might indicate which medications to take, including antibiotics and oral glucocorticoids. The plan should also require patients to contact their GPs or community nurses to allow rapid assessment (see section D).

Home management

Multidisciplinary care may assist home management 108,148,162,163 [evidence level B]

The shortage of hospital beds, especially in winter, has prompted interest in home care for management of COPD exacerbations, with involvement of multidisciplinary teams assisting GPs. Economic studies of such programs have shown mixed results. 108,148,162,163

Up to a quarter of carefully selected patients presenting to hospital emergency departments with acute exacerbations of COPD can be safely and successfully treated at home with support from respiratory nurses. A systematic review of 7 RCTs found no significant differences in readmission rates or mortality, and ‘Hospital at Home’ schemes were preferred by patients and carers 242 [evidence level A]. However, further research is needed because the studies reviewed were small and trialled different interventions.
COPD acute exacerbation plan

Initial assessment of severity

Assessment of severity of the exacerbation includes a medical history, examination, spirometry and, in severe cases (FEV₁ < 40% predicted), blood gas measurements, chest x-rays and electrocardiography. Patients should be provided with and bring a summary of their medical problems and treatment (eg, a personal health record). If available, results of previous stable lung function tests and arterial blood gas measurements are invaluable for comparison.

- **Spirometry:**
  Unless confused or comatose, even the sickest of patients can perform an FEV₁ manoeuvre. An FEV₁ less than 1.0 L (or < 40% predicted) is usually indicative of a severe exacerbation in patients with moderate COPD. For patients with stable levels below these values (ie, severe COPD), the most important signs of a severe exacerbation will be worsening hypoxaemia, acute respiratory acidosis (carbon dioxide retention), or both.

- **Arterial blood gases:**
  Arterial blood gas levels should be measured if the FEV₁ is less than 1.0 L or less than 40% predicted, or if there are signs of respiratory failure or cor pulmonale. Values obtained while breathing room air are the most useful for assessing ventilation–perfusion inequality. A PaO₂ less than 60 mmHg (8 kPa) indicates respiratory failure, while a PaCO₂ greater than 45 mmHg indicates ventilatory failure.

- **Chest x-ray and electrocardiogram:**
  These help to identify alternative diagnoses and complications, such as pulmonary oedema, pneumothorax, pneumonia, empyema, arrhythmias, myocardial ischaemia and others.

Optimise treatment

An acute exacerbation of COPD may involve an increase in airflow limitation, excess sputum production, airway inflammation, infection, hypoxia, hypercarbia and acidosis. Treatment is directed at each of these problems.

- **Bronchodilators:**
  Inhaled beta-agonist (eg, salbutamol, 400–800 mcg; terbutaline, 500–100 mcg) and anticholinergic agent (ipratropium, 80 mcg) can be given by pressurised metered dose inhaler and spacer, or by jet nebulisation (salbutamol, 2.5–5 mcg; terbutaline, 5 mcg; ipratropium, 500 mcg). The dose interval is titrated to the response and can range from hourly to six-hourly.

- **Glucocorticoids:**
  Oral glucocorticoids hasten resolution and reduce the likelihood of relapse. Up to two weeks' therapy with prednisolone (40–50 mg daily) is adequate. Longer courses add no further benefit and have a higher risk of side effects.

- **Antibiotics:**
  Antibiotics are given for purulent sputum to cover for typical and atypical organisms.

- **Controlled oxygen therapy:**
  This is indicated in patients with hypoxia, with the aim of improving oxygen saturation to over 90% (PaO₂ > 50 mmHg, or 6.7 kPa). Use nasal prongs at 0.5–2.0 L/minute or a venturi mask at 24% or 28%. Minimise excessive oxygen administration, which can worsen hypercapnia.

- **Ventilatory assistance:**
  This is indicated for increasing hypercapnia and acidosis. Non-invasive positive pressure ventilation by means of a mask is the preferred method.

  **Inhaled bronchodilators are effective treatments for acute exacerbations**⁶,¹⁴¹,¹⁴²,¹⁶⁴-¹⁶⁶ [evidence level A]

In exacerbations of COPD, the immediate bronchodilator effect is small, but may result in significant improvement in clinical symptoms in patients with severe obstruction.

Studies of acute airflow limitation in asthma indicate that beta-agonists are as effectively delivered by metered dose inhaler and spacer as by nebuliser. This may be applicable to patients with COPD. An adequate dose should be used. The dose equivalent to 5 mg of salbutamol delivered by nebuliser is 8–10 puffs of 100 mcg salbutamol by metered dose inhaler and spacer. Airflow in the nebuliser should be 6 L per
minute or higher to achieve an aerosol. Avoid using high-flow oxygen, which may worsen carbon dioxide retention. High doses of beta-agonists may induce hypokalaemia and predispose to cardiac arrhythmias.

Few studies have examined the use of ipratropium bromide in acute exacerbations of COPD. One study which compared the effectiveness of ipratropium bromide with a beta-agonist showed that each drug produced a small but significant improvement in pulmonary function. 165 Inhaled ipratropium bromide also produced a small but significant increase in PaO2 (average, 6 mmHg, or 0.8 kPa) within 30 minutes of its delivery.

Hospital management of a severe exacerbation usually includes nebulised beta-agonist bronchodilator (eg, salbutamol, terbutaline), given continuously in extremely unwell patients and intermittently in others. This will usually be delivered by means of high flow air. An anticholinergic agent (ipratropium bromide) may be delivered together with the nebulised beta-agonist in patients with severe exacerbations (triage categories 1 and 2) or when response to beta-agonists alone is poor. However, a systematic review213 that included four randomised controlled trials did not demonstrate any additional benefit on FEV1 of the combination of an anticholinergic compared with beta2-agonist alone. [evidence level A] Nebulised medications can also be administered through the assisted ventilation circuit if required. 166

The mode of delivery should be changed to a metered dose inhaler with a spacer device or a dry powder inhaler within 24 hours of the initial dose of nebulised bronchodilator, unless the patient remains severely ill. 167,168

The use of methylxanthines (oral theophylline and IV aminophylline) in the management of acute exacerbations of COPD has diminished because of their potential for toxicity. 169-173 A systematic review of four Randomised Controlled Trials found a transient increase of 101ml in FEV1 after three days and a 4-6 fold increased risk of nausea and vomiting [evidence level A]. The routine use of aminophylline is not recommended for non-acidotic acute exacerbations236 [evidence level B].

Exacerbations with clinical signs of infection (increased volume and change in colour of sputum and/or fever, leucocytosis) benefit from antibiotic therapy 138,139,174-176 [evidence level B]

Bacterial infection may have either a primary or secondary role in about 50% of exacerbations of COPD. Haemophilus influenzae, Streptococcus pneumoniae and Moraxella catarrhalis are most commonly involved. 152,154,159 Mycoplasma pneumoniae and Chlamydia pneumoniae are seen relatively frequently. 152,158 As lung function deteriorates (FEV1 < 35%), Pseudomonas aeruginosa and Staphylococcus aureus are often encountered. 152,154,160

A meta-analysis174 examining the use of oral antibiotics in patients with exacerbations of COPD showed a small but significant clinical and symptomatic benefit. The greatest improvement was seen in patients who had been hospitalised rather than ambulatory.

Therapeutic guidelines: antibiotic177 recommend the use of oral agents such as doxycycline or amoxycillin (alternatively, erythromycin or roxithromycin). If patients do not respond, or if resistant organisms are suspected, amoxycillin–clavulanate should be prescribed. If pneumonia, pseudomonas or staphylococci is suspected, appropriate antibiotics should be used.

Typically, a course of treatment should be over seven to 10 days. A response is usually seen within three to five days, and a change of antibiotic should be considered if the response is unsatisfactory. If parenteral administration was commenced, oral treatment should be substituted within 72 hours.

Radiologically proven pneumonia in patients with COPD, especially in those who have been frequently hospitalised, may not be restricted to the above organisms. Gram-negative organisms, Legionella spp. and even anaerobic organisms may be responsible. Initial empiric antibiotic therapy should be tailored according to clinical and radiographic criteria.

Systemic glucocorticoids reduce the severity of and shorten recovery from acute exacerbations178-180 [evidence level A]

A recent randomised controlled trial of systemic glucocorticoids for acute exacerbations of COPD showed a moderate improvement in clinical outcomes. 179 Maximum improvement was gained within two weeks of therapy, and prolonging the course of treatment thereafter did not result in further benefit. An important side effect was hyperglycaemia, often sufficiently severe to warrant treatment. Blood glucose levels should be monitored. Oral or parenteral glucocorticoids are recommended for treating acute exacerbations of COPD [evidence level A]. The optimal dose has not been established, but 30–50 mg prednisolone daily is sufficient for most patients. If intravenous therapy was commenced, this should be changed to oral therapy within 48 hours. An updated systematic review of systemic corticosteroids for acute exacerbations showed that it would have been necessary to treat nine patients (95% CI 6 to 14) with systemic corticosteroids to avoid one
treatment failure in this time period. Overall, one extra adverse effect occurred for every six people treated (95% CI 4 to 10).

The continued use of inhaled corticosteroids and the administration technique should be reviewed. At discharge, therapy with oral prednisolone (25–37.5 mg daily) may be continued but the optimal duration is unknown. Tapering of glucocorticoid therapy is not necessary after short-term administration. However, patients who have taken glucocorticoids for more than three consecutive weeks may have adrenal suppression, and their glucocorticoid therapy should not be ceased abruptly.

Patients on long-term oral steroid therapy (≥7.5 mg prednisolone daily for more than 6 months) are at risk of developing osteoporosis. Prevention and treatment of steroid-induced osteoporosis should be considered.

Refer appropriately
The risk of death from exacerbations of COPD increases with acute carbon dioxide retention (respiratory acidosis), the presence of significant comorbid conditions (eg, ischaemic heart disease) and complications (eg, pneumonia and empyema). Depending on the nature and severity of the exacerbation, the patient may require urgent specialist review, hospital assessment or admission to a high-dependency or intensive care facility for ventilatory support and appropriate monitoring (see Box 13 and Box 14).

| Box 13 Indications for hospitalisation of patients with chronic obstructive pulmonary disease |
| Marked increase in intensity of symptoms |
| Patient has acute exacerbation characterised by increased dyspnoea, cough or sputum production, plus one or more of the following: |
| ▪ Inadequate response to ambulatory management |
| ▪ Inability to walk between rooms when previously mobile |
| ▪ Inability to eat or sleep because of dyspnoea |
| ▪ Cannot manage at home even with home-care resources |
| ▪ High risk comorbidity condition — pulmonary (eg, pneumonia) or non-pulmonary |
| ▪ Altered mental status suggestive of hypercapnia |
| ▪ Worsening hypoxaemia or cor pulmonale |
| ▪ Newly occurring arrhythmia |

| Box 14: Indications for increased respiratory support or intensive care unit admission |
| ▪ Severe dyspnoea that responds inadequately to initial emergency therapy |
| ▪ Confusion, lethargy or evidence of hypoventilation |
| ▪ Persistent or worsening hypoxaemia despite supplemental oxygen, worsening hypercapnia (PaCO₂ > 70 mmHg), or severe or worsening respiratory acidosis (blood pH < 7.3) |

Assisted mechanical ventilation is required.

Controlled oxygen delivery
Controlled oxygen delivery (28%, or 0.5–2.0 L/min) is indicated for hypoxaemia [evidence level C]

Correction of hypoxaemia to achieve a PaO₂ of at least 55 mmHg (7.3 kPa) and an oxygen saturation of 88%–92% is the immediate priority. Where there is evidence of acute respiratory acidosis (or a rise in PaO₂), together with signs of increasing respiratory fatigue and/or obtunded conscious state, assisted ventilation should be considered. Early non-invasive positive pressure ventilation (NIPPV) may reduce the need for endotracheal intubation (see below for more detail).

Administering oxygen at an inspired oxygen concentration (fraction of inspired oxygen; FiO₂) of 24%–28% by means of a venturi mask is usually sufficient to improve oxygenation in most patients. Nasal cannulas,
although more comfortable, deliver a variable concentration of oxygen, but a flow of 0.5–2.0 L per minute is usually sufficient. Gas flow provided through Hudson-type masks is inadequate when patients are tachypnoeic, so these should not be used. Careful monitoring with oximetry and, where hypercapnia is a potential concern, arterial blood gas measurement is required. There is no benefit in trying to obtain SpO₂ levels over 92%.

High flow oxygen should be avoided, as it is rarely necessary and may lead to hypoventilation and worsening respiratory acidosis. Patients should be weaned off supplementary oxygen as soon as possible, with none for 24–48 hours before discharge, unless home oxygen is prescribed.

Non-invasive positive pressure ventilation

Non-invasive positive pressure ventilation is effective for acute hypercapnic ventilatory failure [evidence level A]

Ventilatory support with intermittent positive pressure ventilation (IPPV) should be considered in patients with rising PaCO₂ levels who are unable to ventilate adequately (ie, acute or acute-on-chronic respiratory acidosis). This can be achieved non-invasively (by means of a face mask, NIPPV) or invasively through an endotracheal tube.

NIPPV is an effective and safe means of treatment of ventilatory failure. Its use allows preservation of cough, physiological air warming and humidification, and normal swallowing, feeding and speech. Early intervention with NIPPV is suggested when the respiratory rate is less than 30 per minute and blood pH is less than 7.35. An improvement in respiratory rate and pH usually occurs within one hour of starting NIPPV. Failure to respond or further deterioration would indicate a need to consider intensive care unit admission (Box 14).

Applying non-invasive ventilation in addition to conventional therapy reduces mortality (Relative Risk 0.5), and the need for intubation (RR 0.4) and its potential complications. NIPPV results in more rapid improvements in respiratory rate, dyspnoea score and blood gas abnormalities than conventional therapy alone. Some studies have also shown an improvement in survival and a reduced length of stay in hospital (Weighted Mean Difference 3.24 days).

Invasive ventilation (intubation)

NIPPV is contraindicated in patients who are unable to protect their airways, are not spontaneously breathing or who have severe facial injury or burns. Relative contraindications (situations where NIPPV may be less effective) include life-threatening refractory hypoxaemia (PaO₂< 60 mmHg, or 8 kPa on 100% inspired oxygen), bronchiectasis with copious secretions, severe pneumonia, and haemodynamic instability. These patients may require intubation. Patients who need mechanical ventilation have an inpatient mortality of 17%–30%.

Weaning from invasive ventilation can be facilitated by the use of non-invasive positive pressure ventilation with outcomes which resulted in decreased mortality (RR 0.41) and reduced hospital length of stay (WMD 7.33 days)

The patient's wishes regarding intubation and resuscitation should ideally be documented before an admission for management of respiratory failure. Patients who require ventilatory support during exacerbations of COPD may have impaired control of breathing or apnoeas during sleep, even when well. Therefore, performing a diagnostic sleep study when the patient's condition is stable should be considered. Narcotic analgesics and sedatives should be avoided, as these may worsen ventilatory failure and hasten the need for positive pressure ventilation.

Clearance of secretions

Patients who regularly expectorate or those with tenacious sputum may benefit from forced expiratory techniques. If patients produce more than 25 mL sputum per day, or if mucus plugging with lobar atelectasis is present, physiotherapy incorporating the use of postural drainage and associated techniques such as percussion and vibration may help.

Monitor and review

The aim is to relieve hypoxaemia and obtain improvement in clinical signs and symptoms.

- **Clinical examination:** Reduction in wheeze, accessory muscle use, respiratory rate, distress.
- Gas exchange: Arterial blood gas levels and/or pulse oximetry levels should be monitored until the patient's condition is stable (SpO₂ 88%–92%).
- **Respiratory function testing**: FEV\(_1\) should be recorded in all patients after recovery from an acute exacerbation.

- **Discharge planning**: Discharge planning should be commenced within 24–48 hours of admission.

**Discharge planning**

Involving the patient's general practitioner in a case conference and developing a care plan may facilitate early discharge\(^{147-149,163}\) [evidence level C]

Discharge planning involves the patient, external lay and professional carers, the multidisciplinary hospital and community team and the patient's regular GP. It should commence on admission and be documented within 24–48 hours (See Box 15). Appropriate patient education and attention to preventive management are likely to reduce the frequency of further acute exacerbations. Assessment of social supports and domestic arrangements are critical in discharge planning.

A discharge pack, which includes general information about COPD, advice on medication use and written instructions on use of inhalation and oxygen devices, if appropriate, as well as a plan for management of worsening symptoms, should be provided. The GP (and respiratory outreach program, if available) should be notified during the patient's admission. A case conference involving the multidisciplinary team and GP may assist successful transition to the community. Medicare Benefits Schedule Enhanced Primary Care item numbers may be claimed for "participation in a case conference" and "contribution to a care plan" (see Section D).

Before discharge, referral to a comprehensive pulmonary rehabilitation program should be considered.

<table>
<thead>
<tr>
<th>Box 15: Criteria for discharge</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Suggested criteria for a patient's readiness for discharge include:</strong></td>
</tr>
<tr>
<td>- The patient should be in a clinically stable condition and have had no parenteral therapy for 24 hours</td>
</tr>
<tr>
<td>- Inhaled bronchodilators are required less than four-hourly</td>
</tr>
<tr>
<td>- Oxygen delivery has ceased for 24 hours (unless home oxygen is indicated)</td>
</tr>
<tr>
<td>- If previously able, the patient is ambulating safely and independently, and performing activities of daily living</td>
</tr>
<tr>
<td>- The patient is able to eat and sleep without significant episodes of dyspnoea</td>
</tr>
<tr>
<td>- The patient or caregiver understands and is able to administer medications</td>
</tr>
</tbody>
</table>

Follow-up and home care arrangements (eg, home oxygen, home-care, Meals on Wheels, community nurse, allied health, GP, specialist) have been completed

**Support after discharge**

Follow-up at home after discharge from hospital may extend the continuum-of-care process begun within the acute environment, although evidence supporting benefit from this practice is still being evaluated. Telephone follow-up may be a way of systematically extending support to patients and increasing their coping strategies at home, but the outcomes of this intervention have not been studied systematically.

**Clinical review and follow-up**

There are no randomised clinical trials that have addressed the best method for follow-up.\(^{197}\) It is recommended that the first review after a hospital admission should be by the GP and within seven days of discharge (Box 16). A decision about the requirement for specialist review should be made at the time of discharge. Follow-up care allows further discussion of self-management plans and future monitoring.\(^{197}\)
**Box 16: Follow-up – initial and subsequent**

- Assessment of the patient’s coping ability and strategies
- Measurement of FEV<sub>1</sub> and performance status
- Reassessment of medication adherence and techniques with inhalation devices
- Review of vaccination status (influenza and pneumococcal)
- Assessment for long-term oxygen therapy (may require reference to specialist facility)
- Consideration of referral for pulmonary rehabilitation
- Assessment of risk of osteoporosis and management
- Smoking cessation — counsel and/or refer

Assess nutritional status (frequent small meals reduce dyspnoea)
### Appendix 1

**Box 17: Use and doses of long-term inhaled bronchodilator and glucocorticoids determined in response trials**

<table>
<thead>
<tr>
<th>Response</th>
<th>Drug</th>
<th>Dose (mcg)</th>
<th>Frequency</th>
<th>Delivery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improved airway function</td>
<td>beta-agonist</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Improved exercise capacity</td>
<td>Salbutamol</td>
<td>200mcg</td>
<td>4–6-hourly</td>
<td>MDI/spacer</td>
</tr>
<tr>
<td>Reduced breathlessness</td>
<td>Terbutaline</td>
<td>500 mcg</td>
<td>6–8-hourly</td>
<td>DPI</td>
</tr>
<tr>
<td>Improved quality of life</td>
<td>Salmeterol</td>
<td>50 mcg</td>
<td>12-hourly</td>
<td>MDI/DPI</td>
</tr>
<tr>
<td></td>
<td>Formoterol</td>
<td>12 mcg</td>
<td>12-hourly</td>
<td>MDI/DPI</td>
</tr>
<tr>
<td>Anticholinergic</td>
<td>Ipratropium</td>
<td>40-80 mcg</td>
<td>6–8-hourly</td>
<td>MDI/spacer</td>
</tr>
<tr>
<td></td>
<td>Tiotropium</td>
<td>18mcg</td>
<td>24-hourly</td>
<td>DPI</td>
</tr>
<tr>
<td><strong>Glucocorticoid</strong></td>
<td>Beclomethasone</td>
<td>400-800 mcg/day</td>
<td>-</td>
<td>MDI/spacer</td>
</tr>
<tr>
<td>(small particle)</td>
<td>Budesonide</td>
<td>800-1600 mcg/day</td>
<td>-</td>
<td>DPI</td>
</tr>
<tr>
<td></td>
<td>Fluticasone</td>
<td>500-1000 mcg/day</td>
<td>-</td>
<td>MDI/DPI</td>
</tr>
</tbody>
</table>

MDI = metered dose inhaler. DPI = dry powder inhaler.
## Appendix 2

**Box 18: Explanation of inhaler devices***

<table>
<thead>
<tr>
<th>Delivery system</th>
<th>Available products</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metered dose inhaler (MDI)</td>
<td>Qvar (beclomethasone 50 mcg, 100 mcg); Flixotide (fluticasone 50 mcg, 125 mcg, 250 mcg); Atrovent (ipratropium bromide 20 mcg); Atrovent Forte (ipratropium bromide 40 mcg); Ventolin, Asmol, Airomir, Epaq (salbutamol 100 mcg); Serevent (salmeterol 25 mcg)</td>
<td>• MDIs should be used with a spacer device, as some people have difficulty coordinating the release of medication with inhalation.</td>
</tr>
</tbody>
</table>
| Spacers | Aerochamber Breath-A-Tech Fisonair Nebuhaler Volumatic | • The spacer chamber acts as a reservoir for the aerosol released from an MDI. The patient can then inhale from this chamber without having to coordinate the release of the medication.  
• Use of spacers with inhaled corticosteroids reduces side effects of oral candidiasis and hoarseness, as well as optimising medication delivery.  
• MDI with spacer is as effective as a nebuliser if an equivalent dose is taken; 10–15 puffs of 100 mcg salbutamol MDI via a spacer is therapeutically equivalent to a 5 mg salbutamol nebul.  
• Spacers are cheap, portable, easily cleaned and maintained, do not require electricity and are simple and quick to use.  
• A small volume spacer is preferable when the vital capacity is less than 1.5 L. |
| Autohaler | Airomir (salbutamol 100 mcg); Qvar (beclomethasone 50 mcg, 100 mcg); Respocort (beclomethasone 50 mcg, 100 mcg) | • Breath-activated MDI containing 200 doses of medication.  
• Use can improve lung deposition in patients with poor MDI inhaler technique. As the patient starts a slow, deep breath through the mouthpiece, a flap valve is triggered and the dose automatically releases. |
(cont.)

<table>
<thead>
<tr>
<th>Delivery system</th>
<th>Available products</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dry powder inhalers (DPI)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| **Accuhaler**    | Serevent (salmeterol 50 mcg); Flixotide (fluticasone 100 mcg, 250 mcg, 500 mcg); Seretide (salmeterol 50 mcg and fluticasone 100 mcg, 250 mcg, 500 mcg) | • Breath-activated multi-dose DPI containing 60 individually sealed doses. A dose counter shows the number of doses remaining. It gives accurate and consistent drug delivery over a range of inspiratory flow rates (30–120 L/minute).  
• Lactose powder is combined with the active medication for patients to taste and reassure them that they have inhaled a dose. |
| **Aerolizer**    | Foradile (formoterol 12 mcg) |                                                                                                                                             |
| **Turbuhaler**   | Bricanyl (terbutaline 500 mcg); Pulmicort (budesonide 100 mcg, 200 mcg, 400 mcg); Oxis (formoterol 6 mcg, 12 mcg); Symbicort (formoterol 6 mcg and budesonide 200 mcg) | • Breath-activated multi-dose inhaler, containing 60 (Oxis, Symbicort) or 200 (Pulmicort, Bricanyl) doses; ensures delivery without the need to coordinate inspiration with drug release.  
• Dose delivery is halved if the patient cannot produce inspiratory flow above 30 L/min. Very few patients with COPD cannot produce a rate of > 60 L/min.  
• Produces very fine powder, so patients often don’t taste anything.  
• Dose indicator shows when there are 20 doses remaining, and then when the inhaler is empty (it contains a drying agent that can be heard when the inhaler is shaken, which can be misinterpreted as available medication). |
<table>
<thead>
<tr>
<th>Delivery system</th>
<th>Available products</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>HandiHaler</td>
<td>Spiriva (tiotropium 18 mcg)</td>
<td>- Breath-activated dry powder inhaler. A capsule containing tiotropium is dropped into the HandiHaler, and pierced by pressing a button. The patient then inhales through the mouthpiece for effective drug delivery. Studies have shown that patients with a wide range of disease severity are able to generate sufficient inspiratory airflow (as low as 20 L/min) to evacuate the powder from the capsule.</td>
</tr>
<tr>
<td>Nebulisers</td>
<td>Most nebulisers are electric. Some ultrasonic nebulisers are battery operated — these models are not heavy duty, but are ideal for travelling. There are also 12-volt pumps that plug into a car cigarette lighter. Use of inhaled glucocorticoids requires a high-flow, heavy-duty pump.</td>
<td>- Glucocorticoid or ipratropium bromide aerosol should not be allowed to enter the eyes to avoid the risk of side effects such as glaucoma or urinary outlet obstruction. Patients should be advised to wipe their face dry after using the nebuliser to remove medication from the skin. - Ipratropium can be combined with beta-agonist, but not with glucocorticoid.</td>
</tr>
</tbody>
</table>
Appendix 3

**Initiating oxygen therapy**

- Before introducing oxygen therapy, ensure optimal treatment of the pulmonary disorder while monitoring improvement with objective tests such as FEV₁ and FVC. Treatment may include maximum therapy for airway obstruction, attention to nutrition and bodyweight, an exercise rehabilitation program, control of infection, and treatment of cor pulmonale.

- In patients selected for oxygen therapy, assess the adequacy of relief of hypoxaemia (PaO₂ > 60 mmHg, or 8 kPa; SpO₂ > 90%) and/or improvement in exercise capacity or nocturnal arterial oxygen saturation while using a practical oxygen delivery system.

**What the patient needs to know**

- Patients receiving oxygen therapy in the home, and their carers, should have the use clearly explained. That is, hours of use and flow rate, and any need to vary flow rates at given times. The equipment and its care, including how to obtain servicing or replacements, needs to be explained. The dangers of open flames (especially cigarettes, gas heaters and cookers) need to be emphasised.

- Flow should be set at the lowest rate needed to maintain a resting PaO₂ of 60 mmHg (8 kPa) or SpO₂ > 88%. For patients with COPD, 0.5–2.0 L/min is usually sufficient. Flow rate should be increased by 1 L/min during exercise.

- Humidifiers are generally not needed at oxygen flow rates below 4 L/min.

- Extrasoft nasal prongs are recommended for continuous oxygen use, but may become uncomfortable at flow rates over 2–3 L/min and in the long term. Facemasks may be preferred for at least some of the time, although there are dangers of rebreathing exhaled CO₂ at flow rates below 4 L/min.

- In some patients needing 24-hour oxygen therapy, transtracheal delivery systems may have advantages.

**Review**

- Reassess 4–8 weeks after starting continuous or nocturnal oxygen therapy, both clinically and by measurement of PaO₂ and PaCO₂, with and without supplementary oxygen. A decision can then be made as to whether the treatment has been properly applied and whether it should be continued or abandoned.

- Patients on intermittent oxygen therapy should also be reassessed periodically. The review can be undertaken by appropriately trained staff using a pulse oximeter to confirm hypoxaemia (SpO₂ < 88%) at rest or during daily activities. They should also check compliance with therapy and smoking status.

- Review at least annually, or more often according to the clinical situation.

**Dangers**

- Supplementary oxygen in patients with increased arterial PaCO₂ may depress ventilation, increase physiological dead space, and further increase arterial PaCO₂. This is suggested by the development of somnolence, headache and disorientation.

- In long-term oxygen therapy, the increase in arterial PaCO₂ is usually small and well tolerated. However, serious hypercapnia may occasionally develop, making continued oxygen therapy impractical. Risk appears greater during acute exacerbations of disease or if the flow of oxygen is increased inappropriately.

- Sedatives (particularly benzodiazepines), narcotics, alcohol and other drugs that impair the central regulation of breathing should not be used in patients with hypercapnia receiving oxygen therapy.

**Choosing the right method**

Domiciliary oxygen therapy can be delivered by three systems:

- **Cylinders:** These contain compressed oxygen gas and deliver 100% oxygen at the outlet. Portable lightweight cylinders are available. Electronic conservation devices trigger oxygen supply on demand, resulting in up to fourfold reduction in oxygen consumption. Reservoir-style conservers are a cost-effective alternative.
Oxygen concentrators: These extract the nitrogen from room air by means of molecular sieves, delivering 90%–95% oxygen at a flow rate of 2 L/min. The percentage falls to about 78% oxygen at a flow of 5 L/min, depending on the model. All units currently available in Australia are imported. A back-up standard D-size oxygen cylinder may be added in case of concentrator breakdown or power failure, but adds to the cost and is rarely necessary. Users may claim a rebate on their electricity account.

Liquid oxygen systems: These systems conserve space by storing oxygen in liquid form. The oxygen is delivered through coils, where it vaporises. Two tanks are needed: a large storage tank, which is filled by the supplier as required (eg, one unit has a 25 800 L gaseous capacity, equivalent to seven E-size cylinders), and a portable unit is filled from the larger tank for ambulatory use.

The prescription should always specify:

- the source of supplemental oxygen (gas or liquid);
- method of delivery;
- duration of use; and
- low rate at rest, during exercise and during sleep.

There is no significant difference in the quality of oxygen delivery among the above methods. However:

- Concentrators are cheaper than cylinders if use is equivalent to or more than three E-size cylinders per month.
- Concentrators can be wheeled around the home but are heavy (about 21–26 kg) and are difficult to move up stairs and in and out of cars.
- Concentrators cannot be used for nebulisation, as the pressure delivered is too low (35–63 kPa, compared with 140 kPa for nebuliser pumps).
- If the anticipated need is for longer than three years, it is cheaper to buy than to rent a unit. The units usually have a five-year guarantee. However, public funding is available for pensioners and Health Care Card holders, subject to means testing.

Appendix 4

Vaccination

NHMRC guidelines recommend pneumococcal vaccination for:

- Over 65s – free vaccination from 1st January 2005, aged 50 for indigenous patients;
- Chronic cardiovascular or pulmonary disease and those who smoke;
- Pneumovax 1 dose 0.5mL re-vaccination at 5 and 10 years for both indigenous and non-indigenous patients.
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