

Chronic obstructive pulmonary disease

This bulletin discusses the diagnosis of chronic obstructive pulmonary disease (COPD) and its appropriate management with inhaled medicines in the primary care setting. It does not discuss the management and treatment of more severe disease or acute exacerbations.

Background

This long-term lung disease is characterised by airflow obstruction that is not fully reversible and is usually progressive, although it does not change markedly over several months.¹ The damage to the lungs is usually caused by an abnormal inflammatory response to noxious particles or gases – the most common cause is smoking.^{1,2} The disease prevalence in Wales, as shown from data collected for the Quality and Outcomes Framework 2005/06, is 1.87% of the population, with more than 57 500 affected people.³ It is thought that there are at least as many people in whom the condition is undiagnosed. The cost burden is substantial as the disease accounts for more than 10% of all hospital admissions and is the largest single cause of lost working days in the UK.²

Diagnosing COPD

The diagnosis of COPD relies on the use of spirometry in association with clinical judgement that is informed by the patient's symptoms and history.¹ A careful and accurate diagnosis is essential as the disease is primarily seen in middle-aged and older smokers or ex-smokers and there are many associated co-morbidities. Weight loss, nutritional abnormalities, and skeletal muscle dysfunction, are well recognised extrapulmonary effects of COPD. However, the disease, its treatment, the patient's age, and other lifestyle factors may also predispose to an increased risk of myocardial infarction, angina, osteoporosis, respiratory infection, sleep disorders, depression, diabetes, anaemia, and glaucoma. There is also a large associated increased risk of lung cancer.⁴

Summary

- ◆ Diagnosis of COPD relies heavily on clinical judgement that is informed by the patient's history, clinical findings, and the results of spirometry.
- ◆ An assessment of severity should be recorded at each clinical review.
- ◆ All COPD patients who smoke should be encouraged to stop and offered help to do so at every opportunity, regardless of age. (See the accompanying supplement.)
- ◆ If a therapy is not effective for a patient it should be withdrawn. This decision should not be based on lung function alone.
- ◆ As relatively high doses of inhaled corticosteroids are used in COPD, patients should be counselled on the risks and benefits of treatment. Issuing a steroid card is recommended.

The National Institute for Health and Clinical Excellence (NICE) guideline stipulates that all health professionals managing patients with COPD should have access to spirometry and be competent in interpreting the results obtained. A diagnosis of COPD should be considered, and spirometry performed, in patients over the age of 35 years who have a risk factor (generally a history of smoking) and who present with:

- ◆ exertional breathlessness
- ◆ chronic cough
- ◆ regular sputum production
- ◆ frequent winter 'bronchitis'
- ◆ wheeze.¹

At diagnosis, such patients should also have:

- ◆ a chest x-ray (to exclude other pathologies)
- ◆ a full blood count (to identify anaemia or polycythaemia)
- ◆ a body mass index (BMI) calculation.¹

Spirometry

Spirometry is the ‘gold standard’ test to confirm COPD and to make an initial assessment of severity. Peak flow measurements are not recommended for diagnosis as they may underestimate the extent of lung impairment.¹

Performing spirometry is primarily a way of assessing the volume of air that the lungs can forcefully expel in one second after a maximal inhalation (forced expiratory volume in one second, **FEV₁**) and the total volume of air a patient can forcefully expel after a maximal inhalation (forced vital capacity, **FVC**). The assessment of the degree of airflow limitation is based on the ratio of FEV₁/FVC, and the comparison of the patient’s FEV₁ to age-, sex-, height-, and race-matched normal healthy predicted values. The diagnosis of COPD is confirmed only if **FEV₁/FVC is <0.7** and **FEV₁ is < 80% of that predicted**.

Spirometry should be repeated periodically; it is recommended that FEV₁ and FVC are measured at least annually in those with mild or moderate disease and at least twice a year in those with severe disease (see below for assessment of disease severity).¹

Is it COPD or asthma?

Clinical features

Both COPD and asthma are associated with chronic inflammation of the respiratory tract. However, there are marked differences in the inflammatory processes, cells, and mediators that account for the differences in physiological effects, symptoms, and response to therapy.⁴ In an untreated patient presenting for the first time, it may be possible to distinguish COPD from asthma based on history and examination (see Table 1). However, ongoing observation using spirometry, peak flow, or symptoms may also be useful in differentiating the two conditions.¹ The possibility that a patient may have both COPD and asthma simultaneously should not be overlooked.

