

# Chronic obstructive pulmonary disease

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**ABSTRACT** Chronic obstructive pulmonary disease is a disease state characterised by airflow obstruction that is not fully reversible. It is predominantly caused by smoking, although other factors such as occupational exposures also contribute to the development. The obstruction arises from chronic inflammation in the airways and lung parenchyma. Chronic obstructive pulmonary disease produces symptoms, disability and impaired quality of life but significant airflow obstruction may be present before the patient is aware of symptoms. Chronic obstructive pulmonary disease is the preferred term for patients who may have been labelled as having chronic bronchitis or emphysema in the past.

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Chronic obstructive pulmonary disease is generally a progressive disease. If the patient stops smoking, the disease may still progress due to the decline in lung function that occurs with the normal aging process. However, ongoing smoking accelerates the process.

**KEYWORDS** Chronic obstructive pulmonary disease, guidelines, management, prevalence

**LIST OF ABBREVIATIONS** 'BMI, Obstruction, Dyspnoea, Exercise capacity' index (BODE index), body mass index (BMI), chronic obstructive pulmonary disease (COPD), forced expiratory volume in one second (FEV1), forced vital capacity (FVC), functional residual capacity (FRC), Global Initiative for Chronic Obstructive Lung Disease (GOLD), inspiratory capacity (IC), long term oxygen therapy (LTOT), Medical Research Council (MRC), modified Medical Research Council (mMRC), monoamine oxidase (MAO), residual volume (RV), total lung capacity (TLC)

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## PREVALENCE

The prevalence of COPD is uncertain since many patients are asymptomatic in the early stages or do not seek medical attention. However, in a national study of patients aged 18–65 in the UK, 10% men and 11% women had an abnormally low FEV1; half of these individuals had not previously been diagnosed. Although the prevalence of COPD in men appears to have reached a plateau, it is still rising in women. In the UK, 27,478 people died as a result of COPD in 2004,<sup>3</sup> representing 5% of all deaths. Morbidity is also high. In 2002, there were 110,000 hospital admissions for COPD in England and Wales, representing 1.1 million inpatient days (Department of Health, Health Solutions Wales). The annual total direct cost of COPD to the NHS is estimated at £491,652,000.

## DIAGNOSIS

A diagnosis of COPD should be considered in patients over the age of 35 with a smoking history who present with one or more of:

- exertional breathlessness

| STAGE |                  | FEV1 (% predicted)• |
|-------|------------------|---------------------|
| 0     | 'at risk'        | Normal              |
| I     | Mild COPD        | ≥ 80%               |
| II    | Moderate COPD    | 50% ≤ FEV1 < 80%    |
| III   | Severe COPD      | 30% ≤ FEV1 < 50%    |
| IV    | Very severe COPD | < 30%               |

**TABLE 1** The five stages of COPD according to 2004 GOLD guidelines.

- chronic cough
- regular sputum production
- frequent winter bronchitis
- wheeze

Spirometry should be performed to confirm the presence of airflow obstruction (FEV1/FVC ratio <70%). Reversibility to bronchodilator or steroids is not usually necessary to make a diagnosis of COPD. However, these investigations may be helpful if there is uncertainty whether the patient has asthma rather than COPD. More detailed investigations such as TLC, RV, IC, FRC and gas

| Points on BODE index | 0    | 1       | 2       | 3    |
|----------------------|------|---------|---------|------|
| FEV 1 (% predicted)  | ≥65  | 50–64   | 36–49   | ≤35  |
| 6 min walk (metres)  | ≥350 | 250–349 | 150–249 | ≤149 |
| mMRC dyspnoea scale  | 0–1  | 2       | 3       | 4    |
| Body mass index      | >21  | ≤21     |         |      |

**TABLE 2** Calculating the BODE score.

transfer calculations may be carried out to estimate further the degree of airflow obstruction and hyperinflation. Additionally, all patients should have a chest radiograph, full blood count (to exclude anaemia and polycythaemia) and BMI calculated.

