CURRENT CONCEPTS IN THE MANAGEMENT OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

Introduction
The Global Initiative for Chronic Obstructive Lung Disease (GOLD) recently published an updated 2016 edition of the global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease (COPD). The aim of the document is to guide healthcare professionals in the diagnosis and management thereof and to differentiate patients with COPD from those with asthma.

COPD definition
COPD is ‘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’. It is a leading cause of morbidity and mortality worldwide. The most important and best studied risk factor for COPD is smoking. However, it is not the only risk factor and, although the prevalence of COPD is higher in smokers, international surveys have also documented a substantial prevalence (3-11%) among people who have never smoked. Indoor air pollution from biomass cooking (e.g. open fires or stoves burning wood, animal dung, crop residues or coal) and heating in poorly ventilated dwellings is another significant risk factor. In South Africa tuberculosis and HIV are also important risk factors, and may accelerate the onset of smoking-related disease. However, it is apparent that genes play a key role in the pathogenesis and epidemiology of COPD, as the majority of smokers (approximately 80%) never develop the disease.

COPD is more common with age, as is associated morbidity, which may also be affected by other comorbid conditions, such as cardiovascular disease, musculoskeletal conditions, diabetes mellitus, osteoporosis, metabolic syndrome and depression.

Pathogenesis of COPD
Pathological changes in COPD occur in the large and small airways, lung parenchyma and pulmonary vasculature consequent on chronic inflammation and structural changes resulting from repeated injury and repair. These changes increase with disease severity and persist after smoking cessation. Airway inflammation differs from that in asthma in that, instead of eosinophilia, it is predominantly associated with lymphocytes, neutrophils and macrophages.

Airway inflammation and narrowing, fibrosis and luminal exudates in the small airways are associated with airflow limitation and air trapping, which correlate with reduction in forced expiratory volume in one second (FEV₁) and FEV₁/FVC ratio. Peripheral airway obstruction progressively traps air during
expiration resulting in hyperinflation, which reduces inspiratory capacity and increases functional residual capacity (FRC), causing exertional dyspnoea and reduced effort tolerance. By reducing air trapping in the peripheral airways, bronchodilator therapy reduces lung volumes and improves symptoms and exercise capacity.

There are multiple causes of gas exchange abnormalities in COPD, which cause hypoxaemia and hypercapnia. They include reduced respiratory drive, airway obstruction, hyperinflation, reduced alveolar ventilation and limitation of the pulmonary vascular bed. Chronic airway irritation is associated with an increased number of goblet cells and enlarged submucosal glands, causing hypersecretion of mucus and the chronic productive cough that is characteristic of many patients with COPD.

Hypoxic vasoconstriction of the small pulmonary arteries and structural changes in the vessel walls may eventually lead to pulmonary hypertension and consequently right ventricular hypertrophy and right-sided heart failure.

Exacerbations of respiratory symptoms are common in patients with COPD. They occur consequent on infection, environmental pollutants or other unidentified factors and are associated with increased inflammation, increased hyperinflation and gas trapping, reduced expiratory flow and worsening of V̇A/Q abnormalities, worsening hypoxaemia and increasing dyspnoea.

**Diagnosis**

Patients with COPD are a heterogeneous population and the clinical presentation may vary markedly. However, a diagnosis of COPD should be considered in symptomatic individuals over the age of 40 with the following:

1. **Persistent dyspnoea** that has been progressively worsening over time (characteristically worse with exercise);
2. **Chronic cough** (may be intermittent and unproductive);
3. **Chronic sputum production**;
4. **History of exposure to risk factors** (e.g. tobacco smoke, indoor smoke pollution, occupational dusts and chemicals).

Although these factors are not diagnostic in themselves, their combined presence increases the probability of COPD. Spirometry is required to support the diagnosis, with post-bronchodilator FEV₁/FVC <0.70 confirming the presence of persistent airflow limitation. Assessment of the degree of reversibility of airflow limitation (e.g. after bronchodilator or corticosteroids) adds nothing to the diagnosis; it does not predict response to long-term bronchodilators or corticosteroids and is no longer recommended.¹

Fatigue, weight loss, anorexia and other symptoms, such as depression and/or anxiety, often occur in severe COPD. They are important in establishing prognosis, but may also be indicative of other diseases and should always be investigated. Importantly, the risk of lung cancer is significantly increased in individuals with COPD.

