

The COPD-X Plan: Australian and New Zealand Guidelines for the management of Chronic Obstructive Pulmonary Disease 2007



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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.



The Australian Lung Foundation gratefully acknowledges the following sponsors who provide unconditional educational grants to fund the program.



This document should be cited as:

David K McKenzie, Michael Abramson, Alan J Crockett, Nicholas Glasgow, Sue Jenkins, Christine McDonald, Richard Wood-Baker, Peter A Frith. The COPD-X Plan: Australian and New Zealand Guidelines for the management of Chronic Obstructive Pulmonary Disease 2007.

Originally published as:

David K McKenzie, Peter A Frith, Jonathan G W Burdon and G Ian Town. The COPDX Plan: Australian and New Zealand Guidelines for the management of Chronic Obstructive Pulmonary Disease 2003. MJA 2003 178(6 Suppl 17 Mar): S1-S40

http://www.mja.com.au/public/issues/178_06_170303/tho10508_all.html

Clinical Practice Update

Michael J Abramson, Alan J Crockett, Peter A Frith and Christine F McDonald. COPDX: an update of guidelines for the management of chronic obstructive pulmonary disease with a review of recent evidence. MJA 2006; 184 (7): 342-345

http://www.mja.com.au/public/issues/184_07_030406/abr10742_fm.html

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
Summary of the COPD-X guidelines	11
C: Confirm diagnosis and assess severity.....	12
Aetiology and natural history	13
Diagnosis	15
History.....	15
Physical examination	15
Spirometry	16
Flow volume tests	17
Assessing the severity of COPD	17
Assessing acute response to bronchodilators.....	18
Confirm or exclude asthma.....	18
Specialist referral	19
Complex lung function tests.....	19
Exercise testing	19
Sleep studies	19
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
Trials of Therapy.....	21
O: Optimise function	21
Symptom relief.....	21
Inhaled bronchodilators.....	21
Long-acting bronchodilators.....	22
Theophyllines.....	23
Assessment of response and continuation of bronchodilator therapy.....	23
Short-course oral glucocorticoids.....	24
Combination inhaled glucocorticoid/long-acting bronchodilator therapy	25
Optimise inhaler technique	25

Surgery	25
Bullectomy	25
Lung volume reduction surgery.....	25
Lung transplantation	26
Identify and treat aggravating factors	26
Sleep apnoea, hypoventilation and hypoxaemia.....	26
Gastro-oesophageal reflux.....	26
Aspiration.....	26
Alcohol and sedatives	27
Hypoxaemia and pulmonary hypertension	27
Osteoporosis.....	28
Improve function	28
Pulmonary rehabilitation	28
Exercise training	29
Patient education / Self-management.....	29
Psychosocial support.....	29
Comprehensive integrated rehabilitation.....	30
Chest physiotherapy (Airway clearance techniques)	30
Weight management and nutrition	30
Opioids.....	31
P: Prevent deterioration	31
Risk factor reduction	31
Smoking cessation.....	31
Nicotine replacement therapy.....	32
Bupropion	33
Prevent smoking relapse.....	34
Prevent infection and exacerbation	34
Influenza vaccination	34
Pneumococcal vaccination	34
Haemophilus influenzae vaccination.....	34
Antibiotics	35
Anticholinergics.....	35
Glucocorticoids	35
Mucolytic agents	35
Regular review.....	36
Oxygen therapy	36
Fitness to fly.....	37
D: Develop support network and self-management plan	37
Pulmonary rehabilitation	38
Support team	38
General practitioner	38
Nurse/respiratory educator	39
Physiotherapist	39

Occupational therapist	39
Social worker	39
Clinical psychologist.....	39
Speech pathologist/therapist.....	39
Pharmacist.....	39
Dietitian.....	39
Non-medical care agencies	40
Multidisciplinary care plans.....	40
Self-management plans.....	40
Maintenance therapy	41
Exacerbations and crises.....	41
Treat anxiety and depression	41
Referral to a support group.....	41
End-of-life issues	42
X: Manage eXacerbations	43
Home management	43
COPD acute exacerbation plan	44
Initial assessment of severity	44
Optimise treatment	44
Refer appropriately	46
Controlled oxygen delivery.....	47
Non-invasive positive pressure ventilation	47
Invasive ventilation (intubation).....	47
Clearance of secretions	48
Monitor and review	48
Pulmonary rehabilitation	48
Discharge planning	48
Support after discharge.....	49
Clinical review and follow-up.....	49
Appendix 1	50
Appendix 2.....	51
Appendix 3.....	54
Initiating oxygen therapy	54
What the patient needs to know	54
Review.....	54
Dangers.....	54
Choosing the right method	55
Appendix 4.....	55
Vaccination	55
References	56
References reviewed but not cited	70

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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,¹ 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,² 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.³

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.⁴ 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,⁵ but differs from previous guidelines on COPD in that it draws from the recently published international Guideline for the Management of Obstructive Lung Disease⁶ 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
Xacerbations.

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.⁵ The Committee agreed to use the Global Initiative for Chronic Obstructive Lung Disease (GOLD) Workshop Report⁶ 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 were originally 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).⁶ The NHLBI scheme is shown in Box 1. For comparison, the National Health and Medical Research Council (NHMRC)⁵ levels of evidence are also shown, along with the equivalent NHLBI categories.

For this update, the COPD Evaluation Committee reclassified NHLBI level A as NHMRC level I and NHLBI level B as NHMRC level II evidence. All citations to NHLBI level C were individually reviewed and reclassified as NHMRC level II, III-2, III-3 or IV evidence. On closer examination, some references originally classified as level C were actually considered level D. As NHLBI level D is not recognised in the NHMRC classification, these levels were removed whilst the bibliographic citations were retained.

Box 1: Levels of evidence

A) National Heart, Lung, and Blood Institute (NHLBI) categories

NHLBI category	Sources of evidence	Definition
A	Randomised controlled trials (RCTs). Rich body of data.	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.
B	Randomised controlled trials (RCTs). Limited body of data.	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.
C	Non randomised trials. Observational studies.	Evidence is from outcomes of uncontrolled or non randomised trials or from observational studies.
D	Panel consensus Judgment.	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.

