Outpatient management of chronic obstructive pulmonary disease

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Chronic obstructive pulmonary disease (COPD) is defined as:

> *a disease state characterised by airflow limitation that is not fully reversible. The airflow limitation is usually both progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases.*[1]

COPD is common and increasing, especially among women (Fig 1).[2] The disease is characterised by an excess decline in lung function as shown on the 'Fletcher diagram' (Fig 2). COPD, like many other chronic disorders, is characterised by a long period of gradually increasing symptoms and deteriorating quality of life (QoL). Most patients are treated for decades outside hospital.

Diagnosis

Essential to all outpatient management of COPD is a proper diagnosis. Spirometry is central in demonstrating airflow limitation. Both the Global Initiative in Obstructive Lung Disease (GOLD) guidelines for diagnosis and management of COPD[1] and the National Institute for Clinical Excellence (NICE) guidelines[3] define airflow obstruction as a ratio of less than 0.7 between forced expiratory volume in one second (FEV_1) and forced vital capacity. This cut-off value will tend to overestimate airflow obstruction in the elderly but, on the other hand, is simple and easy to remember.

In order to diagnose COPD, a diagnosis of asthma must be excluded. In most cases this will not be a problem as asthma is characterised by a larger day-to-day variation, earlier onset, coexistence of other atopic disease and marked nocturnal symptoms. In unclear cases the response to 14 days of systemic steroids or 6–8 weeks of inhaled corticosteroids could be evaluated. Although there are no clear cut-off values, an increase in FEV_1 of 300–400 ml is rarely seen in COPD.

Chest X-ray is not helpful in diagnosing COPD, but should be performed to exclude other intrathoracic pathology – patients with COPD are at high risk of developing lung cancer.

Staging

COPD staging is based on spirometry. Table 1 describes the staging according to GOLD. Unfortunately, the correlation between FEV_1 and symptoms and disability is weak, but it is possible to obtain some prognostic indication by combining spirometry with an assessment of breathlessness, six-minute walking distance and body mass index.

Smoking cessation

In Western Europe and the USA 80% of COPD is caused by tobacco smoking; in other parts of the world, this proportion is often lower. All outpatient management of COPD must include assessment of smoking habits. Participation in active smoking cessation programmes, including use of nicotine replacement therapy and/or bupropion, should be encouraged. Smoking cessation is the only intervention that can effectively slow down further progression of disease.[4]

Progression

Breathlessness, the main symptom of COPD, can be assessed using a number of scales. A recent modification of the thoroughly validated Medical Research Council (MRC) questions on dyspnoea is shown in Table 2. With increasing severity of disease, breathlessness becomes more intense; it eventually leads to anxiety and the patient enters the vicious circles illustrated in Fig 3. With further progression of disease, the patient is disabled not only by breathlessness but also by increasingly frequent exacerbations which are the main cause of the deterioration in health-related QoL.[5] A systemic component to the disease affects muscle function, leading to weight loss.

Non-pharmacological treatment

Deconditioning plays a major role in breathlessness, so patients should be advised to keep physically active despite their disability. Exercise plays an impor-

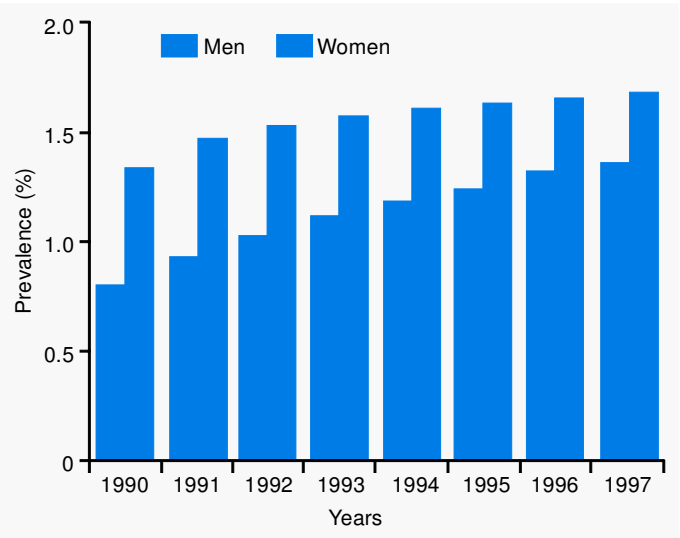

Fig 1. Prevalence (%) of physician-diagnosed chronic obstructive pulmonary disease in the UK in men and women, 1990–1997 (reprinted with permission from Ref 2).

