COPD, a common preventable and treatable disease, is characterized 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. COPD is a preventable and treatable disease. It has two components:

- its **pulmonary** component is characterised by airflow limitation that is not fully reversible
- FEV₁/FVC ratio <70%, post-bronchodilator (measured via spirometry)
- its **extrapulmonary** effects (weight loss, nutritional abnormalities, skeletal muscle dysfunction, and increased risk for myocardial infarction, osteoporosis, etc.) contribute to the severity in individual patients.

**Epidemiology**
An estimated 210 million people have COPD worldwide. Ireland has an estimated 110,000 COPD patients (Murtagh et al, 2005). The worldwide prevalence of COPD is >10%. More than 3 million people died of COPD in 2005, accounting for 5% of all deaths globally that year. Worldwide COPD ranked as the 4th leading cause of death and is expected to become the 3rd leading cause by 2030. Total deaths from COPD are projected to increase by >30% in the next 10 years without interventions to cut risks, particularly exposure to tobacco smoke.

There is an increasing prevalence of COPD in women (MMWR, 2008) with an increased risk of COPD in the economically deprived (Prescott et al, 1999) as socioeconomic status is inversely related to risk of COPD.

In relation to other diseases, COPD is the 4th leading cause of morbidity and mortality, the leading cause of disability and the 6th in prevalence of major conditions (Table 1) (GOLD, 2013)

**Risk factors**
The risk factors for COPD include:

- Exposure to particles such as tobacco smoke, occupational dusts, organic and inorganic, indoor air pollution from heating and cooking with biomass in poorly ventilated dwellings and outdoor air pollution
- Lung growth and development
- Gender – males are more susceptible than females
- Age – risk increases with age
- Respiratory infections
- Socioeconomic status
- Asthma/bronchial hyper-reactivity
- Chronic bronchitis

**Pathophysiology of COPD**
COPD is characterised by airflow limitation, air trapping and decreased exercise tolerance. Frequently, by the time the patient presents with symptoms, many have progressed to moderate COPD. Many patients who have mild COPD on their spirometry will not have symptoms. When airflow is limited, air gets trapped in the lungs which is first recognised by the patient on exercising. Air trapping impacts on the patient by effecting their ability to inhale. It also affects their exercise tolerance and causes patients to limit their activities.

![Graph showing prevalence of COPD in relation to other major conditions](image-url)

Table 1: Prevalence of COPD in relation to other major conditions
The diagnosis and assessment of COPD involves assessing symptoms, airflow limitation, risk of exacerbations and co-morbidities.

Assessing symptoms
The characteristic symptoms of COPD are chronic and progressive dyspnoea, cough, and sputum production that can be variable from day-to-day. Dyspnoea is usually progressive, persistent and characteristically worse with exercise. Patients may have an intermittent and/or unproductive cough but many patients will commonly cough up white/clear non-purulent sputum. Symptoms can be assessed using the COPD Assessment Tool (CAT test) and the Medical Research Council Dyspnoea (MRC) scale. The CAT test is an 8-item measure of health status impairment in COPD (http://catestonline.org). The MRC scale is illustrated in Table 2.

Assessing airflow limitation
Airflow limitation is assessed by spirometry. An FEV₁/FVC ratio post bronchodilator of less than 70% indicates airflow limitation. The severity of airflow limitation is then assessed by the FEV₁. (Table 3). The bronchodilator of choice used for reversibility testing is Salbutamol 200mcg – 400mcg via spacer device with the spirometry repeated 15 minutes post administration.

Assessing risk of exacerbations
If the patient has had two exacerbations or more within the last year or an FEV₁ <50 % of predicted value, they are considered high risk for exacerbations in the future.

Assessing co-morbidities
Patients with are at increased risk for:
- Cardiovascular diseases
- Osteoporosis
- Respiratory infections
- Anxiety and depression
- Diabetes
- Lung cancer

These co-morbid conditions may influence mortality and hospitalizations and should be looked for routinely, and treated appropriately (GOLD, 2014).