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

A	I	Evidence obtained from a systematic review of all relevant randomised controlled trials
B	II	Evidence obtained from at least one properly designed randomised controlled trial
C	III - 1	Evidence obtained from well-designed pseudorandomised controlled trials (alternate allocation or some other method)
C	III - 2	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
C	III - 3	Evidence obtained from comparative studies with historical control, two or more single arm studies, or interrupted time series without a parallel group
C	IV	Evidence obtained from case series, either post-test or pretest/ post-test

Summary of the COPD-X guidelines

C: Confirm diagnosis and assess severity	Evidence level
▪ Smoking is the most important risk factor for COPD	I
▪ Consider COPD in patients with other smoking-related diseases	I
▪ Consider COPD in all smokers and ex-smokers older than 35 years	II
▪ The diagnosis of COPD rests on the demonstration of airflow limitation which is not fully reversible	II
▪ If airflow limitation is fully or substantially reversible, the patient should be treated as for asthma	

O: Optimise function	Evidence level
▪ Inhaled bronchodilators provide symptom relief in patients with COPD and may increase exercise capacity	I
▪ Long-acting bronchodilators provide sustained relief of symptoms in moderate to severe COPD	I
▪ Long term use of systemic glucocorticoids is not recommended	I
▪ Inhaled glucocorticoids should be considered in patients with a documented response or those who have severe COPD with frequent exacerbations	II
▪ Identify and treat hypoxaemia and pulmonary hypertension	I
▪ Prevent or treat osteoporosis	I
▪ Pulmonary rehabilitation reduces dyspnoea, anxiety and depression, improves exercise capacity and quality of life and may reduce hospitalisation	I
▪ In selected patients, a surgical approach may be considered for symptom relief.	III-2

P: Prevent deterioration	Evidence level
▪ Smoking cessation reduces the rate of decline of lung function	I
▪ General practitioners and pharmacists can help smokers quit	I
▪ Treatment of nicotine dependence is effective and should be offered to smokers	I
▪ Pharmacotherapies double the success of quit attempts; behavioural techniques further increase the quit rate by up to 50%	I
▪ Influenza vaccination reduces the risk of exacerbations, hospitalisation and death	I
▪ Long-term oxygen therapy (> 15 h/day) prolongs life in hypoxaemic patients ($\text{PaO}_2 < 55 \text{ mmHg}$, or 7.3 kPa)	I
▪ Inhaled glucocorticoids are indicated for patients with a documented response or who have severe COPD with frequent exacerbations	I
▪ Mucolytics may reduce the frequency and duration of exacerbations	II
▪ Inhaled glucocorticoids are indicated for patients with a documented response or who have severe COPD with frequent exacerbations	I

D: Develop support network and self-management plan	Evidence level
<ul style="list-style-type: none"> ▪ Pulmonary rehabilitation increases patient/carer knowledge base, reduces carer strain and develops positive attitudes towards self-management and exercise 	I
<ul style="list-style-type: none"> ▪ COPD imposes handicaps which affect both patients and carers 	II
<ul style="list-style-type: none"> ▪ Multidisciplinary care plans and individual self-management plans may help to prevent or manage crises 	II
<ul style="list-style-type: none"> ▪ Enhancing quality of life and reducing handicap requires a support team 	
<ul style="list-style-type: none"> ▪ Patients and their family/friends should be actively involved in a therapeutic partnership with a range of professional disciplines 	
<ul style="list-style-type: none"> ▪ Patients should be encouraged to take appropriate responsibility for their own management 	

X: Manage eXacerbations	Evidence level
<ul style="list-style-type: none"> ▪ Inhaled bronchodilators are effective treatments for acute exacerbations 	I
<ul style="list-style-type: none"> ▪ Systemic glucocorticoids reduce the severity of and shorten recovery from acute exacerbations 	I
<ul style="list-style-type: none"> ▪ Non-invasive positive pressure ventilation is effective for acute hypercapnic ventilatory failure 	I
<ul style="list-style-type: none"> ▪ Exacerbations with clinical signs of infection (increased volume and change in colour of sputum and/or fever, leukocytosis) benefit from antibiotic therapy 	II
<ul style="list-style-type: none"> ▪ Multidisciplinary care may assist home management 	II
<ul style="list-style-type: none"> ▪ Early diagnosis and treatment may prevent admission 	III-2
<ul style="list-style-type: none"> ▪ <ul style="list-style-type: none"> • Controlled oxygen in a pre-hospital setting is indicated for hypoxaemia 	
<ul style="list-style-type: none"> ▪ Involving the patient's general practitioner in a case conference and developing a care plan may facilitate early discharge 	

C: Confirm diagnosis and assess severity

Smoking is the most important risk factor in the development of COPD^{7,8} [evidence level I]

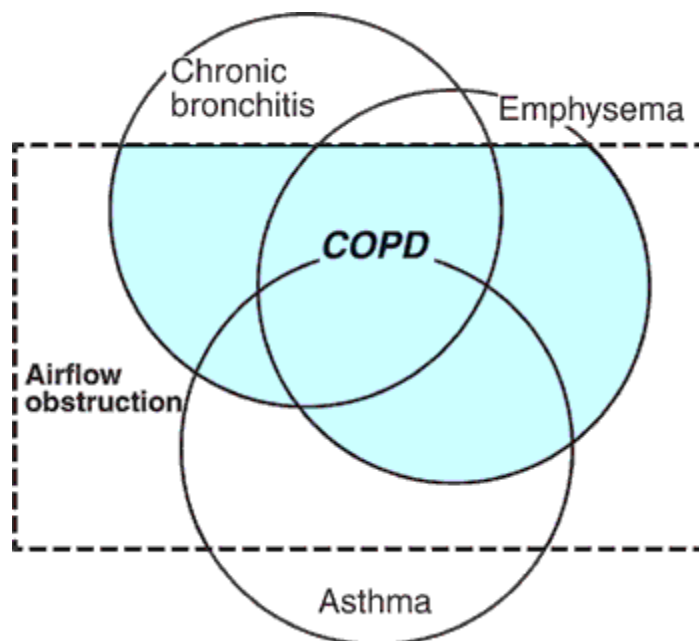
Chronic obstructive pulmonary disease (COPD) is characterised by airway inflammation and airflow limitation that is not fully reversible. It is a progressive, disabling disease with serious complications and exacerbations that are major burdens for healthcare systems.

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 narrowing and impaired gas exchange. The loss of lung elastic tissue in emphysema may result in 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.⁷ 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

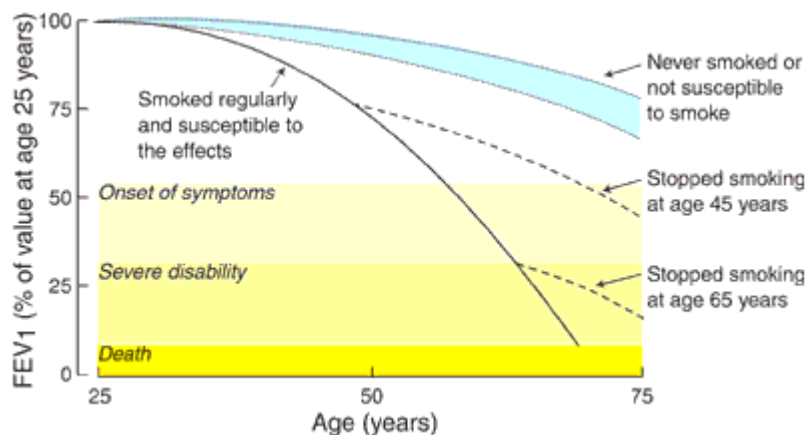
Smoking is the most important risk factor in the development of COPD^{7,8}. [evidence level I]

Cigarette smoking is the most important cause of COPD.^{7,8} 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.⁷ Around half of all smokers develop some airflow limitation, and 15%–20% will develop clinically significant disability.⁷ 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.⁷ 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.⁷

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 C and Peto R. The natural history of chronic airflow obstruction. *BMJ* 1977;1:1645-1648 and reproduced with permission from the BMJ Publishing Group) 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).