**Tools to assess severity of disease**

The COPD assessment test (CAT) is an eight-item questionnaire that measures health status and impairment in COPD (http://www.catestonline.org). Cough, phlegm production, chest tightness, effort tolerance, limitation of activities, anxiety, sleep and energy level are assigned a score between 0 (no symptoms) and 5 (severe) to provide a total score out of 40. The recommended cut-off point for considering regular treatment for COPD symptoms is 10. The Modified British Medical Research Council (mMRC) questionnaire (Table 1) provides an assessment of symptoms and predicts future mortality risk.

Exacerbation in patients with COPD is defined as an acute event characterised by a worsening of the patient’s respiratory symptoms that is beyond normal daily-to-day variations and leads to a change in medication. The rate at which exacerbations occur varies widely from one patient to another and the best predictor is a history of previous treated events. Hospitalisation for COPD exacerbation is associated with a poor prognosis and increased risk of death.

The quadrant model in the GOLD
guidelines uses spirometry, mMRC and CAT to characterise COPD severity and the risk of serious adverse health events in the future, as well as to guide treatment decisions (Figure 1).

When assessing risk, the highest risk according to the GOLD grade or exacerbation history should be selected. Adapted from GOLD, 2016.¹

### Table 1. Modified British Medical Research Council (mMRC) questionnaire²

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>I only get breathless with strenuous exercise.</td>
</tr>
<tr>
<td>1</td>
<td>I get short of breath when hurrying on the level or walking up a slight hill.</td>
</tr>
<tr>
<td>2</td>
<td>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.</td>
</tr>
<tr>
<td>3</td>
<td>I stop for breath after walking about 100 metres or after a few minutes on the level.</td>
</tr>
<tr>
<td>4</td>
<td>I am too breathless to leave the house or I am breathless when dressing or undressing.</td>
</tr>
</tbody>
</table>

### Table 2. Quadrant model of symptom/risk evaluation of COPD

<table>
<thead>
<tr>
<th>Patient category</th>
<th>Characteristics</th>
<th>Spirometric classification</th>
<th>Exacerbations per year</th>
<th>CAT</th>
<th>mMRC</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Low-risk, fewer symptoms</td>
<td>GOLD 1-2</td>
<td>≤1</td>
<td>&lt;10</td>
<td>0-1</td>
</tr>
<tr>
<td>B</td>
<td>Low-risk, more symptoms</td>
<td>GOLD 1-2</td>
<td>≤1</td>
<td>≥10</td>
<td>≥2</td>
</tr>
<tr>
<td>C</td>
<td>High-risk, fewer symptoms</td>
<td>GOLD 3-4</td>
<td>≥2</td>
<td>&lt;10</td>
<td>0-1</td>
</tr>
<tr>
<td>D</td>
<td>High-risk, more symptoms</td>
<td>GOLD 3-4</td>
<td>≥2</td>
<td>≥10</td>
<td>≥2</td>
</tr>
</tbody>
</table>

Figure 1. Quadrant model of symptom/risk evaluation of COPD.
Management

The general principles for the management of all COPD patients are summarised in Table 2.