Combining assessments and classification of COPD
GOLD (2014) recommend combining the assessments from airflow limitation, risk of exacerbations and symptoms (Table 4) to classify patients as A, B, C, or D (Table 5). This classification assists
Abbreviated Prescribing Information. Please consult the Summary of Product Characteristics (SPC) for the full prescribing information. Presentation: Inhalation powder in a white inhaler with an integral dose indicator and a green dosage button. Each delivered dose contains 375 µg aclidinium bromide equivalent to 322 µg of aclidinium. Also, contains lactose. Use: Maintenance bronchodilator treatment to relieve symptoms in adult patients with chronic obstructive pulmonary disease (COPD). Dosage: For inhalation use. Recommended dose is one inhalation of 322 µg aclidinium twice daily. Patients should be instructed on how to administer the product correctly. No dose adjustments are required for elderly patients, or those with renal or hepatic impairment. No relevant use in children and adolescents. Contraindications: Hypersensitivity to aclidinium bromide, atropine or its derivatives, including ipratropium, oxitropium or tiotropium, or to any of the excipients. Warnings and Precautions: Do not use in asthma. Stop use if paradoxical bronchospasm occurs and consider other treatments. Do not use for the relief of acute episodes of bronchospasm. Use with caution in patients with symptomatic prostatic hyperplasia or bladder-neck obstruction or with narrow-angle glaucoma. Do not use in patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption. Interactions: Do not administer with other anticholinergic-containing medicinal products. No other interactions expected. Fertility, pregnancy and lactation: No data on use in pregnancy. Consider risk-benefit before using during lactation. Unlikely to affect fertility at the recommended dose. Side-effects: Common (1-10%): Sinusitis, nasopharyngitis, headache, cough, diarrhoea. Uncommon (0.1-1%): Blurred vision, tachycardia, dysphonia, dry mouth, rash, pruritus, urinary retention. Rare (0.01-0.1%): Hypersensitivity. Not known: Angioedema. Pack sizes: Carton containing 1 inhaler with 60 unit doses. Marketing Authorisation Number: EU/1/12/778/002. Marketing Authorisation holder: Almirall, S.A., Ronda General Mitre 151, ES-08022, Barcelona, Spain. Marketed by: A. Menarini Pharmaceuticals Ireland Ltd., Castlecourt, Monkstown Farm, Monkstown, Co. Dublin. Further information is available on request to A. Menarini Pharmaceuticals Ireland Ltd. or may be found in the SPC. Last updated: May 2014.
There is an increasing prevalence of COPD in women with an increased risk of COPD in the economically deprived as socioeconomic status is inversely related to risk of COPD.

Table 4: Combined assessment of COPD (GOLD, 2014)

<table>
<thead>
<tr>
<th>Symptoms (mMRC or CAT score)</th>
<th>Risk</th>
<th>Exacerbation history</th>
</tr>
</thead>
<tbody>
<tr>
<td>mMRC 0-1 CAT &lt;10</td>
<td>≥2</td>
<td></td>
</tr>
<tr>
<td>mMRC ≥2 CAT ≥10</td>
<td>1-2</td>
<td>≥2 ≥10</td>
</tr>
</tbody>
</table>

Exercise Testing: Objectively measured exercise impairment, assessed by a reduction in self-paced walking distance (such as the 6 min walking test) or during incremental exercise testing in a laboratory, is a powerful indicator of health status impairment and predictor of prognosis.

Differential diagnosis
Asthma is the primary differential diagnosis (Table 4). Other differential diagnoses include congestive cardiac failure, lung cancer, TB, alpha one antitrypsin deficiency and cor pulmonale.

### Table 5: Classification of COPD (GOLD, 2014)

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

Other investigations

**Chest X-ray:** Seldom diagnostic but valuable to exclude alternative diagnoses such as malignancy and establish the presence of significant co-morbidities such as heart failure.

**Lung Volumes and Diffusing Capacity:** Help to characterize severity, but not essential to patient management. These test are carried out in pulmonary function laboratories.

**Oximetry and Arterial Blood Gases:** Pulse oximetry can be used to evaluate a patient’s oxygen saturation and need for supplemental oxygen therapy.

**Alpha-1 Antitrypsin Deficiency Screening:** Should be performed when COPD develops in patients of Caucasian descent under 45 years or with a strong family history of COPD.

the healthcare professional with treatment options and it ensures that patients are prescribed the most appropriate medication for the degree of severity of their COPD.
Asthma maintenance treatment

**Modern aerosol device with a patient-facing dose counter**

flutiform® (FLUTICASONE PROPIONATE AND FORMOTEROL FUMARATE) PRESSURISED INHALATION SUSPENSION.

**Prescribing Information.** Please read the Summary of Product Characteristics before prescribing.

**Presentation:** Pressurised inhalation suspension, in a pressurised metered dose inhaler (MDI), containing fluticasone propionate and formoterol fumarate dihydrate at strengths of 50/2.5 µg, 125/5 µg and 250/10 µg per actuation.