In addition to cigarette smoking, there are a number of other recognised risk factors for COPD²⁶⁴ (see Figure 3-1 adapted from GOLD 2006). COPD almost always arises from a gene environment interaction. The best characterised genetic predisposition is alpha1 antitrypsin deficiency, but multiple other genes each make a small contribution and further investigation is required. The risk of COPD is related to the total burden of inhaled particles²⁶⁴ and oxidative stress in the lung. Occupational dust exposure might be responsible for 20 – 30% of COPD. This has long been recognised in underground miners, but recently biological dust has also been identified as a risk factor, particularly in women.²⁶⁵ Fortunately the air quality in most Australian cities is relatively good and cooking with biomass fuels (wood, dung etc) is uncommon. Failure to achieve maximum lung function increases the risk of COPD in later life. The role of gender is uncertain. Nor is it known whether the increased risk among lower socioeconomic groups is due to greater exposure to pollution, poorer nutrition, more respiratory infection or other factors.²⁶⁴

Figure 3-1. Risk Factors for COPD²⁶⁴

- Genes
- Exposure to particles
- Tobacco smoke
- Occupational dusts, organic and inorganic
- Indoor air pollution from heating and cooking with bio-mass in poorly vented dwellings
- Outdoor air pollution
- Lung Growth and Development
- Oxidative stress
- Gender
- Age
- Respiratory infections
- Socioeconomic status
- Nutrition
- Comorbidities
- Asthma

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.^{11, 274}

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 years⁷ [evidence level II]

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 practice¹⁷ (see Box 4).

Box 4: Medical Research Council grading of functional limitation due to dyspnoea¹⁷

Grade	Symptom complex
1	"I only get breathless with strenuous exercise".
2	"I get short of breath when hurrying on the level or walking up a slight hill".
3	"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".
4	"I stop for breath after walking about 100 yards or after a few minutes on the level".
5	"I am too breathless to leave the house" or "I am breathless when dressing".

Physical examination

The sensitivity of physical examination for detecting mild to moderate COPD is poor.¹⁸ 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

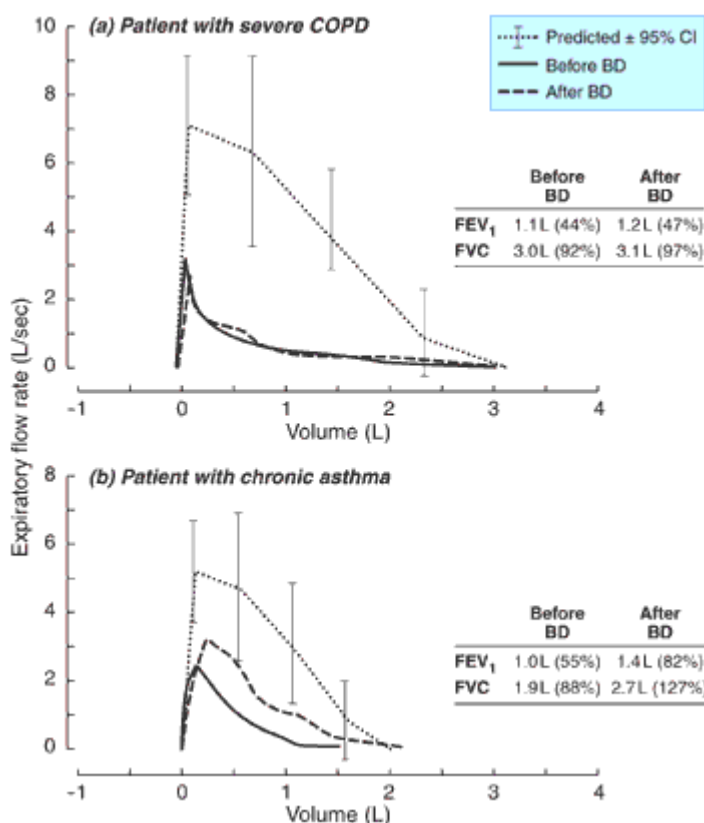
Spirometry

The diagnosis of COPD rests on the demonstration of airflow limitation which is not fully reversible²⁰ [evidence level II]

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 FEV₁ to forced vital capacity (FVC) is < 70% and the FEV₁ is < 80% of the predicted value. The ratio of FEV₁ 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 (FEV₁) was within the normal range (82% predicted). Absolute and per cent predicted values for FEV₁ and forced vital capacity (FVC) before and after BD are shown for each patient.

A recent detailed systematic review states that spirometry, in addition to clinical examination, improves the diagnostic accuracy of COPD compared to clinical examination alone²⁵⁸ (evidence level I). More studies are required to define any benefit from the use of spirometry for case finding in COPD, and to evaluate the effects of spirometric results on smoking cessation.

The spirometric tests require high levels of patient effort and cooperation, and there are important quality criteria that should be met in conducting spirometry (ATS/ERS Guidelines on lung function testing).

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 FEV₁ 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 FEV₁ is the variable most closely associated with prognosis.¹⁰ The grades of severity according to FEV₁ and the likely symptoms and complications are shown in Box 6. However, it should be noted that patients with an FEV₁ > 80% predicted, although within the normal range, may have airflow limitation (FEV₁/FVC ratio < 70%).

Box 6. Classification of severity of chronic obstructive pulmonary disease (COPD)⁶

Factor	COPD Severity		
	Mild	Moderate	Severe
Spirometry findings - postbronchodilator FEV ₁ %	60-80% predicted	40-59% predicted	<40% predicted
Functional assessment (Activities of daily living)	Few symptoms No effect on daily activities Breathless on moderate exertion	Increasing dyspnoea Breathless on the flat Increasing limitation of daily activities	Dyspnoea on minimal exertion Daily activities severely curtailed
Complications	No	Exclude complications; consider sleep apnoea if there is pulmonary hypertension	Severe hypoxaemia (PaO ₂ <60mm Hg or 8kPa) Hypercapnia (PaCO ₂ >45mm Hg or 6kPa) Pulmonary hypertension Heart Failure Polycythaemia
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.^{21, 266} 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

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, to be due to airway remodelling resulting from uncontrolled airway wall inflammation with release of cytokines and mediators.

Furthermore, asthma and COPD are both common conditions, and it must be expected that the two can coexist as least as often as the background prevalence of asthma in adults.