Table 2. General Principles

<table>
<thead>
<tr>
<th>Principle</th>
</tr>
</thead>
<tbody>
<tr>
<td>• All patients who smoke should be encouraged to stop. Smoking cessation may be supported by counselling, social support, pharmacotherapy and nicotine replacement. Second-hand smoke should be avoided.</td>
</tr>
<tr>
<td>• Reduce or avoid indoor air pollution.</td>
</tr>
<tr>
<td>• All COPD patients benefit from regular physical activity and should be encouraged to remain active.</td>
</tr>
<tr>
<td>• Appropriate pharmacological therapy can reduce COPD symptoms, reduce the frequency and severity of exacerbations, and improve health status and exercise tolerance. However, none of the existing medications for COPD has conclusively been shown to modify the long-term decline in lung function.</td>
</tr>
<tr>
<td>• Inhaled therapy is preferred, but choice of treatment depends on the availability of medications and the individual patient’s response in terms of symptom relief and side effects.</td>
</tr>
<tr>
<td>• When inhaled medications are prescribed, training in inhaler technique is essential. The choice of inhaler device will depend on availability, cost, the prescribing physician and the skills and capabilities of the patient.</td>
</tr>
<tr>
<td>• Influenza and pneumococcal vaccination should be offered according to local guidelines.</td>
</tr>
</tbody>
</table>

Pharmacotherapy

The GOLD recommendations for initial pharmacotherapy, depending on COPD severity and risk of future events, are listed in Table 3. Considerations when switching or stepping up therapy include frequency of exacerbations, predominant problems with regular symptoms, exercise limitation and convenience to the patient.

Bronchodilators

Bronchodilator medications, including beta-2-agonists, anticholinergics and theophylline, alone or in combination, are the mainstay of COPD treatment. They improve emptying of the lungs, reduce dynamic hyperinflation at rest and during exercise and improve effort tolerance; they may be administered either as needed or on a regular basis to prevent or reduce symptoms. Long-acting inhaled bronchodilators are convenient and more effective for symptom relief than short-acting bronchodilators. Most patients will require regular treatment with a long-acting bronchodilator, whether it be a long-acting beta-2 agonist (LABA) or long-acting muscarinic antagonist (LAMA).

In stable disease, the dose-response relationship of bronchodilators is relatively flat, although in acute episodes higher doses, especially when administered by nebuliser, may provide some additional subjective benefit. In contrast, side effects and toxicity are dose related.

Regular use of a short-acting beta-2 agonist (SABA) improves both FEV₁ and symptoms, but the effects usually wear off within 4-6 hours and frequent repeated use increases the risk of adverse effects. LABAs are more convenient and significantly improve FEV₁ and lung volumes, reduce exacerbations and related hospitalisations, and improve symptoms (dyspnoea) and health-related quality of life.

Anticholinergic agents include ipratropium, oxitropium, tiotropium and glycopyrronium. The latter two drugs have a duration of action of more than 24 hours and in clinical studies tiotropium has been proven to reduce exacerbations and related hospitalisations, while improving symptoms and health status. Because they are poorly absorbed, inhaled anticholinergics are very safe and do not share the troublesome systemic effects of atropine.

Theophylline may have a modest bronchodilator effect in patients with stable COPD, but inhaled beta-2 agonists and anticholinergic medications are preferred when they are available.

Compared to increasing the dose of a single bronchodilator, combining bronchodilators with different mechanisms and durations of action may improve efficacy and decrease the risk of side effects.
Inhaled corticosteroids (ICSs) and combination ICS/bronchodilator therapy

ICSs are not recommended for all patients with COPD and are frequently inappropriately prescribed, alone or in combination with a bronchodilator.1-5 GOLD (2016) recommends ICSs only for patients classified in groups C and D.

In patients with FEV₁ <60% predicted, an ICS may improve symptoms, lung function and quality of life, while reducing the frequency of exacerbations. Care must be taken when discontinuing an ICS, with gradual tapering of the dose, because sudden withdrawal may lead to exacerbations. Regular ICS therapy does not modify the long-term decline in FEV₁ or mortality, and may be associated with an increased risk of pneumonia.6

For patients who are not controlled on monotherapy with either a LAMA or LABA, step-up to a combination of LAMA plus LABA is a rational and effective choice before considering an ICS and

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**Table 3. Initial pharmacologic management of COPD**

Medications in each box are mentioned in alphabetical order, and therefore not necessarily in order of preference.

