Chronic Obstructive Pulmonary Disease

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Chapter Objectives

1. Describe the epidemiology, pathophysiology and management of chronic obstructive pulmonary disease (COPD).
2. Assess patients with COPD.
3. Identify the red flags in patients presenting with COPD that prompt referral to healthcare practitioners or the emergency department.

Background

Chronic obstructive pulmonary disease (COPD) is "a *treatable* and *preventable* disease characterized by *progressive airflow limitation* (obstruction) that is *not fully reversible* and is associated with an *abnormal inflammatory response* of the lungs to noxious particles or gas" [1]. Pharmacists play an important role in identifying patients that are at risk for COPD, referring for diagnosis and managing drug therapy. Pharmacists assess drug effectiveness and safety but also assess for adherence and proper use of inhalers, which are a mainstay of COPD pharmacotherapy. In collaboration with other healthcare professionals, pharmacists can improve quality of life for patients with this progressive disease and ensure each COPD patient has an action plan and knows what to do in case of an exacerbation.

Epidemiology

COPD is the fourth leading cause of death in Canada [2]. COPD is generally underdiagnosed in Canada. To illustrate, while about 4% of Canadians between 35 and 79 years of age self-report a COPD diagnosis [2], the prevalence of COPD among randomly sampled residents in Vancouver aged 40 or older has been estimated to be 19% (BOLD study) [3]. Additionally, the Canadian Health Measures Survey conducted between March 2007 and February 2008 found that 17% of Canadians aged 35–79 had airflow obstruction compatible with COPD [3]. Conversely, concern surrounds the overdiagnosis of COPD in patients as well, as 60–70% of Canadians between 35 and 79 who reported being diagnosed with COPD did not meet the diagnostic spirometry criteria [3]. Given the potential for over and underdiagnosis of this condition, it is important for pharmacists to be on alert to help identify and refer patients for timely and appropriate diagnosis.

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Risk Factors and Pathophysiology

As COPD is a treatable and preventable disease, early identification of at-risk patients and addressing underlying causes and risk factors to limit disease progression are important roles of the pharmacist. Risk factors for COPD can be *environmental* or *intrinsic*. Environmental factors include cigarette smoking (most common), occupational exposure (e.g., dust, chemicals), and air pollution. Intrinsic host factors include alpha-1-antitrypsin (AAT) deficiency, a rare inherited disorder of airway hyper-responsiveness and impaired lung growth [1].

Inhalation of noxious particles and gas results in an abnormal inflammatory response leading to destructive changes in the airways. The culprit noxious substance in 85–95% of COPD cases is cigarette smoke. It causes inflammation and subsequent cell damage through a number of different mechanisms that are distinct from those seen in asthma. In COPD, neutrophils, macrophages, and CD8 lymphocytes are activated, releasing a variety of inflammatory mediators. This results in lung damage and ciliary destruction, impairing ciliary motility and the ability to expel mucus. Additionally, goblet cell production is stimulated, leading to an increase in mucus production. The result is a vicious cycle of chronic inflammation and mucus production. Small airways (respiratory bronchioles) may become clogged with mucus or distorted by fibrosis. Furthermore, inflammatory cells release proteases that dissolve proteins in the alveolar walls, thereby causing loss of alveolar attachments and loss of elastic recoil. This results in diffuse airway narrowing, plugging with mucus, loss of elastic recoil, air trapping, and lung hyperinflation. Over time, as the disease progresses, there will be inequalities of ventilation/perfusion, destruction of vascular beds, hypoxemia, and carbon dioxide retention [1].

COPD has previously been sub-categorized into "chronic bronchitis" and "emphysema." Cough, chronic inflammation, loss of cilia, and mucus production are associated with chronic bronchitis. Destruction of alveoli and loss of elastic recoil are associated with emphysema. It is now recognized that most patients with COPD have elements of both. An example of an exception is AAT deficiency, which is typically emphysematous [1]. COPD patients typically present with a chronic cough, sputum production, and shortness of breath that progresses and persists over time. Spirometry, which measures airflow limitation, is required for diagnosis [1]. Not all patients with chronic cough have COPD. When assessing a patient with chronic cough, there are other conditions that should be ruled out. These include asthma, lung cancer, tuberculosis, left heart failure, interstitial lung disease, cystic fibrosis, idiopathic cough, chronic allergies, postnasal drip syndrome, upper airway cough syndrome, gastroesophageal reflux, and medication-induced cough [4].