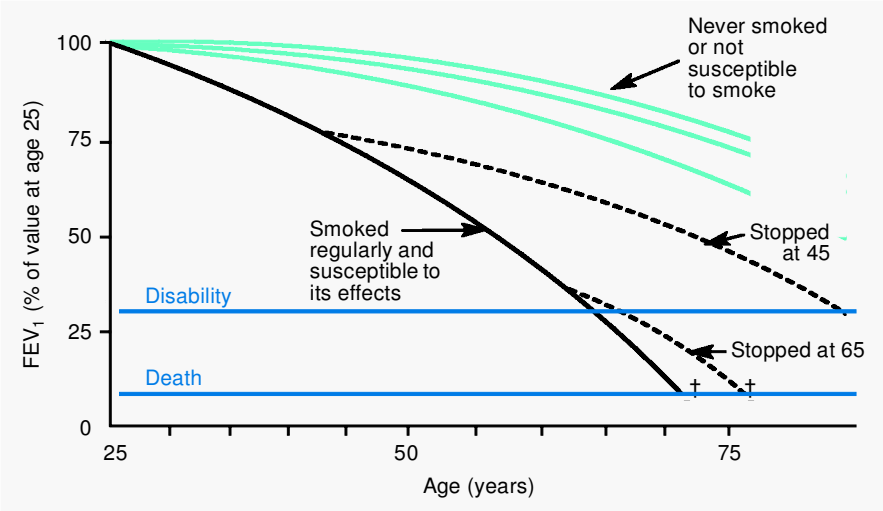

Fig 2. A modification of the 'Fletcher diagram' illustrating the excess decline in forced expiratory volume in 1 second (FEV_1) characteristic of chronic obstructive pulmonary disease.

tant role in rehabilitation programmes, evidence for which has been building up over the last decades.[6] Rehabilitation should be available to all COPD patients with a disability who are motivated to participate in a programme. Multidisciplinary programmes usually last 7–12 weeks and include:

- physical exercise
- teaching of mechanisms of disease and treatment
- dietary advice
- advice on how to cope with COPD.

Weight loss is frequent in severe disease, but may already occur in moderate and even mild disease. There is no evidence that any specific nutritional therapy is useful, but patients able to gain or stabilise weight have a more favourable prognosis than those who continue to lose weight.[7] Obesity should be treated as in non-COPD subjects.

Pharmacological treatment

Most medication for COPD has initially been registered and used for asthma, but both use and effects differ in the two diseases. Proper instruction is a prerequisite to treatment with inhaled medication, and it is crucial to all inhaled therapy that the patient is able to use the chosen inhalation device properly. Pharmacological treatment according to GOLD stages is shown in Fig 4.

Table 1. Staging of chronic obstructive pulmonary disease (COPD), Global Initiative in Obstructive Lung Disease (GOLD) criteria.[1]

Stage	COPD	Criteria
0	At risk	Normal spirometry but chronic symptoms (cough, sputum production)
I	Mild COPD	FEV_1/FVC <70%, FEV_1 ≥80% predicted, with or without chronic symptoms
II	Moderate COPD	FEV_1/FVC <70%, 50% ≥ FEV_1 <80% predicted, with or without chronic symptoms
III	Severe COPD	FEV_1/FVC <70%, 30% ≥ FEV_1 <50% predicted, with or without chronic symptoms
IV	Very severe COPD	FEV_1/FVC <70%, FEV_1 <30% predicted or FEV_1 <50% predicted plus chronic respiratory failure

FEV_1 = forced expiratory volume in one second; FVC = forced vital capacity.

Reversibility testing

Reversibility testing has previously been seen as a way of choosing treatments. Reversibility to bronchodilators and corticosteroids may be helpful in the differential diagnosis of asthma, but in the individual patient with COPD does not help to predict response to treatment. For FEV_1, the variability in post-bronchodilator values is less than for pre-bronchodilator values; this justifies assessing patients after the administration of a bronchodilator. Reversibility in itself does not have prognostic value.[8]

Bronchodilators

Short-acting bronchodilators are often the first choice for treating breathlessness in mild COPD. There is no significant difference between short-acting β_2-agonists (salbutamol, terbutaline, fenoterol) and the short-acting anticholinergic ipratropium bromide, but patients may differ in preference. Controlled studies have shown that combinations of these drugs are more effective than either drug alone.