<table>
<thead>
<tr>
<th>Patient group</th>
<th>Recommended first choice</th>
<th>Alternative choice</th>
<th>Other possible treatments*</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Short-acting anticholinergic pm or Short-acting beta-2 agonist pm</td>
<td>Long-acting anticholinergic or Long-acting beta-2 agonist or Short-acting beta-2 agonist and short-acting anticholinergic</td>
<td>Theophylline</td>
</tr>
<tr>
<td>B</td>
<td>Long-acting anticholinergic or Long-acting beta-2 agonist</td>
<td>Long-acting anticholinergic and long-acting beta-2 agonist</td>
<td>Short-acting beta-2 agonist and/or Short-acting anticholinergic</td>
</tr>
<tr>
<td>C</td>
<td>Inhaled corticosteroid + long-acting beta-2 agonist or Long-acting anticholinergic</td>
<td>Long-acting anticholinergic and long-acting beta-2 agonist or Long-acting anticholinergic and phosphodiesterase-4 inhibitor or Long-acting beta-2 agonist and phosphodiesterase-4 inhibitor</td>
<td>Short-acting beta-2 agonist and/or Short-acting anticholinergic</td>
</tr>
<tr>
<td>D</td>
<td>Inhaled corticosteroid + long-acting beta-2 agonist and/or Long-acting anticholinergic</td>
<td>Inhaled corticosteroid + long-acting beta-2 agonist and long-acting anticholinergic or Inhaled corticosteroid + long-acting beta-2 agonist and phosphodiesterase-4 inhibitor or Long-acting anticholinergic and long-acting beta-2 agonist or Long-acting anticholinergic and phosphodiesterase-4 inhibitor</td>
<td>Carbocysteine or N-acetylcysteine</td>
</tr>
</tbody>
</table>

*Medications in this column can be used alone or in combination with other options in the ‘recommended first choice’ and ‘alternative choice’ columns.
may be more effective in reducing exacerbations than a LABA/ICS combination. However, when exacerbations persist, a LABA/ICS combination is a consideration. In patients with moderate and severe COPD, combining a LABA with an ICS is more effective than the individual components in improving lung function and health status, as well as reducing exacerbations. Twice daily administration is no more effective than once daily.

**Phosphodiesterase-4 inhibitors**
Phosphodiesterase-4 inhibitors (PDE-4i) reduce inflammation by inhibiting breakdown of intracellular cyclic AMP. They have no intrinsic bronchodilator activity and should always be used in combination with at least one long-acting bronchodilator medication. Because of their different mode of action, PDE-4is complement ICSs and bronchodilators. In patients with severe COPD and a history of frequent exacerbations (at least two in the previous year) despite ICS, LABA and LAMA combination therapy, the PDE-4i roflumilast (500 mcg given orally once daily) was shown to improve lung function and reduce exacerbation frequency and hospital admissions. However, roflumilast was associated with more adverse effects than the inhaled medications, including unexplained weight loss. Consequently, weight should be monitored during treatment and roflumilast may not be appropriate for underweight patients.

**Systemic corticosteroids**
The adverse effects associated with long-term systemic corticosteroids are well known and, because of their unfavourable benefit-to-risk ratio, they should generally be avoided. However, a short course of oral corticosteroids for the treatment of an acute exacerbation may help to improve symptoms and lung function, shorten the length of hospital stay and reduce the rate of treatment failure.

**Additional management strategies**
Management strategies that support COPD pharmacotherapy include the following:
1. Antibiotics (indicated for management of acute bacterial exacerbations).
2. Pulmonary rehabilitation, exercise and nutritional support.
3. Oxygen therapy is helpful in patients with chronic respiratory failure and is indicated for patients who have (i) PaO₂ at or below 7.3kPa (55mmHg) or SaO₂ at or below 88%, with or without hypercapnia confirmed twice over a three-week period; or (ii) PaO₂ between 7.3kPa (55mmHg) and 8.0kPa (60mmHg), or SaO₂ of 88%, if there is evidence of pulmonary hypertension, peripheral oedema suggesting congestive cardiac failure, or polycythaemia (haematocrit >55%).
4. Lung volume reduction surgery, either through open resection or with bronchoscopy.

