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Strategies to manage COPD

By Bonnie Bereznicki, Dr Luke Bereznicki and Professor Gregory Peterson

Learning objectives

After reading this article, the reader should be able to:

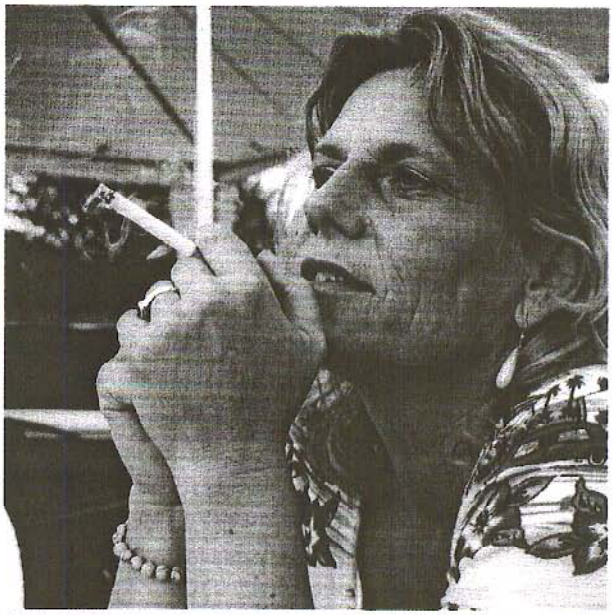
- Understand the range of management strategies available for COPD; and
- Discuss the evidence behind current COPD management strategies, and be confident in making recommendations to patients and GPs.

Case study

Mrs AJ, a 59-year-old female, comes into the pharmacy with a prescription for tiotropium (*Spiriva*). She says she has never used it before, and her doctor prescribed it for her worsening shortness of breath and coughing fits. When asked, she says she started smoking when in her 20s, and still smokes 10 to 15 cigarettes per day. Her doctor told her she should seriously consider quitting, but she is hesitant, particularly when her husband also smokes. She asks if there is anything else that she can do to improve her symptoms.

Introduction

Chronic obstructive pulmonary disease (COPD) is a major cause of disability, hospital admission and premature death in Australia. More than half a million Australians are estimated to have COPD,[1] and the prevalence is likely to escalate as the population ages. Despite COPD being less prevalent in the population than asthma, it is responsible for many more deaths. With about 5,400 deaths attributed to it in 2003, COPD ranks fourth among the common causes of death in Australia.[2] Furthermore, COPD is associated with a significant level of disability in about 34% of sufferers, rising to 68% in those aged 65 years and over.[1] In recognition of the enormous burden that COPD places on the Australian community, the Australian Lung Foundation and Thoracic Society of Australia and New Zealand recently developed clinical practice guidelines to improve the diagnosis and management of COPD. The COPD-X guidelines, as summarised in Table 1, aim to effect changes in clinical practice based on sound evidence, and shift the emphasis from a predominant reliance on pharmacological treatment of COPD to a range of interventions including patient education, self-management of exacerbations and pulmonary rehabilitation.[3] The focus of this article is to review the evidence for the strategies used to optimally manage COPD, as outlined in the COPD-X Guidelines.



Mrs AJ, a 59-year-old female, comes into the pharmacy with a prescription for tiotropium (Spiriva).

Smoking cessation

While there is evidence from epidemiological studies that non-smokers can develop chronic airflow obstruction,[5,6] tobacco smoke remains the most important cause of COPD worldwide, with up to 50% of smokers noted to develop the condition.[7] The forced expiratory volume in one second (FEV_1) declines at about 45mL/year in smokers, compared to

Figure 1. Time-course of COPD[4]