Long-acting β_2-agonists (salmeterol, formoterol) and anticholinergics (tiotropium) are recommended in recent guidelines, but they may not be necessary in mild COPD and are more expensive. They relieve breathlessness, improve

Table 2. Scaling of breathlessness.

PLEASE TICK IN THE BOX THAT APPLIES TO YOU (ONE BOX ONLY)	
☐	I only get breathless with strenuous exercise.
☐	I get short of breath when hurrying on the level or walking up a slight hill.
☐	I walk slower than people of the same age on the level because of breathlessness or I have to stop for breath when walking at my own pace on the level.
☐	I stop for breath after walking about 100 yards or after a few minutes on the level.
☐	I am too breathless to leave the house or I am breathless when dressing or undressing.

Key Points

- Chronic obstructive pulmonary disease (COPD) is a common progressive disease mainly caused by smoking
- Spirometry is central in diagnosis, staging and follow-up of patients
- Pulmonary rehabilitation has been proven effective in improving exercise capacity and increasing quality of life (QoL) and should be made available to all COPD patients motivated to participate
- Bronchodilators reduce breathlessness, improve QoL and can to some extent reduce exacerbation rate. Long-acting bronchodilators should be used in patients with moderate and severe disease
- Inhaled corticosteroids reduce exacerbation rate and improve QoL and may have an impact on mortality; they are indicated in patients with severe COPD and frequent exacerbation
- Most exacerbations in COPD can be treated outside hospital using bronchodilators and courses of systemic corticosteroids and antibiotics

KEY WORDS: antibiotics, bronchodilators, chronic obstructive pulmonary disease, corticosteroids, epidemiology, exacerbations, rehabilitation, smoking

QoL,[9–11] can to some extent reduce exacerbations, and have a clear role in moderate and severe disease. Again, there is no major difference in efficacy between the β_2-agonists and anticholinergics.

In general, the low efficacy and high frequency of side effects and interactions make *theophyllines* a less suitable group of bronchodilators.

With the large number of drugs available, and because of the variation in response between individual patients and the normal variation in symptomatology, repeat individual evaluation of bronchodilators is crucial.

Nebulised short-acting bronchodilators are often used during exacerbations and in stable severe disease. Nebuliser treatment can almost always be substituted with a metered dose inhaler used through a spacer device, provided a high dose is given (eg 1–2 mg). Nebuliser treatment requires thorough assessment before initiation, for which patients should be referred to a specialist.

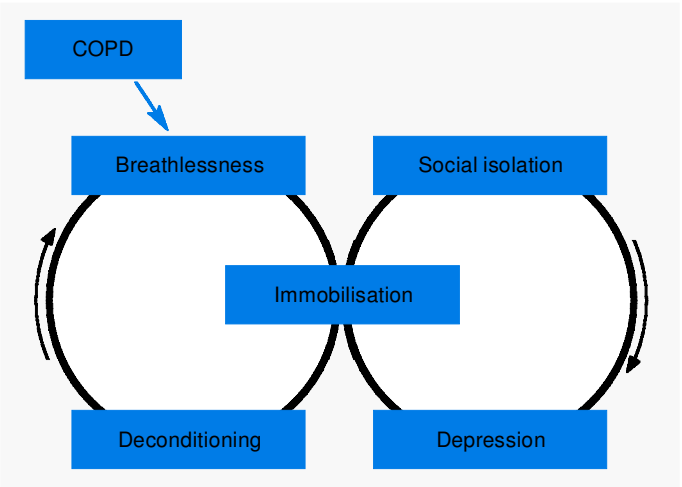

Fig 3. Vicious circles of breathlessness (COPD = chronic obstructive pulmonary disease).

Inhaled corticosteroids

Inhaled corticosteroids (ICS) are indicated in patients with severe or very severe COPD with previous documented exacerbations (β_2 requiring treatment per year). The purpose of treatment with ICS is primarily to prevent exacerbations and improve QoL. They have no effect in mild disease and only a small effect (if any) on FEV_1 decline.[12] Pharmacoepidemiology indicates that the effect on exacerbations could have an impact on mortality.[13]

ICS can be combined with long-acting bronchodilators. Fixed combinations with β_2-agonists are available. Trials have shown them to be efficacious[14] and better for most outcomes than single drug treatment. Doubt remains as to whether or not long-term ICS treatment of patients with severe COPD and/or exacerbations could have long-term side effects, especially osteoporosis. This and the possible effect of combination treatment on mortality are now being examined in a large controlled trial. Maintenance therapy with systemic corticosteroids increases the risk of mortality and should be avoided.