**Management approaches according to COPD phenotype**
COPD phenotype is defined as ‘a single disease attribute or combination of disease attributes that describe differences between individuals with COPD as they relate to clinically meaningful outcomes (symptoms, exacerbations, response to treatment, speed of progression of the disease or death)’. It is important to point out that the aim of this phenotypic classification is not to quantify the many different aetiopathogenic, clinical and morphological presentations of COPD per se, but rather to guide in determining a likely prognosis and deciding on the most appropriate therapy that will have a therapeutic impact (Table 4). In addition to the phenotypes listed in the table, others have been described (e.g. fast decliner, chronic bronchitis, current smoker), but they offer little additional practical guidance from a clinical point of view.

**Emphysema-hyperinflation phenotype**
In patients with COPD, dyspnoea, exercise capacity and hyperinflation predict mortality independently of lung function. The emphysema-hyperinflation phenotype describes patients who present with these symptoms predominating. They have a tendency towards a lower body mass index (BMI). Unless it is associated with chronic bronchitis, the presence of emphysema has not been associated with greater risk for exacerbations.
Bronchodilators (LABA plus LAMA) improve hyperinflation, dyspnoea and exercise capacity. In contrast, anti-inflammatory therapy with an ICS or PDE-4i, the main objective of which is to reduce exacerbations, is not effective in this phenotype.

**Exacerbator phenotype**

Some patients with COPD suffer repeated exacerbations, whereas others do not experience any. Frequent exacerbations may be associated with a more rapid decline in lung function, increased dyspnoea, reduced exercise capacity and greater decline in health status. These patients are at high risk of morbidity and mortality, and up to 40% of those requiring hospitalisation may die within the subsequent 12 months. Although exacerbations may occur with any severity of COPD, they become more common as the disease progresses. Causes are multifactorial. Viral infection and levels of air pollution may exacerbate existing airway inflammation, predisposing to secondary bacterial infection. The presence of a chronic cough and cough expectoration is associated with a greater risk of repeated exacerbations. Comorbid conditions, such as cardiovascular disease, hypertension and diabetes may increase the risk of exacerbation-associated hospital admissions and mortality.

The two most important strategies to reduce the frequency of exacerbations are active immunisation, including pneumococcal and influenza vaccines, and chronic maintenance pharmacotherapy. LABAs, LAMAs and combination therapy with ICSs reduce the mean rate of COPD exacerbation and reduce hospitalisation and healthcare utilisation. The addition of the PDE-4i, roflumilast, may further reduce the exacerbation rate in patients with severe COPD who experience frequent exacerbations.9,11-13 Prophylactic use of macrolide antibiotics over an extended period may be helpful in a carefully selected subgroup of patients with COPD and frequent exacerbations, despite optimisation of COPD management. In addition to their antimicrobial activity, macrolides have anti-inflammatory and immunomodulatory properties, which may be associated with a reduction in duration of individual exacerbations, extended periods between exacerbations, reduced number of hospitalisations and improved quality of life.14-17

**Mixed asthma-COPD (ACOS): Does it exist and does it matter?**

Risk factors and pathophysiological changes in the airways overlap in asthma and COPD and many patients share clinical characteristics of both diseases, which makes classifying them as asthmatic or having COPD difficult in everyday clinical practice. Within the spectrum of chronic airway obstruction there are asthmatics who smoke and who do not respond as well to ICSs as non-smokers, asthmatics who have airway obstruction that is not fully reversible, symptoms or signs of increased reversibility.