Reversibility testing

It is possible that asthma may show similar abnormalities on spirometry to COPD. Reversibility testing can be carried out where diagnostic doubt remains despite patient history, examination, and longitudinal observation of spirometry, peak flow, or symptoms. NICE states that the test should not be used routinely for

Table 1. Clinical features differentiating COPD and asthma.^{1,5}

Feature	COPD	Asthma
Smoker or ex-smoker	Nearly all	Possibly
Symptoms < 35 years	Rare	Often
Chronic productive cough	Common	Uncommon
Breathlessness	Persistent/ progressive	Variable
Night time waking with breathlessness / wheeze	Uncommon	Common
Significant diurnal or day-to-day symptom / peak flow variability	Uncommon	Common
Family history	Uncommon unless smokers	Common
Concomitant eczema or allergic rhinitis	Possible	Common

diagnosis or to plan initial therapy because results can show small, spontaneous fluctuations or inconsistencies that may be unhelpful or misleading.¹ However, the new Quality and Outcomes Framework (2008/09) requires that patients have the diagnosis of COPD confirmed with ‘post-bronchodilator spirometry’.

Reversibility testing can be carried out by obtaining a baseline spirometry reading, and then comparing that with another reading following use of a bronchodilator (details regarding the methods of testing are documented in Spirometry in Practice).⁶ A significant degree of reversibility (>400ml FEV₁) is strongly suggestive of asthma.^{1,7} Smaller improvements in FEV₁ (e.g. >200ml) are less discriminatory but may suggest an asthmatic component to disease.^{4,7}

Assessment of severity

The severity of COPD has implications both on prognosis and therapy. Assessment is based on degree of spirometric abnormality (see Table 2), symptoms, and the presence of complications.

Table 2. Assessment of the severity of airflow obstruction based on FEV₁ as a percentage of predicted value.

(Adapted from NICE and Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines.)^{1,4}

NICE	FEV ₁	GOLD
-	> 80%	Stage I: Mild
Mild	50-80%	Stage II: Moderate
Moderate	30-49%	Stage III: Severe
Severe	< 30%	Stage IV: Very Severe

The Medical Research Council (MRC) Dyspnoea Scale (see Table 3) is a widely-used and useful tool, particularly as the symptoms a patient experiences and the degree of airway obstruction seen on spirometry may not be commensurate. The grading, based on patient self-reporting, relates well to other measures of health and is predictive of mortality risk.⁴

Table 3. The MRC Dyspnoea Scale.⁸

Grade	Degree of breathlessness
1	Breathlessness only on strenuous exercise.
2	Short of breath when hurrying or walking up slight hill.
3	Walks slower than contemporaries on level ground because of breathlessness, or has to stop for breath walking at own pace.
4	Stops for breath after walking for about 100 metres, or for a few minutes, on level ground.
5	Too breathless to leave the house or breathless on dressing and undressing.

Referral for specialist advice

Referral may be indicated at any stage of disease. Reasons include diagnostic uncertainty, symptoms that are disproportionate to lung function deficit, severe or worsening disease (based on symptom assessment and/or rapid decline in FEV₁, i.e. of >100ml per year), onset of cor pulmonale, dysfunctional breathing, age <40 years or family history of alpha₁-antitrypsin deficiency, frequent exacerbations, haemoptysis, and assessment for other therapies such as pulmonary rehabilitation, oxygen, nebulised medicines, oral corticosteroids, and lung surgery.¹

Treatment of stable COPD

Initial treatment intensity should be tailored to the individual patient, taking into account the level of disease severity and symptoms at diagnosis. Patient preference should also be considered. It is important that any therapy that is not effective for a patient is discontinued. The assessment of effectiveness should include factors such as extent and rapidity of symptom improvement, ability to carry out activities of daily living, and exercise tolerance; it should not be determined solely by changes in lung function.¹

Some suggested questions to help assess effectiveness of therapy are:⁹

- ◆ Has your treatment made any difference to you?
- ◆ Is your breathing easier in any way?
- ◆ Can you do things now that you couldn't do at all before, or do the same things but faster?

- ◆ Can you do the same things as before but are now less breathless when you do them?
- ◆ Has your sleep improved?