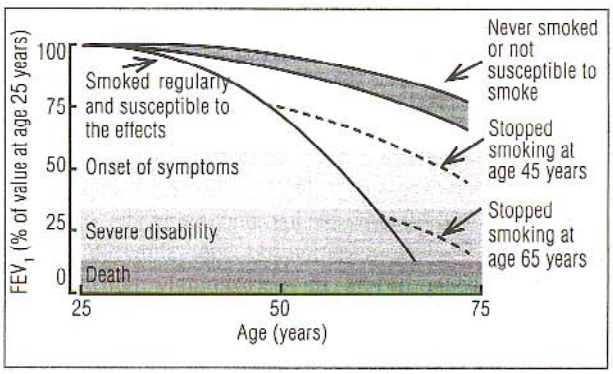


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Table 1. Summary of the COPD-X guidelines[4]

C: Confirm diagnosis and assess severity	Evidence level*
• Smoking is the most important risk factor for COPD	I
• Consider COPD in patients with other smoking-related diseases	I
• Consider COPD in all smokers and ex-smokers older than 35 years	II
• The diagnosis of COPD rests on the demonstration of airflow limitation which is not fully reversible	II
O: Optimise function	Evidence level*
• Inhaled bronchodilators provide symptom relief in patients with COPD and may increase exercise capacity	I
• Long-acting bronchodilators provide sustained relief of symptoms in moderate to severe COPD	I
• Long term use of oral corticosteroids is not recommended	I
• Inhaled corticosteroids should be considered in patients with a documented response or those who have severe COPD with frequent exacerbations	II
• Pulmonary rehabilitation reduces dyspnoea, anxiety and depression, improves exercise capacity and quality of life and may reduce hospitalisation	I
P: Prevent deterioration	Evidence level*
• Smoking cessation reduces the rate of decline of lung function	I
• General practitioners and pharmacists can help smokers quit	I
• Treatment of nicotine dependence is effective and should be offered to smokers	I
• Pharmacotherapies double the success of quit attempts; behavioural techniques further increase the quit rate by up to 50%	I
• Influenza vaccination reduces the risk of exacerbations, hospitalisation and death	I
• Inhaled corticosteroids are indicated for patients with a documented response or who have severe COPD with frequent exacerbations	II
• Mucolytics may reduce the frequency and duration of exacerbations	I
D: Develop a support network and self-management plan	Evidence level*
• Pulmonary rehabilitation increases patient/carer knowledge base, reduces carer strain and develops positive attitudes towards self-management and exercise	I
• Multidisciplinary care plans and individual self-management plans may help to prevent or manage crises	II
X: Manage eXacerbations	Evidence level*
• Inhaled bronchodilators are effective treatments for acute exacerbations	I
• Oral corticosteroids reduce the severity of and shorten recovery from acute exacerbations	I
• Exacerbations with clinical signs of infection benefit from antibiotic therapy	II
• Multidisciplinary care may assist home management	II

*NHMRC levels of evidence:
I Evidence obtained from a systematic review of all relevant randomised controlled trials.
II Evidence obtained from at least one properly designed randomised controlled trial.

the decline associated with normal ageing of approximately 30mL/year in non-smokers.[8]

Smoking cessation is the single most effective – and cost effective – intervention to reduce the risk of developing COPD and stop its progression.[9] While smoking cessation may lead to minimal improvements in lung function, more importantly it will slow the rate of decline and delay the onset of disablement. Smoking cessation has been shown to reduce the rate of decline of FEV_1 to approximately that of never-smokers (Figure 1). It has also been demonstrated that the slowed decline in FEV_1 is sustained years after quitting.[10]

There is good evidence that health professionals can substantially increase quitting and readiness to quit in the population. Even a brief (3-minute) period of counselling to urge a smoker to quit results in smoking cessation rates of 5-10%.[11] Furthermore, collaborative efforts among health professionals are more effective than interventions by only one type of health professional; a recent US Tobacco Survey of 1,723 smokers found that being asked about smoking by two or more types of professionals substantially increased the odds of recent quitting (odds ratio [OR] = 2.37; 95% confidence interval [CI] = 1.15 to 4.88). Moreover, it is imperative that smoking cessation interventions involve