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

Circumstances possibly requiring specialist review	Role of respiratory specialist
1. Moderate or severe chronic obstructive pulmonary disease (COPD)	Confirm diagnosis and optimise therapy. Cease inappropriate or ineffective therapies. Assess side effects. Determine need for nebulised therapy. Assess complications.
2. Uncertain diagnosis (< 10 pack-year smoking history or < 40 years of age or rapid decline in FEV ₁)	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).
3. Recurrent infections, exacerbations	Exclude other conditions (eg, bronchiectasis, cystic fibrosis, immunological abnormality, aspiration).
4. Symptoms out of proportion to lung function impairment	Exclude complications of COPD or comorbidities (eg, pulmonary hypertension, cardiac disease). Consider sleep study.
5. Cor pulmonale	Confirm diagnosis and optimise treatment, including assessment for oxygen or other ventilatory support.
6. Suspect chronic hypoxaemia	Confirm chronic hypoxaemia or nocturnal hypoxaemia. Assess for ambulatory oxygen therapy.
7. Bullous lung disease or severe emphysema	Determine suitability for bullectomy or lung volume reduction surgery.
8. Severe disability or respiratory failure	Determine suitability for lung volume reduction surgery or lung transplantation or home ventilation.
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. Helical 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 or left heart failure are suspected.

Consider COPD in patients with other smoking-related diseases^{22, 267, 268, [evidence level I]}

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.

Trials of Therapy

The evidence supporting the utility of specific diagnostic tests in COPD is typically not of the same strength as that for specific therapies reviewed in subsequent sections. The evidence base for tests used in the diagnosis and monitoring of a number of respiratory diseases at one specialist referral clinic was reviewed by Borrill et al.²⁴⁴ They were unable to identify any evidence to support the use of peak flow charts to assess treatment with inhaled steroids in patients with pre-diagnosed COPD. Studies were found that did not support the diagnostic use of trials of therapy with inhaled or oral steroids in COPD. There was no evidence to support the diagnostic use of trials of therapy with short or long acting bronchodilators or oral theophyllines in COPD. However, it should be remembered that absence of evidence is not the same as evidence of absence of utility.

O: Optimise function

Summary	Evidence level
Inhaled bronchodilators provide symptom relief in patients with COPD and may increase exercise capacity	I
Long-acting bronchodilators provide sustained relief of symptoms in moderate to severe COPD	I
Long term use of systemic glucocorticoids is not recommended	I
Inhaled glucocorticoids should be considered in patients with a documented response or those who have severe COPD with frequent exacerbations	II
Identify and treat hypoxaemia and pulmonary hypertension	I
Prevent or treat osteoporosis	I
Pulmonary rehabilitation reduces dyspnoea, anxiety and depression, improves exercise capacity and quality of life and may reduce hospitalisation	I
In selected patients, a surgical approach may be considered for symptom relief.	III-2

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 capacity²³⁻³⁰ [evidence level I]

Regular short-acting beta-agonists improve lung function and daily breathlessness scores. A systematic review of randomised controlled trials²⁷³ found a significant increase in post-bronchodilator spirometry when compared to placebo; weighted mean difference = 140mls (95% CI 40 to 250) for FEV1 and 300mls (95% CI 20 to 580) for FVC. There were also improvements in post-bronchodilator morning and evening PEF: weighted mean difference = 29.17 l/min (95% CI 0.25 to 58.09) for morning and 36.75 l/min (95% CI 2.57 to 70.94) for evening measurements. The relative risk of dropping out of the study was 0.49 (95% CI 0.33 to 0.73), giving a number needed to treat of 5 (95% CI 4 to 10) to prevent one treatment failure. There was no significant benefit on functional capacity, measured by walking tests, or symptoms other than breathlessness, although one randomised controlled trial has found a significant improvement in six-minute walking distance and quality of life.²⁸ Short-acting beta-agonists are now usually prescribed for use as "rescue" medication, i.e. for relief of breathlessness, rather than for regular use.

The duration of action of short-acting anticholinergics is greater than short-acting beta-agonists. A systematic review of randomised controlled trials comparing ipratropium bromide alone, or in combination with short-acting beta-agonists, against short-acting beta-agonists alone found significant benefits for regimens containing ipratropium bromide.²⁶⁹ Ipratropium bromide improved pre-drug spirometry over short-acting beta-agonists alone, weighted mean difference = 30mls (95% CI 0 to 60) for FEV₁ and 70mls (95% CI 10 to 140) for FVC, although there was no significant difference between peak post-drug measurements. Ipratropium bromide improved quality of life, with a statistically significant improvement in all domains of the Chronic Respiratory Disease Questionnaire. These benefits occurred with fewer adverse drug effects, Peto odds ratio = 0.71 (95% CI 0.53 to 0.97), number needed to harm = 32 (95% CI 20 to 316). There was a lesser need to add or increase the dose of oral corticosteroids for participants receiving ipratropium bromide, Peto odds ratio = 0.52 (95% CI 0.37 – 0.74), with 15 (95% CI 12 – 28) people requiring treatment with ipratropium bromide to prevent one receiving additional oral corticosteroids.

For combination therapy with ipratropium bromide and short-acting beta-agonists, there was no significant difference in pre-drug spirometry compared to ipratropium bromide alone. There was a significant benefit for the combination for post-drug spirometry measurements; weighted mean difference = 70 mls (95% CI 50 to 90) for FEV₁ and 120mls (95% CI 80 to 160) for FVC. There was no significant difference between interventions for quality of life or adverse drug effects, but combination treatment decreased the need to add or increase oral corticosteroids compared to ipratropium bromide alone, Peto odds ratio = 0.69 (95% CI 0.50 to 0.94), number needed to treat = 20 (95% CI 12 to 108).

In summary, short-acting bronchodilators, either beta-agonists or ipratropium bromide, significantly increase lung function measurements in COPD. Ipratropium bromide has a significantly greater effect on lung function compared to beta-agonists, in addition to improving quality of life and decreasing need for oral corticosteroid treatment. These benefits occurred with a decreased risk of adverse drug effects.

Box 9: Initial treatment with short-acting bronchodilators*

Severity	FEV ₁	Suggested treatment
Mild COPD	60%–80%	Intermittent bronchodilator - salbutamol (200 mcg) or ipratropium bromide (40 mcg) as needed before exercise
Moderate COPD	40%–59%	Intermittent or regular bronchodilator — salbutamol (200–400 mcg four times daily) or ipratropium bromide (40 mcg four times daily). Combination bronchodilators may be considered
Severe COPD	< 40%	Regular combination bronchodilator — salbutamol (200–400 mcg four times daily) and ipratropium bromide (40–80 mcg four times daily)

* Modified from GOLD⁶ [evidence level D].
 FEV₁ = forced expiratory volume in one second.
 COPD = chronic obstructive pulmonary disease.

Long-acting bronchodilators

Long-acting beta-agonists (eg salmeterol, eformoterol) cause prolonged bronchodilatation, for at least 12 hours, and can thus be administered twice daily. A systematic review of randomised controlled trials²⁷⁰ found that compared to placebo, long-acting beta-agonists used for at least four weeks produce statistically significant benefits in lung function, quality of life, use of 'reliever' short-acting bronchodilators and acute exacerbations. This review compared different drugs and doses independently, the commonest being salmeterol 50 mcg daily which involved up to 3363 participants.