Other treatment options

Long-term oxygen therapy prolongs survival in hypoxic COPD patients. Treatment requires assessment of arterial blood gases and often takes place in specialist clinics. Patients should be screened for hypoxia when:

- it is clinically suspected
- FEV_1 in stable phase drops to 40% of predicted, or
- saturation drops to 93% measured with pulse oximetry.

Influenza vaccination should be given to all COPD patients with stage II+, but the evidence for pneumococcal vaccination is more dubious. *Long-term antibiotics* and expectorants have no effect on exacerbation rate.

Comorbidities often deserve attention. As a result of smoking and often a sedentary lifestyle, especially ischaemic heart disease and osteoporosis often coexist.

Exacerbations

An exacerbation can be defined as:

> *a sustained worsening of the patient's condition, from the stable state and beyond normal day-to-day variations, that is acute in onset and necessitates a change in regular medication in a patient with underlying COPD.*[15]

Exacerbations are often caused by viral and/or bacterial infection of the tracheobronchial tree and air pollution, but in a substantial number of cases a cause

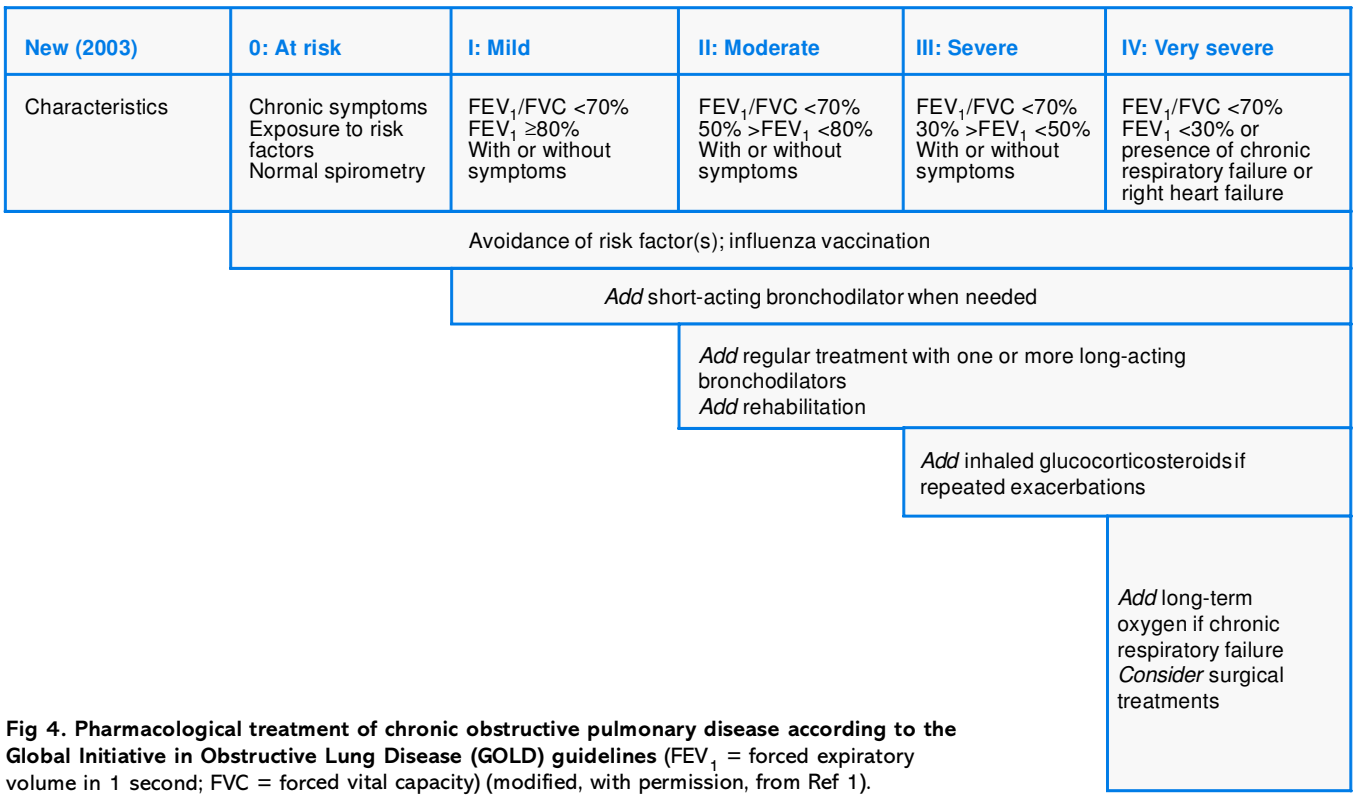

Fig 4. Pharmacological treatment of chronic obstructive pulmonary disease according to the Global Initiative in Obstructive Lung Disease (GOLD) guidelines (FEV_1 = forced expiratory volume in 1 second; FVC = forced vital capacity) (modified, with permission, from Ref 1).