Initial Assessment of a Patient with Chronic Cough

PK is a 52-year-old female patient presenting to your pharmacy or clinic requesting something for her chronic cough. What initial assessments might contribute to the diagnosis of COPD?

Screening

Screening for COPD and possible referral to primary care providers for diagnosis is an important step in assessing patients presenting with chronic cough. The following questions are helpful in screening patients [2]:

1. Are you 40 years of age or older?
2. Are you a current or former smoker?
3. Do you have a history of occupational exposure to dusts and chemicals?
4. Do you cough regularly?
5. Do you cough up phlegm regularly?
6. Do simple chores make you short of breath?
7. Do you wheeze when you exert yourself or at night?
8. Do you get frequent colds that persist longer than those of other people you know?

Patients who are 40 years or older, with a history of smoking or exposure to dusts or chemicals, AND answered YES to any of questions 4–8 above should be referred for further assessment.

Patient History

Additional targeted questions that are valuable in the assessment of COPD include the following:

- *Social history*: exposure to environmental or occupational risk factors such as smoking
- *Family history*: family history of COPD or other respiratory diseases, e.g., history of AAT deficiency.
- *Past medical history*: history of exacerbations or hospitalizations for respiratory disorders in the last 12 months. It is also important to keep in mind that COPD is associated with a number of comorbid conditions such as ischemic heart disease, anemia, cachexia, osteoporosis, depression, anxiety, and cancer to name a few [1, 2].
- *Symptoms*: In addition to the symptoms described in the initial screening questions above, the patient may also experience difficulty sleeping. This may be due to awakening resulting from episodes of coughing and shortness of breath or sleep apnea. It may also be related to anxiety or depression, which is a common comorbidity in patients with COPD. The patient may also report a loss of energy or fatigue. This may be due to the extra work it takes to breathe, poor oxygen exchange in the lungs, and/or polycythemia. Furthermore, assessment of symptom severity is important (see below).
- *Red flag symptoms* that require immediate referral include excessive shortness of breath, chest pain, blood in sputum, and change in mental status (e.g., confused and/or drowsy).

Physical Assessment

In addition to targeted questions, depending on the clinical setting, the pharmacists might utilize the following physical assessment skills.

Inspection

Pharmacists can observe any of the following findings consistent with COPD:

- Barrel chest
- Accessory muscle use
- Pursed lip breathing
- Prolonged expiration
- Cyanosis (bluish discoloration of the skin and lips)
- Tachypnea (respiratory rate > 20 breaths per minute)
- Signs of being a smoker: smell of nicotine and yellow stained fingers and nails

Auscultation

Auscultation might identify breath sounds more commonly associated with COPD:

- Rhonchi: sounds that resemble snoring that occur when air is blocked or becomes rough through the airways.
- Wheezing: high-pitched sounds produced by narrow airways that sometimes can be heard without a stethoscope.
- Diminished breath sounds

Laboratory

Arterial blood gasses (ABGs) provide information on pulmonary function and how well gas exchange is occurring. Hypoxemia is low PaO_2 (partial pressure of oxygen) in the blood. Hypercapnia is high $PaCO_2$ (partial pressure of carbon dioxide) and indicates hypoventilation [7]. There is no specific blood test to measure whether inadequate oxygen is being delivered to tissues (hypoxia). However, chronic hypoxia can stimulate increased production of red blood cells to carry more oxygen. This manifests

Table 16.1 Normal arterial blood gases [7]

Arterial blood	Normal (range)
pH	7.4 (7.35–7.45)
PaO_2	80–100 mm Hg (10.6–13.3 kPa)
$PaCO_2$	35–45 mm Hg (4.7–6.0 kPa)
SaO_2	95%

PaO_2 partial pressure of oxygen, *$PaCO_2$* partial pressure of carbon dioxide, *SaO_2* saturation of arterial oxygen, *kPa* kilopascal

as "polycythemia" or elevated hematocrit and/or hemoglobin. Table 16.1 depicts the normal ranges for ABGs.