**Indications:** Regular treatment of asthma where the use of a combination product (inhaled corticosteroid and long-acting ß2-agonist) is appropriate; for patients not adequately controlled on ICS alone.

**Dosage and administration:** For inhalation use. The patient should be shown how to use the inhaler correctly by a physician or other healthcare professional. Patients should be provided with a spacer device as required, with the exception of the 250 µg/10 µg combination product.

**Use of a spacer device may also cause an increased systemic exposure. Increased exposure can be expected in patients with severe hepatic impairment.**

**Flutiform** contains a small amount of ethanol; however this negligible amount does not pose a risk to patients.

**Adverse events:** Adverse events should be reported. Reporting forms and information can be found at http://www.imb.ie/EN/Safety--Quality/Online-Forms/Human-Medicine-Adverse-Drug-Reaction.aspx. Adverse events should also be reported to Mundipharma Pharmaceuticals Limited on 01 206 3800/1800 991830 or via your local Mundipharma office.

**Combinations:** Flutiform should be discontinued immediately if there is evidence of paradoxical bronchospasm. Systemic effects with an ICS may occur particularly at high doses for prolonged periods or when combined with potent CYP3A4 inhibitors.

**Side-effects:** Potentially serious side-effects: hyperglycaemia; depression; aggression; behavioural changes (predominantly in children); paradoxical bronchospasm; agitation; vertigo; palpitations; ventricular extrasystoles; angina pectoris; tachycardia; hypertension; dyspnoea; peripheral oedema; immediate allergic reactions, including angioedema and anaphylaxis; retinal haemorrhage; visual disturbances; death.

**Contraindications:** Flutiform should be discontinued immediately if there is evidence of paradoxical bronchospasm. Systemic effects with an ICS may occur particularly at high doses for prolonged periods or when combined with potent CYP3A4 inhibitors. Patients should be reviewed as soon as possible if there is any indication of deteriorating asthma control. The use of inhaled corticosteroids may be associated with an increased risk of dental candidiasis. If candidiasis occurs, use of an antifungal agent may be required.

**Long-term use of an ICS in asthma:**

- **Potentially serious side-effects:** hyperglycaemia; depression; aggression; behavioural changes (predominantly in children); paradoxical bronchospasm; agitation; vertigo; palpitations; ventricular extrasystoles; angina pectoris; tachycardia; hypertension; dyspnoea; peripheral oedema; immediate allergic reactions, including angioedema and anaphylaxis; retinal haemorrhage; visual disturbances; death.

- **Contraindications:** Flutiform should be discontinued immediately if there is evidence of paradoxical bronchospasm. Systemic effects with an ICS may occur particularly at high doses for prolonged periods or when combined with potent CYP3A4 inhibitors.

- **Side-effects:** Potentially serious side-effects: hyperglycaemia; depression; aggression; behavioural changes (predominantly in children); paradoxical bronchospasm; agitation; vertigo; palpitations; ventricular extrasystoles; angina pectoris; tachycardia; hypertension; dyspnoea; peripheral oedema; immediate allergic reactions, including angioedema and anaphylaxis; retinal haemorrhage; visual disturbances; death.

**Monitoring of serum potassium levels is recommended during these circumstances.**
Management

Key Points for therapeutic options for COPD (GOLD, 2013)

Smoking cessation has the greatest capacity to influence the natural history of COPD. Healthcare providers should encourage all patients who smoke to quit.

Pharmacotherapy and nicotine replacement reliably increase long-term smoking abstinence rates.

All COPD patients benefit from regular physical activity and should repeatedly be encouraged to remain active.

Appropriate pharmacologic therapy can reduce COPD symptoms, reduce the frequency and severity of exacerbations, and improve health status and exercise tolerance.

None of the existing medications for COPD has been shown conclusively to modify the long-term decline in lung function.

Influenza and pneumococcal vaccination should be offered depending on local guidelines.

Counseling delivered by physicians and other health professionals significantly increases quit rates over self-initiated strategies. Even a brief (3-minute) period of counseling to urge a smoker to quit results in smoking quit rates of 5-10%.

Nicotine replacement therapy (nicotine gum, inhaler, nasal spray, transdermal patch, sublingual tablet, or lozenge) as well as pharmacotherapy with varenicline, bupropion, and nortriptyline reliably increases long-term smoking abstinence rates and are significantly more effective than placebo.