The GOLD guidelines (2004) identified five stages of COPD based on the FEV1 (See Table 1).

The 'at risk' category is a controversial one and represents patients with a chronic cough and sputum production, but normal lung function. It is best seen as a pointer to alert patients to their risk of disease rather than as a true stage in COPD development as not all patients report these symptoms. Indeed, the revised guidelines in 2006 removed stage 0.

The forced expiratory volume in one second is the single best variable to stratify COPD severity. However, it does not accurately predict dyspnoea intensity, exercise tolerance, or mortality. In light of this, the BODE index<sup>1</sup> has been devised (BMI, Obstruction, Dyspnoea, Exercise capacity) which is a useful prognostic tool (see Table 2).

In a prospective study of 625 COPD patients,<sup>1</sup> the hazard ratio for death from any cause per one-point increase in the BODE score was 1.34, and the hazard ratio for death from respiratory causes was 1.62.

## MANAGEMENT

### Smoking cessation

Chronic obstructive pulmonary disease patients who stop smoking show significantly smaller declines in FEV1, along with less cough, wheeze, chronic phlegm production and dyspnoea than patients who continue to smoke.

All COPD patients who continue to smoke should be encouraged to stop at every opportunity. This is more easily achieved with the help of a support programme and the use of nicotine replacement therapy and/or bupropion (unless contraindicated; such contraindications would include seizure disorders including a current or prior diagnosis of bulimia or anorexia nervosa and concurrent administration of bupropion with a MAO inhibitor.) A new smoking cessation agent, varenicline, has recently been introduced.

### Inhaled bronchodilator therapy

#### Short-acting beta 2 agonists (salbutamol, terbutaline)

These act directly on bronchial smooth muscle to cause bronchodilation and are the most widely used bronchodilators for COPD. Their effects last up to four hours. They improve FEV1 along with dyspnoea and fatigue and are as effective taken on an 'as needed' basis as when taken as regular therapy.

#### Short-acting anticholinergics (atrovent)

These block the bronchoconstrictor effect that arises from increased resting tone in the cholinergic nerves in COPD patients. Short-acting anticholinergics improve FEV1, however, while some studies have shown improvement in dyspnoea and quality of life, other studies have not. Nonetheless, they are commonly prescribed, often in the form of a combined inhaler containing salbutamol and atrovent ('combivent').

#### Long-acting beta 2 agonists (salmeterol, formoterol)

These bronchodilators have a duration of action of around 12 hours and may be commenced in patients who are using their short-acting beta 2 agonists regularly. A large multicentre randomised controlled trial showed that salmeterol reduced the rate of COPD exacerbations compared with placebo. However, other studies have shown variable results in assessing whether there is benefit in health related quality of life.

#### Long-acting anticholinergics

Tiotropium is currently the only such agent available and it is taken once daily. This drug is associated with improved FEV1, reduced dyspnoea and exacerbation rates, and improved health related quality of life when compared with placebo and short-acting anticholinergics.

#### Long-acting bronchodilators

Long-acting bronchodilators should be used in patients who remain symptomatic despite short-acting bronchodilators or have had two or more exacerbations in the past year.

#### Inhaled corticosteroids

Although not currently licensed for use alone in COPD in the UK, there is evidence that inhaled corticosteroids do reduce exacerbation rates in more severe COPD. Inhaled steroids increase the risk of oral candidiasis. There are concerns about longer term effects such as cataracts and osteoporosis, although a definite association is not yet proven.

Inhaled corticosteroids should be prescribed for patients with FEV1 ≤50% predicted who have had two or more exacerbations in a 12 month period.

#### Combination inhalers (salmeterol / fluticasone, formoterol / budesonide)

These preparations are associated with a sustained

improvement in FEV1, breathlessness scores and exacerbation rates which is greater than with either of the components separately. There is now emerging data suggesting that these combination inhalers may also impact on mortality in COPD patients.