Imaging

If available, chest x-ray might show hyperinflation and depressed diaphragm.

PK is over 40 years old and said she quit smoking 10 years ago. She has been coughing regularly over the last several months and sometimes brings up phlegm. PK should be referred for spirometry, as this test is the "gold standard" and required to establish a COPD diagnosis.

Diagnosis

Spirometry

Spirometry is a commonly used test to assess pulmonary function. It assesses how much and how quickly air can be expelled from the lungs. It helps to differentiate obstructive (air cannot get out) and restrictive (air cannot get in) lung disease by measuring lung volumes. All lung volumes are compared to normal values from healthy subjects (predicted values). The test itself takes about 15–20 minutes and carries no risk to patients (see standard spirometry volume/time curve, Fig. 16.1) [8]. Postbronchodilator forced expiratory volume over 1 second (FEV_1) over forced vital capacity (FVC) ratio (FEV_1/FVC) of less than 0.70 confirms the presence of an obstructive disorder.

PK was referred for diagnosis, and spirometry reveals an FEV_1/FVC ratio of 0.56, which is less than 0.70 and confirms the presence of persistent airflow limitation/obstruction.

The World Health Organization launched the Global Initiative for Chronic Obstructive Lung Disease (GOLD) in 2001 [1]. These international strategies are updated annually based on the most recent evidence. The Canadian Thoracic Society (CTS) provided a 2017 position

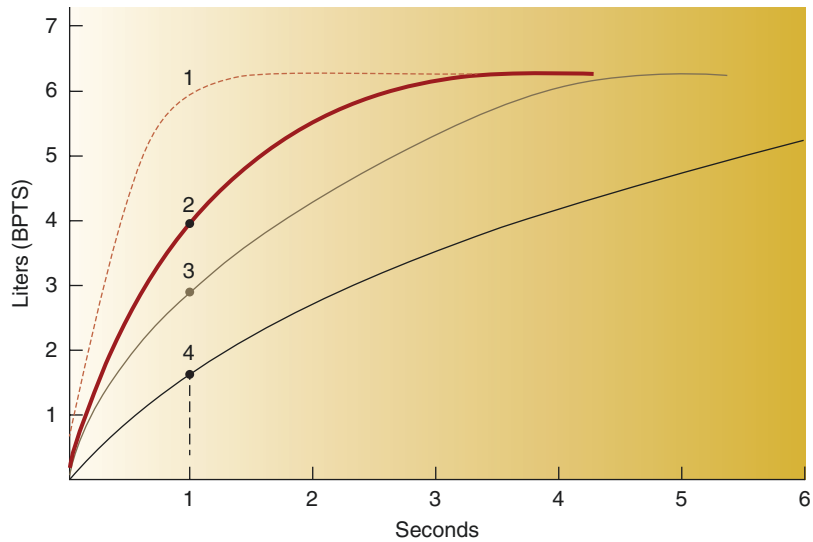

Fig. 16.1 Standard spirometry. Curve 1 is for a normal subject with normal forced expiratory volume over 1 second (FEV_1); curve 2 is for a patient with mild airway obstruction; curve 3 is for a patient with moderate airway obstruction; curve 4 is for a patient with severe airway obstruction. BPTS, body temperature saturated with water vapor. (Reprinted with permission from McGraw-Hill Education. Velez et al. [8]. Available at: https://accesspharmacy.mhmedical.com/content.aspx?bookid=1861&sectionid=146078873. Accessed: July 30, 2018)

Table 16.2 Classification of airflow obstruction in COPD [1, 2, 4]

Degree of impairment	Spirometry
Mild	FEV_1 is greater than or equal to 80% predicted
Moderate	FEV_1 is greater or equal to 50% predicted and less than 80% predicted
Severe	FEV_1 is greater or equal to 30% predicted and less than 50% predicted
Very severe	FEV_1 is less than 30% predicted