**Table 4. Common clinical phenotypes of COPD**1,11,12

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Characteristics</th>
<th>Treatment considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emphysema-hyperinflation</td>
<td>Predominating symptoms are dyspnoea, exercise intolerance, frequently accompanied by signs of hyperinflation. Presence of emphysema: tendency towards lower body mass index, not associated with exacerbation risk.</td>
<td>• Combination bronchodilator therapy (LABA/LAMA) • Respiratory rehabilitation • ICSs not effective</td>
</tr>
<tr>
<td>Exacerbator</td>
<td>≥2 exacerbations per year separated by ≥2 weeks after end of treatment of previous exacerbation or ≥6 weeks after start if no treatment has been received. Implies worse prognosis, with high risk for morbidity and mortality.</td>
<td>Potential treatment includes: • Long-acting bronchodilator • Anti-inflammatories (e.g., ICS, PDE-4 inhibitor) • Antibiotics (e.g. macrolides)</td>
</tr>
<tr>
<td>Mixed asthma-COPD (ACOS)</td>
<td>Airflow obstruction that is not completely reversible, symptoms or signs of increased reversibility. History of asthma and/or atopy, reversibility in the bronchodilator test, eosinophilia, high IgE, positive prick test to pneumoallergens.</td>
<td>• ICS • Long-acting bronchodilators</td>
</tr>
</tbody>
</table>
completely reversible or who progress to develop a COPD-like syndrome, non-smokers who develop chronic airflow obstruction and patients with COPD who have increased reversibility. This has led to the characterisation of an asthma-COPD overlap syndrome (ACOS). The exact prevalence of this subgroup is unknown, but it may be as high as 20-40% among patients with COPD. Notably, this patient group has generally been excluded from clinical studies, because asthma studies often exclude smokers and COPD studies exclude those with a history of asthma.\(^1\)\(^{11,18-20}\)

The clinical importance of this group is that they respond to early introduction of an ICS (in addition to a long-acting bronchodilator) with improved lung function and improvement of symptoms. In clinical practice patients characterised as having ACOS may have more severe disease, with increased exacerbations and hospitalisations relative to some asthma and COPD patients.\(^1\)\(^9\)

Patients with overlapping symptoms are a very heterogeneous group and the diagnosis can be confusing. Although young asthmatics who smoke and develop airflow obstruction that is incompletely reversible differ significantly from patients with COPD who have no history of asthma (Table 5), the lack of specific biomarkers makes a diagnosis of ACOS difficult, especially in an older individual where a previous history of asthma is uncertain or not known. Furthermore, bronchial hyperresponsiveness, a hallmark of asthma, is common in patients with COPD and is demonstrable in up to two-thirds of them.\(^1\)\(^2\)\(^{18,19}\)

Nevertheless, asthma and COPD differ markedly in respect of overall approach to management, prognosis and expectations from treatment, and the importance of making a correct diagnosis of either asthma or COPD (with or without features of asthma) cannot be over-emphasised (Table 6). Rather than defining a patient with ACOS, a more appropriate clinical approach is to describe a patient with COPD as completely as possible, with regard to characteristics that determine treatment response (e.g. eosinophilic inflammation) and prognosis (such as smoking status, exacerbation rate, fixed airflow limitation, hyperresponsiveness, comorbidities).\(^2\)\(^1\)

In general, in patients with COPD the neutrophil-predominant inflammatory response responds poorly to ICSs and long-term use of an ICS at high doses is associated with increased risk of adverse effects. Therefore it is important to attempt to identify the subgroup of patients where eosinophilic inflammation predominates and where an ICS may be effective.\(^1\)\(^2\)

**Table 5. Characteristics of patients with asthma (>40 years of age) who smoke and develop not fully reversible airflow obstruction\(^1\)\(^2\)\(^{18,19}\)**

- More likely to have a history of allergic rhinitis
- Bronchial hyperresponsiveness and presence of wheezing
- Higher plasma concentrations of IgE
- Dyspnoea
- Chronic cough and chronic sputum production

**Table 6. Why it is important to differentiate COPD from asthma\(^1\)**

- The natural history differs
- The package of care is different
- COPD requires bronchodilators as mainstay of therapy, including LAMAs
- ICSs may not be effective in COPD and, where indicated, should never be used as monotherapy
- All patients with asthma should be treated with an ICS (with or without a LABA), but monotherapy with long-acting bronchodilators is contraindicated
- Smoking cessation is important in both asthma and COPD, and may improve response to therapy in asthma
- Expectations and outcomes of therapy are different
- COPD exacerbations need to be recognised and managed appropriately
- Pulmonary rehabilitation and O\(_2\) are important management strategies in COPD
The GOLD COPD management guideline recommends a detailed stepwise approach to differentiate between asthma and subgroups of COPD. This includes a careful history (age of onset, pattern of symptoms, past and family histories), chest x-ray and spirometry, and early referral for confirmatory investigations and management, because of the worse outcomes among patients with overlapping symptoms (Table 7).^{1}