cannot be identified. Bacteria present are most often *Streptococcus pneumoniae*, *Haemophilus influenzae* or *Moraxella catarrhalis*. *Pseudomonas aeruginosa* plays a role in patients with severe disease who have received frequent courses of antibiotics or when bronchiectases are present.

Exacerbations can often be treated outside hospital. Depending on severity, outpatient treatment includes increased use of bronchodilators, a course of systemic corticosteroids[16] and, in the presence of signs of infection such as purulent sputum, antibiotics.[17] Criteria for hospital admission of COPD exacerbations are shown in Table 3. Exacerbations will often lead to deterioration in QoL, loss of muscle mass and increased disability; these patients would often gain with follow-up rehabilitation.

Table 3. Criteria for hospital admission of patients with chronic obstructive pulmonary disease (COPD) exacerbations (modified from Ref 1).

- Marked increase in intensity of symptoms (eg development of resting dyspnoea)
- Severe underlying COPD
- Onset of new physical signs (eg cyanosis, peripheral oedema)
- Failure to respond to initial medical management
- Significant comorbidities
- Newly occurring arrhythmias or hypotension
- Confusion
- Older age
- Insufficient home support

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Community acquired pneumonia

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Community acquired pneumonia (CAP) is common in adults. Annual incidence rates increase from six per 1,000 population in the 16–59 age group to 34 per 1,000 population in those aged 75 and over.[1] Hospital admission is needed in 20–40% of patients with CAP, 5–10% of whom require admission to an intensive care unit. Most studies report an overall mortality of 5–10%. In recognition of the importance of CAP, several countries have published national guidelines for its management. The latest British Thoracic Society (BTS) guidelines were published in 2001 and have recently been updated.[2,3,4]

This review will discuss key aspects of the management of CAP, including changes or new issues to be covered in the BTS guidelines 2004 update.

How to recognise community acquired pneumonia

The diagnosis of CAP in hospital is defined by the BTS as the presence of symptoms and signs of an acute lower respiratory tract infection (LRTI) together with new radiographic shadowing for which there is no other explanation. Diagnosing CAP in the community in the absence of a chest X-ray (CXR) is less straightforward. Even in patients with symptoms of an LRTI plus focal chest signs, there is radiographic evidence of pneumonia in only about 40%.[5] Furthermore, the classic symptoms and signs of an LRTI (eg fever and cough) may not always be present in the elderly, while non-specific symptoms such as mental confusion are more common than in younger patients.[6] A healthy index of suspicion is required in such patients. Ultimately, the CXR remains the definitive test for diagnosing CAP.

What are the likely pathogens implicated in community acquired pneumonia in the UK?

Streptococcus pneumoniae continues to be the most frequently isolated organism in CAP (Table 1).

Other pathogens should be considered when there is a coincidence of certain epidemiological features (Table 2). *Chlamydia pneumoniae* has been identified in up to 20% of cases; it is often isolated together with another pathogen, most commonly *S. pneumoniae*.[7] Specific antibiotic therapy against *C. pneumoniae*

Key Points

- **Streptococcus pneumoniae remains the most important pathogen in community acquired pneumonia (CAP), even in patients with underlying chronic obstructive pulmonary disease**
- **Patients with three or more of the following features have severe CAP: (a) Confusion, (b) Urea >7 mmol/l, (c) Respiratory rate 30 per min, (d) Blood pressure (systolic <90 mmHg or diastolic #60 mmHg), (e) Age 65 years (CURB-65)**
- **Patients who do not have severe CAP may not require intravenous antibiotics**
- **Hospitalised patients with severe CAP should be treated with a beta-lactam based antibiotic in combination with a macrolide (eg cefuroxime, clarithromycin)**
- **The new 'Gram-positive' fluoroquinolones (eg levofloxacin, moxifloxacin) should not be used in the community or as first-line treatment of CAP**

KEY WORDS: adult, antibiotics, community acquired pneumonia, fluoroquinolone, guidelines, respiratory tract infection, review, *Streptococcus pneumoniae*