FEV1 post-bronchodilator forced expiratory volume over 1 second

statement update for pharmacotherapy in COPD [6]. Other international guidelines offer similar recommendations. Readers should refer to the most recent evidence-based guidelines to direct care. The GOLD 2017 Strategy recommends assessment of lung function. In addition to being required for diagnosis (FEV_1/FVC), spirometry provides baseline FEV_1 [4]. Postbronchodilator FEV_1 indicates the degree of airflow obstruction or limitation (impairment of lung function) and is recommended to be repeated annually as a measure of disease progression (Table 16.2) [4]. There is a poor correlation between FEV_1, symptom intensity, exercise capacity, and quality of life. The most recent GOLD Strategy (2017) no longer includes FEV_1 as a factor in exacerbation risk assessment [4]. Degree of airflow obstruction or limitation is categorized as shown in Table 16.2 [1, 2, 4].

ABCD Classification

The GOLD Strategy recommends assessment of *frequency of exacerbations* and *severity of symptoms* to determine the ABCD classification of patients with COPD, which stratifies patients by risk of exacerbations and symptoms, to assist in directing initiation of pharmacologic care (Table 16.3).

Frequency of Exacerbations If there have been two or more exacerbations in the last 12 months or at least one exacerbation leading to hospital admission, the patient is considered at "higher risk" for exacerbations [4].

Table 16.3 GOLD 2017 ABCD Classification of patients with COPD based on exacerbation history and symptoms [4]

History of exacerbations	ABCD classification	
Higher risk (two or more exacerbations in the last 12 months or at least one leading to hospital admission)	C	D
Low risk	A	B
Symptom assessment	mMRC 0–1 (1–2 MRC) or CAT < 10 less symptoms	mMRC > 2 (>3 MRC) or CAT > 10 more symptoms

CAT COPD Assessment Test, *mMRC* modified Medical Research Council dyspnea scale, *MRC* Medical Research Council dyspnea scale

Symptom Severity There are a number of different tools that can be used to measure symptom severity. The most commonly used tools are the modified Medical Research Council (mMRC) or Medical Research Council (MRC) dyspnea scale and the COPD Assessment Test (CAT).

- MRC and mMRC dyspnea scales classify patients according to the severity of symptoms (Table 16.4). The Canadian Thoracic Society (CTS) Guidelines use the MRC scale, (1–5), whereas the GOLD Strategy uses the modified scale from 0 to 4 [2, 4].
- CAT includes eight statements about symptoms and activities. The patient scores each statement on a scale of 1–5. The impact of COPD symptoms is assessed by a cumulative score (0–40) [1]. CAT can found at http://www.catestonline.org.
- Patients with mMRC score of 0–1 (1–2 MRC scale) or a CAT score of less than 10 are considered to have "less symptoms." If patients have mMRC score of 2–4 (3–5 MRC scale), they are considered to have "more symptoms."

PK has an FEV1 67% (predicting moderate lung function impairment) with no exacerbations in the last year (low risk). She is breathless with moderate exercise (mMRC score = 0 (MRC = 1), few symptoms). Therefore, PK would be classified as risk Group A.

Table 16.4 GOLD mMRC and CTS MRC dyspnea scoring scale and corresponding definition [2, 4]

GOLD mMRC scoring	CTS MRC scoring	Definition
Grade 0	Grade 1	Breathless with strenuous exercise
Grade 1	Grade 2	Shortness of breath when hurrying on the level or walking up a slight hill
Grade 2	Grade 3	Slower than people of the same age on the level or stops for breath when walking at own pace on the level
Grade 3	Grade 4	Stops for breath after walking about 100 yards (90 meters) or after a few minutes on the level
Grade 4	Grade 5	Too breathless to leave the house or breathless with dressing

GOLD Global Initiative for Chronic Obstructive Lung Disease, *mMRC* modified Medical Research Council dyspnea scale, MRC Medical Research Council dyspnea scale

Table 16.5 COPD goals of therapy [1, 5]

Symptoms	Alleviate breathlessness and other respiratory symptoms Improve exercise tolerance and daily activity Improve overall health status
Risk	Prevent disease progression Reduce the frequency and severity of exacerbations Treat exacerbations and complications of the disease Reduce mortality

Management

COPD goals of therapy are to manage symptoms and reduce risks as described in Table 16.5. Management involves pharmacologic and non-pharmacologic measures for both prevention and treatment. Prevention strategies include [1, 2]:

- *Smoking cessation*: is beneficial at any stage of COPD (with or without pharmacologic intervention).
- *Vaccinations*: pneumococcal and annual influenza vaccinations.
- *Supplementary oxygen*: goal is to maintain oxygen saturation greater than 90%.
- *Avoiding drugs that exacerbate COPD*: these include antitussives, sedating antihistamines, and beta-blockers. Opioids and benzodiazepines should also be avoided, if possible, but may be used as part of end-of-life care.
- *Education and pulmonary rehabilitation*: patients should be educated on COPD and proper use of inhaler devices. They should be encouraged to have a healthy lifestyle and be referred to a pulmonary rehabilitation program.
- Currently, the use of prophylactic antibiotics to prevent exacerbations of COPD is controversial.

Pharmacological management of COPD primarily includes inhaled bronchodilators including beta-agonists (short-acting "SABA" and long-acting "LABA") and muscarinic antagonists (short-acting "SAMA" and long-acting "LAMA"). Figure 16.2 depicts the CTS COPD treatment pyramid [6], and Table 16.6 outlines the different classes of drugs utilized in the management of COPD. Controversy surrounds the use of low dose inhaled corticosteroids (ICS) as add-on treatment as they carry the potential for side effects such as pneumonia and cataracts [6]. ICS should never be used as monotherapy for COPD. When ICS/LABA combinations are used, high doses of ICS are not required to achieve optimum benefit. Oral therapies such as systemic steroids are used short term for exacerbations. Oral phosphodiesterase inhibitors, methylxanthines, and mucolytics are reserved for patients not responding to inhaled therapy as they also have the potential for significant side effects. The 2017 Canadian Thoracic Society Guidelines (Fig. 16.3) [6] mirror the GOLD approach of stepping up or stepping down drug management if symptoms fail to improve or continue to progress [4]. Initial therapy recommendations from GOLD and the CTS is presented in Table 16.7.

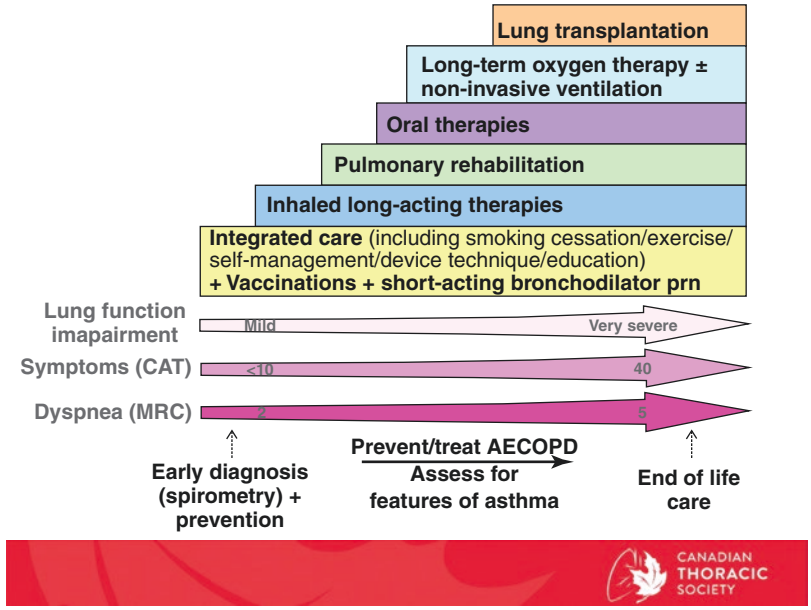

Fig. 16.2 COPD pyramid for comprehensive Management of COPD. Integrated approach of care that includes COPD diagnosis with spirometry, evaluation of symptom burden and risk for future exacerbations with ongoing monitoring, assessment for features of asthma, and comprehensive management, both nonpharmacologic and pharmacologic. CAT, COPD assessment test; MRC, Medical Research Council; SABD PRN, short-acting bronchodilator as needed; AECOPD, acute exacerbation of COPD; Inhaled Long-Acting Therapies, long-acting muscarinic antagonist and/or long-acting beta2-agonist and/or inhaled corticosteroid; LTOT, long-term oxygen therapy. (Reprinted from Bourbeau et al. [6]. With permission from Taylor & Francis Ltd., http://www.tandfonline.com)