Table of outcomes for salmeterol 50 mcg/day vs placebo*

Outcome	WMD	95% CI
FEV ₁ =	55.13	38.16 to 72.09
Morning PEF =	15.81	11.96 to 19.67
Use of short-acting bronchodilator =	-0.78	-1.03 to -0.53
St George's Respiratory Questionnaire =	-2.17	-2.88 to -1.46
	Odds Ratio	
Exacerbations	0.80	0.67 to 0.95

*Results for all studies in COPD irrespective of baseline FEV₁ response to bronchodilator

The review did not find evidence that higher doses of salmeterol were more beneficial than 50mcg/day. Fewer studies of the effect of eformoterol were included and they were not combined in a meta-analysis, but some benefits similar to those of salmeterol were seen for a range of outcomes across a range of doses. Adverse drug effects were not reported.

The efficacy of long-acting beta-agonists compared to ipratropium bromide, alone or in combination, have also been combined in a systematic review.²⁶⁹ Comparisons of monotherapy found a greater increase in FEV₁, weighted mean difference = 60 mls (95% CI 0 to 110), and morning PEF, weighted mean difference = 10.96 l/min (95% CI 5.83 to 16.09) for salmeterol over ipratropium bromide. There were no significant differences between interventions for quality of life, functional capacity, symptoms, acute exacerbations or adverse events. Comparisons of the combination of ipratropium bromide and salmeterol with ipratropium bromide alone showed varying effects on lung function and symptoms, but a small, significant reduction in reliever use; weighted mean difference = -0.67 puffs/day (95% CI -1.11 to -0.23).

Tiotropium is a long-acting anticholinergic agent with duration of action of over 24 hours and is used once daily. Two systematic reviews of randomised controlled trials of its clinical effects have been published.^{271 272} These had differing inclusion criteria, particularly the duration of treatment, and consequently slightly different results. Compared to placebo, the reviews found tiotropium produced a significant increase in FEV₁ in the order of 130mls and improved quality of life, decreasing the mean St George's Respiratory Questionnaire by about 3 units. Tiotropium had a beneficial effect on acute exacerbations, odds ratio of 0.75, and hospitalisation, odds ratio 0.64. These effects came at the cost of an increased risk of adverse drug effects, particularly dry mouth which is 4-5 times more likely with tiotropium. Comparisons of tiotropium with ipratropium bromide or long-acting beta-agonists are limited by scanty data, producing conflicting results.

In summary, long acting bronchodilators produce significant improvements in lung function, symptoms and quality of life, as well as decrease exacerbations. Tiotropium increases the likelihood of developing hoarseness, while adverse effects associated with long-acting beta-agonists were not well reported.

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 effects^{45, 217} [evidence level I]. 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. Theophylline is effective in COPD but due to its potential toxicity, inhaled bronchodilators are preferred when available.²⁶⁴

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 (eg, 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 (eg, 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 I]

The long-term use of systemic glucocorticoids in COPD is not recommended⁵²⁻⁵⁶ [evidence level I]. 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.^{6,57} 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 exacerbations⁵⁷⁻⁶¹ [evidence level II]

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, as these patients probably have mixed asthma and COPD.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. Withdrawal of inhaled steroids may be associated with a decline of FEV1, increased symptoms and a greater rate of mild exacerbations²⁴⁸ [evidence level II]. However, it is not clear whether this applies to patients who have not responded to oral steroids.

Combination inhaled glucocorticoid/long-acting bronchodilator therapy

A systematic review of six randomised controlled trials involving 4,118 participants 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. There was a statistically significant reduction in exacerbation rate for budesonide and formoterol, or fluticasone and salmeterol when compared to placebo, rate ratio 0.76 (95% CI 0.68, 0.84). There was also a statistically significant reduction in exacerbation rate for combination therapy versus long-acting beta₂-agonists, rate ratio 0.85 (0.77, 0.95) but not for combination therapy compared to inhaled corticosteroids. There were conflicting results for Quality of Life and symptom scores for both treatment comparisons and combinations (budesonide and formoterol, or fluticasone and salmeterol). Possible explanations for these conflicts include study design and differential drop outs for interventions between 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 I]

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 cost of inhaler devices varies between products. As there are no differences in patient outcomes for the different devices, the cheapest device the patient can use adequately should be prescribed as first line treatment.²⁵² 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 relief⁶²⁻⁷² [evidence level III-2].

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. The National Emphysema Treatment Trial was a large randomised multicentre study which investigated the effectiveness and cost-benefit of this procedure.⁶⁸ A total of 1,218 patients with severe emphysema underwent pulmonary rehabilitation and were then randomised to LVRS or continued medical therapy. There was no overall survival advantage of surgery, but after 24 months there was significant improvement in exercise capacity in the surgical group. Among patients with predominantly upper lobe emphysema and impaired exercise capacity, mortality was significantly lower in the surgical than the medical group. However, high risk patients with diffuse emphysema and well preserved exercise capacity are poor candidates for surgery because of increased mortality and negligible functional gain²⁶⁰ [evidence level II].

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.^{71,72} The procedure is most successful when lung disease is the recipient's only medical problem and is usually offered to younger patients (eg, 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 awakenings 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.⁷³ 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 transcutaneous 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.⁷⁵ Patients with COPD who also have OSA have a higher prevalence of pulmonary hypertension and right ventricular failure than those without OSA.⁷⁵ 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, limiting food intake within 4 hours of bed-time, 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/pathologist and videofluoroscopy.

Treatment involves retraining in safe swallowing techniques, which may include:

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

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 hypertension⁷⁶⁻⁸⁵ [evidence level I]

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.⁶ The presence of hypercapnia is strongly associated with cor pulmonale.⁶

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; and
- nocturnal hypoxaemia due to hypoventilation or supine gas exchange problems.

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.^{262 263} Nitric oxide worsens V/Q mismatching and is therefore contraindicated in patients with COPD.^{86,87}

Osteoporosis

Prevent or treat osteoporosis⁸⁸ [evidence level I]

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 currently available in Australia and New Zealand 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 II]. Australian Guidelines on the prevention and treatment of osteoporosis, including glucocorticoid-induced osteoporosis have been published.²⁴⁰ Higher doses of inhaled glucocorticoids have been associated with biochemical markers of increased bone turnover, but data on BMD and fractures at these doses are not available²³¹ [evidence level I]. Those who have had long-term steroid therapy at lower doses and who have other risk factors should be screened for osteoporosis.

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.⁸⁸ Oral bisphosphonates, particularly risedronate, have been shown to be effective in preventing and treating bone loss in men and women taking corticosteroids.^{88,219} 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 I]^{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 hospitalisation⁸⁹⁻¹⁰⁷ [evidence level I]

An online toolkit is available to assist health professionals to implement a Pulmonary Rehabilitation Program. See www.pulmonaryrehab.com.au

Pulmonary rehabilitation is one of the most effective interventions in COPD⁸⁹⁻⁹³ 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.^{101,104-106} 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 II] 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 I]. Improvements in muscle strength and self-efficacy have also been reported.^{89-100,103} Exercise training also improves exercise tolerance in individuals with more mild disease.²⁴⁷

Inspiratory muscle training (IMT), performed in isolation using a threshold loading device or target-flow resistive device, has been demonstrated to increase inspiratory muscle strength and endurance and reduce dyspnea in patients with COPD^{255, 256} [evidence level I]. It remains unclear whether IMT combined with a program of whole-body exercise training confers additional benefits in dyspnea, exercise capacity or health-related quality of life in subjects with COPD. 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 encouraged.^{6,105}

Patient education / Self-management

There is limited evidence that education alone can improve self-management skills, mood and health-related quality of life¹⁰⁵⁻¹⁰⁷ [evidence level III-2]. Providing information and tools to enhance self-management in an interactive session is more effective than didactic teaching.^{105,108}

One multicentre randomised clinical trial provides evidence that a multicomponent, skill-oriented disease-specific self-management program "Living Well with COPD - www.livingwellwithcopd.com reduced hospitalisations for COPD exacerbations, all cause admissions, emergency department visits and unscheduled physician visits and improved health-related quality of life compared to a usual care group (Evidence level II). These benefits were seen at one and two years following the intervention.^{275 276} The patients in this study were recruited within 12 months of a hospital admission for a COPD exacerbation. The intervention involved weekly home visits by a health professional to deliver the self-management program over a 7-8 week period, an action plan for COPD exacerbations and advice regarding a home exercise program. The health professional acted as a case manager and provided advice and monthly phone calls. This program however failed to improve functional exercise capacity. The findings of this RCT were not replicated in another randomised controlled trial²⁷⁷ of a disease specific skill-oriented self-management program. The patients in the latter study²⁷⁷ had less severe disease.

A systematic review of self-management education for COPD²⁷⁸ concluded that the data available were insufficient for forming recommendations (Evidence level I).

Self-management programs may be especially beneficial for patients with reduced health status and a high frequency of exacerbations. Self-management programs that are combined with a supervised exercise training program are likely to be more effective in improving exercise tolerance and health status.

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 alone^{102,105} [evidence level III-2]. 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 I]. 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 100 groups throughout Australia can be contacted via LungNet.

Australia	New Zealand
LungNet	Asthma and Respiratory Foundation of New Zealand
toll-free phone number 1800 654 301	phone +64 4 499 4592
http://www.lungnet.com.au	http://www.asthmanz.co.nz

Chest physiotherapy (Airway clearance techniques)

The aims of airway clearance techniques in patients with COPD are to assist sputum removal and improve lung ventilation in an attempt to slow the decline in lung function and relieve symptoms. Chest x-ray/ CT findings and auscultation help determine the regions of the lung to be treated. Short-acting inhaled bronchodilators prior to treatment may assist with sputum clearance in some patients.

A variety of techniques are available including conventional chest physiotherapy (defined as any combination of gravity-assisted drainage, percussion, vibrations and directed coughing), the Active Cycle of Breathing Techniques (ACBT), Positive Expiratory Pressure (PEP) therapy, oscillating devices (Flutter[®], or Acapella[®]).

A systematic review of bronchopulmonary hygiene therapy in COPD and bronchiectasis showed a significant increase in sputum production and isotope clearance from the lung with no change in lung function or health status²⁷⁹ [Evidence level I]. However, the trials were all small and not generally of high quality. Further, the results could not be combined as the trials addressed different patient groups and outcomes.

Given the heterogeneity of lung disease in COPD it is unlikely that one technique is superior for all patients. The choice of technique depends on the patient's condition (e.g. extent of airflow limitation, severity of dyspnoea); sputum volume; the effects of the different techniques on lung volumes, expiratory flow and dynamic airway compression; cognitive status of the patient and acceptability of the technique to the patient especially where long-term treatment is required.²⁸⁰ Re-evaluation of the choice of airway clearance technique is necessary during an acute exacerbation of COPD when deterioration in lung function, increased sputum volume and increased work of breathing are likely to be present.

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 I]. 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 outcomes²³² [evidence level I]. 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 intractable dyspnoea²³⁵ [evidence level I]. 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

P: Prevent deterioration	Evidence level
Smoking cessation reduces the rate of decline of lung function	I
General practitioners and pharmacists can help smokers quit	I
Treatment of nicotine dependence is effective and should be offered to smokers	I
Pharmacotherapies double the success of quit attempts; behavioural techniques further increase the quit rate by up to 50%	I
Influenza vaccination reduces the risk of exacerbations, hospitalisation and death	I
Long-term oxygen therapy (> 15 h/day) prolongs life in hypoxaemic patients (PaO ₂ < 55 mmHg, or 7.3 kPa)	I
Inhaled glucocorticoids are indicated for patients with a documented response or who have severe COPD with frequent exacerbations	I
Mucolytics may reduce the frequency and duration of exacerbations	II
Inhaled glucocorticoids are indicated for patients with a documented response or who have severe COPD with frequent exacerbations	I

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 recommended.⁶ Influenza vaccination reduces the risk of exacerbations and death [evidence level I], while long term oxygen therapy reduces mortality [evidence level I].

Risk factor reduction

Smoking cessation

Smoking cessation reduces the rate of decline of lung function^{7, 11, 274} [evidence level I]

A comprehensive review of smoking cessation in patients with respiratory diseases has been published by the European Respiratory Society (www.ersnet.org/ers/lr/browse/viewPDF.aspx?id_attach=17030).²⁸³

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 available^{6,120} [evidence level I].

Smoking cessation (see Box 3) has been shown to halt the accelerated decline in lung function seen with COPD^{7, 11, 274} [evidence level I]. 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 I]

Brief counselling is effective [evidence level I] 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 move between various 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 counselling¹²⁴⁻¹³² [evidence level I]

Pharmacotherapies for nicotine dependence, including nicotine replacement and bupropion (sustained-release), are effective [evidence level I].¹²⁴⁻¹³² At least one of them should be added to counselling if necessary and in the absence of contraindications⁶ [evidence level I]. 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 I].^{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.¹²⁹⁻¹³² It is recommended as first-line pharmacotherapy for smoking cessation alongside NRT [evidence level I],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.¹²² The contradictions and adverse effects for bupropion hydrochloride are shown in Box 11.

Box 11. Advantages and disadvantages of pharmacological treatments for smoking cessation ^{6,121-132}		
Treatment	Advantages	Disadvantages
Nicotine patch	Easy to use, few compliance problems. Available over the counter.	Half of the users have skin reactions. Some sleep disturbances with the 24-hour patch.
Nicotine gum	2 mg strength available over the counter; good to use as a safety valve in times of stress. Provides oral substitute for smoking.	Need to spend time explaining correct use. Common adverse effects are mouth soreness, hiccups, dyspepsia and jaw ache. Effectiveness limited by under-use and excessive chewing. Patients can become dependent on the gum.
Nicotine lozenges	Easy to use; useful for denture wearers as alternative to gum. No special technique.	Hiccups
Nicotine inhaler	Mimics hand-to-mouth behaviour of cigarette smoking.	Low nicotine levels. Mild throat irritation and cough.
Bupropion hydrochloride	Non-nicotine; can be used with patch. Reduces urge to smoke and withdrawal symptoms.	Contraindicated in patients with history of seizures, significant head injury, drugs which lower seizure threshold and alcohol abuse. Adverse effects are mild insomnia and dry mouth, headache, rash and tremor. These are generally transient.