The hallmark of COPD is airflow limitation that cannot reverse to normality. Patients who have COPD with features of asthma should be started on treatment appropriate for asthma, including an ICS and LABA, but not bronchodilators alone. Conversely, those without asthma symptoms should not receive ICS monotherapy. All patients should receive advice about other therapeutic strategies for COPD, including smoking cessation, pulmonary rehabilitation, vaccinations and treatment of comorbidities.

### Table 7. Features suggestive of asthma, COPD and overlap^{1}

<table>
<thead>
<tr>
<th></th>
<th>Asthma</th>
<th>COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age of onset</strong></td>
<td>Before age 20 years</td>
<td>After age 40 years</td>
</tr>
<tr>
<td><strong>Pattern of symptoms</strong></td>
<td>• Variable over minutes, hours or days</td>
<td>• Persistent despite treatment</td>
</tr>
<tr>
<td></td>
<td>• Worse at night or early morning</td>
<td>• Always daily symptoms with exertional dyspnoea</td>
</tr>
<tr>
<td></td>
<td>• Triggers</td>
<td>• Chronic cough and sputum</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Unrelated to triggers</td>
</tr>
<tr>
<td><strong>Past history, family history</strong></td>
<td>Asthma &amp; other allergic conditions (allergic rhinitis, eczema)</td>
<td>Personal history of COPD diagnosis, exposure to tobacco smoke, biomass fuels</td>
</tr>
<tr>
<td><strong>Time course</strong></td>
<td>Variable, with spontaneous improvement, no worsening or progressive worsening over years</td>
<td>Progressively worsens over years</td>
</tr>
<tr>
<td><strong>Response to medication</strong></td>
<td>Immediate to bronchodilators, progressive improvement with ICS</td>
<td>Limited relief with bronchodilators</td>
</tr>
<tr>
<td><strong>Chest x-ray</strong></td>
<td>Normal</td>
<td>Severe hyperinflation</td>
</tr>
<tr>
<td><strong>Spirometry</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal FEV₁/FVC pre- or post BD</td>
<td>Compatible</td>
<td>Not compatible</td>
</tr>
<tr>
<td>Post BD FEV₁/FVC &lt;0.7</td>
<td>Indicates airflow limitation, but may improve spontaneously or on treatment</td>
<td>Required for diagnosis</td>
</tr>
<tr>
<td>FEV₁</td>
<td>May be ≥80% or &lt; 80% predicted</td>
<td>If post BD FEV₁/FVC is &lt;0.7, FEV₁ ≥80% predicted is compatible with GOLD categories A and B; FEV₁ &lt;80% predicted is an indicator of severe airflow limitation and risk of mortality and exacerbations</td>
</tr>
<tr>
<td>Post-BD increase in FEV₁ &gt;12% and 200 ml from baseline (reversible airflow limitation)</td>
<td>Usual at some times, but may not be present if well controlled or on ICS</td>
<td>Common</td>
</tr>
<tr>
<td>Post-BD increase in FEV₁ &gt;12% and 400 ml from baseline (marked reversibility)</td>
<td>High probability of asthma</td>
<td>Unusual</td>
</tr>
</tbody>
</table>

BD: bronchodilator; FEV₁: forced expiratory volume in 1 second; FVC: forced vital capacity; GOLD: Global Initiative for Obstructive Lung Disease; ICS: inhaled corticosteroid
Conclusion

COPD is a common incurable, progressive disease that carries significant morbidity and mortality. Although its heterogeneous nature can complicate diagnosis, its primary characteristic is airflow limitation that cannot be reversed to normality. Systematic history taking and careful investigation help to guide a treatment programme specific to the individual that will improve symptoms, reduce the risk of exacerbations and hospitalisations, and improve quality of life.

References