Table 16.6 Classes of drugs used in the management of COPD

Drug class	Drug names (available delivery mechanism)
Inhaled beta-agonists	
Short-acting (SABA) Long-acting (LABA)	Salbutamol (MDI, Dk, Neb), terbutaline (TH) Formoterol (TH, Aerolizer – Inh Caps), Salmeterol (Dk), indacaterol (BH) Olodaterol (Rs) Not available as single agent: vilanterol
Inhaled muscarinic antagonists	
Short-acting (SAMA) Long-acting (LAMA)	Ipratropium (MDI, Neb) Tiotropium (HH, Rs), glycopyrronium (BH), aclidinium (PI), umeclidinium (E)
Inhaled combination beta-agonists/muscarinic antagonists	
Short-acting (SABA/SAMA) Long-acting (LABA/LAMA)	Salbutamol/ipratropium (Neb, Rs) Formoterol/aclidinium (PI) Olodaterol/tiotropium (Rs) Indacaterol/glycopyrronium (BH) Vilanterol/umeclidinium (E)
Inhaled combination beta-agonists/corticosteroids	
Long-acting (LABA/ICS)	Salmeterol/fluticasone propionate (Dk) Formoterol/budesonide (TH) Vilanterol/fluticasone furoate (E)
Phosphodiesterase inhibitors	Roflumilast capsules – oral
Methylxanthines	Theophylline, – oral, aminophylline - intravenous
N-acetylcysteine	Oral N-acetylcysteine: the injectable solution is administered orally, or powder could be compounded into capsules

BH Breezehaler, *Dk* Diskus, *E* Ellipta, *HH* HandiHaler, *Inh Caps* inhaled capsules, *MDI* metered dose inhaler, *Neb* nebule, *PI* Pressair inhaler, *Rs* Respimat, TH Turbuhaler

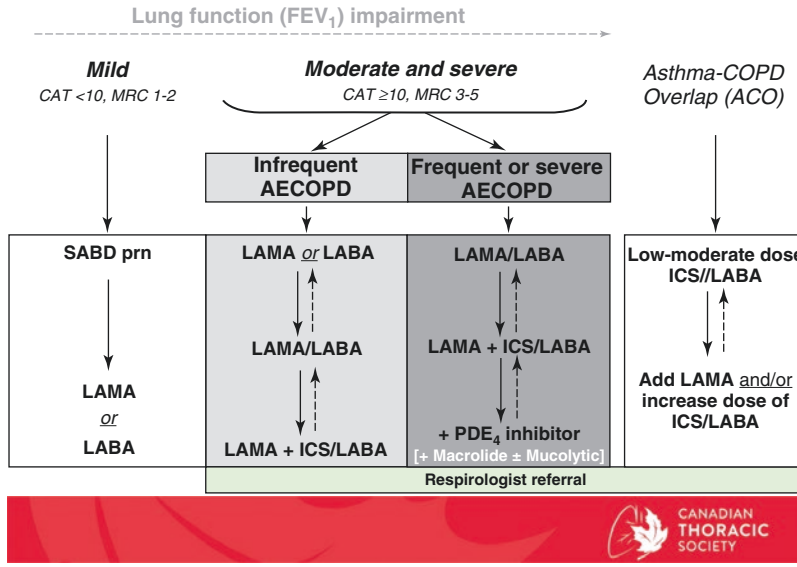

Fig. 16.3 COPD pharmacotherapy. Suggested COPD pharmacotherapy promoting an approach that matches treatment decisions with symptom burden and risk of future exacerbations. Solid arrows indicate step up therapy to optimally manage symptoms of dyspnea and/or activity limitation, as well as the prevention of AECOPD where appropriate. Dashed arrows indicate potential step down of therapy, with caution, and with close monitoring of the patient symptoms, exacerbations, and lung function. Frequent AECOPD is ≥2 events requiring antibiotics ± systemic corticosteroids over 2 years or ≥ 1 severe AECOPD requiring hospitalization. As-needed (prn) use of short-acting bronchodilator should accompany all recommended therapies. CAT, COPD assessment test; MRC, Medical Research Council; SABD prn, short-acting bronchodilator as needed; AECOPD, acute exacerbation of COPD; LAMA, long-acting muscarinic antagonist; LABA, long-acting B2-agonists; ICS, inhaled corticosteroid; PDE4, phosphodiesterase-4. (Reprinted from Bourbeau et al. [6]. With permission from Taylor & Francis Ltd., http://www.tandfonline.com)