Non-pharmacological therapeutic management of COPD

1. Smoking cessation

Smoking cessation is of paramount importance in the management of COPD regardless of disease severity. Support given by health professionals significantly increases quit rates over self-initiated strategies. Even a brief (3-minute) period of counseling to urge a smoker to quit results in smoking quit rates of 5-10%.

Dyspnoea is usually progressive, persistent and characteristically worse with exercise.

Table 6: COPD vs Asthma

Key Points for diagnosis & assessment of COPD (GOLD, 2013)

- A clinical diagnosis of COPD should be considered in any patient who has dyspnea, chronic cough or sputum production, and a history of exposure to risk factors for the disease.
- Spirometry is required to make the diagnosis; the presence of a post-bronchodilator FEV1/FVC < 0.70 confirms the presence of persistent airflow limitation and thus of COPD.
- The goals of COPD assessment are to determine the severity of the disease, including the severity of airflow limitation, the impact on the patient’s health status, and the risk of future events.
- Comorbidities occur frequently in COPD patients, and should be actively looked for and treated appropriately if present.

Table 7: Pharmacological therapeutic options for stable COPD (GOLD, 2014)

<table>
<thead>
<tr>
<th>Patient</th>
<th>Recommended First choice</th>
<th>Alternative choice</th>
<th>Other Possible Treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>SAMA prn or SABA prn</td>
<td>LAMA or LABA or SABA and SAMA</td>
<td>Theophylline</td>
</tr>
<tr>
<td>B</td>
<td>LAMA or LABA</td>
<td>LAMA and LABA</td>
<td>SABA and/or SAMA and LABA</td>
</tr>
<tr>
<td>C</td>
<td>ICS + LABA or LAMA</td>
<td>LAMA and LABA or PDE4-inh. or LABA and PDE4-inh.</td>
<td>SABA and/or SAMA and PDE4-inh.</td>
</tr>
<tr>
<td>D</td>
<td>ICS + LABA and/or LAMA</td>
<td>ICS + LABA and PDE4-inh.</td>
<td>Carbocysteine SABA and/or SAMA</td>
</tr>
</tbody>
</table>

GOLD, GOLD; prn, as needed; Theophylline; SABA, short-acting bronchodilator; LABA, long-acting bronchodilator; SAMA, short-acting muscarinic antagonist; ICS, inhaled corticosteroid; PDE4-inh, PDE4 inhibitor.
**HOW MUCH IS TOO MUCH?**

- **43%** of mature* drinkers consume alcohol two or more times a week\(^1\)
- During any single drinking occasion **51%** of female and **30%** of male mature* drinkers consumed at a high risk level\(^1\)

Why not discuss drinking habits with your patients today?

---

### Daily risk levels of drinking\(^2\)

<table>
<thead>
<tr>
<th></th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very High Risk</td>
<td>Over 6 standard drinks</td>
<td>Over 10 standard drinks</td>
</tr>
<tr>
<td>High Risk</td>
<td>4-6 standard drinks</td>
<td>6-10 standard drinks</td>
</tr>
</tbody>
</table>

\(^*\) Aged 30+. 10g alcohol = 1 standard drink. Irish standard drink approximations are one ½ pint of beer; one small glass of wine (12.5% volume); or one pub measure of spirits (35.5 ml). One bottle of wine contains 8 standard drinks.\(^*\)