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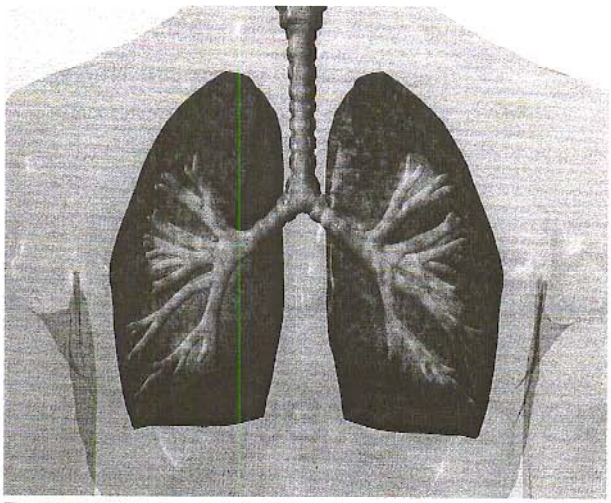


The COPD-X Guidelines state that 'inhaled bronchodilators provide symptom relief in patients with COPD and may increase exercise capacity'.

combinations of psychological and social support mechanisms, and pharmacotherapy.[12]

Self-management plans

Self-management interventions improve various outcomes for many chronic conditions. Research in self-management plans for COPD is relatively new, and variable results have been reported in the literature. A Canadian multicentre randomised controlled trial (RCT) involving 191 patients from seven hospitals evaluated an intervention consisting of a comprehensive patient education program administered through weekly visits by trained health professionals over a two-month period with monthly telephone follow-up.[13] After 12 months, hospital admissions for exacerbation of COPD were reduced by 40% in the intervention group compared to the usual care group ($P < 0.05$), and admissions for other health problems were reduced by 57% ($P < 0.05$). Emergency department visits were reduced by 41% ($P < 0.05$) and unscheduled physician visits by 59% ($P < 0.01$).

In contrast, a New Zealand RCT of structured one-hour education sessions on the use of a written self-management plan and patient-initiated short courses of antibiotics and oral corticosteroids failed to show any added health benefit, in terms of health utilisation, or self-reported outcomes, compared to usual care.[14] A recent systematic review on self-management education in COPD could not draw any conclusions about the effectiveness of self-management because of the large variation of outcome measures used in a limited number of included studies, and noted the evident need for additional large RCTs featuring long-term follow-up, before more conclusions can be drawn.[15]

Pulmonary rehabilitation

Pulmonary rehabilitation programs involve patient assessment, exercise training, nutritional intervention and psychosocial support, and are designed to reduce symptoms, optimise functional status, increase participation and reduce health care costs through stabilising or reversing systemic manifestations of COPD.[16] The components of pulmonary rehabilitation are shown in Table 2.

Table 2. Components of comprehensive pulmonary rehabilitation programs [17]

1. Education, including self-management strategies
2. Upper and lower extremity exercise training, resistance training
3. Psychosocial support, when indicated
4. Encouragement of activity and exercise in the home setting
5. Outcome assessment
6. Promotion of long-term adherence.

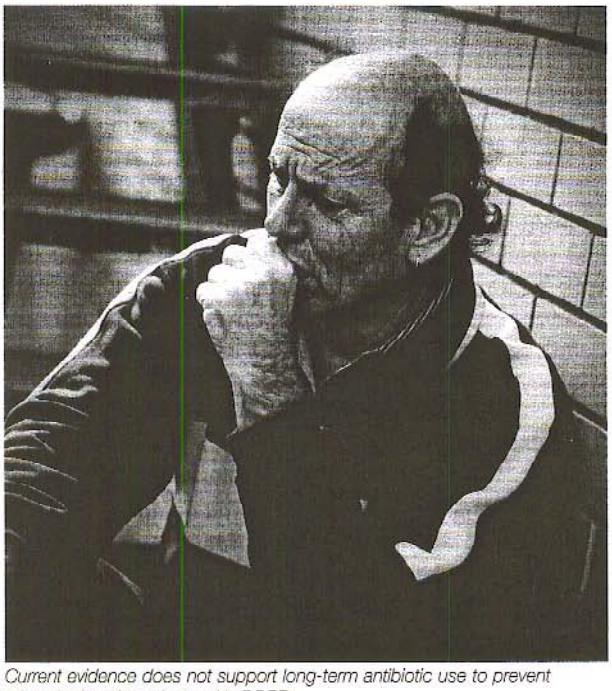
Although pulmonary rehabilitation has not been shown to have a substantial effect on the specific respiratory impairment in COPD,[18] a large body of scientific evidence demonstrates its beneficial effects over multiple outcome areas. A recent systematic review including 31 RCTs of pulmonary rehabilitation for COPD on disease-specific health status was conducted. This review reported that in four important quality of life domains (Chronic Respiratory Questionnaire scores for Dyspnoea, Fatigue, Emotional Function and Mastery), the effect was larger than the minimal clinically important difference of 0.5 units.[19] The authors concluded that the improvements for all outcomes were moderately large and clinically significant, and that the results strongly support pulmonary rehabilitation as part of the spectrum of the management of patients with COPD.

Pharmacological therapy

Inhaled bronchodilators

The COPD-X Guidelines state that 'inhaled bronchodilators provide symptom relief in patients with COPD and may increase exercise capacity'.[4] The inhaled bronchodilators include short- and long-acting beta-2-agonists (LABAs), and short- and long-acting anticholinergics. Systematic reviews comparing the efficacy of salbutamol and ipratropium found no major differences between the responses to either drug or the combination for the treatment of acute exacerbations of COPD[20] or stable COPD.[21]

A recent systematic review of RCTs comparing tiotropium to other bronchodilators used in patients with stable COPD found that tiotropium reduced the odds of a COPD exacerbation (OR 0.74; 95% CI 0.66 to 0.83) and related hospitalisations (OR 0.64; 95% CI 0.51 to 0.82) compared to placebo or ipratropium. Reductions in these endpoints compared to LABAs were not statistically significant.[22]



Current evidence does not support long-term antibiotic use to prevent exacerbations in patients with COPD.

A recent report from the manufacturer of *Spiriva*, Boehringer Ingelheim, to the United States Food and Drug Administration (FDA) raised alarms about a possible increased risk of stroke in patients using tiotropium. Pooled analysis from 29 placebo controlled clinical studies estimated that the risk of stroke was eight per 1000 patients treated for one year with tiotropium, and six per 1000 patients treated for one year with placebo.[23] The FDA warned that these preliminary results should be interpreted with caution, as while the analysis provides early information about potential safety issues, it has inherent limitations and further investigation using other data sources is required. The FDA will announce conclusions and recommendations to the public later this year after data from a four-year study have been received and analysed.

Corticosteroids

Inhaled corticosteroids (ICS) have proven benefit in the treatment of airway inflammation in asthma, but their role in COPD has been the subject of much controversy. A systematic review of 47 RCTs found that long-term use of ICS (>6 months) did not significantly reduce the rate of decline in FEV_1 or mortality in COPD patients. However, long-term use of ICS reduced the mean rate of exacerbations and slowed the rate of decline in quality of life, as measured by the St. George's Respiratory Questionnaire. The authors concluded that patients and health professionals should balance the potential benefits of ICS (reduced rate of exacerbations, slowed decline in quality of life) against the adverse effects (oral thrush, hoarseness and unknown long-term side effects).[24]

A recent study compared the relative efficacy of salmeterol/fluticasone 50/500µg twice-daily and tiotropium 18µg once-daily in preventing exacerbations and related outcomes over two years in severe and very severe COPD.[25] Interestingly, the study showed no difference in reduction of exacerbations between the treatment groups, although patients receiving the salmeterol/fluticasone combination had better health status as measured by the St George's Respiratory Questionnaire ($P < 0.01$) and had better survival (all-cause mortality rate 3% versus 6% with tiotropium, $P < 0.05$). This was the first study to directly compare an ICS/LABA combination and a long-acting anticholinergic, and has important implications for the choice of therapy in the management of severe COPD.

The long-term use of oral corticosteroids for COPD is not recommended.[4] Systematic review found that long-term use did not slow the decline in lung function, and increased the risk of side effects such as diabetes and osteoporosis.[26] However, there was some evidence that high doses (≥ 30mg prednisolone/day) improved FEV_1 over a short period (weighted mean difference 53mL; 95% CI 22 to 84mL, after two weeks treatment).

Methylxanthines

There is evidence that theophylline improves FEV_1 (weighted mean difference 100mL; 95% CI 40 to 60mL) and arterial blood gas tensions (PaO_2: weighted mean difference 3.2mm Hg; 95% CI 1.2 to 5.1, and $PaCO_2$: weighted mean difference -2.4mm Hg; 95% CI -3.5 to -1.2) compared to placebo.[27] However, methylxanthines are rarely used because of their narrow therapeutic index and potential for significant adverse effects and drug interactions. With close monitoring of individual patients and their serum drug levels, it appears that beneficial effects may be obtained in COPD patients who remain symptomatic despite first-line bronchodilator therapy.

Antibiotics

Current evidence does not support long-term antibiotic use to prevent exacerbations in patients with COPD. Systematic review found that prophylactic antibiotics in chronic bronchitis/COPD had a small but statistically significant effect in reducing the days of illness due to exacerbations.[28] However, they do not have a place in routine treatment because of concerns about the development of antibiotic resistance and the possibility of adverse effects.

A systematic review of the value of antibiotics in acute COPD exacerbations found that their use, regardless of choice, reduced the risk of short-term mortality by 77%, decreased the risk of treatment failure by 53% and the risk of sputum purulence by 44%; with a small increase in the risk of diarrhoea.[29] Antibiotics are therefore recommended for exacerbations with an increase in cough, dyspnoea, sputum volume or purulence.

Vaccinations

The COPD-X Guidelines recommend that all patients with moderate to severe COPD should receive annual influenza vaccinations.[4] Data from RCTs demonstrate that administration

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of an inactivated influenza vaccine to COPD patients significantly reduces exacerbations.[30]

Pneumococcal vaccination is known to be highly effective in preventing invasive bacteraemic pneumococcal pneumonia, but may be less effective in elderly or immunocompromised patients. There is no direct evidence of its efficacy in preventing pneumococcal exacerbations of COPD,[31] but the prevention of pneumonia in these patients with already reduced respiratory reserve is a worthy goal in its own right.[4]

Mucolytics

A systematic review reported a 20% reduction in the number of exacerbations per patient with oral mucolytics compared to placebo.[32] However, no differences in lung function or in adverse effects between the treatments were reported. Bearing in mind that significant quality of life and health care costs result from COPD exacerbations, health professionals and patients need to judge whether the reduction in exacerbation rate is large enough to warrant daily treatment with these medicines. Benefit may be greater in individuals who have frequent or prolonged exacerbations, or those who are repeatedly admitted to hospital with COPD, although data from RCTs is not presently available to support this recommendation.[32]

Case study

You dispense the tiotropium prescription for Mrs AJ, supply her with the appropriate inhalation device, and counsel her on its use. Knowing that collaborative efforts among health professionals are more effective than smoking cessation interventions by only one type of health professional, you reinforce what her doctor told her about the benefits of smoking cessation (for both her and her husband) and recommend nicotine replacement therapy. You also give her the Pharmacy Self Care Fact Cards on Smoking, Nicotine Replacement Therapy, and Staying a Non-Smoker. You determine that she will be receiving influenza and pneumococcal vaccines in several weeks. In addition, you tell her that there is extensive evidence for pulmonary rehabilitation programs in improving wellbeing and quality of life, and refer her to a local rehabilitation program.*

**The Australian Lung Foundation maintains a comprehensive national database of programs and can supply contact details for programs Australia-wide. Patients can enter a program either by asking for a referral from their GP and/or respiratory specialist. Many programs will also accept patients who contact them directly. Go to: www.lungnet.org.au/copd/pr_pulmon_rehab.html or call 1 800 654 301 for more information.*

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CPD questions on pages 492-4