Table 16.7 COPD initial pharmacotherapy based on ABCD classification (GOLD and CTS recommendations)

Classification of risk Group (GOLD) [4]	Initial therapy (GOLD 2017) [4]	CTS COPD 2017 update [6]
A Low-risk, less symptoms	SABD as needed or LABD	SABD as needed or LABD
B Low-risk, more symptoms	LABA or LAMA	LAMA is superior to LABA
C High-risk, less symptoms	LABA/LAMA	Prefer step up to LABA/LAMA over LABA/ICS in patients who do not have asthma overlap syndrome
D High-risk, more symptoms	LABA/LAMA/ICS	In patients with high symptom burden and poor health despite LABA/LAMA dual therapy – triple therapy may be considered Consider oral therapies when the patient is experiencing exacerbations despite optimized inhaled therapies

CTS Canadian Thoracic Society, *GOLD* Global Initiative for Chronic Obstructive Lung Disease, *SABD* short-acting bronchodilator, *LAMA* long-acting bronchodilator, *LABA* long-acting beta-agonist, *LAMA* long-acting muscarinic antagonist, *ICS* inhaled corticosteroid

As PK is in risk Group A and is not currently on any therapy, it would be appropriate to initiate short-acting bronchodilator (SABD) therapy and monitor frequency of use and response.

Follow-Up Assessment

In order to optimize therapy, ongoing follow-up should occur regularly to monitor efficacy, exacerbations, adverse effects, and most importantly adherence.

Adherence

One of the most common problems with inhalers is adherence and appropriate inhaler technique. Incorrect inhaler use is a potential obstacle to achieving good COPD control [6]. Patients should be assessed at each refill for *how* and *when* they are using their inhalers to ensure optimal drug therapy [4]. There are many alternative inhaler devices available that allow for modification of therapy based on the patient's ability to administer medications [9]. When assessing adherence, consider the patient's manual dexterity to load capsules into inhaler devices and ability to take deep breaths to inhale dry powders. Consider coordination of hand and breaths when using a metered dose inhaler (MDI) and if a valved holding chamber (VHC) is appropriate. Other questions to consider are whether once daily versus twice daily dosing is important and if the patient is better able to manage more than one inhaler type (i.e., MDI versus Turbuhaler versus Breezehaler). Table 16.8 provides examples of different types of delivery devices.

Table 16.8 Examples of available inhaler devices per drug and drug class [9]

Type of delivery	Type of device	Drug name	Drug class
Aerosolized (doses in a canister)	MDI (it can be used with valved holding chamber with or without mask)	Salbutamol Ipratropium	SABA SAMA
Dry powder (doses in a reservoir)	Turbuhaler	Terbutaline Formoterol Formoterol/ budesonide	SABA LABA LABA/ ICS
Dry powder (doses as single blisters within the device)	Diskus	Salbutamol Salmeterol Salmeterol/ fluticasone propionate	SABA LABA LABA/ ICS
	Pressair	Aclidinium Formoterol/ aclidinium	LAMA LABA/ LAMA
	Ellipta	Umeclidinium Vilanterol/ umeclidinium Vilanterol/ fluticasone furoate	LAMA LABA/ LAMA LABA/ ICS
Dry powder (doses as capsule to be loaded and punctured)	Aerolizer	Formoterol	
	HandiHaler	Tiotropium	LAMA
	Breezehaler	Indacaterol Glycopyrronium	LABA LAMA
Soft mist (doses in a canister)	Respimat	Salbutamol/ ipratropium Olodaterol/ tiotropium Tiotropium Olodaterol	SABA/ SAMA LABA/ LAMA LAMA LABA

MDI pressurized metered dose inhaler, *SABA* short-acting beta-agonist, *SAMA* short-acting muscarinic antagonist, *LABA* long-acting beta-agonist, *LAMA* long-acting muscarinic antagonist

Control

Signs and Symptoms

Assess if there have been any changes to symptoms from baseline (cough, sputum production, dyspnea, etc.) and severity using the same scale used previously (MRC, mMRC, CAT). COPD is a progressive disease therefore, overtime, it is expected that the patient will require more therapy to control symptoms, especially if underlying modifiable risk factors are not addressed (i.e., smoking cessation).