Although the British Thoracic Society guidelines have not allocated a definite place for combination inhalers, they are generally being prescribed for severe patients (FEV1  $\leq$ 50% predicted) who are exacerbating two or more times per year.

#### Nebulisers

Short-acting beta 2 agonists, anticholinergics and steroids can be delivered through a nebuliser. Nebulisers are often administered in acute exacerbations. However, studies have shown that nebulisers in stable COPD are no more effective than bronchodilators taken properly through an inhaler. Nebulised therapy is also more likely to lead to side effects (tremor and tachycardia.) Nebulisers require regular servicing and electrical checks, along with regular cleaning and changes of tubing, nebuliser chambers and masks. Failure to do so is common, and could result in deleterious health effects. For these reasons, hand-held inhalers (with or without a spacer device) should be used in the first instance, and with appropriate training most patients should be able to receive their medications effectively via an inhaler. Only patients with disabling or distressing breathlessness, despite maximal therapy with inhalers, should be considered for nebulised therapy.

#### Oral therapy

##### Oral corticosteroids

Due to significant systemic side effects, maintenance use of oral corticosteroids is not recommended. Apparent short-term improvements in patient wellbeing are bought at the cost of major systemic complications and an increased risk of premature death. Oral corticosteroid reversibility tests do not predict response to inhaled corticosteroid therapy.

##### Theophyllines

These drugs relax smooth airway muscle and may increase diaphragmatic strength and improve mucociliary clearance in COPD patients. They improve FEV1 and exacerbation rates, but do not significantly improve breathlessness, wheeze, or walking distance compared with placebo. Side effects (nausea and palpitations) are common, and there are interactions with other medications.

Theophyllines should be used only after a trial of short and long-acting bronchodilators, and plasma levels should be monitored.

#### Oxygen

As COPD progresses, patients may become hypoxaemic either at rest and/or on exertion. When the PaO<sub>2</sub> falls

below 8 kPa, some patients start to develop cor pulmonale. Untreated, such patients have a five-year survival below 50%.

Oxygen is often prescribed as short burst therapy to relieve symptoms, although the evidence to support this is very weak. In contrast, there is good evidence that ambulatory oxygen improves exercise endurance and LTOT prolongs life.

Long-term oxygen is indicated in COPD patients with a PaO<sub>2</sub> <7.3 kPa when stable, or PaO<sub>2</sub> <8 in the presence of secondary polycythaemia, nocturnal hypoxaemia, peripheral oedema or evidence of pulmonary hypertension. In these patients, LTOT used for more than 15 hours per day improves survival.

Inappropriate oxygen delivery can cause respiratory depression in COPD patients. There are now comprehensive guidelines for oxygen prescribing following an overhaul of the home oxygen service by the Department of Health in England that came into effect in February 2006. With these new guidelines, most home oxygen (all LTOT and ambulatory oxygen) will be prescribed from secondary care; this has been the situation in Scotland for a number of years.

#### Pulmonary rehabilitation

Pulmonary rehabilitation involves an individualised programme of exercises and education with the aim of reversing deconditioning and helping the patient cope with their disease. Pulmonary rehabilitation leads to improved exercise capacity, health related quality of life and less hospitalised days.

Pulmonary rehabilitation should be offered to all patients who consider themselves functionally disabled by COPD (Usually MRC dyspnea scale 3 and above.)

#### Vaccination

Chronic obstructive pulmonary disease patients should be offered annual influenza vaccinations and 5–10 yearly pneumococcal vaccinations.

#### Lung surgery

Bulectomy, lung volume reduction surgery and lung transplantation may be performed in selected COPD patients.