Prevent smoking relapse

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

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.⁶

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

Australia	New Zealand
131 848	0800 778 778
http://www.quitnow.info.au	http://www.quit.org.nz

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 I]

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 I]. 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,²⁸¹ 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 II].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 vaccine²¹⁶ 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 I] Furthermore, this is not currently available in Australia or New Zealand.

Antibiotics

Current evidence does not support long-term antibiotic use to prevent exacerbations in patients with COPD^{138,139} [evidence level I]. 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

Anticholinergics

A systematic review of 22 trials with 15,276 participants found that anticholinergic use significantly reduced severe exacerbations (pooled RR 0.67, 95% CI 0.53 to 0.86) and respiratory deaths (RR 0.27, 95% CI 0.09 to 0.81) compared with placebo. It would be necessary to treat 278 patients with anticholinergic agents to prevent one death²⁵⁹ [evidence level I].

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 I]. A 2003 meta-analysis by Highland et al²²² 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 al²²³ 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 exacerbations⁵⁸⁻⁶¹ [evidence level II]

In patients with severe COPD, high-dose inhaled corticosteroids may reduce the rate of acute exacerbations²³⁸ [evidence level I] However, it has been suggested that the rate of exacerbations may not have been correctly analysed²⁴⁵ and a Cochrane Review is awaited.²⁴⁶ High-dose inhaled corticosteroids may slow the rate of decline of quality of life⁶⁰ [evidence level II]. A pooled analysis of individual patient data from 7 RCTs of inhaled steroids suggested that all cause mortality was reduced by 25% compared to placebo²⁵³ [evidence level I]. However because death is relatively uncommon in clinical trials, 94 patients with COPD would need to be treated (NNT) with inhaled steroids to prevent one death. Results from a large randomised controlled trial powered to detect significance of changes in mortality over three years are awaited. Long term risks require further study. Cessation of therapy is recommended if no benefit is seen, although caution is recommended, given the observations that abrupt ICS withdrawal may be associated with increased symptoms or exacerbation.²⁴⁸. Detailed discussion appears in section O and section X.

Mucolytic agents

Mucolytics may reduce the frequency and duration of exacerbations¹⁴⁰ [evidence level I]

These drugs (eg, bromhexine, N-acetylcysteine, ambroxol, potassium iodide and glycerol guaiacolate) have multiple potential actions in COPD. These include decreasing the viscosity of sputum, or as antioxidant, antiinflammatory, or antibacterial agents.

A Cochrane Review concluded that, in patients with COPD or chronic bronchitis who have a higher than average rate of exacerbations, chronic treatment with oral mucolytic agents was associated with a small, but significant, reduction in acute exacerbations and total number of days of disability.¹⁴⁰ However, the trials in the review are not consistent in this finding. A recent large RCT of N-acetylcysteine at 600 mg/day 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 steroids²⁴¹ [evidence level II].

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 There is at present no evidence to support this hope.

Oxygen therapy

Long-term oxygen therapy (more than 15 h/day) prolongs life in hypoxaemic patients (PaO₂ < 55 mmHg, or 7.3 kPa)^{12,13,80-82,141-143} [evidence level I]

Long term oxygen therapy reduces mortality in COPD.^{12,13,80-82,141-143} It may also have a beneficial impact on haemodynamics, haematological status, exercise capacity, lung mechanics and mental state.^{80,82,143}

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 I]. 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%)^{141,142}. Continuous oxygen therapy is of most benefit for patients with increased arterial PaCO₂ (> 45 mmHg, or 6 kPa).¹³

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.¹⁴⁴ However, use of intermittent oxygen therapy may be considered for:

- People who experience oxygen desaturation on exertion.¹⁴⁴ A Cochrane review of 31 studies found that ambulatory oxygen was efficacious in single assessment studies when comparing an exercise test performed breathing oxygen or air in patients with moderate to severe COPD. Benefits were shown in endurance exercise capacity, dyspnoea at isotime and oxygen saturation.²⁴⁹ However, the minimum clinically important difference in these variables with oxygen therapy is unknown. Because of the heterogeneity of the studies, subgroup analyses were not possible to determine which patients were more likely to benefit. Benefit cannot be predicted by a resting test. Acute benefit may be established by comparing exercise endurance on a walking test (e.g. six minute walk test, incremental or endurance shuttle walk test or treadmill test) when breathing oxygen and when breathing room air. The oxygen system used in the assessment should be the same as the system the patient would use if oxygen were prescribed (e.g. trolley or shoulder bag to transport the cylinder). A stationary bicycle should not generally be used for the test as oxygen desaturation is significantly greater in COPD patients when walking as compared to cycling;^{225, 250, 251}
- 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%. 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.^{142,145}

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

<i>D: Develop support network and self-management plan</i>	<i>Evidence level</i>
Pulmonary rehabilitation increases patient/carer knowledge base, reduces carer strain and develops positive attitudes towards self-management and exercise	I
COPD imposes handicaps which affect both patients and carers	II
Multidisciplinary care plans and individual self-management plans may help to prevent or manage crises	II
Enhancing quality of life and reducing handicap requires a support team	
Patients and their family/friends should be actively involved in a therapeutic partnership with a range of professional disciplines	
Patients should be encouraged to take appropriate responsibility for their own management	

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

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.² 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.

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, though more evidence is required.

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^{89-108,111-116,141,142} [evidence level I]

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 team¹⁴²

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. Since relapse to smoking is common, GPs should make enquiries about smoking status routinely at each visit. There are several smoking cessation programs that have been developed for use in general practice (outlined in the RACGP "Green Book"¹⁴⁶). 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 disciplines^{89,90,92,105-108} [evidence level II]

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 for those with severe disease 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 This is particularly important where multiple comorbid conditions require treatment with multiple medications that have potential interactions, or when confusion exists about timing of medication administration:

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 crises¹⁰⁸ [evidence level III-2]

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 who take appropriate responsibility for their own management may have improved outcomes^{108,142,147-149} [evidence level III-2]

Patients with chronic illness who participate in self-management have better outcomes, including reduced healthcare costs, than those who do not.¹⁰⁸ 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.¹⁰⁵

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.¹⁴⁷⁻¹⁴⁹ Whether such treatment is cost-effective remains controversial.⁴⁷⁻¹⁴⁹

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 al²⁴³ 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. 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.¹⁰⁵ 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.¹⁰⁹ 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.¹⁰⁵ 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 II]^{224, 235}

X: Manage eXacerbations

X: Manage eXacerbations	Evidence level
Inhaled bronchodilators are effective treatments for acute exacerbations	I
Systemic glucocorticoids reduce the severity of and shorten recovery from acute exacerbations	I
Non-invasive positive pressure ventilation is effective for acute hypercapnic ventilatory failure	I
Exacerbations with clinical signs of infection (increased volume and change in colour of sputum and/or fever, leukocytosis) benefit from antibiotic therapy	II
Multidisciplinary care may assist home management	II
Early diagnosis and treatment may prevent admission	III-2
Controlled oxygen in a pre-hospital setting is indicated for hypoxaemia	
Involving the patient's general practitioner in a case conference and developing a care plan may facilitate early discharge	

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.¹⁴ 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 admission²⁸² [evidence level III-2]

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 II]

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 carers²⁴² [evidence level I]. 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 ($FEV_1 < 40\%$ 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 FEV_1 manoeuvre. An FEV_1 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 FEV_1 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 PaO_2 less than 60 mmHg (8 kPa) indicates respiratory failure, while a $PaCO_2$ 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 mg; terbutaline, 5 mg; 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% ($PaO_2 > 50$ 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 I]

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.^{165,166} 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 I] 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 vomiting²²⁶ [evidence level I]. The routine use of aminophylline is not recommended for non-acidotic acute exacerbations²³⁶ [evidence level II].

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

Bacterial infection may have either a primary or secondary role in about 50% of exacerbations of COPD.^{152,155,160,175} *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 systematic review of RCTs has confirmed the overall benefit of antibiotics given for at least five days in acute exacerbations (although most of the data is from the hospital setting).²⁶¹ Antibiotics for increased cough and sputum purulence decreased mortality, treatment failure and end of treatment sputum purulence at a cost of an increased risk of diarrhoea. A significant decrease in mortality (RR 0.23; 95% CI 0.10 to 0.52) was found, meaning 8 (95% CI 6 to 17) people needed antibiotic treatment to prevent one death. Treatment increased adverse events, most notably diarrhoea (RR 2.86; 95% CI 1.06 to 7.76), meaning antibiotic treatment in 20 (95% CI 10 to 100) people would result in one additional episode of diarrhoea. Unfortunately, these data are limited by participant numbers and setting, the majority of studies being performed in the hospital setting. Generalisability, especially to the primary care setting where most exacerbations are seen, is unclear.

Therapeutic guidelines: antibiotic¹⁷⁷ recommend the use of oral agents such as doxycycline or amoxicillin (alternatively, erythromycin or roxithromycin). If patients do not respond, or if resistant organisms are suspected, amoxicillin–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 I]

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 I]. 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,^{179,180} 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 ($\text{PaCO}_2 > 70$ 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 hypoxaemia¹⁸¹

Correction of hypoxaemia to achieve a PaO_2 of at least 55 mmHg (7.3 kPa) and an oxygen saturation of 88%–92% is the immediate priority.⁶ Where there is evidence of acute respiratory acidosis (or a rise in PaO_2), 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; FiO_2) 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 SpO_2 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^{85,182-196} [evidence level I]

Ventilatory support with intermittent positive pressure ventilation (IPPV) should be considered in patients with rising PaCO_2 levels who are unable to ventilate adequately (ie, acute or acute-on-chronic respiratory acidosis).¹⁸²⁻¹⁸⁶ This can be achieved non-invasively (by means of a face mask, NIPPV) or invasively through an endotracheal tube.^{187,188}

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.¹⁸²⁻¹⁸⁶ 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).^{85,182-196,229} [evidence level I].

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.¹⁸⁸ Relative contraindications (situations where NIPPV may be less effective) include life-threatening refractory hypoxaemia ($\text{PaO}_2 < 60$ 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%.¹⁸⁹

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)²³³

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.^{117,139}

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:** FEV₁ 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.

Pulmonary rehabilitation

A pulmonary rehabilitation program that includes supervised exercise training can be initiated immediately following an acute exacerbation. Such a program involves functional exercise capacity, health-related quality of life, and may reduce unplanned hospital admissions and mortality²⁵⁷ [evidence level I].

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 III-2]

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.

Box 15: Criteria for discharge

Suggested criteria for a patient's readiness for discharge include:

- The patient should be in a clinically stable condition and have had no parenteral therapy for 24 hours
- Inhaled bronchodilators are required less than four-hourly
- Oxygen delivery has ceased for 24 hours (unless home oxygen is indicated)
- If previously able, the patient is ambulating safely and independently, and performing activities of daily living
- The patient is able to eat and sleep without significant episodes of dyspnoea
- The patient or caregiver understands and is able to administer medications

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 nurse-led chronic disease management for people with COPD is absent²⁵⁴ [evidence level I]. 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 FEV₁ 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

Response	Drug	Dose (mcg)	Frequency	Delivery	
Improved airway function	beta-agonist				
	Salbutamol	200mcg	4–6-hourly	MDI/spacer	
Improved exercise capacity	Terbutaline	500 mcg	6–8-hourly	DPI	
	Salmeterol	50 mcg	12-hourly	MDI/DPI	
Reduced breathlessness	Formoterol	12 mcg	12-hourly	MDI/DPI	
	Anticholinergic				
Improved quality of life	Ipratropium	40-80 mcg	6–8-hourly	MDI/spacer	
	Tiotropium	18mcg	24-hourly	DPI	
	Glucocorticoid			Inhaled	
	Beclomethasone (small particle)	400-800 mcg/day	-	MDI/spacer	
	Budesonide	800-1600 mcg/day	-	DPI	
	Fluticasone	500-1000 mcg/day	-	MDI/DPI	
	Ciclesonide	80-320mcg/day		MDI – spacer not recommended	
	MDI = metered dose inhaler. DPI = dry powder inhaler.				

Appendix 2

Box 18: Explanation of inhaler devices*

Delivery system	Available products	Considerations
Metered dose inhaler (MDI)	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); Alvesco (ciclesonide 80mcg, 160mcg)	<ul style="list-style-type: none"> ▪ MDIs should be used with a spacer device, as some people have difficulty coordinating the release of medication with inhalation.
Spacers	Aerochamber Breath-A-Tech Fisonair Nebuhaler Volumatic	<ul style="list-style-type: none"> ▪ 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 nebule. ▪ 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); Respicort (beclomethasone 50 mcg, 100 mcg)	<ul style="list-style-type: none"> ▪ 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.)

Delivery system	Available products	Considerations
Dry powder inhalers (DPI)		
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)	<ul style="list-style-type: none"> ▪ 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)	<ul style="list-style-type: none"> ▪ Breath-activated single-dose powder inhaler that comes with a sheet of 60 capsules in push-out foil sheet. One capsule is loaded into the inhaler and pierced before inhaling. ▪ Gives consistent drug delivery over a range of inspiratory flow rates.
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)	<ul style="list-style-type: none"> ▪ 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).

(cont.)

Delivery system	Available products	Considerations
HandiHaler	Spiriva (tiotropium 18 mcg)	<ul style="list-style-type: none"> ▪ 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.
Nebulisers	<p>Most nebulisers are electric. Some ultrasonic nebulisers are battery operated — these models are not heavy duty, but are ideal for travelling.</p> <p>There are also 12-volt pumps that plug into a car cigarette lighter. Use of inhaled glucocorticoids requires a high-flow, heavy-duty pump.</p>	<ul style="list-style-type: none"> ▪ 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.

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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