Smoking cessation

For smokers, cessation is the single most effective intervention to prevent disease progression.⁴ All COPD patients who smoke should be encouraged to stop and offered help to do so at every opportunity, regardless of age (see accompanying supplement).¹

Inhaled bronchodilators

Bronchodilators are central to symptom control in COPD and a **short-acting bronchodilator**, given on an 'as required' basis, is the initial, empirical treatment of choice for breathlessness and exercise limitation.¹ A short-acting β_2 -agonist [SABA] (salbutamol or terbutaline sulphate) or an antimuscarinic preparation (ipratropium bromide) may be used. A systematic review has concluded that the differences between the treatments are small with regard to improvements in lung function, symptoms, and exercise tolerance.¹⁰ The choice will depend on the patient's response to a trial of the drug, potential adverse effects, patient preference, and cost.¹ If 'as required' therapy is ineffective it is reasonable to give an adequate trial of regular treatment, or to change to a product from the other drug class (i.e. from SABA to antimuscarinic, or vice versa). If this also proves inadequate, combining the two classes of therapy can be considered.^{1,10}

If a patient remains symptomatic despite receiving an adequate trial of short-acting bronchodilators as above, or has two or more disease exacerbations in a year, then consideration should be given to the regular use of a **long-acting bronchodilator**.¹ Choices include a long-acting β_2 -agonist [LABA] (salmeterol or formoterol) or a long-acting antimuscarinic (tiotropium). It is important to note that ipratropium and tiotropium should not be used together due to the risk of additive antimuscarinic adverse effects.¹¹

There is a need for large, well designed studies to directly compare the efficacy and safety of medicines from the two available drug classes. It is difficult to draw conclusions from many currently available studies as patients often received concomitant therapies, and serious endpoint event rates can be low.¹² Furthermore, definitions of 'exacerbations' and 'change in quality of life' are not uniform. One systematic review reports that the

long-acting inhaled therapies were similarly effective in reducing exacerbations.¹³ Likewise, a cohort study comparing LABAs and tiotropium in patients registered in a UK primary care database suggests that the rates of all-cause mortality, most cardiac events, COPD exacerbations, and pneumonia reported with these medicines are essentially the same.¹⁴ If one long-acting bronchodilator fails to be effective alone, NICE stipulates that a drug from the other class may be added (i.e. if tiotropium is ineffective add a LABA, or vice versa).¹ However, again due to study limitations,^{13,15} assessing evidence regarding such a combination is difficult.

Inhaled corticosteroids (ICS)

NICE recommends that ICS are only used when FEV₁ is $\leq 50\%$ of that predicted* (i.e. moderate and severe disease) **and** oral corticosteroids or antibiotics are required for two or more exacerbations a year.¹ ICS should be withdrawn if they fail to help improve symptoms (e.g. breathlessness) following a four week trial.¹ Any effect on exacerbations is harder to assess and may take longer to become apparent. Relatively high doses of ICS are used in COPD and it is essential that all patients receive counselling regarding the risks and benefits of treatment. Issuing a steroid card is recommended.^{1,11}

There is debate surrounding the use of inhaled corticosteroids in COPD. No monocomponent ICS preparations are licensed for use, but combination ICS/LABA products (breath-actuated fluticasone/salmeterol and budesonide/formoterol) are available and have been the subject of several recently published systematic reviews.^{13,16-18} One such review concluded that there is no advantage in using combinations of ICS/LABA over LABA alone.¹³ However, a Cochrane meta-analysis, which used different criteria for including studies in the investigation of exacerbations,¹⁹ found inhaled ICS/LABA combinations improved quality of life and reduced exacerbations compared with a LABA alone. To put the results in context, the reported reduction of approximately one in five exacerbations will be relevant only in patients experiencing frequent exacerbations. The effects on hospitalisations were inconclusive and mortality was not significantly reduced.¹⁸ Interpretation of the data from one more recent trial of fluticasone/salmeterol versus tiotropium therapy is difficult as treatments were associated with high withdrawal rates.²⁰

Oral candidiasis and hoarseness are commonly seen adverse effects of ICS treatment.¹¹ Of concern are reports of an increased risk of pneumonia (primarily from studies of fluticasone-containing regimens).^{15,17-21} Some caution regarding these reports is warranted as criteria for reporting pneumonia (e.g. confirmatory x-ray) has differed between studies. However, the Medicines and Healthcare products Regulatory Agency recommends clinicians are vigilant for signs of pneumonia in any patient with COPD treated with ICS, because the clinical features of such infection and exacerbation often overlap. They advise that patients with severe COPD who develop pneumonia while receiving ICS should have their treatment reconsidered.²²

Pulmonary rehabilitation

Pulmonary rehabilitation is established as a core therapy for patients with COPD, although access to services remains limited in some areas. It is recommended for patients with COPD who are on optimal therapy but who are breathless at MRC Dyspnoea Scale grade 3 or worse.¹

*Marketing authorisations differ and the Summaries of Product Characteristics should be consulted for full prescribing information.

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