#### Mucolytic therapy

These are oral agents which reduce the viscosity of sputum. Overall, the benefits of this therapy appear to be small. A Cochrane Review<sup>4</sup> found a lower exacerbation rate in COPD and chronic bronchitis

patients taking mucolytic compared with placebo. However, a large randomised trial in COPD patients has failed to confirm this, at least when inhaled corticosteroids are also prescribed.<sup>5</sup>

#### Anxiety and depression

Chronic obstructive pulmonary disease can cause disabling and distressing symptoms and the limited activity of COPD patients can lead to social isolation. Such patients are at high risk of anxiety and depression, especially patients with more severe disease. Healthcare professionals should be alert to the presence of depression in COPD patients, and, where appropriate, antidepressant pharmacotherapy should be commenced.

#### Nutritional factors

Many COPD patients are underweight as a result of decreased food intake due to breathlessness, and increased resting energy expenditure as a result of the increased work of breathing. Reduced BMI is associated with increased mortality, as exemplified in the BODE scoring system.

The BMI should be calculated in all patients with COPD. If the BMI is high or low or changing, the patient should be referred for dietetic advice. Chronic obstructive pulmonary disease guidelines recommend that nutritional supplements should be given when the BMI is low. However, a Cochrane Review<sup>6</sup> showed that nutritional support in stable COPD patients had no significant effect on anthropometric measures, lung function or exercise capacity.

#### Education, self-management plans and follow-up

Patients should be given self-management plans that may include self initiation of steroids and/or antibiotics at the onset of an exacerbation. Most COPD patients with mild–moderate, or stable severe disease can be followed up by the General Practitioner with access to specialist care where needed. They should be reviewed at least once per year with monitoring of smoking status, symptom control, inhaler technique, and the need for LTOT or pulmonary rehabilitation. Forced expiratory volume in one second and FVC, BMI and MRC dyspnoea score should also be assessed at least once per year.

#### FURTHER READING

- Patient version of British Thoracic Society/NICE guideline: [www.nice.org.uk](http://www.nice.org.uk)
- The full British Thoracic Society guidelines can be obtained from: Chronic obstructive pulmonary disease: National clinical guideline for management of chronic obstructive pulmonary disease in

#### Exacerbations

Periodic worsening of symptoms like breathlessness and sputum production, secondary to viral and bacterial infection and/or atmospheric pollution, produce extended periods of ill health and can be life-threatening. A short (ten day or less) course of oral steroids, antibiotics if the sputum is purulent and increased bronchodilator therapy are the mainstays of management. Hospitalisation with the use of controlled oxygen is needed in more severe cases. Non-invasive ventilation can be life-saving in those with respiratory acidosis and is now the evidence-based standard of care for these patients.<sup>7</sup>

The presence of COPD as a co-morbidity increases the risk of death from other conditions, especially cardiovascular disease, and this relationship may be more than simply coincidental. Increasing awareness of COPD as a major cause of disability and ill health is now a priority area for action in the UK and overseas, a belated recognition of the importance of this common, but neglected, disorder.

#### KEYPOINTS

- Chronic obstructive pulmonary disease results from airflow obstruction which may not be reversible and is the preferred term for patients who may in the past have been labelled as having chronic bronchitis or emphysema.
- Chronic obstructive pulmonary disease is predominantly caused by cigarette smoking, although occupational exposure can contribute to its development.
- Symptoms may not be present until the more advanced stages of the disease.
- Ten to eleven per cent of the UK adult population may have COPD.
- The volume of air that can be forced out in one second after taking a deep breath (FEV1) classifies disease severity.
- Treatment centres on bronchodilation, steroids and control of infection in the acute presentation.
- Pulmonary rehabilitation should be offered to all functionally disabled patients.

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- The GOLD guidelines are available from: [www.goldcopd.com](http://www.goldcopd.com)
- Useful information is also available from: The British Thoracic Society: [www.brit-thoracic.org](http://www.brit-thoracic.org) and The British Lung Foundation: [www.lunguk.org](http://www.lunguk.org)

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