COPD Action Plan

All patients with COPD should have an individualized action plan (https://cts-sct.ca/wp-content/uploads/2018/03/4915_THOR_COPDActionPlanUpdate_Editable_Eng_v006.pdf). The COPD action plan includes information on what the usual daily symptoms look like for the patient (sputum color and level of activity) and what to do if there is a change in usual symptoms over at least 2 days. Action strategies include increasing use of the short-acting bronchodilator, a prescription for an antibiotic for sputum changes, and a short course of oral prednisone for increased shortness of breath. It also provides guidance on when to seek urgent or emergency care.

Adverse Drug Reactions

Table 16.9 lists the adverse reactions of drug therapy in patients with COPD.

Disease Complications

Acute Exacerbation of COPD

An acute exacerbation of COPD (AECOPD) has been likened to a "lung attack," where an exacerbation is to COPD what a myocardial infarction is to coronary artery disease [6]. It is an acute event with worsening of symptoms that are beyond the day-to-day normal variation [1]. Goals of therapy for AECOPD are to prevent hospitalization, acute respiratory failure, and death and to return symptoms to baseline [1].

Classification

Spirometry tests are not useful in the management of an AECOPD. AECOPD is classified according to the presenting symptoms. Patients presenting with three cardinal symptoms are considered to have a severe AECOPD, while those presenting with two cardinal symptoms have a moderate AECOPD [1]. Cardinal symptoms include:

Table 16.9 List of adverse reactions of drug therapy in patients with COPD

Drug	Common adverse reactions/precautions
Beta-agonists [10]	Tremors, headache, dizziness, sleep disturbances, nausea Hypokalemia, sinus tachycardia, and rhythm disturbances in predisposed individuals
Muscarinic antagonists [11]	Dry mouth, metallic taste, blurred vision Urinary retention, caution in narrow angle glaucoma, severe cardiovascular disorders (arrhythmias)
Inhaled corticosteroids [12]	Oropharyngeal candidiasis, dysphonia, cough Systemic side effects (adrenal insufficiency, skin thinning, osteoporosis) with long-term high-dose usage
Phosphodiesterase inhibitors (roflumilast) [13]	Nausea, diarrhea, weight loss, headache, decreased appetite, dizziness, insomnia, anxiety Neuropsychiatric effects (potential for suicidal thoughts, worsening depression)
Methylxanthines (theophylline) [14]	Anorexia, nausea, vomiting, abdominal cramps, headaches, nervousness, tremor, insomnia Toxicity associated with theophylline serum concentrations >110 umol/L Notable drug interactions: antibiotics (ciprofloxacin, norfloxacin, erythromycin), antiepileptics (carbamazepine, phenytoin), smoking, allopurinol, fluvoxamine
Oral/systemic corticosteroids [15]	*Short-term use* Hypertension, weight gain (due to sodium/water retention), hyperglycemia, nausea, mood changes, insomnia, appetite stimulation, leukocytosis, flushing *Long-term use* Cushing's syndrome, adrenal suppression, gastrointestinal ulcerations, osteoporosis, cataract

- Worsening of dyspnea
- Increase in sputum volume
- Increase in sputum purulence

A mild AECOPD presents with one of the cardinal symptoms above plus at least one of the following:

- Upper respiratory tract infection in the last 5 days
- Fever without other explanation
- Increased wheezing
- Increased cough
- Increase in respiratory rate or heart rate (20% above baseline)

Management of AECOPD [1, 4]
Management of AECOPD will depend on the severity of the exacerbation. Severe AECOPD requires hospital admission. Nonpharmacologic management may include oxygen with a target oxygen saturation of 88–92%. