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COPD management

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COPD management
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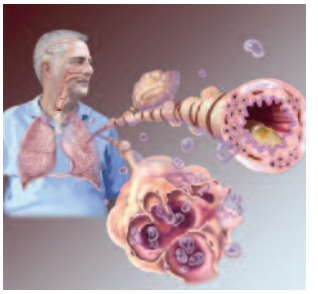

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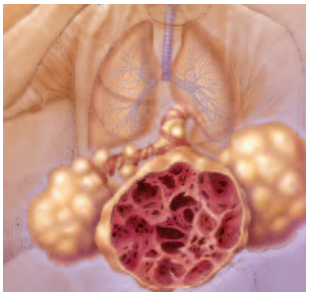

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PEER REVIEWED FEATURE ARTICLES

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PEER REVIEWED FEATURE
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COPD management

An integrated approach

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Chronic obstructive pulmonary disease (COPD) has major impacts on quality of life and mortality in a large number of people in Australia. The Australian COPD-X guidelines advocate a stepwise approach for early diagnosis and effective management of patients with COPD involving nonpharmacological and pharmacological interventions, which are outlined in this article. This is the first in a series of articles on COPD.

Key points

- **Chronic obstructive pulmonary disease (COPD) affects about two million people in Australia, if mild disease is included, and this prevalence is expected to more than double by 2050.**
- **COPD is a clinical diagnosis confirmed by spirometric evidence of airflow limitation that is not fully reversible.**
- **A multidimensional assessment approach, including spirometry and symptom assessment, has been advocated by international guidelines and expert clinicians for assessment of COPD severity.**
- **A stepwise approach to managing patients with COPD involves risk reduction (especially smoking cessation), promotion of physical activity, optimisation of weight and nutrition, prevention of infection by vaccinations, pulmonary rehabilitation, and use of inhaled medications to treat airflow obstruction and reduce exacerbations.**
- **Addressing comorbidities and psychosocial needs, and providing self-management education and action plans, can help patients to cope better with this chronic lung disease and reduce its impact.**

Chronic obstructive pulmonary disease (COPD) is described by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) as a 'common, preventable and treatable disease characterised by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. Exacerbations and comorbidities contribute to the overall severity in individual patients'.[1]

EPIDEMIOLOGY

COPD is a highly prevalent disease affecting about two million people in Australia if mild disease is included. This is expected to more than double by 2050 as a consequence of the interaction between lifetime cumulative exposures, the delay in development of tobacco-related disease, the impact of ageing and the improved outcomes in previously fatal diseases such as ischaemic heart disease and some cancers. Additionally, a proportion of patients with asthma develop significant fixed airway narrowing, which contributes to the burden of COPD. About half of patients with COPD have moderate-to-severe disease with symptoms that affect their daily lives.[2,3]

Recent prevalence estimates of COPD undertaken through standardised spirometry and questionnaires show that in over 3000 randomly tested men and women in Australia, the prevalence of COPD (defined as post-bronchodilator forced expiratory volume in

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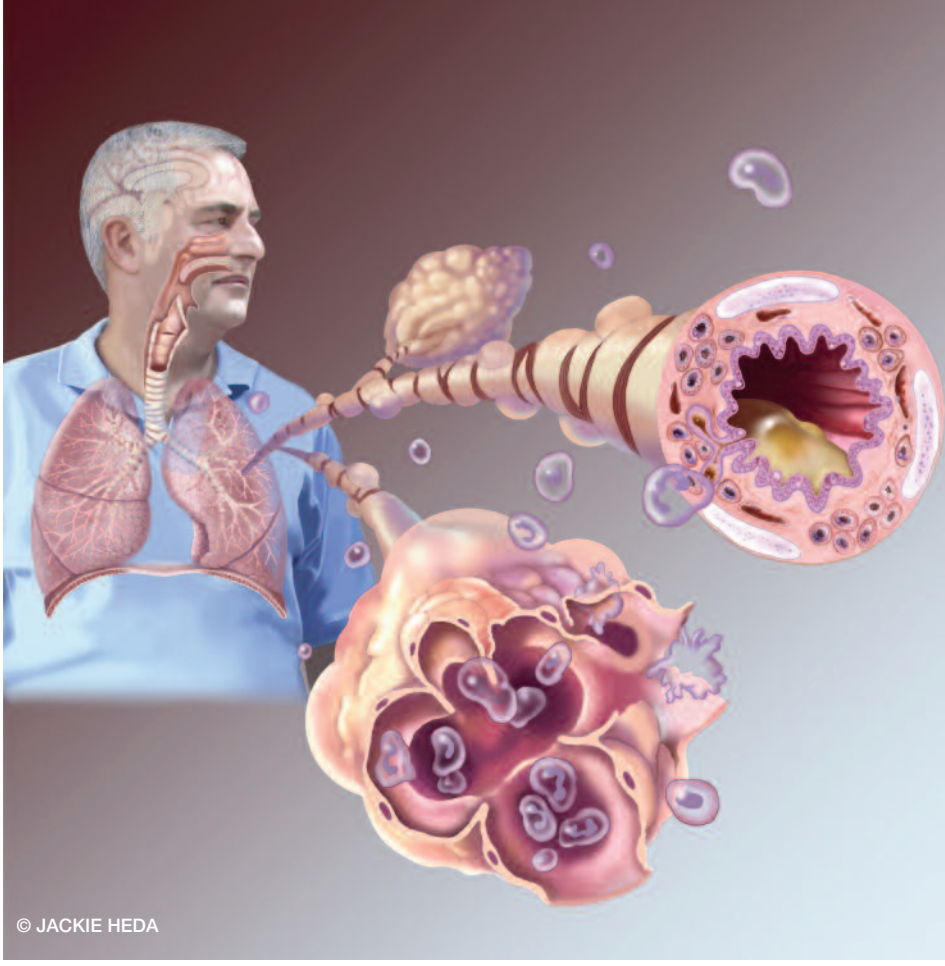

1 second [FEV_1]/forced vital capacity [FVC] ratio of less than 0.7 and FEV_1 less than 80% predicted) was 7.5% in people aged 40 years and over and 29% in those aged 75 years and over.[3] The prevalence of symptoms was significantly higher, but the many potential explanations for dyspnoea and cough make it essential to demonstrate the presence of airway obstruction and not rely on symptoms alone to diagnose COPD.

COPD costs the Australian community an estimated $8.8 billion annually in direct health costs and indirect costs such as lost productivity and lower employment.[4] COPD has major impacts on quality of life and social participation, even in people who may have infrequent exacerbations and relatively mild symptoms. It is the second leading cause of avoidable hospital admissions in Australia and is also a leading cause of death and disease burden after heart disease, stroke and cancer.

CAUSES

Cigarette smoking is the most important cause of COPD in most Western countries. Fortunately in Australia, smoking rates in the general population are now down to 15%, even though globally up to 45% of people with COPD smoke.[5] Many patients with COPD have been ex-smokers for over 10 years, but the interaction of previous exposures and age results in clinical expression of the disease later in life. Other dusts and fumes, particularly from biomass fuel burning, passive smoking, outdoor air pollution and occupational exposures, significantly increase the risk of developing COPD. In Australia, biological dusts and fumes in rural settings, inherited predisposition such as airway hyper-responsiveness and atopy, and environmental factors such as childhood respiratory infections, long-standing asthma and low socioeconomic status all contribute to the risk of developing COPD.

DIAGNOSIS

When patients present with breathlessness, it is essential to identify risk factors and assess the potential causes, which include chronic heart and lung disease, lack of fitness, obesity and anaemia. GPs are in the frontline to identify COPD in patients with recurrent winter bronchitis. COPD should be considered the most likely diagnosis if the patient has been a smoker and there are additional respiratory symptoms suggestive of airways disease, including exertional breathlessness, a productive cough for three months over two consecutive years, a history of exposure to any risk factors, and no features suggesting asthma (such as a history dating back to childhood, variable wheeze, atopy, a history of significant prevention of symptoms by inhaled corticosteroids [ICS]).

To confirm a clinical suspicion of COPD, spirometry should be performed. Many algorithms exist to assist clinicians in making a definite diagnosis of COPD (see the web resources box on page 16), but most importantly, COPD is a clinical diagnosis confirmed by spirometric evidence of airflow limitation that is not fully reversible. COPD is present when the FEV_1/FVC ratio is less than 0.7 after bronchodilator therapy (200 to 400 μg of salbutamol or equivalent).

In the Australian COPD-X guidelines severity is graded as mild when FEV_1 is 60 to 80% predicted, moderate if 40 to 60% predicted and severe if less than 40% predicted.[6] Much has been written about overdiagnosis of COPD based on spirometry in older people because an FEV_1/FVC ratio of less than 0.7 can be within

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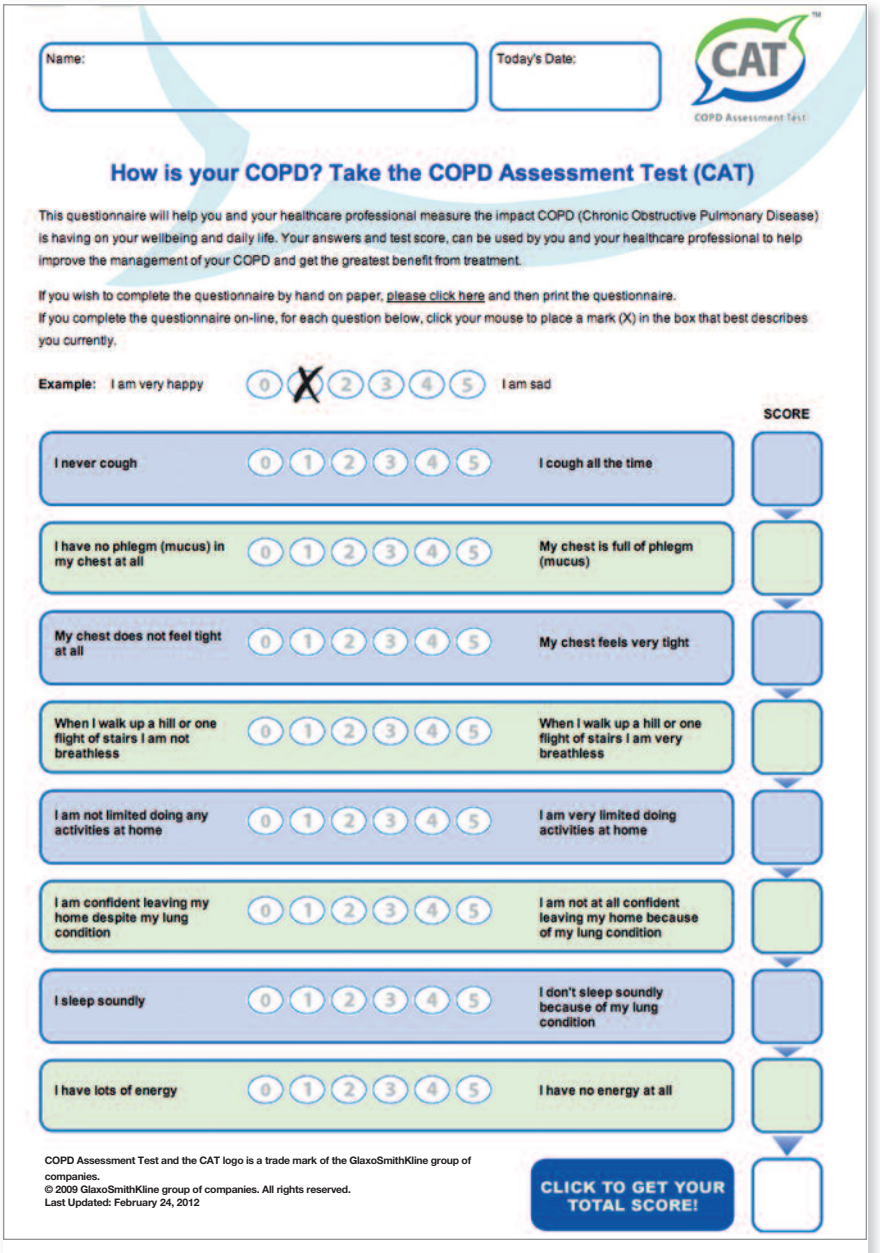
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CAT™
COPD Assessment Test

How is your COPD? Take the COPD Assessment Test (CAT)

This questionnaire will help you and your healthcare professional measure the impact COPD (Chronic Obstructive Pulmonary Disease) is having on your wellbeing and daily life. Your answers and test score, can be used by you and your healthcare professional to help improve the management of your COPD and get the greatest benefit from treatment.

If you wish to complete the questionnaire by hand on paper, please click here and then print the questionnaire.
If you complete the questionnaire on-line, for each question below, click your mouse to place a mark (X) in the box that best describes you currently.

Example: I am very happy 0 X 2 3 4 5 I am sad

			SCORE
I never cough	0 1 2 3 4 5	I cough all the time	
I have no phlegm (mucus) in my chest at all	0 1 2 3 4 5	My chest is full of phlegm (mucus)	
My chest does not feel tight at all	0 1 2 3 4 5	My chest feels very tight	
When I walk up a hill or one flight of stairs I am not breathless	0 1 2 3 4 5	When I walk up a hill or one flight of stairs I am very breathless	
I am not limited doing any activities at home	0 1 2 3 4 5	I am very limited doing activities at home	
I am confident leaving my home despite my lung condition	0 1 2 3 4 5	I am not at all confident leaving my home because of my lung condition	
I sleep soundly	0 1 2 3 4 5	I don't sleep soundly because of my lung condition	
I have lots of energy	0 1 2 3 4 5	I have no energy at all	

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Last Updated: February 24, 2012

CLICK TO GET YOUR TOTAL SCORE!

Figure 1. The COPD Assessment Test (CAT). Available online at: www.catestonline.org/images/pdfs/CATest.pdf.

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normal limits in people over 60 years of age. However, in Australia, spirometry is infrequently performed in primary care and overdiagnosis most frequently results from lack of spirometry and a diagnosis based on symptoms alone.

Severity assessment

Traditionally, COPD guidelines have advocated performance of spirometry and grading of severity of disease based on the FEV_1. Although the FEV_1 is strongly predictive of mortality, it correlates poorly at an individual level with functional exercise capacity, quality of life and risk of exacerbations.

More recently a multidimensional assessment approach including spirometry and symptom assessment has been advocated by international guidelines and expert clinicians. The recent GOLD strategy includes three domains:

- the current level of dyspnoea or COPD symptoms
- the severity of the spirometric abnormality
- the prior 12 months' history of exacerbations.[1]

In this model, dyspnoea is assessed by either the COPD Assessment Test (Figure 1) or the modified Medical Research Council dyspnoea scale (Table 1). The resulting assessment allocates a disease impact grade of A to D and is expressed in a schematic (Figure 2), which is linked to choice of treatment later in the guidelines. The groups can be summarised as follows:

- group A: low risk, less symptoms
- group B: low risk, more symptoms
- group C: high risk, less symptoms
- group D: high risk, more symptoms.

The GOLD strategy document advocates initially assessing COPD symptoms and then the number of exacerbations and the severity of spirometry to place the patient in one of four categories. The GOLD spirometry stages are:

- GOLD 1 (mild), $FEV_1/FVC < 0.7$; $FEV_1 \geq 80\%$ predicted
- GOLD 2 (moderate), $FEV_1/FVC < 0.7$; $50\% \leq FEV_1 < 80\%$ predicted
- GOLD 3 (severe), $FEV_1/FVC < 0.7$; $30\% \leq FEV_1 < 50\%$ predicted
- GOLD 4 (very severe), $FEV_1/FVC < 0.7$; $FEV_1 < 30\%$ predicted.

The presence of comorbidities adds additional prognostic information and may affect management. This multi-dimensional approach and particularly the link to treatment choice has not yet been tested prospectively. It is not yet included in the Australian COPD-X

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guidelines,[6] but it reflects the current understanding of COPD as a disease with systemic manifestations and impact.

Evidence already supports a multi-faceted assessment for people with COPD. For example, a large multinational study of over 2000 patients with COPD showed that broad categories of FEV_1 impairment correlated weakly with health status, six-minute walk distance and probability of having an exacerbation.[7] The strongest independent predictor of risk of exacerbation was exacerbation history in the previous 12 months. In addition to FEV_1, elevated total white cell count and a history of gastroesophageal reflux disease were independent risk factors for exacerbations.[7] Although it is acknowledged that the management of patients with COPD requires more than spirometry alone, more evidence is needed to support the links between patient groups A to D (Figure 2) and the recommendations about drug treatment.

TABLE 1. MODIFIED MEDICAL RESEARCH COUNCIL QUESTIONNAIRE FOR ASSESSING THE SEVERITY OF BREATHLESSNESS

Symptom description	Score
I only get breathless with strenuous exercise	0
I get short of breath when hurrying on the level or up a slight hill	1
I walk slower than people of the same age walking on the level because of breathlessness; or I have to stop for breath when walking at my own pace on the level	2
I stop for breath when walking at my own pace after a few minutes on the level or after walking 100 m	3
I am too breathless to leave the house; or I am breathless when dressing or undressing	4

MANAGEMENT

The Australian COPD-X guidelines advocate a stepwise approach to managing patients with COPD that involves non-pharmacological and pharmacological interventions. Nonpharmacological interventions include risk reduction by removing exposures (especially addressing ongoing cigarette smoking), promotion of physical activity, optimising weight and nutrition, prevention of infection by use of vaccinations, and addressing mood and psychosocial needs (Table 2). Pharmacological interventions include the use of inhalers, treatment of comorbidities and assessment of the requirements for long-term oxygen therapy, and are covered elsewhere in this supplement.

Nonpharmacological management

Smoking cessation

The most important measures to prevent COPD and slow its progression are smoking avoidance and smoking cessation. Smoking cessation can be achieved with behavioural counselling and nicotine replacement therapy,[8] or with oral pharmacological agents such as the nicotinic receptor partial agonist varenicline[9] or the non-nicotine agent bupropion (see: www.racgp.org.au/guidelines/smokingcessation). There is evidence of additive effects when multiple modalities are employed. Although cigarette smokers are undoubtedly at high risk of permanent lung damage, patients with COPD who have recently quit smoking do show improvements in lung function, respiratory symptoms, functional state and mental state within the first three months of abstinence, providing further incentive for those with COPD to quit smoking.[10]

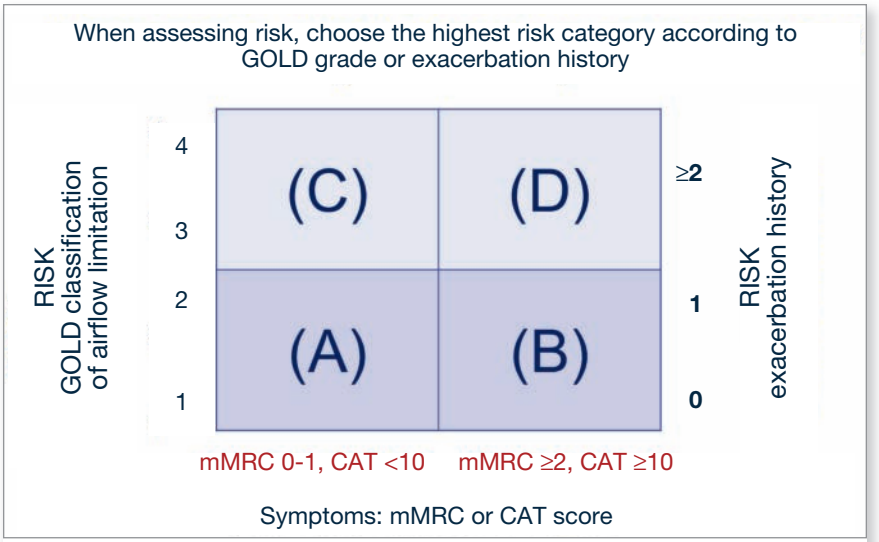

Figure 2. GOLD assessment. Association between symptoms, spirometric classification and future risk of exacerbations.

ABBREVIATIONS: CAT = COPD Assessment Test; GOLD = Global Initiative for Chronic Obstructive Lung Disease; mMRC = modified Medical Research Council.

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TABLE 2. AUSTRALIAN LUNG FOUNDATION STEPWISE MANAGEMENT PLAN: NONPHARMACOLOGICAL INTERVENTIONS

Intervention	Specific items and comments
Risk reduction	Check smoking status, support smoking cessation, recommend annual influenza and pneumococcal vaccination according to The Australian Immunisation Handbook
Optimise function	Encourage physical activity, review nutrition, provide education, develop GP management plan and initiate regular review
Consider comorbidities	Especially osteoporosis, coronary disease, lung cancer, anxiety and depression
Refer for pulmonary rehabilitation	Also consider psychosocial needs, agree on a written action plan
Consider oxygen therapy	At this stage of the disease, also consider surgery, palliative care and advanced care directives

Vaccinations

All patients with COPD should be offered yearly influenza vaccination, which reduces COPD exacerbation rates.[11] Pneumococcal vaccination is usually also recommended because it provides protection against invasive pneumococcal disease in the general population and people with chronic illness (although it does not prevent all-cause pneumonia or mortality).[12] There have been few studies of pneumococcal vaccination specifically in patients with COPD,[13] and there is currently no evidence for reduction of acute exacerbations of COPD.

Pulmonary rehabilitation

There is level 1 evidence from large randomised controlled trials showing that pulmonary rehabilitation improves exercise capacity and quality of life and reduces hospitalisations and length of stay in people with COPD.[14] Even after an acute exacerbation of COPD, pulmonary rehabilitation substantially reduces the subsequent risk of hospital admissions and mortality, and improves health-related quality of life.

In a recent Cochrane review, 57% of patients in the control group, who had no pulmonary rehabilitation, were readmitted to hospital after an exacerbation of COPD compared with 14% of patients in the pulmonary rehabilitation group.[15] The number needed to treat was 2.3 to prevent one hospital admission. As many regional and rural centres do not have access to pulmonary rehabilitation programs, The Australian Lung Foundation has developed an online module enabling health professionals to develop the skills and knowledge to implement and evaluate a program, which includes the essential components of physical activity training and education in resource poor settings.[16]

Education, self-management and action plans

Effective self-management can help patients with COPD to initiate the early use of antibiotics and oral corticosteroids, which can shorten and minimise the severity of the COPD exacerbation, also reducing the risk of hospital admission.[17,18] Patients with COPD may need repeated assistance and regular review to ensure they are using their inhaler correctly. Regular reinforcement of medication timing and appropriate use of short-acting reliever medication is important to minimise symptom burden.

Individualised written action plans, especially those that include supportive care provided by a case manager or frequent contact with a respiratory specialist unit can help reduce the impact of COPD exacerbations.[19,20] In most studies it is clear that some patients find it particularly difficult to learn these skills and are better managed by proactive care and ongoing regular clinical review. A useful action plan template is available on The Australian Lung Foundation website (http://www.lungfoundation.com.au/).

Inhaler technique and adherence

Patients with COPD often have suboptimal inhaler technique;[21] therefore, inhaler technique and adherence should be checked by direct observation at each visit.[22] Coaching by a trained practice nurse or referral to a respiratory educator can improve inhaler technique. The National Asthma Council website has useful 'how-to videos' to demonstrate inhaler technique (see: www.nationalasthma.org.au/).

Pharmacological management

Respiratory symptoms in people with COPD are mainly due to chronic airflow limitation (from small airway obstruction and loss of elastic recoil) and chronic airway inflammation. Hence, bronchodilators are useful for reducing breathlessness across all stages of COPD severity and, in more severe patients, inhaled corticosteroids are potentially useful as anti-inflammatory agents.

Bronchodilators

Short-acting bronchodilators

Salbutamol and terbutaline are short-acting β_2-agonists used as relievers at any stage of COPD. Ipratropium is a short-acting anticholinergic bronchodilator given as needed or on a regular basis. Ipratropium is now less commonly used than the once daily long-acting

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WEB RESOURCES ON COPD

Patient resources

- Patient educational material: Better Living with COPD booklet http://www.lungnet.org.au/lung- information/patient-educational-material
- LungNet patient resource group – contacts and practice nurse online training http://www.lung foundation.com.au/get-involved/events/about-world-copd-day/copd-patient-support-lungnet

Health professional resources

Useful resources from the Australian Lung Foundation http://www.lungfoundation.com.au/ include:

- COPD-X complete http://www.lungfoundation.com.au/professional-resources/guidelines/copd-x-plan
- Stepwise management of COPD http://www.lungnet.org.au/professional-resources/general-practice/stepwise-management-of-stable-copd
- GP toolkit for screening and to assess lung age http://www.lungfoundation.com.au/professional-resources/general-practice/primary-care-respiratory-toolkit/about

muscarinic antagonist tiotropium, which provides more sustained bronchodilation.[23] Ipratropium and tiotropium should not be used together because both are anticholinergics.

Long-acting bronchodilators

Salmeterol and eformoterol are long-acting β_2-agonists (LABA) with a duration of action of 12 hours and indacaterol is an ultra-LABA with 24 hours' duration of action. These long-acting bronchodilators improve lung function, reduce the risk of exacerbations, [24,25] and can be used at any stage of COPD. Indacaterol is not licensed for use in people with asthma. Side effects of β_2-agonists include tremor and tachycardia, although these do not usually trouble patients.

Tiotropium is a once-daily, long-acting muscarinic antagonist that can be commenced at any stage of COPD. As an anticholinergic with a 24-hour duration of action, it reduces dyspnoea, improves quality of life and decreases risk of exacerbations.[26,27] In patients with moderate COPD, tiotropium has been shown to slow the rate of decline of lung function to a small extent and possibly reduce mortality.[28,29] It can cause dry mouth and urinary retention[30] and should not be used in people with narrow-angle glaucoma. A meta-analysis concluded that anticholinergic inhalers may increase cardiovascular events.[31] However, tiotropium delivered in a Handihaler did not appear to increase cardiac complications in a large randomised controlled trial.[26] Use of a LABA with tiotropium provides small improvements in quality of life and bronchodilation compared with use of tiotropium alone.[32]

Inhaled corticosteroids

People with COPD are less responsive to corticosteroids than people with asthma.[33] However, a Cochrane systematic review has shown that ICS, when used alone without a LABA, can reduce the risk of exacerbations and slow the rate of decline of quality of life.[34] On a cautionary note, use of ICS may increase risk of pneumonia in patients with COPD.[34] Their anti-inflammatory actions (reduced rate of exacerbations) should be weighed up against their potential to promote infection (increased risk of pneumonia). ICS alone (as a monocomponent inhaler) is not available on the PBS for people with COPD, but is available with a LABA in a combination inhaler (see below).

Combination inhalers

ICS/LABA combination inhalers (fluticasone/salmeterol, budesonide/eformoterol) have been shown in placebo-controlled randomised controlled trials to reduce exacerbations, slow the rate of decline of quality of life, potentially slow the rate of decline of lung function and possibly reduce mortality.[35-37] In several large randomised controlled trials, combination inhalers have been shown to be more effective than either of the ICS or LABA monocomponents alone.[38]

ICS/LABA combinations are available on the PBS for use in symptomatic patients with moderate-to-severe COPD (FEV_1 <50% predicted) who have a history of repeated exacerbations with significant symptoms despite regular β_2-agonist bronchodilator therapy.

Triple therapy

Each inhaled therapy individually has at best a modest benefit in patients with COPD because of the chronic damage in the lungs. Although it has slightly smaller magnitude of effect on COPD exacerbations, tiotropium appears to be similar in overall benefit to salmeterol/fluticasone.[39,40] Tiotropium in conjunction with an ICS/LABA combination inhaler (triple therapy) appears to be more beneficial than the individual treatments alone,[41,42] and is commonly used in clinical practice for patients with moderate-to-severe COPD with repeated exacerbations.

Emerging treatments

Roflumilast

Roflumilast is an oral anti-inflammatory agent (phosphodiesterase-4 inhibitor), which reduces exacerbations and improves symptoms.[43] Roflumilast is not yet available in Australia.

Azithromycin

A 12-month randomised controlled trial showed that azithromycin reduced exacerbation rates and improved quality of life in some patients with COPD.[44] However,

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hearing decrements were more common in the azithromycin than in the placebo group, as were macrolide-resistant organisms. Azithromycin is not indicated on the PBS for long-term use in COPD.

Lung volume reduction

Lung volume reduction surgery[45,46] is now less commonly used in Australia, although new methods of bronchoscopic lung volume reduction are emerging using valves, stents or steam.[47,48] Selected patients with very severe emphysema may be referred for consideration for lung transplantation.

Other treatments

Theophylline is an oral bronchodilator[49] that is now infrequently prescribed due to its side effects. An NHMRC-funded randomised controlled trial of low-dose theophylline and low-dose oral corticosteroids is currently underway.

Support network and multidisciplinary team

Systems for integrated care may be beneficial for patients with severe COPD.[19,20] Important components include self-management education, appropriate use of decision support systems, co-ordinated care and access to community resources.[50]

Significant reductions in emergency department visits and admissions can be achieved by programs that involve self-management education and information about COPD, and access to a readily available case manager or nurse practitioner. Integrated care programs combining self-management education and case management can decrease rates of COPD-related hospital admissions.[17-19,50] Integrated self-management programs should include having a supply of oral corticosteroids and/or antibiotics to start at the beginning of an exacerbation and access to medical help when needed.

Over time most patients with COPD experience progressive worsening of their disease and develop deconditioning that adds to their disability. They may also experience significant anxiety and depression.[51] Their exacerbations may ultimately require assisted ventilation or intensive care admission. All such patients should be given the opportunity to discuss their future treatment and be assisted in making choices to reduce the probability of unnecessary prolongation of their lives when there is no further chance of recovery to independence or reasonable quality of life. Palliative interventions that are planned and discussed with close family and trusted friends can be initiated appropriately, especially if a plan is agreed on and written into an advance directive.[52,53]

WHEN TO REFER TO A SPECIALIST

COPD is a complex disease and although management in its initial stages may be straightforward, later in the disease comorbidities and the complications of COPD create a complex spectrum of problems that require specialist management, especially for those who experience frequent exacerbations.[53,54] Most patients will benefit from specialist review to optimise their management and ensure all complicating factors and comorbidities are being addressed.

Patients who are experiencing frequent exacerbations, persistent or recurrent infection, rapid functional decline or troublesome side effects from treatment should be referred for specialist opinion. Any patient requiring long-term oxygen should have at least one assessment by a specialist and subsequent review to ensure eligibility, appropriate adherence and benefit. The need for interventions such as endobronchial stents and valves or pulmonary resection requires a full assessment in specialist care. Referral of patients to a respiratory specialist or educator may assist with device technique and self-management.

CONCLUSION

Avoidance of cigarette smoke and other environmental exposures remains important to prevent COPD. New approaches, including multidimensional assessment of symptoms and spirometry, show great promise for improving the assessment and management of people with COPD. Although COPD often has a major impact on patients' lives, a stepwise approach to management – both nonpharmacological and pharmacological – is recommended to reduce the disease burden of COPD and improve quality of life for affected patients. MT

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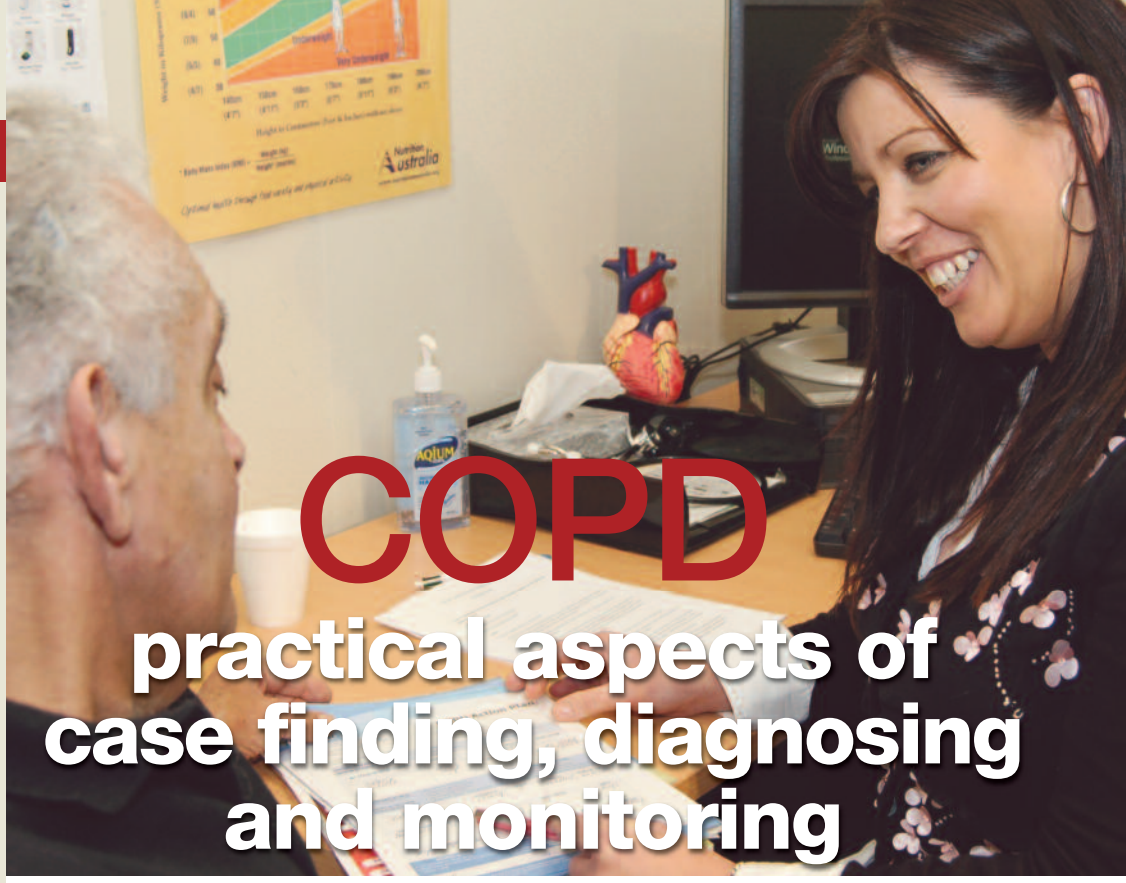

COPD
practical aspects of case finding, diagnosing and monitoring

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Key points

- Diagnosis of COPD is often delayed and a high proportion of cases in primary care are unrecognised.
- COPD is often misdiagnosed in primary care, probably as a result of not using spirometry for diagnosis.
- Screening systematically or opportunistically with questionnaires can be used to case-find in general practice. Expiratory flow devices are used to determine the need for diagnostic testing.
- Spirometry is essential to diagnose COPD. COPD is present if the post-bronchodilator FEV_1/FVC ratio is below 0.7 and FEV_1 is less than 80% predicted.
- Telling smokers their 'lung age' after spirometry increases their chances of successfully quitting.
- The results of spirometry together with symptoms and exacerbation frequency guides the management of COPD.
- Complex lung function tests to distinguish between asthma and COPD are not usually required.

Does my patient have chronic obstructive pulmonary disease (COPD), and does it matter?

Many patients with COPD remain undiagnosed, unknown even to doctors they consult regularly, until they have advanced stages of the disease. Patients may ignore limitations and symptoms of COPD or attribute them to other causes, such as increasing age, lack of fitness and weight gain. A delayed diagnosis may deny potentially effective treatment and result in lost opportunity to prevent progression. Only smoking cessation and prevention of exacerbations have been shown to reduce progression of COPD.

COPD is mainly thought of in terms of its pulmonary component: airflow limitation that is progressive and not fully reversible, due to an abnormal inflammatory response of the lungs to cigarette smoking or other noxious particles.[1] However, there are also significant extrapulmonary consequences and comorbidities, such as deconditioning, exercise intolerance, skeletal muscle dysfunction, osteoporosis, metabolic impacts, anxiety and depression, that contribute to the overall impact and severity.[2,3] Patients with COPD have an increased risk of conditions that have the same risk factors (advanced age, smoking, low socioeconomic status and sedentary lifestyle) – cancer (a 15-fold increased risk of lung cancer), cardiovascular disease (a fivefold increased risk), stroke (a threefold increased risk) and diabetes mellitus (double the risk).[4]

By taking a systematic approach in general practice, people at risk of lung disease can be

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identified using simple questionnaires such as the Lung Foundation Australia's one-minute Lung Health Checklist, then screened rapidly using a COPD screening device and have diagnostic spirometry for COPD if appropriate.

This article explains the benefits of recognising COPD and discusses the issues of identifying patients with COPD early in the course of the disease and the challenges of making an accurate diagnosis.

BENEFITS OF RECOGNISING COPD

Although there is no cure for COPD, stopping smoking will reduce the progression of the condition and treatment can help reduce the symptoms (Figure 1).[5] Recognising and understanding the cause of symptoms and participating in pulmonary rehabilitation to combat deconditioning can greatly improve quality of life, reduce anxiety and increase exercise tolerance.

Stopping smoking is the most important target for people with COPD as it is the most effective intervention to reduce symptoms and prevent progression of COPD and lung function impairment.[1,6] Smoking cessation advice and support should be offered to all smokers. Pharmacotherapy should also be considered to help patients in their smoking cessation attempts.[7] Supporting patients' self-management for COPD, such as by being proactive and providing or enabling access to appropriate medications in case of symptom flare-up during an exacerbation, can prevent more rapid deterioration.

Preventive options recommended in the Australian COPD-X guidelines can be maximally implemented through use by the primary care team and allied health professionals of the Medicare Benefits Schedule (MBS) chronic disease management items GP Management Plan (GPMP; MBS item 721), Team Care Arrangement (TCA; item 723) and Review of GPMP or Co-ordinate Review of TCA (item 732), and also the chronic disease management nurse monitoring and support item (item 10997).[8] Resources are also available for clinicians to provide patients with information about COPD, its symptoms and management. The Lung Foundation has a range of booklets, fact sheets, DVDs and interactive tools (http://lungfoundation.com.au).

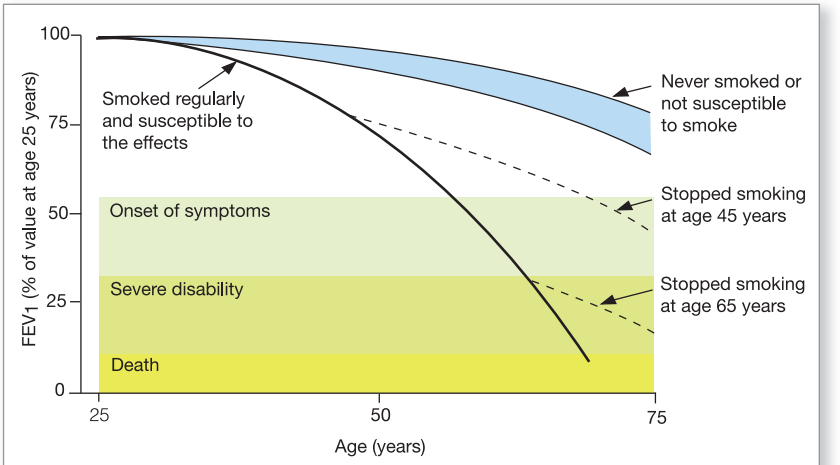

Figure 1. The Fletcher–Peto diagram. Smoking causes lung function to worsen at a faster rate. Quitting smoking at any age is beneficial.

Adapted from Fletcher C, Peto R. Br Med J 1977; 1: 1645-1648.[5]

HOW TO IDENTIFY PATIENTS WITH COPD

The early identification of patients with COPD can be achieved using a systematic process with targeted case finding as well as by opportunistically screening those at risk.

Patients may not recognise or report their symptoms of coughing, decreasing physical activity/exertion and breathlessness, assuming they result from normal physiological changes (e.g. ageing or gaining weight).[9] Many patients, however, have symptoms of COPD noted at general practice consultations over long periods before the diagnosis is actually made, an average of three years in one study.[10] It is important to be attuned to the tendency to dismiss early COPD symptoms and to be aware that protracted or frequent episodes of acute bronchitis may be the first sign of COPD.[11] Breathlessness may occur later, when around 50% of lung function has been lost.

Opportunistic or systematic approach

Routine untargeted screening for COPD in primary care settings is not cost-effective.[12] However, the possibility of COPD should be considered in patients over the age of

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Figures 2a and b. Digital COPD screening devices. a (left). PiKo-6, with mouthpiece adaptor and one-way valved cardboard mouthpiece attached. b (right). Vitalograph COPD-6, with one-way valve mouthpiece attached.

Images courtesy of Lung Foundation Australia.

35 years who are current smokers or ex-smokers (who continue to be at higher risk), as recommended in the Australian COPD-X guidelines.[8] In these patients, the presence or history of risk factors such as smoking, exacerbations (acute bronchitis episodes), occupational exposure to particles or family history of COPD should be specifically sought. There are suitable tools readily available to help in this, such as the Lung Foundation's Lung Health Checklist, which is accessible as an online tool and as pdfs in English, Arabic, Hindi, Samoan, Spanish and Vietnamese from the Lung Foundation Australia website (http://lungfoundation.com.au/lung information/lung-health-checklist/interactive-checklist).

The Lung Health Checklist asks the questions listed below.

- Are you a smoker or ex-smoker?
- Do you or have you worked in a job that exposed you to dust, gas or fumes?
- Do you cough several times most days?
- Do you cough up phlegm or mucus most days?
- Do you get out of breath more easily than others your age?
- Do you experience frequent chest infections?

A positive answer to any question indicates that the patient is at risk of having COPD and needs further investigation by full diagnostic spirometry, with or without preliminary lung function screening with a lung function screening device (Figures 2a and 2b).

Adopting a systematic approach to identify COPD may involve other members of the practice team, as recommended in the RACGP's *Guidelines for Preventive Activities in General Practice* (the 'red book').[13] Practices are encouraged to make organisational changes and use clinical audit to identify middle-aged patients who have not had preventive activity, and to then implement a recall system or opportunistically arrange a health check. Planned health checks for middle-aged adults and patients over 75 years (MBS health assessments items 701, 703, 705 and 707) and indigenous patients (MBS health assessment item 715) are opportunities for case finding; these checks can be facilitated by the involvement of practice nurses.

COPD education for practice nurses is available online from the Lung Foundation and will equip nurses with the knowledge and skills to support a systematic approach to identifying and managing patients with COPD (http://lungfoundation.com.au/professional-resources/training/copd-nurse-training-online).

Lung function screening devices

There are several expiratory flow devices available to follow up patients at risk of COPD and to rule out or confirm the need for diagnostic testing with spirometry. These devices are relatively inexpensive and easy-to-use, and require minimal training to conduct the procedure and interpret the results. They are suitable for most patients because they do not require complete emptying of the lungs as the test assesses expiratory volumes at one and six seconds (forced expiratory volume in one second, FEV_1 and in six seconds, FEV_6).

Validated devices in Australia are the PiKo-6 and Vitalograph COPD-6 (Figures 2a and b). The Lung Foundation has a short online video for training in operating both devices, and printed materials for interpreting and following up the results (http://lungfoundation.com.au/professional-resources/1692-2/health-professional-training-and-courses/copd-screening-devices-in-the-community). Both devices use colour-coded interpretation to make them easy to use in screening.

DIAGNOSING COPD – SPIROMETRY

The diagnosis of COPD rests on the demonstration of airflow limitation that is not fully reversible, and thus spirometry is the gold standard for diagnosis and should be performed before confirming a diagnosis to avoid potential misclassification (Figure 3).[8] Identification of the severity of COPD by spirometry allows progression of the disease to be monitored objectively, and the result can be used along with symptoms to guide appropriate interventions for each patient.

However, spirometry is underused in general practice in Australia, leading to under-recognition and also misdiagnosis of COPD. Studies have shown COPD misdiagnosis in 31% to 44% of cases in Australian general practices.[14,15] In a survey of 45- to 70-year-old Australian adults, of those with confirmed moderate or severe COPD, 49% reported no diagnosis of a respiratory condition, and

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among those with COPD or asthma who had seen a GP (for any reason) in the previous 12 months, only one-third had undergone a respiratory function test.[16]

Diagnostic criteria

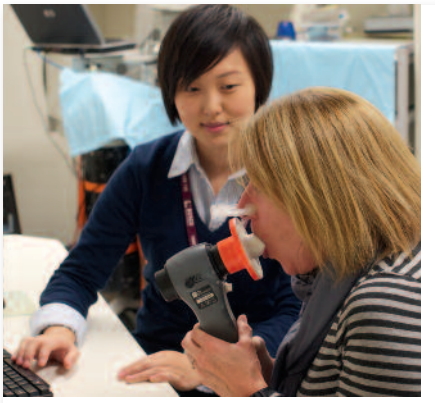
Airflow limitation is considered not fully reversible when, after administration of bronchodilator medication (such as two puffs of salbutamol or terbutaline), the ratio of FEV_1 to forced vital capacity (FVC) is less than 70% (FEV_1/FVC ratio) and the FEV_1 is less than 80% of the predicted value.[8] Recent studies have criticised this definition, suggesting that the use of a fixed FEV_1/FVC ratio of less than 70% will lead to overdiagnosis of COPD in older populations and underdiagnosis in younger people, and may lead to gender imbalances as women have a higher FEV_1/FVC ratio than men.[17,18]

The most recent (2005) international statement on lung function interpretation has proposed alternative criteria, defining airflow obstruction based on the FEV_1/FVC lower limit of normal (LLN).[19] However, both the Australian and international guidelines (the COPD-X guidelines and the GOLD guidelines, respectively) continue to recommend the fixed cut-off values for COPD diagnosis.[1,8]

Spirometry testing

Several factors can be barriers to spirometry, and need to be addressed in general practice. Although spirometer ownership may appear high in general practices, the selection of suitable spirometers is important, the rate of use is often low and the test results obtained are frequently of low quality (due in part to lack of expertise).[11,20] An information paper describing spirometer selection in general practice is available from the National Asthma Council Australia (http://www.nationalasthma.org.au/health-professionals/spirometry-resources/spirometer-users-buyers-guide).

It is well recognised that GPs may not feel confident performing spirometry and interpreting results, and referral to a spirometry service or pulmonary function laboratory is an appropriate alternative.[21] Factors such as equipment costs and the low reimbursement level for a spirometry test with bronchodilator reversibility (MBS item 11506) may also contribute to a practice policy to refer patients elsewhere for testing and interpretation of results.



Figures 3a and b. a (left). Spirometry is the gold standard for diagnosis of COPD. b (right). A digital spirometer.

Training in spirometry

If spirometry is performed in the practice, effective training and ongoing quality control of tests are essential. Training programs for GPs and practice nurses endorsed by the Australian and New Zealand Society of Respiratory Science are available through the National Asthma Council Australia and other providers (listed on the National Asthma Council Australia website, http://www.nationalasthma.org.au/health-professionals/spirometry-resources/spirometry-training).

Ongoing assessment of spirometry quality in primary care has been limited in the past. A recent development is an online training program (Spirometry 360) that also addresses the need for quality feedback (available on the website http://www.spirometry360.org). This program provides monthly analysis by clinical experts of spirometry performed in the practice setting after training.

The Lung Foundation's online Spirometry Calculator (part of the Primary Care Respiratory Toolkit) can help with interpretation of spirometry results (http://www.lungfoundation.com.au/professional-resources/general-practice/primary-care-respiratory-toolkit).

Value of spirometry for smoking cessation

The most important preventive measure in COPD is smoking cessation, and spirometry can be used as a tool to motivate smokers to quit. In a UK study in general practice, telling smokers their lung age (the age of the average healthy individual who would perform similar to them on spirometry) significantly improved the likelihood of successful quitting, and an almost twofold increase in long-term quit rates was achieved.[22] The Lung Foundation has developed an online, interactive Lung Age Estimator as part of its Primary Care Respiratory Toolkit. This motivational tool provides a personalised graphic presentation of an individual's estimated lung age based on spirometry results and the person's age, height and gender, and demonstrates how much stopping smoking can prevent lung function decline.

In addition, use of the 'Fletcher-Peto' diagram to demonstrate that smoking increases the loss of lung function and

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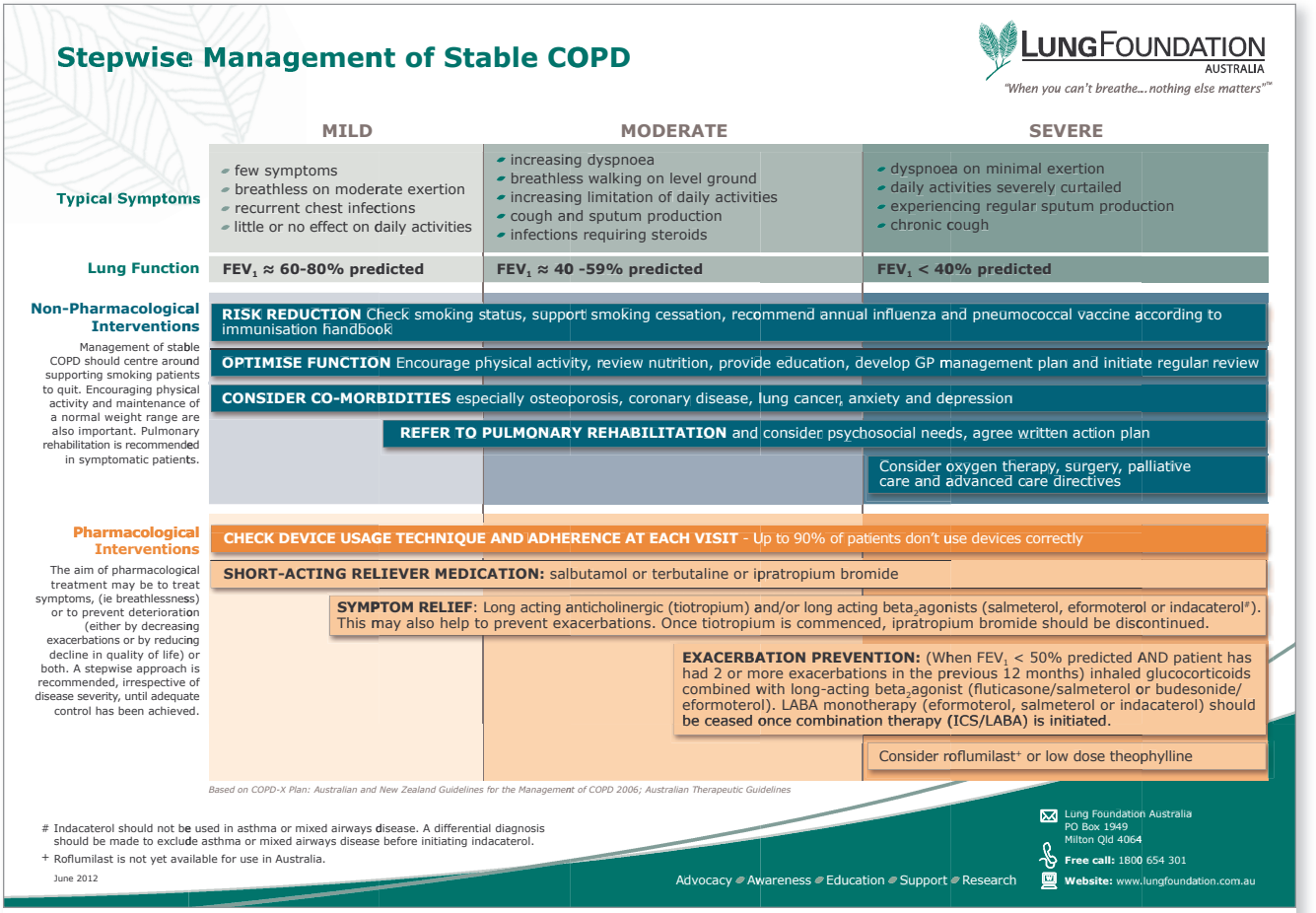

Figure 4. Stepwise management of stable COPD – the Lung Foundation (until 2013, The Australian Lung Foundation).

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quitting returns the decline to the normal ageing-related rate may assist smokers to decide which path they will follow (see Figure 1).[5] A patient fact sheet containing this graph, *Smoking and Lung Health – Patients*, is available from the Lung Foundation (http://lungfoundation.com.au/wp-content/uploads/2012/06/Smoking-and-lung-health-Patients.pdf).

MONITORING DISEASE PROGRESSION

Monitoring disease progression and patient outcomes is an important aspect of COPD management. COPD is a progressive condition associated with frequent acute exacerbations, and patients are required to make significant behavioural changes to manage their disease well.[2] Monitoring disease severity by spirometry together with symptoms and exacerbation frequency will inform management. An example of a COPD management summary is shown in Figure 4 (available from the Lung Foundation, http://lungfoundation.com.au/wp-content/uploads/2012/01/ALF-Stepwise-Management-of-COPD-A4-April-2013.pdf).

Once COPD is diagnosed, patients require ongoing and regular monitoring because treatment recommendations change as the disease progresses. An example of an annual cycle of care in general practice for a patient with COPD is shown in Figure 5 (available online from the Lung Foundation, http://lungfoundation.com.au/wpcontent/uploads/2012/06/mbs_flow_charts_for_copd.pdf).

Frequent exacerbations of COPD are associated with an accelerated decline in lung function, accelerated decrease in health status and decreased survival. Review and monitoring of patients during and after exacerbations is important as not only are these events an immediate concern but also, after recovery, they can have a negative effect on disease trajectory. Follow up after an exacerbation is an appropriate time to refer a patient for pulmonary rehabilitation to help him or her return to previous activity and health status.[8] Recent evidence also indicates

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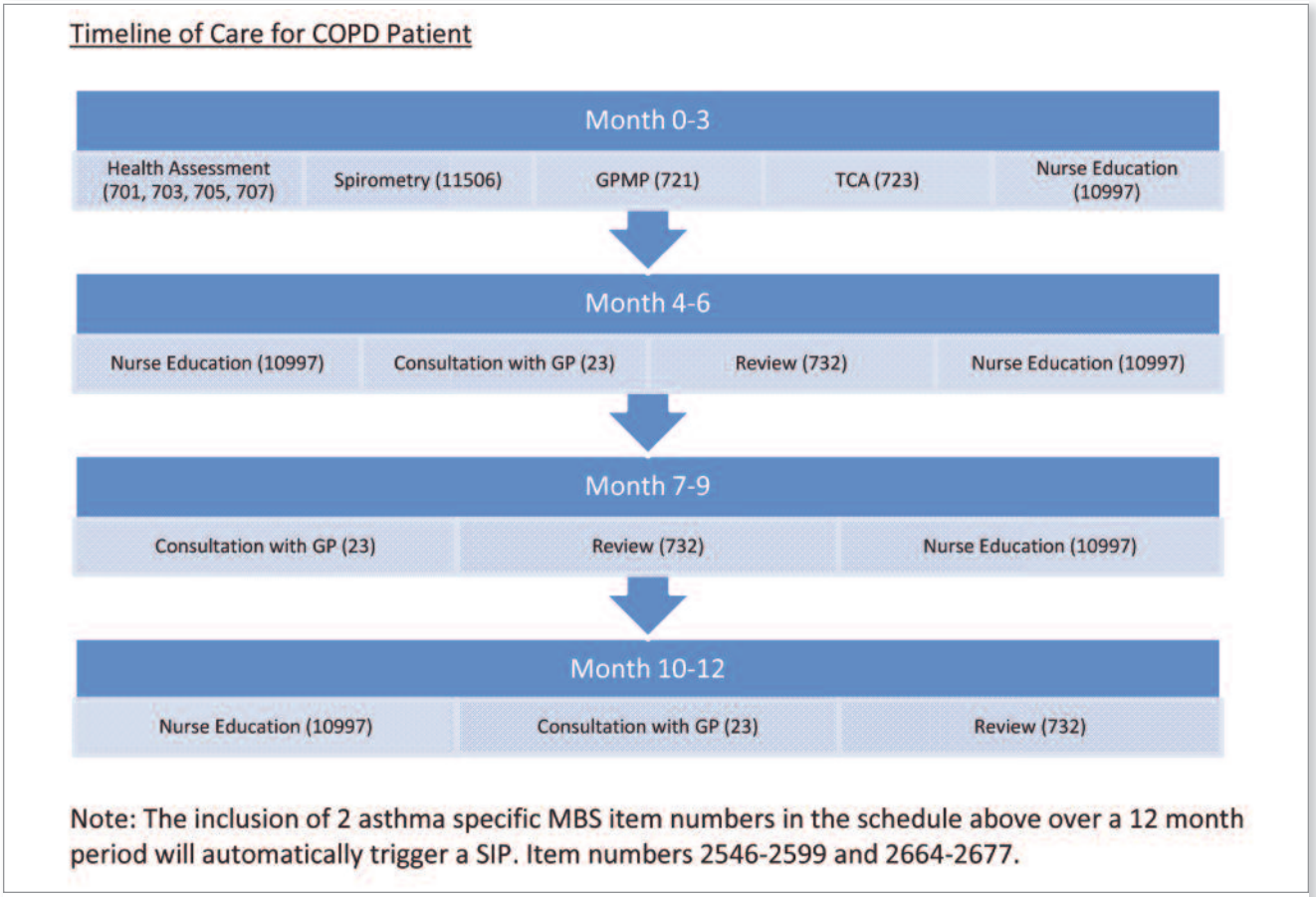

Figure 5. The Lung Foundation's COPD cycle of care showing MBS item numbers.

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that exacerbations cluster together in time and that after one exacerbation the risk of a second is heightened.[23]

ASTHMA–COPD OVERLAP

Overlap of asthma and COPD is common, occurring in up to half of older people with obstructive airway disease, and often causes diagnostic and management difficulties.[2,24,25] Asthma and COPD are usually considered distinct conditions, with their own diagnostic and management approaches; in practice, however, older patients often demonstrate features of both conditions (Table).[2]

Airflow obstruction in COPD is not highly variable and is largely irreversible, unlike in asthma, which is a disease of variable airflow obstruction. Symptoms may be common to both conditions and there is considerable overlap as many people with asthma smoke and long-standing asthma may have a degree of irreversibility.[25]

Overlap syndrome is recognised by the coexisting features on spirometry of increased variability of airflow in a patient with incompletely reversible airway obstruction. There is no strong justification for more complex lung function tests to distinguish between asthma and COPD. Pharmacological treatment in both conditions may include inhaled corticosteroids and long-acting beta agonists.[8] Nonpharmacological therapies and risk factor reduction such as self-management, pulmonary rehabilitation (in the presence of airflow obstruction and symptoms), smoking cessation and exacerbation avoidance are beneficial and recommended in both conditions.[2,26,27]

To overcome the complexities of management in patients with asthma–COPD overlap, it has been recommended that clinicians undertake a systematic and multidimensional assessment to determine the clinical problems and then apply individualised management recommendations.[2,25]

CHALLENGES AND PITFALLS IN DIAGNOSING COPD

In the absence of spirometry, breathlessness due to obesity, which is now prevalent

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TABLE. COMPARING FEATURES OF COPD AND ASTHMA

COPD	Asthma
Onset in mid-life	Onset early in life (often childhood)
Symptoms progress slowly	Symptoms vary from day to day
Dyspnoea during exercise	Symptoms provoked by a range of triggers
May not have atopy	Allergy, rhinitis and/or eczema may be present
Uncommon family history (genetic deficiency of alpha 1-antitrypsin)	Common family history

in the primary care population, may be wrongly attributed to COPD.[14] Additionally, COPD symptoms in women are often mistakenly attributed to asthma, as historically COPD was a disease of older men.[28] More recently, there is a higher incidence of COPD in younger women, due to increased smoking among women. The Australian mortality rate in women reflects this, with the death rate for women from COPD rising and approaching the rate for men.[29]

CONCLUSION

COPD is a common condition that is underdiagnosed and undertreated. A delay in diagnosis may deny patients potentially effective treatment and result in lost opportunities to prevent progression. Current Australian guidelines (the COPD-X guidelines) recommend that COPD should be considered in people over the age of 35 years who are current smokers or ex-smokers.

Patients with COPD can be identified using a systematic process with targeted case finding as well as by opportunistically screening those at risk. Lung function screening devices may be used to follow up patients at risk of COPD and to rule out or confirm the need for diagnostic testing with spirometry.

Spirometry is underutilised in primary care, and its improved use is essential for diagnosing COPD and monitoring disease progression, which informs patient management. Information about training programs in spirometry is provided.

Complex lung function tests to distinguish between asthma and COPD are not usually required. MT

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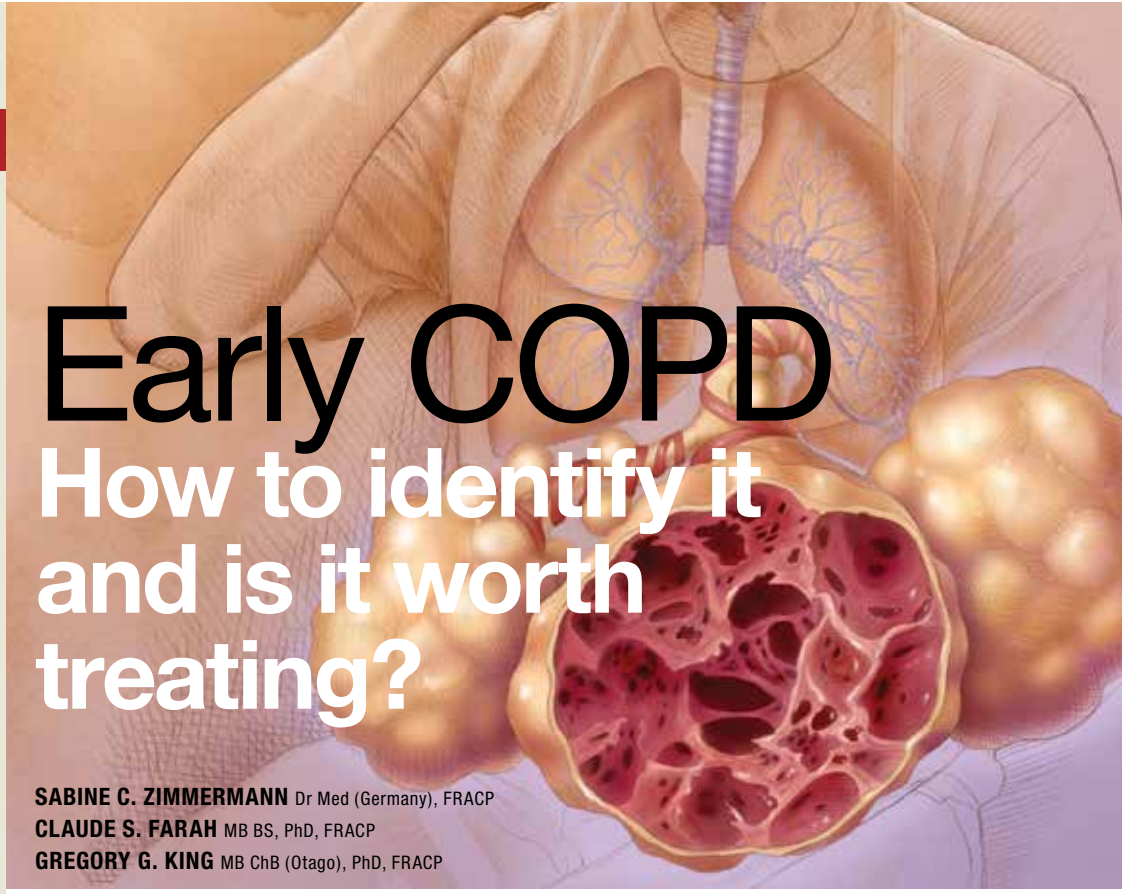

Early COPD
How to identify it and is it worth treating?

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Key points

- **Detecting airflow limitation when the patient has no symptoms and confirming the diagnosis of COPD by spirometry identifies individuals at risk of future symptoms, increased decline in FEV_1 and complications of the condition.**
- **Better stratification of future risk by actively diagnosing COPD (case finding) may alter management in those with additional risk factors for COPD progression and cardiovascular risk.**
- **Performing spirometry in current smokers may increase smoking cessation.**
- **An asymptomatic patient with a new diagnosis of airflow limitation should be monitored for decline in FEV_1, onset of COPD symptoms and occurrence of exacerbations.**
- **Confirmation or exclusion of COPD allows appropriate drug prescription and helps avoid diagnostic confusion.**
- **Management of COPD continues to evolve as understanding of the disease increases, particularly appreciation of its heterogeneity.**

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Case finding of airflow limitation and COPD is an important step to be undertaken by GPs in individuals at risk to help address the increasing burden of this condition in the community.

Chronic obstructive pulmonary disease (COPD) is an important disease globally because of its massive societal, economic and personal burden. It is defined by airflow limitation (measured by spirometry) that does not normalise after administration of a short-acting bronchodilator and by typical symptoms of breathlessness on exertion and cough productive of sputum.[1]

AN OVERVIEW OF COPD

Two important guidelines on COPD are the Australian COPD-X plan and the international Global Initiative for Chronic Obstructive Lung Disease (GOLD)'s strategy document; these contain practical information that is regularly updated.[1,2] Both documents describe the severity of COPD based on impairment of forced expiratory volume in one second (FEV_1). The GOLD document also incorporates symptoms and exacerbations to assign COPD severity.

It is predicted that the burden of COPD will increase due to tobacco-related morbidity so that by 2020 it will be the fifth leading cause of disability worldwide.[3] Therefore, in addition to measures aimed at preventing smoking and helping patients quit smoking, there has been a drive to find strategies to identify people at risk of COPD and to reduce their risk of the condition developing as a result of a sustained excess decline in lung function.[4] Similarly, there is interest in diagnosing COPD in its earlier stages in the hope that the course of the disease can be altered if the pathophysiological changes are not advanced.

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There is also a greater appreciation of the heterogeneity in disease expression and considerable effort is being made to better characterise patients with established COPD, with the long-term goal of targeting treatment.

A deeper understanding of COPD and its underlying processes is therefore needed to enable advances in its management.

SPIROMETRY FOR DIAGNOSIS OF COPD

The prevalence of airflow limitation in the population varies between countries. The most comprehensive study to date on the prevalence of airway obstruction is the Burden of Obstructive Lung Disease (BOLD) study, which involved 12 sites in 12 different countries and 9425 subjects. The investigators reported the presence of moderate or greater airway obstruction (ratio of FEV_1 to forced vital capacity [FVC] less than 0.70 and FEV_1 less than 80% of predicted on post-bronchodilator spirometry testing) in 6 to 20% of the population over 40 years of age.[5] The reported prevalence is a surprisingly large proportion of the population. The study did not include any developing countries where environmental pollutant exposure and tobacco consumption are high and, therefore, where COPD could be even more prevalent. In Australia, the prevalence of COPD in women and men aged 40 years or older was found to be 7.5%.[6]

Other studies have reported that when the largest at-risk population in western societies – current and former smokers of 10 pack-years or more and 40 years of age and older – is screened, between one in seven and one in three people have COPD.[7-9] The proportion varies depending on the prevalence of COPD in the population being tested. Considering the relation between pack-years and severity of airway obstruction, the likelihood of finding airway obstruction will be even higher if individuals who have smoking histories exceeding 20 pack-years are targeted.

Is spirometry really necessary for diagnosis?

The diagnosis of COPD needs confirmation in individuals who have symptoms. As the symptoms associated with COPD are nonspecific, such as productive cough that could be due to bronchitis without COPD, bronchiectasis or postnasal drip, diagnosis by clinical symptoms and signs alone is highly inaccurate. The implications of misdiagnosis are significant: treating a patient with drugs for an erroneous diagnosis is wasteful of resources, needlessly exposes patients to potential drug side effects and may delay the correct diagnosis and appropriate management.

Arguably spirometry is mandatory in any patient who presents with worsening breathlessness or wheeze during a respiratory tract infection because such a scenario constitutes an exacerbation, which in itself has significant clinical connotations. An exacerbation of COPD is commonly defined as worsening symptoms (cough, sputum production or breathlessness) for three or more days. Apart from the short-term consequences, exacerbations are associated with increased rate of decline in lung function, further exacerbations, increased risk of death, reduced quality of life and increased health care utilisation.[10]

AIRFLOW LIMITATION

Although the most common cause of COPD is cigarette smoking, it is not the sole cause. Other causes include domestic and occupational inhalants and asthma. Although long-standing asthma can cause airflow limitation that is incompletely reversible by acute bronchodilator inhalation, the pathology of long-standing asthma is very different from that of COPD and the clinical features frequently differ. In COPD, neutrophilic inflammation in the large and small airways, including the respiratory and terminal bronchioles, is characteristic and leads to tissue destruction that also involves the lung parenchyma, resulting in emphysema.[11] Even after smoking cessation, inflammation persists when COPD is established and severe.[12] In asthma, however, inflammation is commonly eosinophilic, although neutrophilic inflammation becomes more common with more long-standing asthma.[13]

The combination of smoking and asthma results in additive effects on decline in lung function.[14] If asthma is severe and smoking exposure has been heavy, the chances of having incompletely reversible airflow limitation are increased, and all such patients should have spirometry performed. The value of making a diagnosis of asthma versus a diagnosis of COPD or a diagnosis of 'overlap' is open to debate. The criteria on which such diagnostic splitting is based are also a matter of opinion. Whether such diagnostic labelling should alter management or affect outcomes is even more complex and will probably be influenced by greater understanding of different clinical subtypes, or phenotypes, of obstructive airways disease.

CASE FINDING IN COPD

The practical aspects of case finding in COPD have been discussed in the article 'COPD: practical aspects of case finding, diagnosing and monitoring', published in the February 2013 issue of *Medicine Today* and reproduced in this publication (see pages 10 to 16).[15] COPD should be actively sought in all current or former smokers, and in particular in those who have respiratory symptoms (typically cough, wheeze or breathlessness) as they may have more severe disease than asymptomatic smokers. The German research team who were part of the BOLD study of COPD prevalence, together with primary care physicians, found that a new COPD case would be identified in one of every two individuals if they screened all smokers older than 40 years of age who also had symptoms of cough or breathlessness.[16]

There is good evidence that screening with spirometry is helpful for successful smoking cessation. In a study performed

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in a primary care setting in the UK, smoking cessation rates in those aged over 35 years were increased by telling individuals their estimated lung age (the age of the average healthy individual who would have similar spirometry to them), independently of whether the results were normal or abnormal.[17] Such evidence may be sufficient justification for mass screening with spirometry in all smokers for some healthcare givers. However, the US Preventive Services Task Force in 2009 stated that there was no net benefit in mass screening for COPD with spirometry in terms of the overall cost–benefit ratio.[18] Nevertheless, we believe there is sufficient evidence to support case finding of COPD with spirometry in high-risk populations, including current and ex-smokers older than 35 years of age. The box on this page lists the target population for COPD case finding.[2]

Successful smoking cessation before there is loss of lung function will have larger potential benefits in preserving lung function. In early COPD, lifestyle changes (optimisation of weight, exercise, dietary changes) should be instituted as early as possible, with or without pharmacological treatment, depending on the presence of symptoms and exacerbations. The diagnosis of COPD should also alert GPs and other physicians to the increased risk of mortality from any cause, importantly cardiovascular disease, respiratory failure, cerebrovascular disease and cancer, which may have implications for patient management in relation to risk modification.[19]

POTENTIAL TO IMPROVE CLINICAL OUTCOMES

The aim of early detection of airflow limitation is to allow early intervention and, as a result, to improve outcomes. The benefits of early diagnosis of COPD and airflow limitation are poorly studied but the natural history of COPD strongly suggests that intervention should be as early as possible. The earlier the intervention, the greater the potential benefits in terms of improved life expectancy and health outcomes; therefore, the earlier patients can quit smoking, the greater the benefits in terms of preserving lung function.[20] Furthermore, as symptoms usually do not occur until there has been about a 50% loss of FEV_1,[4] then early diagnosis of COPD clearly mandates case-finding: that is, performing spirometry in smokers.

All smokers should be strongly encouraged to quit smoking and, therefore, the presence of COPD should not influence management in terms of smoking cessation. However, there is evidence that smoking cessation is more likely if the subject has airway obstruction. In a smoking cessation program in Poland involving 100,000 people, about 4500 individuals with a history of at least 10 pack-years of smoking were invited to attend a smoking cessation session.[21] More than two-thirds of subjects attended the sessions where spirometry was used as a tool to help quitting. The presence of airway obstruction was associated with higher quit rates at one year (verified by exhaled carbon monoxide level), with the difference being highest in those with severe airflow limitation (16.3% versus 12% in those with normal spirometry results).

After airflow limitation is detected with spirometry, it should be interpreted in the context of the individual patient, as for any test result. Patients are concerned about the consequences to them, in terms of current or future impairment and disability, and possible treatment requirements. Although there is a sound evidence base to inform treatment in some instances, given the heterogeneity of COPD, there are many instances where there is little evidence to inform treatment strategy. Examples include people with asthma who have smoked and those with asthma who have not smoked but have fixed airway obstruction. These people are usually excluded from both asthma studies and COPD studies, so the evidence from studies may not be generalisable to these populations. However, management that is based on identifying and treating clinical problems such as frequent exacerbations, breathlessness, obesity and anxiety in patients who have airways disease may result in greater clinical benefits than the more narrow approach of prescribing an inhaler as specific treatment for the airways.[22] This approach seems logical as the quality of life in patients with airways disease is impaired in proportion to the number of identifiable comorbidities.[23]

The management of patients with COPD, symptomatic and asymptomatic, is summarised in the Figure.[24]

TARGET POPULATION FOR COPD CASE FINDING[2]

Case finding should be considered in individuals aged at least 35 years who meet at least one of the following risk factor or symptom criteria:

- current or ex-smoker
- current or previous occupational dust, gas or fume exposure
- coughs several times on most days, with or without mucous production
- gets more easily short of breath than other people of the same age
- feels wheezy or tight in the chest
- suffers from frequent chest infections

CAN WE ALTER PROGRESSION OF THE DISEASE?

Smoking cessation is the only intervention that can alter the progression of COPD. Although the rate of decline in FEV_1 was shown to be reduced in patients with moderate COPD by treatment with a high-dose, combination inhaled corticosteroid/long-acting β_2-agonist or a long-acting antimuscarinic agent, the effects were small and of uncertain clinical significance.[18,25] Treatment with short-acting antimuscarinic drugs has no effect on the rate of decline in FEV_1.[26] Nevertheless, there is great heterogeneity in the rate of decline in FEV_1, presence of symptoms, systemic disease and exacerbation rates between patients, with some progressing

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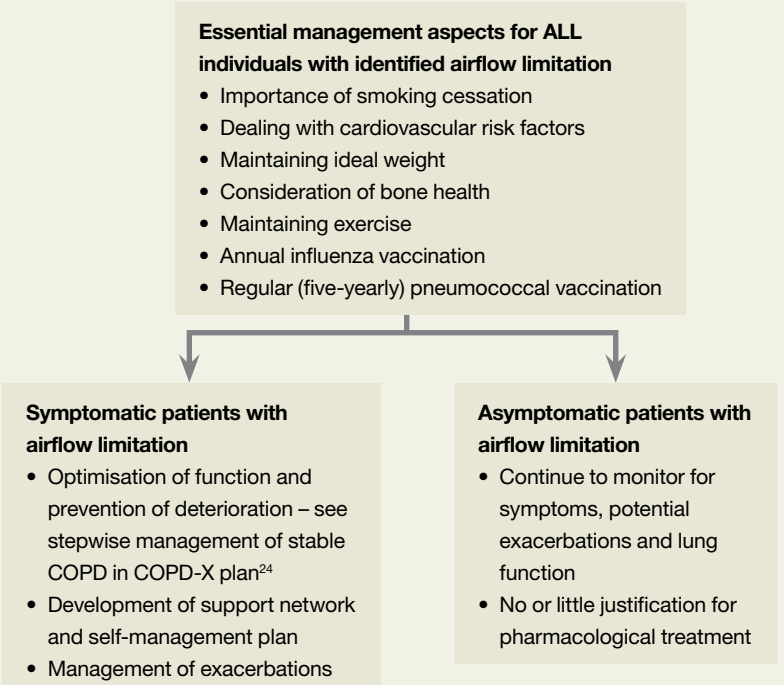

Figure. Management after case finding for COPD in symptomatic and asymptomatic individuals.[24]

quickly in terms of COPD severity while others remain stable for many years.

Currently, there are no clinically useful markers to identify patients with COPD who will decline rapidly or to predict those in whom drug treatment reduces the rate of decline. Although it is known that airway hyperresponsiveness, acute bronchodilator reversibility, respiratory symptoms, reduced FEV_1/FVC ratio, low baseline FEV_1, emphysema, mucus hypersecretion and episodes of lower respiratory tract illness are associated with increased rate of loss of FEV_1, their predictive ability in an individual is likely to be poor and they are not routinely used for this purpose.[27-34]

It is recognised that for a given impairment in FEV_1, there is a wide range of symptom severity and exacerbation risk in COPD. This heterogeneity is reflected in the updated international GOLD strategy document, in which symptoms are included in the severity assessment.[1] The presence of symptoms as defined by the revised GOLD severity classification is associated with an increased risk of exacerbation as well as of mortality for the same degree of airflow limitation defined by spirometry.[35] Following publication of the new GOLD classification, a study involving a large population of COPD patients showed that the presence of symptoms did indeed signify an increased risk of exacerbations and also mortality.[35]

Drug treatment with either single or combination inhaled corticosteroids, long-acting β-agonists or long-acting anti-muscarinic agents improves symptoms and exacerbation risk in patients with moderate COPD (FEV_1, 50 to 80% of predicted), as well as in patients with more severe COPD.[36,37] Although such individuals in the general population are less likely to report any symptoms than those with lower FEV_1, there is great variability. Overall, such patients benefit from pharmacological treatment in terms of improved quality of life and reduced exacerbation risk, with the decision ideally based on a risk–benefit assessment in each individual. It is worthwhile noting that patients entering clinical studies are more likely to be symptomatic because their symptoms identified them as having COPD prior to enrolment. The absence of symptoms or previous exacerbations after thorough history-taking in a patient with moderate airflow limitation (moderate COPD) is associated with a very low risk of exacerbations in the following year – around 2%.[36] Mortality risk is also low at 0.6%.[36] Therefore, asymptomatic individuals who have COPD do not necessarily warrant drug treatment, particularly if they have only mild to moderate FEV_1 impairment.

Thus, the most important treatment in a patient newly diagnosed with airflow limitation whose FEV_1 is greater than 50% of predicted and who is asymptomatic is smoking cessation. Other considerations in such a patient are dealing with cardiovascular risk factors, maintaining ideal weight, considering bone health and maintaining exercise. However, there is no or little justification for pharmacological treatment for COPD because there is little known of the benefits of such treatment in patients with asymptomatic, mild to moderate COPD. This is an area that requires further research.

FUTURE DEVELOPMENTS IN COPD

There is widespread agreement about the need for more research into COPD phenotyping (i.e. clinical, biochemical and inflammatory characterisation) because of the potential for clinic benefit.[38-40] COPD represents a spectrum of disorders that share airflow limitation as their common underlying pathophysiological process but behave differently in many aspects between individuals. Understanding the heterogeneity of COPD better might allow earlier detection as well as development of treatment methods that are

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targeted specifically at certain phenotypic subgroups.

Current methods in practice to phenotype COPD include CT imaging to establish, for example, the presence of underlying emphysema. Although there is firm evidence to support a correlation between the extent of emphysema determined by CT and by histological examination,[41-46] using CT imaging for this purpose has the disadvantages of cost and radiation exposure. New methods being used in research, such as the multiple breath nitrogen washout technique as a measure of small airway function, might potentially allow such phenotypic classification.[47-49]

Disease phenotyping is a current area of research because of the potential to help improve COPD outcomes. Certain COPD phenotypes might respond differently to different treatments (e.g. differing bronchodilator responsiveness), which raises the possibility of individualised management regimens. The tools used to phenotype disease could also identify markers of COPD susceptibility (because only about 20% of smokers develop COPD), allowing very early detection of disease, even before spirometry results have become abnormal.[49]

Ultimately, being able to identify the clinical links between phenotypes and the complex relation with genetic, molecular, cellular and environmental components may translate into the ability to practise individualised medicine rather than a generalised 'one-fits-all' approach to COPD. This could lead to better patient outcomes in terms of morbidity and mortality by delaying progression of disease and improving overall survival.[39,40] Such an approach would be of particular relevance for patients with mild COPD.

SUMMARY

It is worthwhile identifying patients with mild COPD and early disease, but this is possible only if case finding occurs in primary care. Detection of airflow limitation when the patient is asymptomatic and confirmation by spirometry of a diagnosis of COPD identifies individuals at risk of future symptoms and complications of the condition. Better stratification of future risk by actively diagnosing COPD may alter the management in individuals who have additional risk factors for COPD progression and a cardiovascular risk. Performing spirometry in current smokers may increase their chances of smoking cessation.

It is important to recognise that when a previously asymptomatic patient with newly diagnosed airflow limitation develops respiratory symptoms, this represents an exacerbation of COPD. This exacerbation needs to be managed accordingly, and not be misdiagnosed as a simple lower respiratory tract infection. Confirmation or exclusion of COPD allows appropriate drug prescription and helps avoid diagnostic confusion.

Management of COPD, including its pharmacotherapy, continues to evolve as understanding of the condition increases, particularly the appreciation of the heterogeneity of the disease. Case finding of COPD raises complex arguments about cost effectiveness, clinical benefit and appropriate treatment. There are a great number of clinical questions that still need answering by well-designed clinical studies to provide a stronger evidence base to guide management in early COPD. MT

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PEER REVIEWED FEATURE
POINTS: 2 CPD/2 PDP

Optimising function in COPD

Physical activity and pulmonary rehabilitation

JENNIFER ALISON PhD, MSc, DipPhty
SUE JENKINS PhD, GradDipPhys

National and international guidelines strongly endorse the benefits of physical activity and exercise training via pulmonary rehabilitation in patients with COPD.

Key points

- Physical activity levels are reduced in people with chronic obstructive pulmonary disease (COPD).
- Lower physical activity levels in patients with COPD are associated with poorer outcomes.
- People with COPD should be encouraged to meet the recommended guidelines for physical activity.
- Pulmonary rehabilitation, which includes exercise training and education, is an essential component in the management of COPD.
- Pulmonary rehabilitation improves exercise capacity and quality of life, reduces hospitalisations for acute exacerbations and may improve physical activity levels.
- All people with COPD should be offered pulmonary rehabilitation.

In Australia, chronic obstructive pulmonary disease (COPD) is estimated to affect about 14% of people aged 40 years or older.[1] It is the second leading cause of avoidable hospital admissions,[2] and in some rural and remote regions, it is the leading cause.[3] Although the role of pharmacology in the management of COPD is well recognised, physical management is often neglected. This is despite high-level evidence for the positive impact of physical activity and exercise training via pulmonary rehabilitation on the outcomes of the disease, and the recommendations of national and international guidelines that strongly endorse the benefits of physical activity and referral to pulmonary rehabilitation programs.[4-6]

This article outlines the impact of COPD on physical activity levels and highlights the adverse consequences of low levels of physical activity. In addition, the benefits of pulmonary rehabilitation on important patient outcomes are described. GPs have a vital role in the management of COPD. Optimising management by referring patients with COPD to pulmonary rehabilitation programs and

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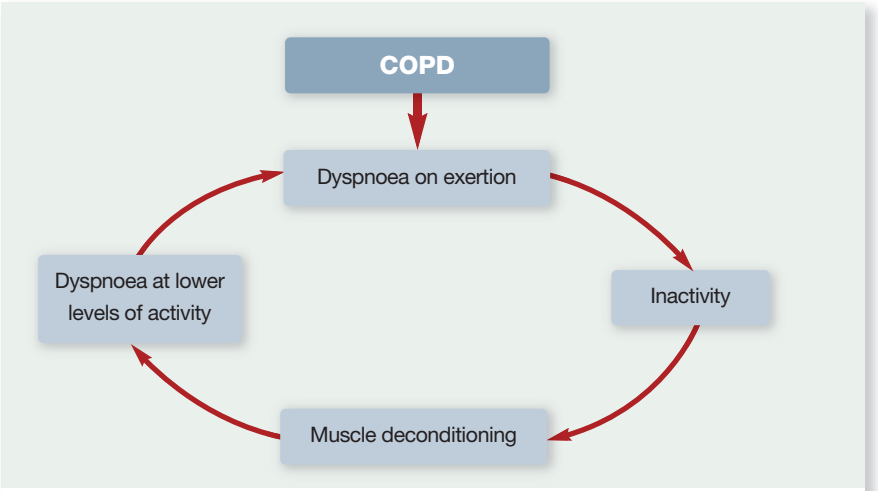

Figure. The disability spiral in COPD.

encouraging patients to be more active will lead to improved patient outcomes.

PHYSICAL ACTIVITY

Physical activity is defined by the World Health Organization (WHO) as 'any bodily movement produced by skeletal muscles that requires energy expenditure'.[7]

In the context of COPD, physical activity can be simply defined as the activity that a person chooses to do within their available exercise capacity. This implies that physical activity levels are not only affected by physiological impairments such as those in the pulmonary, cardiovascular and musculoskeletal systems but also by other factors such as climate, habits or behaviours, self-efficacy and health beliefs.

Are people with COPD inactive?

Dyspnoea on exertion is common in people with COPD and leads to avoidance of the daily activities that elicit this symptom. This results in a downward spiral of progressive inactivity with adverse consequences that includes peripheral muscle deconditioning (Figure), depression, social isolation and poor quality of life.

Measurement of physical activity levels confirm that, compared with an age-matched healthy population, people with COPD have reduced levels of physical activity and that the decline in physical activity progresses as disease severity increases.[8] People with COPD are often sedentary and, compared with age-matched healthy people, have been shown to spend less time walking (46% less) and standing (35% less), and to spend more time sitting (22% more) and lying down (200% more).[9]

Why is physical activity important in COPD?

In people with COPD, higher levels of physical activity are associated with a reduction in the number of hospital admissions due to exacerbations,[10,11] as well as reduced all-cause and respiratory mortality.[10,12,13] Moderate to high levels of physical activity may also have a role in slowing lung function decline and reducing the risk of developing COPD among smokers.[14]

There is strong evidence in the general population that older adults who are physically active have lower rates of all-cause mortality, coronary heart disease, hypertension, stroke, type 2 diabetes and colon and breast cancer, and a higher level of cardiorespiratory and muscular fitness. Also of relevance to older adults are the benefits of exercise as a means of preserving bone mass and reducing the risk of falls.[15] Since people with COPD are mostly in the 'older adult' population, and also have high rates of comorbid conditions, the health benefits from physical activity described above should also be applicable to COPD.

How is physical activity measured?

Physical activity can be assessed using questionnaires, although such self-reporting methods are prone to recall bias (i.e. individuals overestimate their physical activity) and are most useful in large population studies.[16] Objective measures of physical activity use devices such as pedometers, accelerometers and global positioning system (GPS) devices. Pedometers provide a simple and inexpensive method for recording the number of steps taken. However, pedometers do not measure walking duration, speed or grade and are less accurate when people walk very slowly, as is the case in people with very severe COPD. In addition, pedometers do not provide information on other activities not related to walking. Accelerometers and GPS devices offer more detailed information; however, they are expensive. In clinical practice, a combination of a pedometer to record step count and a diary card to record walking duration and nonwalking-based activities may be useful.[17]

What are the recommended levels of physical activity?

In the age category of most people with symptomatic COPD (i.e. 65 years and above), the WHO,[18] the American College of Sports Medicine[15] and the Australian Department of Health and Ageing[19] recommend the following:

- At least 150 minutes of moderate-intensity aerobic physical activity should be undertaken each week (equivalent to 30 minutes a day, five

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days a week). If a pedometer is available patients can be advised that walking at 100 steps/minute is equivalent to moderate-intensity exercise.
- Aerobic activity should be performed in bouts of at least 10 minutes' duration.
- Muscle-strengthening activities, involving major muscle groups, should be done on two or more days a week.
- An overall recommendation for daily exercise is walking at least 7000 steps each day.

If people with severe COPD are unable to perform the recommended amounts of physical activity they should be as physically active as their condition allows.

Can any intervention change the habitual physical activity level?

It is difficult to alter habitual behaviour, especially in relation to exercise and physical activity. There is evidence that exercise training performed within a pulmonary rehabilitation program can result in a small but significant increase in physical activity in people with COPD.[20] Reassuring patients that breathlessness during daily activities is not harmful, and encouraging increased physical activity, may help to enhance participation in regular physical activity.

PULMONARY REHABILITATION

Pulmonary rehabilitation is an evidence-based intervention for patients with chronic lung disease.[5] Its aims are to reduce dyspnoea and fatigue, optimise functional status, increase exercise tolerance and daily physical activity, improve quality of life and decrease the healthcare burden. Pulmonary rehabilitation programs include patient assessment, exercise training and education about disease management.

Why does pulmonary rehabilitation work?

Exercise training is the component of pulmonary rehabilitation that has the strongest level of evidence for benefit.[5,6] Endurance training involving the large muscle groups in the legs induces physiological changes in the exercising muscles. This, in turn, improves the oxidative capacity of the muscles, reduces lactate build-up during exercise and leads to a decrease in ventilation and dyspnoea. Further, significant psychological benefits occur as the patient becomes more confident to undertake physical activities. This helps to reduce anxiety and depression and social isolation and improves quality of life.

The self-management training included in pulmonary rehabilitation programs may enhance the patient's confidence to manage their condition and to continue with regular exercise on completion of the program.

What are the outcomes of pulmonary rehabilitation?

The outcomes of pulmonary rehabilitation are summarised in the box on this page.[6,20-24] Pulmonary rehabilitation has been shown to produce clinically significant improvements in symptoms (dyspnoea and fatigue), exercise tolerance and quality of life.[6,21] Importantly, it reduces hospitalisations for acute exacerbations of COPD and is cost effective.[22,25]

What is involved for the patient?

Most pulmonary rehabilitation programs provided within Australia last for at least eight weeks.[26] Although most participants in these programs have COPD, individuals with other respiratory conditions, such as interstitial lung disease, bronchiectasis or asthma, and patients undergoing lung surgery may also attend classes.

Patients usually participate in two supervised exercise classes each week and complete an individually prescribed home exercise program on an additional two or three days a week. The exercise classes typically last between 60 and 75 minutes and involve groups of six to 10 patients. An example of a pulmonary rehabilitation program session is given in the box on page 26.[27]

BENEFITS OF PULMONARY REHABILITATION IN COPD[6,20-24]

Reduces
- Symptoms (dyspnoea and fatigue)
- Anxiety and depression
- Hospitalisations for exacerbations
- Mortality*

Improves
- Exercise tolerance
- Quality of life
- Physical activity levels

* When pulmonary rehabilitation commences after an exacerbation.

Within Australia, physiotherapists are responsible for exercise prescription and training in over 90% of programs, with nurses or exercise physiologists who have undergone training in pulmonary rehabilitation providing supervision in the remaining programs.[26]

Before starting rehabilitation, patients undergo an assessment that involves a walking test with pulse oximetry to measure exercise capacity and oxygen desaturation during exercise, and assessment of dyspnoea and quality of life. These measures are repeated at the end of the program to evaluate the patient's response to rehabilitation. In addition, at the initial assessment comorbid conditions that might impact on the ability or safety to exercise, such as cardiovascular, musculoskeletal or neurological impairments and psychological status, are documented. The minimum requirements for patient assessment and the safety considerations, including emergency procedures, are detailed elsewhere.[28]

Although patients exercise with a group, each patient has his or her own individually tailored exercise program. Performing exercise in the group setting is beneficial, as patients see other people who are breathless and gain support and

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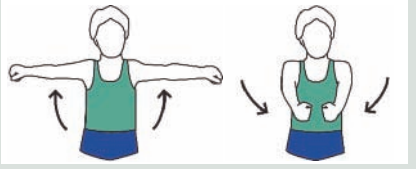
PULMONARY REHABILITATION PROGRAM: EXAMPLE SESSION

Step 1. 20 to 30 minutes
Lower limb endurance exercise
– e.g. walking and cycling

Step 2. 15 minutes
Upper limb endurance exercises
– e.g. arm reaches



Step 3. 10 minutes
Lower limb strengthening exercises
– e.g. wall squats

Step 4. 10 minutes
Upper limb strengthening exercises
– e.g. arm raises

Refer to the Lung Foundation Australia's Pulmonary Rehabilitation Toolkit for examples of other exercises to include in each step noted above. The toolkit can be viewed online at: http://www.pulmonaryrehab.com.au/welcome.asp[27]

Drawings courtesy of Lung Foundation Australia.

motivation from their peers.

Supplemental oxygen is used during training in patients receiving long-term oxygen therapy (LTOT) and those who have normal oxygen levels at rest but demonstrate profound oxygen desaturation during exercise and are shown to benefit from oxygen. Some patients use short-acting inhaled bronchodilators prior to training if spirometry results confirm that such use provides benefits beyond that provided by the long-acting bronchodilators that the patient may be prescribed.

Many programs also include a component of education, which may involve several members of the multidisciplinary team. The education may include topics such as understanding COPD, disease management, the benefits of exercise and physical activity, nutrition, medications, how to use devices for delivery of medications, oxygen therapy and breathing techniques.

Following the supervised pulmonary rehabilitation program, it is essential that patients continue to maintain a regular home exercise program, as the benefits of a pulmonary rehabilitation program decline over the following 12 to 18 months if regular exercise is not maintained.[5] Where resources permit, participating in a weekly supervised maintenance exercise class or attending pulmonary rehabilitation periodically for assessment of exercise tolerance are strategies that may assist patients to continue with a regular exercise regimen.[29,30]

What types of exercise are important?

Training the muscles of ambulation with a walking or cycling program is an essential component of a pulmonary rehabilitation program. To achieve benefits, patients need to perform walking or cycling exercise for at least 30 minutes per session three to five days each week.[6] A minimum of 20 sessions of exercise training are required to achieve a physiological benefit.[5,6]

Walking is an activity that people who are breathless avoid; however, it is an essential component of everyday life. Therefore, most programs emphasise walking training as an important mode of lower limb endurance exercise. Walking and cycling training are often undertaken in an intermittent manner so that the patient takes frequent short rests during the 30-minute exercise period to avoid intolerable dyspnoea or muscle fatigue. A simple circuit of exercises aimed at improving the strength and endurance of the arm and leg muscles so that the patient is able to undertake more easily activities of daily living is also prescribed. The exercise prescription is tailored to the individual based on assessment findings.

Patients need reassurance that breathlessness during activity is not harmful. It is important that exercise is continued long term, so most programs use simple equipment to allow replication of the exercises in the home setting. In addition to regular exercise, patients participating in a pulmonary rehabilitation program are encouraged to increase their level of daily physical activity.

Where resources for carrying out exercise training are limited, a program that

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CRITERIA FOR REFERRAL TO PULMONARY REHABILITATION

Inclusions

- Clinical diagnosis of COPD confirmed by spirometry
- Optimised medical management
- Dyspnoea during physical activity
- Current smokers should not be excluded

Exclusions

- Comorbidities that compromise safety or ability to participate in exercise testing or training – e.g. unstable cardiovascular disease, uncontrolled diabetes, recent exertional syncope, severe neurological impairment, severe cognitive impairment
- No motivation to attend

comprises only walking training provides a simple, readily available alternative that requires no resources and has been shown to be beneficial.[31] Details of strategies for exercise training when resources are limited have been described elsewhere.[28]

Which patients benefit from pulmonary rehabilitation?

The box on this page details the criteria for referral to pulmonary rehabilitation. The referring doctor can increase the likelihood of a patient participating in a pulmonary rehabilitation program by being enthusiastic and advocating the benefits.[32,33]

Improvements following rehabilitation have been demonstrated in patients with mild, moderate and severe COPD. Any patient with lung disease whose lifestyle is affected by dyspnoea may gain benefits from a pulmonary rehabilitation program. Often, mild symptoms such as dyspnoea only when walking up inclines or climbing stairs are ignored and attributed to ageing, weight gain or lack of exercise and not the underlying lung problem. As a result, many patients who potentially would benefit are not identified as candidates for rehabilitation.

When determining whether a patient is likely to benefit from a pulmonary rehabilitation program, the COPD Assessment Test (CAT, available online: http://www.catestonline.org) may also be useful, as it elicits information about limitation in the ability to perform activities of daily living and symptoms of exertional dyspnoea and fatigue.

Where can pulmonary rehabilitation programs be found?

Lung Foundation Australia has a list of pulmonary rehabilitation programs offered throughout Australia (http://lungfoundation.com.au/professional-resources/pulmonary-rehabilitation/programs). Most take place in hospitals, although some take place in community centres. More pulmonary rehabilitation programs are urgently required to meet the need for this effective intervention.

CONCLUSION

Appropriate management of the physical consequences of COPD through pulmonary rehabilitation can have a significant positive impact on patient outcomes. By referring patients with COPD to pulmonary rehabilitation programs and encouraging them to increase daily physical activity, GPs can help to improve the outcomes of these patients. MT

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PEER REVIEWED FEATURE
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Managing severe COPD
Much can be done

Key points

- Management of patients with severe COPD is challenging, but with a combination of therapeutic approaches much can be achieved.
- Pulmonary rehabilitation may improve symptoms and quality of life and reduce exacerbations in patients at all stages of disease severity.
- Detecting and managing comorbidities, including cardiac disease, osteoporosis, anxiety and depression, are important in improving patient outcomes.
- Oxygen therapy improves prognosis in patients with chronic hypoxaemia.
- Noninvasive ventilation is useful in managing acute hypercapnic exacerbations of COPD.
- Clear communication focusing on likely disease trajectory, prognosis, goals of care and advance care planning is essential.
- Patients with very severe COPD may require palliative care, ideally provided by their usual care providers, but some patients require specialist palliative care referral.

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Severe COPD may be challenging to manage as patients often experience debilitating symptoms that fail to respond completely to disease-specific treatment. Clear communication about the goals of care combined with management of symptoms and comorbidities should enable patients to enjoy a better quality of life.

Chronic obstructive pulmonary disease (COPD) is a common and progressive disease associated with significant morbidity and mortality. Access Economics estimated in 2008 that more than one million Australians had moderate COPD, with a further 150,000 having severe COPD.[1] A careful history and clinical examination may suggest a diagnosis of COPD, but they do not reliably predict airflow obstruction and spirometry is essential to confirm the diagnosis.

COPD is defined as severe in spirometric terms when the postbronchodilator forced expiratory volume in 1 second (FEV_1) is less than 40-50% predicted,[2,3] with very severe disease defined by a post-bronchodilator FEV_1 less than 30% predicted.[3] Although the FEV_1 correlates well with prognosis, the degree of airflow obstruction alone may be poorly predictive of symptoms. Guidelines recommend assessing symptom burden (especially the degree of dyspnoea), degree of activity limitation and frequency of exacerbation, along with FEV_1, when determining treatment needs.[3]

This article discusses the management of patients who are severely symptomatic with an FEV_1 at the 'very severe' or 'severe' end of the COPD spectrum. The specific management of acute exacerbations of COPD has been discussed in the article 'COPD exacerbations: improving outcomes', published in the April 2013 issue of *Medicine Today* (see pages 36 to

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41 of this supplement),[4] although the use of acute noninvasive ventilation for hypercapnic exacerbations is discussed briefly here.

MANAGING SYMPTOMS IN SEVERE COPD

Patients with very severe COPD may have symptoms as debilitating as those with advanced cancer.[5] A cardinal feature of very severe COPD is profound dyspnoea. Cough, fatigue, poor social functioning, high rates of depression and anxiety and poor quality of life are also prominent symptoms.[6,7] Carers of people with very severe COPD also have significant morbidity.[7] Despite intensive treatment, disease-specific symptom relief may be inadequate and many patients receive inadequate palliative care.[8] Throughout the range of disease severity, treatments for COPD are largely directed at:

- improving symptoms
- preventing deterioration, notably through reducing exacerbations, with their known impact on disease progression and quality of life.

Both nonpharmacological and pharmacological therapies have a role.

NONPHARMACOLOGICAL THERAPIES

Smoking cessation

In patients with mild-to-moderate COPD, smoking cessation reduces lung function decline and mortality[9] and improves respiratory symptoms and health-related quality of life.[10] Although similar long-term studies are not available in those with severe COPD, health benefits are likely from smoking cessation at all stages of the disease, and counselling (with additional pharmacotherapy if needed) should be offered to all patients.

Physical activity and pulmonary rehabilitation

Patients with COPD typically reduce their participation in activities that induce breathlessness and fatigue; none more so than those with very severe disease. Continued limitation of daily activities and worsening symptoms (despite reduced activities) induces deconditioning. This results in an ongoing dynamic of symptoms affecting activities, and vice versa, often referred to as the 'dyspnoea spiral' or downward cycle of deconditioning with worsening symptoms and further restriction of activity.

Regular physical activity is recommended for all people with COPD, and has been associated with reduced hospital admissions.[11] Pulmonary rehabilitation is an evidence-based, multidisciplinary program involving graded exercise, education, behaviour modification and psychosocial support, typically provided on an outpatient basis, two or three times weekly over six to eight weeks. Pulmonary rehabilitation improves dyspnoea, exercise capacity and health-related quality of life as well as improving symptoms of anxiety and depression and reducing health care utilisation.[12]

Although patients may be hesitant to consider exercise when their dyspnoea is severe, support from their primary care physician is key,[13] and even patients with very severe COPD can achieve benefits. Pulmonary rehabilitation programs in Australia are generally run through hospital outpatient departments or community health centres. Information about local programs can be obtained through Lung Foundation Australia's website (http://lungfoundation.com.au).

Vaccination

Influenza vaccination reduces acute exacerbation of COPD, although its effect on health care utilisation and mortality is unclear. Guidelines recommend yearly influenza vaccinations and up-to-date pneumococcal vaccination for all people with COPD.[2]

PHARMACOTHERAPY

Inhaled therapies

Titration of inhaled therapy for COPD is recommended using a stepwise approach to enable evaluation of each additional medication before adding another and to minimise side effects.[2,3] Treatment should be based on the patient's symptoms, exacerbation risk and response until, ideally, adequate disease control is achieved. Short-acting beta agonists (SABAs) or anticholinergics (SAMAs) are effective in providing acute symptom relief,[14,15] while longer-acting beta agonists (LABAs)[16,17] or anticholinergics (LAMAs)[18-21] may improve quality of life and reduce exacerbation frequency.

The inflammatory response in COPD is relatively corticosteroid-insensitive. Although inhaled corticosteroids may reduce exacerbation frequency and decline in quality of life when prescribed in combination with LABAs for patients with FEV_1 less than 50% predicted and frequent exacerbations (two or more in 12 months), the improvement over LABA alone is of questionable significance. In addition, benefits need to be weighed against the known increased risk of pneumonia with their use.[22] There is some evidence that the combination of a LAMA and LABA is better than either monotherapy.[23] However, evidence for triple therapy (LABA, LAMA and inhaled corticosteroid) is conflicting. It is important to note that using more than one agent from each class does not confer additional benefit and should be avoided, suggesting the need for careful and regular review of patients' pharmacotherapy.

When changing pharmacotherapy, the clinician should consider treatment response in terms of dyspnoea, functional status, history of exacerbations and patient preference. In an individual with severe COPD, decisions about which therapies to continue will likely be based on various factors, including:

- severity of symptoms
- frequency of exacerbations with or without the need for hospitalisation
- device preference
- adverse effects
- potential long-term benefits

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- other comorbidities and their treatments
- cost and minimisation of polypharmacy.

Longer-term therapeutic trials are needed to determine the impact of changing therapies on exacerbations.

Inadequate device use is very common in patients with COPD, and many primary care as well as specialty physicians and nurses are inadequately equipped to instruct patients in proper inhaler use.[24] Health professionals should ensure they are capable of instructing patients and caregivers on inhaler use, and review should be repeated at each visit to ensure maintenance of proper technique.[24]

Other therapies

Unfortunately, patients with severe COPD may continue to experience significant symptoms despite the use of evidence-based therapies. Theophylline is considered a third- or fourth-line bronchodilator because of its narrow therapeutic window and significant side effects. Although it may be helpful in some individuals with severe COPD, its role in patients who are already receiving various combination therapies is unclear.

Mucolytic drugs may be beneficial in decreasing sputum viscosity and reducing disability and exacerbations, but their role in patients who are already receiving inhaled corticosteroids is, similarly, unclear.[25]

MANAGING SYSTEMIC EFFECTS AND COMORBIDITIES

COPD is often associated with comorbidities, many of which share common systemic inflammatory features with COPD. Most common among these are systemic hypertension, dyslipidaemia, diabetes, coronary heart disease, heart failure and osteoporosis.

Some of the management principles described above can also be applied to preventive and therapeutic interventions for these common comorbidities. Smoking cessation, exercise and rehabilitation all have the potential to benefit a range of chronic diseases. Specific treatments such as the use of statins to manage hyperlipidaemia have provoked considerable interest because of studies suggesting they may have beneficial effects in patients with COPD over and above their impact on cardiac risk.[26] Prospective studies are awaited.

Cardiovascular disease

Cardiovascular disease is the most frequent and important of all COPD comorbidities and may contribute significantly to disease burden. Beta blockers have proven mortality benefits in the management of cardiac disease but their use is limited in patients with COPD because of their potential to cause acute bronchospasm, increase airway hyper-responsiveness and worsen respiratory symptoms. Concerns have been allayed to some extent by a recent meta-analysis suggesting that cardioselective beta blockers are safe in patients with COPD, even in those with severe airflow obstruction.[27] Nonetheless, the included studies were of short duration and the absolute numbers included were small, thus providing little guidance about long-term safety and potential morbidity. European Society of Cardiology guidelines state that COPD is not a contraindication to the use of beta blockers; however, low-dose initiation and gradual up-titration is recommended.[28]

Osteoporosis

Osteoporosis is a major comorbidity in COPD and patients are at increased risk even in the absence of corticosteroid use. Although no clear association has been demonstrated between the inhaled corticosteroids most commonly used in Australia and increased bone fragility, regular courses of oral corticosteroids will further increase osteoporosis risk. Index of suspicion should be high and treatment should proceed according to standard guidelines.

Anxiety and depression

Patients with COPD have an increased prevalence of both anxiety disorders and depression compared with the general population. These conditions increase disability and social isolation and impair functional status, resulting in reduced quality of life and poorer prognosis.

Standard management principles apply, although evidence for the effectiveness of specific pharmacotherapy is limited in patients who also have COPD and further clinical trials are needed.[3] Exercise in the context of pulmonary rehabilitation has proven beneficial in management.[29]

Other comorbidities

Other comorbidities that may compromise survival and add considerably to the overall burden of COPD include diabetes mellitus, hypertension and vasculopathy, as well as systemic consequences of COPD, such as weight loss and muscle dysfunction due to inactivity and deconditioning. The metabolic and vascular issues should be investigated and treated appropriately, and pulmonary rehabilitation is again important in managing the consequences of inactivity and deconditioning.

Although low body weight is associated with a poorer prognosis, and nutritional advice should be provided, the effects of nutritional supplementation in underweight patients with COPD have been disappointing.[30] In the absence of guidelines for the management of multimorbidities, other comorbidities should be managed according to relevant disease-specific guidelines.

OXYGEN THERAPY

Long-term continuous oxygen therapy

Oxygen therapy may be appropriate in patients with severe COPD for the management of hypoxaemia. When PaO_2 is 55 mmHg or below, or PaO_2 is 59 mmHg or below in the presence of pulmonary hypertension, right heart failure or

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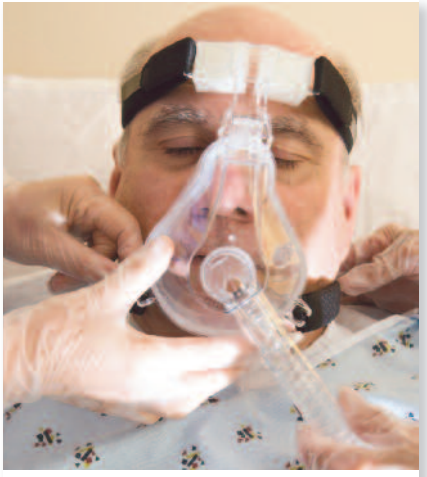

Figure. NIV mask being placed on patient.

polycythaemia, continuous oxygen therapy for at least 15 hours per day (or as long as 24 hours, if tolerated) has been shown to prolong life.[31,32]

Right heart failure presenting as ankle oedema or raised jugular venous pressure in a patient with COPD should flag the need for arterial blood gas measurement. Other indicators suggesting a need for measurement of arterial blood gases include the presence of cyanosis or polycythaemia, known very severe COPD with FEV_1 less than 30%, and pulse oximetry reading less than 92%.[3] Australian guidelines recommend oxygen therapy should only be provided to those who have ceased smoking.[33]

In patients with COPD, low flow rates of oxygen (2 L/minute) via nasal cannula are generally sufficient to raise oxygen saturations to satisfactory levels and there is usually no requirement to increase flow rates nocturnally.[34] It is important to explain to patients that the indication for long-term oxygen use is the presence of hypoxaemia but that there may be no improvement in dyspnoea through its use. In addition, a recent randomised controlled trial found no benefit over placebo air in terms of breathlessness for patients who are not hypoxic.[35]

Ambulatory oxygen

Ambulatory oxygen may be used for patients with COPD requiring continuous oxygen in order to maximise relief of hypoxaemia throughout the 24-hour period and to increase mobility. Portable cylinders are available through a range of government-supported schemes (which vary between states and territories)[36] and are generally used with a conservation device. Generally, portable oxygen concentrators are not provided through government-subsidised programs, but many patients find the concept of these light-weight, battery-operated devices, attractive, even though they are expensive. It is, as yet, unclear what role they offer in terms of long-term oxygen use.

Although laboratory-based studies have shown that supplemental oxygen can reduce ventilation and improve exercise capacity in breathless patients with COPD who do not fulfil criteria for the requirement of continuous oxygen therapy, use of oxygen in the ambulatory setting for relief of breathlessness is of questionable benefit. A recent large, randomised controlled trial demonstrated no benefit of oxygen therapy over medical air in relieving breathlessness or improving exercise capacity or quality of life.[37] The indistinguishable benefits over the period of the study of both oxygen and air raise the possibility that inhaled therapy with either gas provides a powerful placebo effect.

Nocturnal oxygen therapy

Hypoxaemia may occur during sleep in patients with severe COPD due to hypo - ventilation or worsening ventilation-perfusion. Clinical consequences of isolated nocturnal hypoxaemia are unknown and results of clinical trials of nocturnal oxygen therapy in such patients have been contradictory. Further studies are needed, but current consensus suggests that nocturnal oxygen therapy may be indicated in patients whose nocturnal arterial oxygen saturation repeatedly falls below 88% or who have evidence of hypoxia-related sequelae. Any contributing factors such as obstructive sleep apnoea or cardiac failure must first have been treated optimally.

NONINVASIVE VENTILATION

Noninvasive ventilation (NIV) is any form of ventilatory assistance delivered without the need for an endotracheal tube.[38] It consists of an electronically powered device, fitted to the patient via a mask, which provides ventilatory support. Some authors include continuous positive airways pressure (CPAP), in this definition, while others include only BiLevel CPAP (Figure). CPAP provides a single pressure throughout the respiratory cycle whereas BiLevel CPAP alternates between two pressures; a higher pressure at inspiration and a lower pressure at expiration. Most BiLevel devices have the capacity to respond to the patient's respiratory efforts or to provide extra 'breaths' if the patient's respiratory rate is low.

NIV in acute respiratory failure

NIV plays a key role in the routine management of patients with acute hypercapnic respiratory failure requiring ventilatory support due to acute exacerbations of COPD. Before the availability of NIV, such patients often required invasive ventilation in the ICU, with consequent poor acute outcomes. Used in combination with other treatments for acute exacerbations of COPD, NIV is clearly superior to intubation in terms of mortality, morbidity and length of stay.[39,40] In addition, complications associated with intubation, such as ventilator-associated pneumonia, are much reduced.[39,40] NIV can be delivered outside the ICU setting and may be a more agreeable option for patients compared with intubation as they are able to eat, talk and receive physiotherapy during the period of NIV support. The utility of NIV in relieving breathlessness is less certain.[41]

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NIV in chronic respiratory failure

NIV in overlap syndrome

Both obstructive sleep apnoea (OSA) and COPD are common diseases, and the occurrence of both in a single patient is termed the 'overlap syndrome'. The morbidity and mortality of the overlap syndrome is greater than that of either COPD or OSA alone.[42] A recent observational trial of CPAP in patients with overlap OSA/COPD found decreased hospitalisations and mortality in the treated group.[43]

The impact of coexistent OSA on the natural history of COPD is not yet known. When evaluating a patient with either OSA or COPD, a high index of suspicion is crucial to diagnose the overlap syndrome. Daytime hypercapnia and pulmonary hypertension out of proportion to the severity of the disease in patients known to have only one disease (either OSA or COPD) should prompt assessment for the other disorder. Currently, CPAP (with oxygen therapy as needed) is the treatment of choice for the overlap syndrome.

Home nocturnal NIV in COPD

Patients with severe COPD may develop significant oxygen desaturation and hypoventilation nocturnally.[44,45] Respiratory muscle fatigue is believed to contribute to both gas exchange abnormalities and symptoms, and some studies have found both sleep and respiratory failure parameters are improved by domiciliary nocturnal NIV.[46,47] However, the reported impact on daytime function, breathlessness, quality of life and mortality of home-delivered nocturnal NIV has been contradictory. For instance, a large Australian trial found that although nocturnal NIV improved survival, this was at the expense of decreased quality of life, tempering enthusiasm for the use of NIV in this population.[48] The decision to initiate chronic nocturnal NIV remains contentious and is generally made by specialist providers, often following an inpatient admission for acute hypercapnic respiratory failure. Ongoing research is required to delineate the role of NIV for COPD in the home setting.

SURGERY AND DEVICES

Occasional patients with severe, disabling COPD may be suitable for consideration of lung transplantation (younger patients with fewer comorbidities), whereas those who have predominant upper lobe emphysema with marked hyperinflation or 'gas trapping' may benefit from lung volume reduction surgery. Alternative nonsurgical approaches include a type of 'bronchoscopic lung volume reduction'. Discussions about such highly specialised palliative approaches necessitate referral of patients to a specialist centre.

ADVANCE CARE PLANNING IN COPD

Advance care planning (ACP) is the process by which patients, families and health professionals discuss and establish future goals of care according to the patient's values and preferences. It includes clarifying a patient's understanding of their illness and treatment options, identifying their wishes and appointing a substitute decision maker.[49,50] It is an ongoing process, and decisions may change as COPD progresses.

ACP can improve patient and family satisfaction with care,[49,50] limit burdensome treatment at the end of life in line with patient preferences,[49,50] and reduce stress, anxiety and depression in surviving relatives.[51] Many patients with COPD and their families want information about the diagnosis, its likely progress and prognosis and what dying might be like, and they want to participate in ACP.[52] Despite this, many patients with advanced COPD lack knowledge about the disease and its likely time course and may be unaware that the disease will progress and may be fatal.[53]

Patients expect their doctors to initiate conversations about ACP,[54,55] and appreciate it when they do. Some doctors may find these conversations difficult, and may be unsure as to how to get started. The Victorian Quality Council has recently developed 'The Next Steps' program to assist doctors in undertaking ACP conversations. Materials including videos of patient scenarios and access to a patient ACP e-simulation are available on the council's website (http://www.health.vic.gov.au/qualitycouncil/activities/training.htm).

PALLIATIVE CARE

Definition of palliative care

Palliative care is an approach that improves the quality of life of those facing life-threatening illness, through early identification, assessment and treatment of pain and other problems, physical, psychosocial and spiritual.[56] Importantly, palliative care and end of life care are not synonymous. A palliative approach, focusing on symptom relief, may be applicable for quite some time before death. End of life care refers to the period just prior to death.

Need for palliative care in COPD

The need for palliative care in COPD is increasingly being recognised. As dyspnoea may be difficult to relieve in patients with very severe COPD despite maximal standard therapy, evidence-based symptom-directed therapy may be appropriate. Treatment may include nonpharmacological therapies such as fans or the use of low doses of opioids that have a demonstrated role in the palliation of intractable dyspnoea.[57,58] Other common symptoms include fatigue, xerostomia, cough and chest pain. The Australian *Therapeutic Guidelines: Palliative Care* offers excellent practical guidance regarding symptom-directed strategies.[59]

COPD is characterised by repeated exacerbations, any of which might be fatal. Patients' palliative care needs may increase during exacerbations and decrease afterward, and access to palliative care should be on the basis of need rather than prognosis. Specialist palliative care involvement may vary to accommodate these changing needs but some changes in service models are required.[60] (For example,

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models of care are required that facilitate shared care involving specialist palliative care providers when needs are especially high or complex and other providers when needs are less.)

Usual care providers (GPs, community nurses, specialist physicians) may be best placed to provide most patients' palliative care needs,[61-62] but may need additional training to do so.[64-68] Specialist expertise should be reserved for treating complex symptomatology or for discussions when there are complex psychosocial factors impeding care. Clear, effective communication is important and excellent Australian guidelines may aid such conversations.[69]

When to refer to palliative care

There is no consensus on when to refer patients with COPD to palliative care, but clinical pointers include:

- repeated hospital admissions
- being housebound or chairbound
- an FEV_1 less than 30% predicted
- on long-term oxygen, or
- a BMI below 20 kg/m^2.[70]

An exacerbation requiring NIV might also prompt referral, given the one-year survival after such an episode is only 50%.[71] In addition, referral may be considered for patients with difficult-to-manage symptoms, who are unresponsive to usual therapy or with complex psychosocial situations and/or complex ACP needs.

END OF LIFE CARE

Although some patients die of COPD, many die with the disease.[72,73] However, patients with COPD are more likely to die in the ICU than those with lung cancer, despite having an equal desire to die at home.[73] This may be due to the final, fatal exacerbation being indistinguishable from previous exacerbations, compounded by a medical and social culture that strives for restitution of pre-morbid health.[74]

End of life care for patients with COPD requires clear communication about the goals of care, assessment and management of symptoms and attempts to promote and maintain dignity. This implies the ability to 'diagnose' dying,[74] which can be challenging in patients having a COPD exacerbation. A time-limited trial of usual exacerbation treatments (antibiotics, corticosteroids, bronchodilators and/or ventilatory support with NIV or even invasive ventilation) may be appropriate.[75,76] If the patient fails to improve, the diagnosis of dying is made and comfort becomes the focus. The Liverpool Care Pathway for the Dying Patient may be helpful to guide such care.[77]

Although a detailed discussion of end of life care is beyond the scope of this article, medications that may be used include opioids for breathlessness, antipsychotics and benzodiazepines for agitation and anticholinergics for the management of terminal secretions. Guidance may be found in *Therapeutic Guidelines: Palliative Care*.[59]

CONCLUSIONS

Patients with severe COPD require maximal tolerated standard treatment for targeted at symptom control, prevention of exacerbations and treatment of comorbidities, including cardiovascular disease, anxiety and depression. Hypoxaemia may warrant consideration of long-term oxygen therapy. Pulmonary rehabilitation improves exercise capacity and dyspnoea, even in patients with severe COPD.

Intractable breathlessness may be treated by nonpharmacological methods and/or judicious use of pharmacological treatments. A palliative approach to COPD care focusing on symptom relief should be considered as exacerbations become more frequent and symptom control becomes more difficult. Specialised palliative care services may be involved at this stage.

End of life care in COPD requires clear communication about the goals of care, ideally should involve the patient and their caregivers and should be initiated through advance care planning. Discussions should preferably occur well before death is imminent, and continue through to the end of life. MT

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PEER REVIEWED FEATURE
POINTS: 2 CPD/2 PDP

COPD exacerbations

Improving outcomes

PAUL KING PhD, FRACP

Early diagnosis and treatment of exacerbations of chronic obstructive pulmonary disease (COPD) may improve outcomes and avoid the need for hospital admission.

Key points

- **An exacerbation of COPD is characterised by a change in the patient's baseline symptoms of dyspnoea, cough and/or sputum production that is acute in onset and may warrant a change in medication.**
- **An increased respiratory rate and/or airway inflammation may result in dynamic hyperinflation and gas trapping.**
- **Appropriate management of exacerbations includes the use of bronchodilators, systemic corticosteroids, antibiotics and, in severe exacerbations, noninvasive positive pressure ventilation.**
- **Patients who have had one exacerbation are highly likely to have a recurrence. An appropriate follow-up management plan and early initiation of therapy may improve outcomes.**

An exacerbation of COPD is an event in the natural course of the disease characterised by a change in the patient's baseline dyspnoea, cough and/or sputum production that:

- is beyond normal day-to-day variations
- is acute in onset
- may warrant a change in regular medications in a patient with underlying COPD.[1]

As such, exacerbations vary markedly in their severity and clinical features. They are the main reason for treatment and hospitalisation of patients with COPD, and are closely associated with functional decline and mortality.

Exacerbations also become more frequent as COPD worsens. A recent major study found that the main predictor of exacerbations was previous exacerbations. There is, therefore, a proportion of patients who have the frequent exacerbator phenotype.[2]

The topic of COPD exacerbations has been comprehensively reviewed in the COPD-X guidelines, which are available from Lung Foundation Australia (http://lungfoundation.com.au) and directly from the COPD-X website (http://www.copdx.org.au).[3,4]

PATHOPHYSIOLOGY

By definition, COPD is characterised by airflow limitation that is not fully reversible. This results in a longer period required to exhale gas from the lung because of reduced diameter of the airways. Any factor that increases the respiratory rate results in a decreased time period available for expiration (as typically occurs in exercise). In patients with airway obstruction, an increased respiratory rate may not allow enough time to exhale fully before another breath needs to be taken, and this can cause air-trapping and dynamic hyperinflation. When patients stop exercising, the respiratory rate typically reduces and the increased period available for exhalation allows deflation of the lung.

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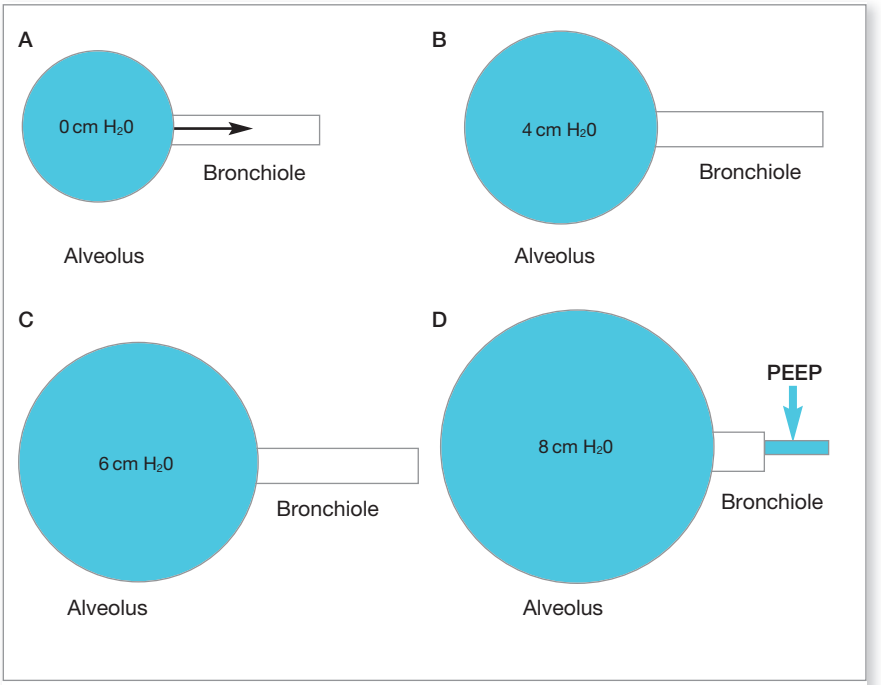
In exacerbations there is often increased airway inflammation and obstruction and an increased respiratory rate. As shown in work by O'Donnell and colleagues, and illustrated in Figure 1, this can result in a progressive increase in end-expiratory pressure and high intrathoracic pressures during exhalation (positive end expiratory pressure; PEEP).[5] This has two key functional effects:

- as alveolar pressures are positive at the end of expiration, a significant respiratory effort is required to expand the lungs enough to create a flow of air into the lungs
- the significant expiratory effort required to breathe out compresses the airways, further exacerbating the airflow obstruction.

In severe cases this results in progressive dynamic lung hyperinflation and patient exhaustion with consequent respiratory failure.



Figures 1a to d. Dynamic hyperinflation in COPD. a (top left). At the end of expiration (i.e. just before inspiration) pressure in the alveolus should normally be close to 0 cm H_2O. b to d (top right, bottom left and right). In an exacerbation of COPD there is air trapping, which leads to progressive dynamic hyperinflation of the alveolus and a positive pressure at the end of expiration. In addition, the strong effort to exhale causes positive end expiratory pressure (PEEP), which collapses the bronchiole, worsening obstruction (d; bottom right).

PRECIPITATING FACTORS

Exacerbations of COPD may be precipitated by various factors, particularly infections and airway pollutants. The most common cause is bacterial infection, responsible for about half of all exacerbations of COPD.[6] The main bacterial pathogens are *Haemophilus influenzae, Streptococcus pneumoniae* and *Moraxella catarrhalis*. Viral infections may also cause exacerbations.[7] A recently recognised entity is viral and bacterial co-infection, which may result in worse exacerbations.[8]

DIAGNOSIS AND ASSESSMENT OF SEVERITY

The diagnosis of an exacerbation of COPD may not be straightforward. Most cigarette smokers do not have severe COPD, and COPD may also occur in nonsmokers. In addition, there is considerable overlap in the symptoms with other conditions such as pneumonia and chronic congestive heart failure.

Lung function testing that has confirmed airflow obstruction previously with minimal or no reversibility is very helpful, as is a history of exacerbations. Increased sputum production and a change in sputum colour (e.g. white to green) are important symptoms (Figure 2) and correlate with airway inflammation.[9]

A key decision to make is whether patients can be managed at home or should be referred and admitted to hospital. Those who have documented previous severe exacerbations with respiratory failure or have clinical evidence of significant respiratory distress should generally be referred to hospital. The box on page 38 lists factors that may indicate the need for admission of patients attending the emergency department.

Assessment of all patients with COPD exacerbations who attend an emergency department should include measurement of urea, electrolytes and arterial blood gases and a chest x-ray. Patients who have acute respiratory failure with a low pH and elevated pCO_2 are likely to be candidates for assisted ventilation.

Shorr and colleagues have described the BAP-65 score, which uses age, blood urea,

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Figure 2. A key symptom of an exacerbation is a change in sputum colour (typically from white to yellow/green).

FACTORS INDICATING THE NEED FOR HOSPITAL ADMISSION

- Previous severe exacerbation
- Failure to improve on outpatient therapy
- Significant respiratory distress
- Major comorbidities
- Altered mental status
- Tachycardia
- Respiratory failure
- Abnormalities in blood gases, blood urea
- Lack of social support

KEY STEPS IN ACUTE TREATMENT

Regular bronchodilators
Inhaled short-acting beta-agonist and/or anticholinergic agents via spacer/nebuliser 1–6 hourly

Systemic glucocorticoids
Oral prednisolone 30–50 mg daily (not tapered), typically for 1 week

Antibiotics
Amoxycillin/doxycycline for 7–10 days. Parenteral or broader spectrum antibiotic if required

Oxygen
Low-dose to maintain saturation at 88–92%

Noninvasive positive pressure ventilation
For those with severe exacerbations and ventilatory failure

acute confusion/delirium and pulse rate (greater than 100 beats/min) to stratify the risk of exacerbations of COPD;[10] however, this is not widely used.

ACUTE MANAGEMENT

The acute management of exacerbations of COPD usually involves the use of a combination of bronchodilators, antibiotics and glucocorticoids and, for those with acute respiratory failure, the use of oxygen and/or noninvasive ventilation (see the box on this page).

Inhaled bronchodilators

Short-acting inhaled beta-agonists (e.g. salbutamol and terbutaline) and anticholinergic agents (e.g. ipratropium) can be given effectively by metered-dose inhaler with a spacer or by a jet nebuliser. The frequency of administration is governed by clinical response but typically ranges from hourly to six hourly. Dry powder inhalation of the long-acting beta-agonist eformoterol may also be helpful, given typically from hourly to six hourly, but patients may have difficulty inhaling dry powders during exacerbations.

The bronchodilator effect of these medications is usually small (in contrast to their effect in asthma) but may produce significant clinical improvement, particularly in terms of dyspnoea.

Systemic glucocorticoids

Systemic glucocorticoids are typically given orally at a daily dose of 30 to 50 mg, for a maximum of two weeks. There is no clear benefit in giving a tapering dose, nor in giving this medication parenterally.[11] Systemic glucocorticoids have been shown to reduce 30-day treatment failure, hospital stay and severity of symptoms.[12] Long-term use is associated with side effects, particularly osteoporosis, and should be avoided.

Antibiotics

Bacterial infections have a role in about half of all COPD exacerbations. Patients with exacerbations with at least two out of three features of increased dyspnoea, increased sputum and change in sputum characteristics are the most likely to benefit from antibiotics.[13] Antibiotics have been shown clearly to improve outcomes in patients hospitalised for acute exacerbations.[14,15]

Randomised controlled trials have found that short duration of antibiotics (up to five days) were as effective as longer courses. There may also be a lower incidence of side effects with shorter dose therapy.[16]

Therapeutic Guidelines: Respiratory recommends initial oral use of antibiotics such as amoxycillin or doxycycline.[17] Patients should respond within three to five days. If there is failure to respond then broader spectrum antibiotics such as amoxycillin–clavulanic acid can be used or if specific resistant pathogens such as *Pseudomonas* spp. are present then appropriate therapy directed at the pathogen should be given. Generally most inpatients are initially treated with

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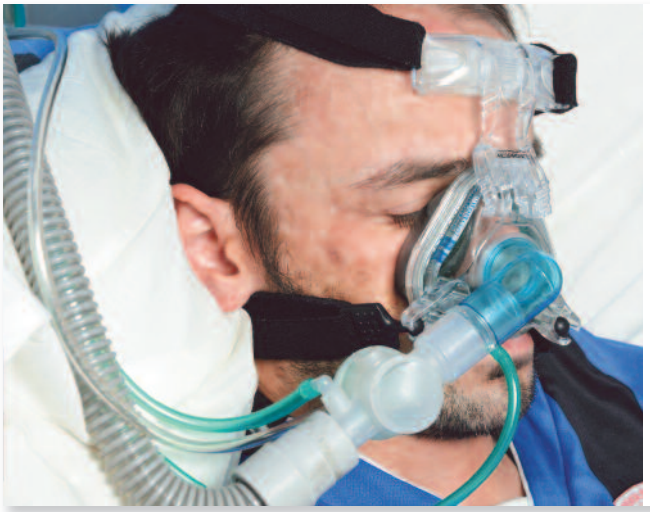

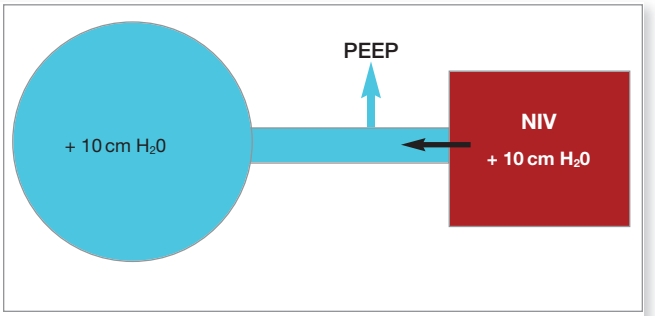

Figures 3a and b. a (left). The use of noninvasive positive pressure ventilation (NIV) for COPD exacerbations. b (above). NIV reverses the effect of PEEP, holds the airways open in expiration and facilitates inspiration by reducing the gradient between mouth and alveolar pressure.

parenteral antibiotics and within 72 hours switched to oral therapy. Antibiotics are most commonly given for a course of seven to 10 days.

Combined therapy with systemic glucocorticoids and antibiotics produces a significantly higher rate of clinical cure than glucocorticoids alone.[18]

Some patients have a persistent fever, which may indicate of a resistant pathogen such as *Pseudomonas aeruginosa* or a complication, particularly an infected parapneumonic effusion or empyema. Appropriate therapy should be given.

Clearance of secretions

Patients with significant sputum production may benefit from sputum clearance techniques. Mechanical vibration or positive expiratory pressure therapy may be helpful for hospitalised patients.

Oxygen therapy

Oxygen therapy is given to maintain a PaO_2 above 55 to 60 mmHg (corresponding to an oxygen saturation of greater than 88 to 92%). Oxygen therapy does not reverse the primary pathophysiological process of dynamic hyperinflation in COPD. It is also very important not to give patients too much oxygen and risk suppressing hypoxic drive, further suppressing ventilation (with the potential for respiratory arrest). Nasal cannula-administrated oxygen, given at a flow rate of 0.5 to 2 L/min to maintain an oxygen saturation of 88 to 92%, is generally sufficient.

Noninvasive ventilation

The advent of noninvasive ventilation (NIV) has dramatically improved the treatment of severe exacerbations of COPD with acute ventilatory failure.[19] NIV is typically used when patients have an acute respiratory acidosis (pH less than 7.35 and elevated pCO_2 levels on arterial blood gas measurements) with tachypnoea.

A full-face mask is put on the patient and NIV is given using either continuous positive airway pressure (CPAP) or bi-level airway pressure (BiPAP). A significant clinical improvement usually occurs within an hour. NIV has an immediate effect on reversing the underlying pathophysiology of exacerbations of COPD, the with improvement in both the expiratory and inspiratory phases of ventilation.

The effect of NIV is shown in Figure 3b. Not all patients can tolerate NIV; some may panic, have increased respiratory effort or vomit into the mask. As such, the implementation of this treatment requires expert and, ideally, continuous nursing care.

Invasive ventilation

Invasive ventilation may be considered for patients who fail to improve with NIV, have respiratory arrest or are unable to protect their airways. Mechanical ventilation for COPD is associated with a high inpatient mortality of 39%.[20] Follow-up studies of patients treated with invasive ventilation have shown a mild decrease in quality of life, but most patients would elect to receive this treatment again.[20] If possible, the need for ventilation should be discussed with the patient and/or family before an acute severe deterioration occurs.

FOLLOW-UP MANAGEMENT

A key component of the management of exacerbations of COPD is organising appropriate follow up.

Hospital discharge planning

Features that indicate a patient who has been hospitalised for an exacerbation can be discharged include:

- no longer requiring parenteral therapy
- not requiring bronchodilators more often than four hourly
- being independent with activities of daily living and ambulation
- having an appropriate level of social support.

Patients should be given general

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IMPORTANT STEPS IN FOLLOW-UP MANAGEMENT

- Appropriate hospital discharge planning
- Oxygen therapy for those who meet criteria
- Referral to pulmonary rehabilitation
- Lung function testing (to confirm COPD)
- Assessment of appropriate use of medications (including education about inhaler technique) and compliance
- Assurance of smoking cessation
- Regular influenza and pneumococcal vaccination
- Development of a management plan for future exacerbations
- Early institution of acute treatment
- Baseline assessment of risk of osteoporosis and nutritional status
- Specific treatment, if required, for anxiety, a prominent feature of severe COPD
- Management, as appropriate, of other important comorbidities, including depression, right-heart failure and obstructive sleep apnoea

information about COPD, use of medications and the importance of maintaining and increasing activity levels, as well as a plan for the management of future exacerbations. The GP should be informed of the admission and ideally patients should have at least one review in a hospital-based clinic. For patients who continue smoking, appropriate management to optimise smoking cessation should be undertaken.

Use of oxygen

A significant proportion of patients who come into hospital have hypoxia that persists throughout the admission, and they are discharged home on oxygen therapy. Domiciliary oxygen can be given as continuous oxygen for those with low oxygen saturation levels at rest (i.e. PaO_2 less than 56 mmHg) or ambulatory oxygen for those who significantly desaturate on walking (although the use of ambulatory oxygen is controversial). To qualify for ongoing oxygen therapy, patients need to be reassessed one to two months after discharge (at this time many do not require ongoing oxygen owing to clinical recovery).

Continuous oxygen therapy is the only treatment that has been shown to prolong life in patients with COPD. It needs to be taken for more than 16 hours a day so patients need to use this when they are sleeping.[21,22] It is imperative that patients do not smoke while on oxygen.

Lung function testing

For all patients who have not had lung function testing, this should be performed in a formal laboratory to confirm the presence of COPD and categorise severity. Lung volumes, bronchodilator effect and lung diffusing capacity should be measured.

Referral for pulmonary rehabilitation

Pulmonary rehabilitation has been shown to be associated with a variety of benefits including improved exercise capacity and reduced admissions and mortality.[23] All patients who have been hospitalised for an exacerbation should be referred to a pulmonary rehabilitation service. This will generally involve attendance for half a day a week for several months with a multidisciplinary team to improve patient understanding, self-management and fitness.

General management

Several issues need to be followed up after an exacerbation and are summarised in the box on this page.

Management of future exacerbations

Patients who have had previous COPD exacerbations are highly likely to have further exacerbations. Early diagnosis and treatment of exacerbations may improve outcome and avoid the need for hospital admission. Patients should be educated to recognise the symptoms and signs of an exacerbation and should have a plan to institute appropriate management. This would typically involve seeking medical attention within 24 hours and may also involve self-initiation of medications (e.g. glucocorticoids and antibiotics).

SUMMARY

Exacerbations of COPD are extremely common, but in the absence of previous lung function testing the diagnosis may not be straightforward. Increased airway inflammation and/or increased respiratory rate results in air trapping and dynamic lung hyperinflation and may lead to respiratory failure. Early initiation of appropriate therapy and follow-up management is vital to patient outcome. MT

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PEER REVIEWED FEATURE
POINTS: 2 CPD/2 PDP

COPD is complicated: the story of its comorbidities

PETER FRITH MB BS, FRACP, FCCP

COPD is increasingly being considered a systemic disease because of the over-representation of an extraordinary range of comorbid conditions associated with biomarkers of systemic inflammation.

Key points

- **COPD is common, costly, and associated with many comorbidities, including heart disease, osteoporosis, mental health disorders, diabetes, renal dysfunction, anaemia, lung cancer and other respiratory conditions.**
- **Systemic inflammation is common to most of the observed chronic comorbid conditions, leading to a proposed unifying hypothesis that their association and consequences are due to systemic inflammation.**
- **Almost all people with moderate-to-severe COPD aged over 65 years are estimated to have at least one comorbidity.**
- **The implications of comorbidities in patients with COPD include diagnostic confusion, inappropriate use of treatment, and increased rates of hospitalisation and mortality.**
- **Clinical practice guidelines for COPD do not currently provide evidence-based guidance on how to account for the comorbid conditions.**

COPD – chronic obstructive pulmonary disease – has enormous global and national importance. It is the second most common cause of avoidable hospital admissions in Australia,[1] the third most common cause of morbidity globally,[2] will be the third most common cause of death by 2020,[3] and its economic impact is prodigious.[4]

WHAT IS COPD?

Learned bodies in Australia[1] and internationally[5] define COPD as a progressive but preventable disease caused by dysregulated inflammation, now recognised as systemic.[6,7] Inflammation is triggered by repeated exposure to multiple inhaled noxious agents or unregulated inflammatory remodelling of asthmatic airways,[6] resulting in chronic airway narrowing and parenchymal lung destruction (chronic airflow limitation and emphysema).[8]

Usually the inflammation in COPD is described as neutrophilic, which distinguishes it from the inflammation seen in asthma (eosinophil-predominant),[5] and resembles that seen in ageing.[9] This may have important therapeutic implications since corticosteroids are less effective in controlling neutrophilic inflammation. (These differences have recently been blurred by findings of non-eosinophilic asthma and non-neutrophilic COPD, leading to the idea that treatments could be targeted to the inflammatory cells rather than to the clinical features.[10])

Symptoms include daily cough and/or sputum production, breathing discomfort with tasks considered normal for age, easy fatigue, and reduced health-related quality of life. COPD is increasingly being considered a systemic disease[11] due to the over-representation of an extraordinary range of comorbid conditions, thought by many to be due to systemic spillover of the inflammation,[12] and a proportion of patients who demonstrate biomarkers of inflammation in the systemic circulation.[13] Alternatively, COPD and its comorbidities could be consequences of a systemic inflammatory (possibly autoimmune)

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disorder,[14] or an inflammatory phenomenon associated with obesity.[15] This article seeks to alert the wider medical community to the importance of these comorbidities and their impact in people with COPD.

EPIDEMIOLOGY AND IMPACT OF COPD

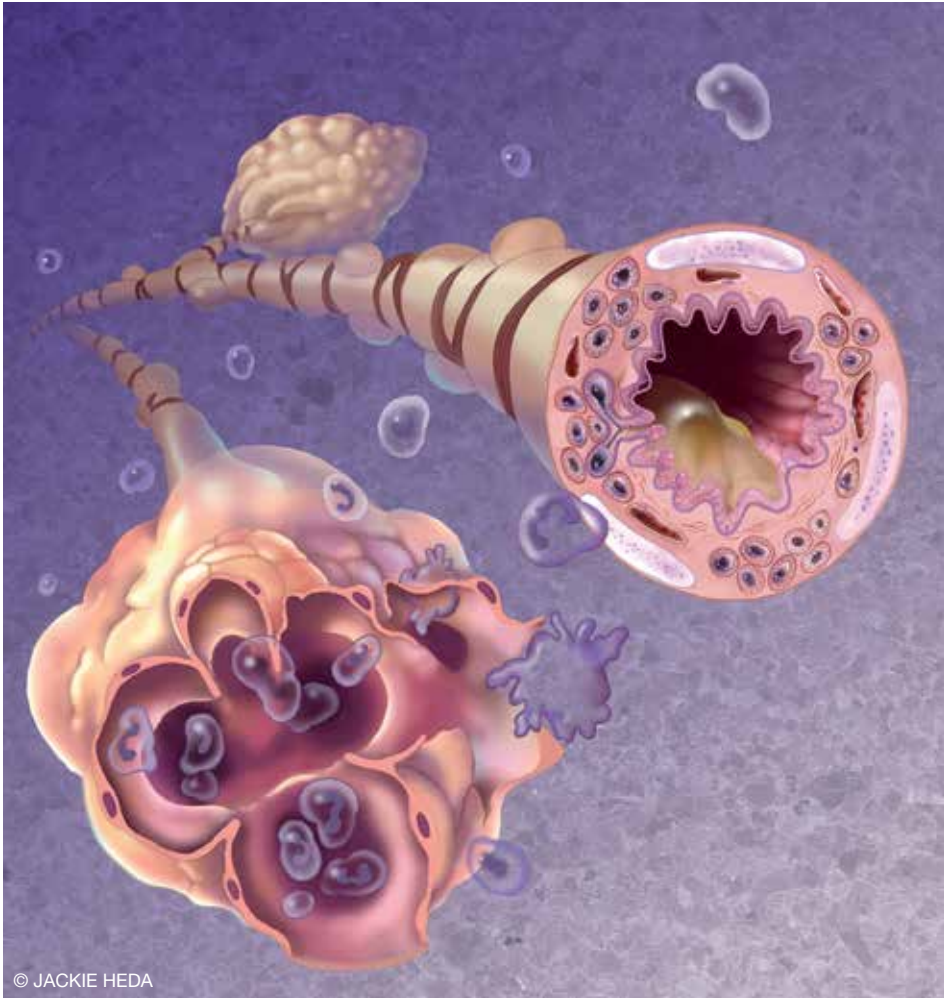
In Asian countries of the Asia-Pacific region, mortality and hospitalisation rates of people with COPD are even higher than in developed nations of the region.[16] In those developing nations males with COPD predominate, whereas in developed nations like Australia the trend is for prevalence and death rates to be almost equal in the sexes, and increasing in females.[16]

More than one in 10 people aged over 40 years has COPD.[17] About three in four of these have been smokers (or continue to smoke);[18] however, in some developing nations smoking is less prominent and biomass fuel pollution assumes greater importance, especially in women.[19] Other significant risk factors are second-hand smoke[20] and chronic (usually poorly controlled) asthma.[21]

Most people with COPD will die prematurely, usually after a prolonged decline in overall health. They may die, usually in hospital, of respiratory failure or, more commonly,[22] from one of the comorbid illnesses. Unfortunately many patients are only diagnosed with COPD when their disease has already begun to disable them or they have a severe exacerbation leading to hospitalisation. Greater awareness of this fact, a recognition of the clinical imperative to question adult patients more carefully and improved skills to undertake appropriate diagnostic tests or wider access to respiratory laboratories are pressing needs worldwide.[23]

COEXISTING MEDICAL CONDITIONS

The conditions often coexisting with COPD are mostly in epidemic proportions in themselves. Many of them share the same lifestyle or ageing factors. However, the associations addressed in this article go well beyond background prevalence rates, and each interacts with the other conditions to worsen their impact. One study has shown the median number of comorbidities in COPD is nine,[24] and comorbidity burden determines higher use of healthcare resources.[25] Systemic inflammation is common to most of the observed chronic conditions, leading to a proposed unifying hypothesis that their association and consequences are due to systemic inflammation.[26]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Patient data from the UK General Practice Research Database were analysed to quantify rates of comorbidities in 2699 patients with COPD compared with age-, sex-, practice- and time-matched controls. The authors of this study found that COPD is associated with many comorbidities, particularly cardiovascular, bone and other smoking-related conditions (Table).[27]

Heart disease

Not surprisingly, the most common comorbidity is heart disease – ischaemic coronary disease (IHD) and chronic heart failure (CHF) in particular, but arrhythmias also complicate medical care in patients with COPD, even allowing for background tobacco consumption. CHF is seen in about 20% of individuals with COPD,[28] and COPD occurs in up to 35% of patients with CHF[29] in studies that have used rigorous diagnostic criteria for each. COPD is an independent predictor of cardiovascular mortality in patients who also have hypertension.[30] In a large primary care survey in Madrid, people with coexisting COPD and heart disease were more disabled,

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TABLE. INCREASED RISK OF COMORBIDITIES IN PATIENTS WITH COPD*[27]

Disorder	Relative risk
Pneumonia	16.00
Osteoporosis	3.14
Respiratory infection	2.24
Myocardial infarction	1.75
Angina	1.67
Fractures	1.58
Glaucoma	1.29

* Relative risk of comorbidities in 2699 patients with COPD compared with age-, sex-, practice- and time-matched controls without COPD (all except glaucoma p<0.05). Data from the UK General Practice Research Database (Soriano, et al).[27]

had worse quality of life and used more healthcare resources and their direct health care costs were substantially higher than those with COPD and no cardiac disease.[31]

Both COPD and worse lung function are independent and major cardiovascular risk factors[32] as well as predictors of cardiovascular death.[33] There is growing evidence that the main reason for this comorbidity is systemic inflammation,[34] in addition to the shared risk of smoking.

Mental health disorders

Mental health disorders are also overrepresented in patients with COPD. It may not be surprising that patients become despondent and frankly depressed, or that they assume avoidance behaviours. It is also not surprising that panic becomes entrenched when a person repeatedly becomes uncomfortably breathless.

Diagnosable depression and anxiety (either alone or together) occur at least five times as often in patients with COPD than in the general population.[35] In a large observational cohort 26% of patients with moderate to severe COPD had diagnosable depression,[36] with frequent symptoms and poor quality of life being the most important determinants. There is gross underdiagnosis of depression in the general population, and this is just as big an issue in COPD. The use of screening instruments suited to general practice is highly recommended, although clinical confirmation of abnormal scores and diagnosis of specific depression subtypes is equally important.[35]

Quite separately, cognitive function is impaired in patients with COPD (reported in 18.5% of subjects with COPD),[37] especially in those who have chronic hypoxaemia.[38]

Diabetes and osteoporosis

Diabetes is more common in patients with COPD compared with the general population (16.3%),[37] as is osteoporosis (16.9%).[37,39] In both cases, use of corticosteroids may be considered the cause, but the prevalence of both is excessive beyond the use of these drugs. Their development has been attributed to a range of pathophysiological mechanisms.

Osteoporosis may be caused by any combination of systemic inflammation, smoking (notably in women), hypoxaemia, vitamin D deficiency due to nutritional difficulties or lack of exposure to sunlight and reduced weight-bearing activity.[40]

Obesity and the metabolic syndrome

Obesity, elevated triglyceride and high-density lipoprotein cholesterol levels, elevated blood pressure and fasting hyperglycaemia (the metabolic syndrome) have been identified in 47% of patients with COPD compared with 21% of control patients without COPD.[41] Obesity has been linked to systemic inflammation and increased prevalence of cardiovascular disease.[15] In older patients with COPD who have relatively mild disease, however, high BMI is associated with significantly lower risk of mortality than those with normal BMI,[42] confirming previous observations from Dutch workers over many years.

On the other hand, it is recognised that cachexia is associated with greater risk of early death,[43] especially so in older patients with more severe COPD. This may reflect merely the energy consumption or reduced food assimilation that occurs in end-stage COPD, or high levels of systemic inflammation.

Polycythaemia, anaemia and renal failure

Secondary polycythaemia as a consequence of chronic hypoxia is now less often seen in patients with COPD and other conditions since appropriate long-term oxygen therapy has been more widely used. On the other hand, anaemia is increasingly being recognised. In a large Spanish population cohort, almost 10% of patients admitted to hospital with COPD had anaemia,[44] supporting an earlier systematic review.[45] This appears to be a consequence of systemic inflammation.

Linked with anaemia, renal failure is highly prevalent in patients with COPD,[46] and microalbuminuria is a common occurrence if sought, especially if those who have chronic hypoxaemia. Microalbuminuria can be reversed with long-term oxygen therapy.[47]

Muscular disorders

Muscle weakness is most usually thought to be due to atrophy secondary to inactivity

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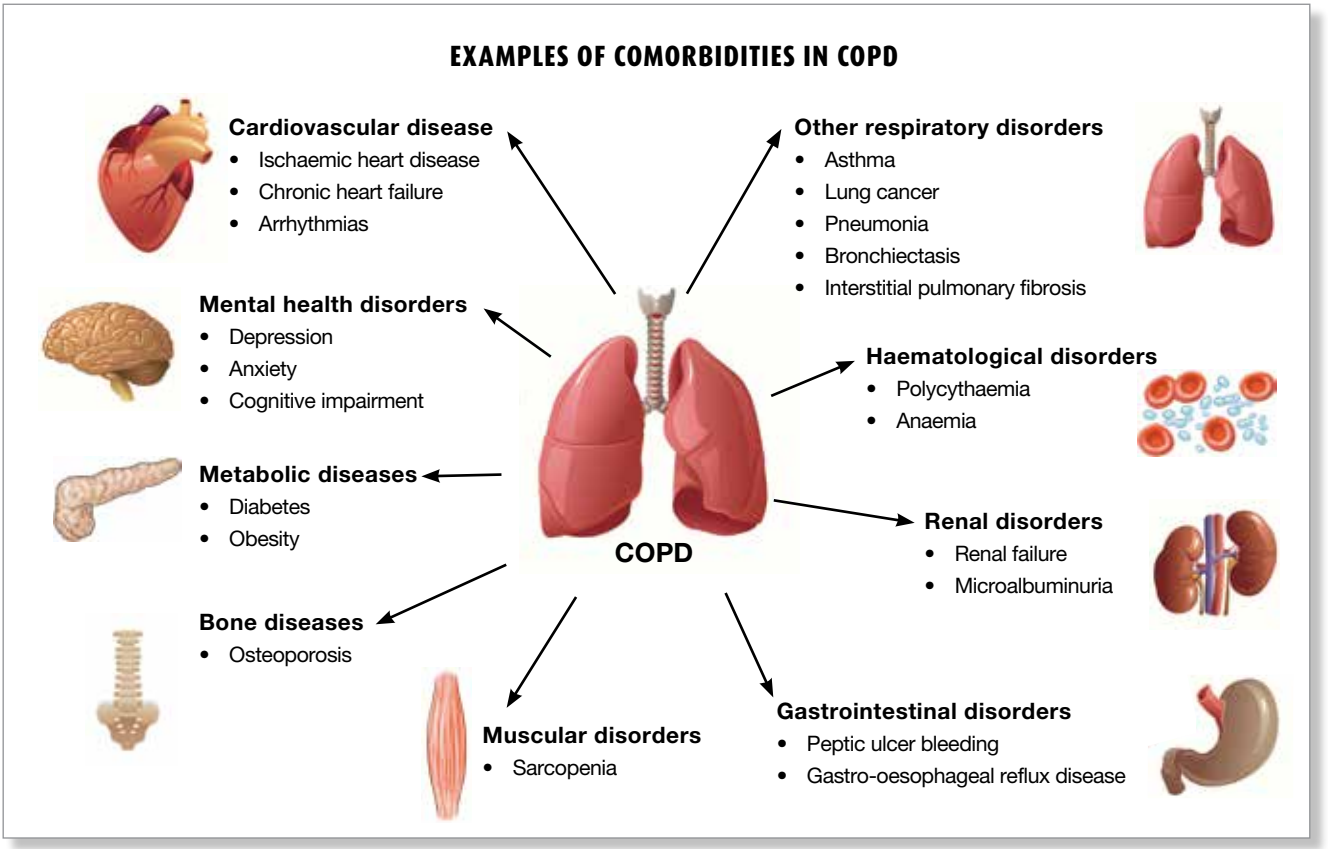

and poor nutrition,[48,49] but increasing evidence shows us that there is an almost specific form of COPD-associated sarcopenia, most probably a result of chronic systemic inflammation.[50] Skeletal weakness leads to fatigue[51] (along with depression and dyspnoea), a potent predictor of both poor quality of life and hospital readmissions of patients for COPD management.[52]

Gastrointestinal disorders

Gastric ulcers were once considered excessively common in patients with COPD, but since smoking rates have declined, and the diagnosis and treatment of peptic ulcer disease have improved, this comorbidity is not as prevalent. In a large Taiwanese database analysis, however, COPD was found to be a major independent risk factor for peptic ulcer bleeding, with almost a doubling of risk compared with age-matched controls.[53] Gastro-oesophageal reflux disease (GORD) is a vital condition to recognise as it is both more common and has greater importance to COPD progression and exacerbations than peptic ulcers.[54]

Other respiratory conditions

Other respiratory conditions occur more often with COPD.

- Smoking is now recognised to be responsible for some cases of interstitial pulmonary fibrosis.
- Bronchiectasis, a condition not due to smoking *per se* (even in those without cystic fibrosis), is increasingly identifiable on CT scans of the lungs of patients with COPD.
- Lung cancer is more common than could be predicted from the background smoking rate in people with COPD. FEV_1 has been proposed as a means of pre-screening risk of lung cancer in smokers because lung cancer is more often found in patients with a reduced FEV_1 independent of smoking history.[55]
- Asthma is even more common in those with COPD than in the general population, and itself can lead to COPD.[56]
- Patients with COPD are at increased risk of pneumonia.

Each of these conditions shares one or more clinical features with COPD. In turn, dyspnoea with exertion, chronic sputum production and recurrent lower respiratory infections (LRTI), haemoptysis, clubbing and weight loss, wheezing and exacerbations of respiratory symptoms can confuse the clinician as well as the patient and family.

Obstructive sleep apnoea, although not over-represented in patients with COPD,[57] compromises ventilation further when it coexists with COPD and increases the likelihood of worse respiratory and cardiovascular outcomes.

Some examples of the important comorbidities of COPD are illustrated in the box above.

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IMPLICATIONS OF COMORBIDITIES IN COPD

Diagnostic confusion

Diagnostic confusion is not unusual when patients with COPD present with their symptom complex.[58] This is especially so when patients present with exacerbated symptoms, so pneumonia or pulmonary emboli might be missed in a patient who seems to have a COPD exacerbation. In addition, in patients with both COPD and heart failure, symptoms are shared (notably dyspnoea) and may cause diagnostic confusion for the patient as well as the doctor. Diagnostic investigations can also be confusing in such patients – notably chest x-ray cardiac size may be underestimated and echocardiographic images can be difficult to obtain when there is lung hyperinflation.

It behoves us to take extra care with our diagnosis as the outcomes hinge on correct medical management and the use of inappropriate drugs could make a patient worse. Take, for example:

- prescribing beta blockers for heart failure in a patient with asthma and COPD
- increasing doses of beta agonists or anticholinergic drugs for COPD too much in a patient with recurrent life-threatening cardiac arrhythmias and/or accelerating coronary artery narrowing
- assuming dyspnoea is due to COPD and ignoring anaemia
- patients taking increasing doses of sedatives or anxiolytics for panic when they have respiratory failure.

Treatments are tailored for uncomplicated COPD

Clinical practice guidelines for COPD (or any of the other conditions), while hinting at the comorbidities, cannot give evidence-based guidance for how to account for the comorbid conditions. The evidence within guidelines is mainly based on randomised controlled trials, and patients in these trials are as 'pure' as possible – i.e. with no comorbidities. Treatments are usually tailored for uncomplicated COPD – not a 'real-world' set of circumstances by any means.

Furthermore, the treatment applicable to one condition may complicate the others, and some treatments for stabilising a chronic condition may be underused, contributing to worse outcomes. Some examples are noted below.

- Beta blockers may be withheld when CHF or paroxysmal tachyarrhythmia coexists with COPD.
- Overuse of beta agonists or anticholinergics increases the risk of decompensation of CHF or tachyarrhythmia.
- Coexisting chronic renal failure may increase drug toxicity when CHF, arrhythmia or infections are being treated.
- Use of systemic corticosteroids may complicate the control of diabetes, contributing to the observed increased length of hospitalisation and mortality.[59]
- Use of inhaled corticosteroids (ICS) for mild to moderate COPD (i.e. when not indicated) appears to increase the risk of lower respiratory tract infection and/or pneumonia.[60]
- ICS interfere with bone metabolism, increasing the likelihood of osteoporotic skeletal fractures.[61]
- Cognitive impairment or mental health comorbidities contribute to poor medication adherence, particularly early response to exacerbating symptoms.[37]

Despite these issues, there is some encouraging evidence relating to cotreatments.

- Retrospective data in large cohorts suggest statins may have beneficial effects on COPD outcomes.[62,63]
- Use of cardioselective beta blockers for CHF or arrhythmia in patients with COPD is safe[64] and improves overall and COPD outcomes.[65,66]
- Large databases have attested to the safety of, and even improved cardiovascular outcomes from, tiotropium administered via HandiHaler.[67]
- Although traditionally avoided because of fears of respiratory depression, low-dose opioids have proven effective and safe in controlling intractable dyspnoea.[68]

Increased rates of hospitalisation, morbidity and mortality

The US National Hospital Discharge Survey, 1979-2001, which evaluated more than 47 million hospital discharges of patients aged 25 years or older with COPD found there was:[22]

- a significantly higher rate of hospitalisation of patients with important medical conditions (notably hypertension, ischaemic heart disease, pneumonia and diabetes) in those with COPD than in those without
- a significantly increased rate of in-hospital mortality from common medical conditions in patients with a codiagnosis of COPD than in those who had no such diagnosis.

Other studies have shown:

- length of hospital stay for COPD exacerbations is prolonged in patients with increasing numbers of comorbidities[69]
- patients seen in primary care have worse respiratory and general health-related quality of life during exacerbations, especially if there are more than three comorbidities[70]
- survival is significantly worse in patients with comorbid heart and lung disease,[22,71] irrespective of which condition developed first,[72] and especially so in those with more severe disease[29]
- the risk of death has been shown to be more than double in patients discharged from hospital following a diagnosed COPD exacerbation if they also had diabetes mellitus than in those without diabetes.[73]

Most costs relating to COPD are derived from hospital admissions, usually due to exacerbations. Exacerbations are not only costly to governments (and therefore society) but they also:

- are distressing for patients and their families

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- worsen health-related quality of life for several weeks or months
- increase markedly the risk of further hospitalisations in the next year[74]
- increase depression and anxiety
- reduce physical activity, itself a risk factor for further exacerbations and permanent disablement.

In addition, exacerbations are now more deadly than myocardial infarctions, with reported in-hospital mortality as high as 7.4%,[75] and higher in those requiring ICU treatment (8 to 26%).[76] Exacerbations increase with advancing age: there is a 36% increase in hospitalisation rates for every five years after age 65 years.[77] After apparent recovery from exacerbations, studies from the UK, USA and Netherlands have shown that 14 to 20% of patients die within the next three months[78,79] and 23 to 43% within 12 months.[79,80]

CONCLUSION

Chronic noncommunicable diseases represent the new global epidemic. COPD ranks highly as a cause of death and prolonged disablement, with exacerbations consuming large amounts of our health budget. These exacerbations are more deadly than myocardial infarctions, and their severity is complicated by coexisting medical conditions.

All the chronic conditions that occur as comorbidities of COPD occur more often in patients with COPD than they do in the general age-matched population, and some estimates suggest almost all people with moderate-to-severe COPD aged over 65 years have at least one of these comorbidities. The most common are probably cardiovascular and osteoporosis, but mental health, endocrine, renal, haematological and other conditions occur in frequencies between 30 and 60% of people with COPD.

It is a matter of concern that there is no guidance from evidence-based guidelines for any chronic disease on how we should handle these circumstances, and patients are undeniably confused. Although this article documents the high prevalence and impacts of each comorbidity, and acknowledges the shortcomings of expert guidance, we can only await research that addresses the complexities, and demand that expert bodies develop clear integrated guidelines. MT

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