**References:**
Table 8: Bronchodilator and anti-muscarinic [cholinergic] inhaler options

<table>
<thead>
<tr>
<th>DRUG NAME</th>
<th>FORMULATION</th>
<th>DOSE FREQUENCY</th>
<th>SIDE EFFECTS</th>
<th>AVAILABILITY AS COMBINATION THERAPY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salbutamol (SABA) Ventolin</td>
<td>Syrup, injection</td>
<td>Up to 4 times per day</td>
<td>Tachycardia, skeletal muscle tremor, headache and irritability. At very high doses, hyperglycaemia, hypokalemia.</td>
<td>Yes – with Ipratropium bromide (Combivent) (available only as UDU's)</td>
</tr>
<tr>
<td>Gerivent Novolizer Salbutamol Salamol Salbul</td>
<td>Nebule, infusion/injection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Terbutaline (SABA) Bricanyl</td>
<td>Inhaler, injection</td>
<td>Up to 4 times per day</td>
<td></td>
<td>No</td>
</tr>
<tr>
<td>Salmeterol (LABA) Serevent</td>
<td>Inhaler</td>
<td>Twice daily</td>
<td></td>
<td>Yes – with Fluticasone (Seretide)</td>
</tr>
<tr>
<td>Formoterol (LABA) Oxis</td>
<td>Inhaler</td>
<td>Twice daily</td>
<td>Yes – with Fluticasone (Flutiform) and with Budesonide (Symbicort)</td>
<td></td>
</tr>
<tr>
<td>Indacaterol (LABA) Onbrez</td>
<td>Inhaler</td>
<td>Once daily</td>
<td>Yes – combined with Glycopyrronium (Ultibro)</td>
<td></td>
</tr>
<tr>
<td>Ipratropium bromide Atrovent</td>
<td>Inhaler, nebulne</td>
<td>Up to four times per day</td>
<td>Mouth dryness, bad taste in mouth</td>
<td>Yes – with Salbutamol (Combivent) (available only as UDU's)</td>
</tr>
<tr>
<td>Tiotropium bromide Spiriva Olodasterol Striverdi</td>
<td>Inhaler</td>
<td>Once daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glycopyrronium Seebri</td>
<td>Inhaler</td>
<td>Once daily</td>
<td>Yes – combined with Indacaterol (Ultibro)</td>
<td></td>
</tr>
<tr>
<td>Aclidinium bromide (EkliraGenuair)</td>
<td>Inhaler</td>
<td>Twice daily</td>
<td>Headache, cough, sinusitis, nasopharyngitis,</td>
<td>No</td>
</tr>
</tbody>
</table>

Table 9: Combined therapeutic options

<table>
<thead>
<tr>
<th>DRUG NAME</th>
<th>FORMULATION</th>
<th>DOSE FREQUENCY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluticasone and Salmeterol (Seretide)</td>
<td>Inhaler</td>
<td>Twice daily</td>
</tr>
<tr>
<td>Budesonide and Formoterol (Symbicort)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Budesonide and Formoterol (Bufomix)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluticasone and Formoterol (Flutiform)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vilanterol and Fluticasone furoate (Relvar)</td>
<td>Inhaler</td>
<td>Once daily</td>
</tr>
</tbody>
</table>

Table 10: Xanthine preparations

<table>
<thead>
<tr>
<th>DRUG NAME</th>
<th>METHOD OF ADMINISTRATION</th>
<th>DOSE FREQUENCY</th>
<th>SIDE EFFECTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Theophylline Uniphyllin</td>
<td>Oral</td>
<td>Twice daily</td>
<td>GI upset, arrhythmias, tremors, transient increased urination</td>
</tr>
<tr>
<td>Aminophylline Phyllocontin</td>
<td>Oral</td>
<td>Twice daily</td>
<td>Nausea, gastric irritation, CNS stimulation, headache</td>
</tr>
</tbody>
</table>

muscarinic agents (LAMAs), short-acting bronchodilator (SABAs) and short-acting muscarinic agents (SAMAs). Other bronchodilator treatments include theophyllines which require regular patient monitoring as these agents interact with other commonly used drugs. Tables 7, 8 and 9 illustrate the inhaled treatment options for patients with COPD.

The use of inhaled corticosteroids in patients with COPD has been debated at length in recent years and should be reserved for patients who experience more than 2 exacerbations per year as combined therapy is associated with an increased risk of pneumonia (GOLD, 2014).

Phosphodiesterases 4 (PDE4s) are the ‘new kids on the block’ in COPD and are yet to become available in Ireland. Cilomilast and Rofamilast are currently in development. PDE4 is expressed in airway smooth muscle and in vitro, PDE4 inhibitors relax lung smooth muscle. They also address the inflammatory process associated
Managing co-morbidities
Many patients with COPD will have other co-morbidities. The presence of co-morbidities should not alter COPD treatment and co-morbidities should be managed as if the patient does not have COPD. Co-morbidities include ischaemic heart disease, atrial fibrillation, heart failure, hypertension, osteoporosis, anxiety, depression, lung cancer, metabolic syndrome and diabetes mellitus. Many patients will have more than one co-morbidity and consideration should be given to length of appointment when reviewing these patients.

Conclusion
COPD is a complex multiple system condition whereby patients can experience severe limitations to their quality of life. Patients require a skilled practice nurse to assist them in optimising their full potential. Education, empowerment and self-management are key to the success of preventing exacerbations and avoiding hospital admission. Practice nurses are well placed to provide these supports to patients by ensuring optimal inhaler technique, educating the patient in recognition of acute exacerbations and management of these and assisting with smoking cessation. With the development in recent times of a number of new therapies, people with COPD now have much more therapeutic options available to them and health professionals have much more to offer.

References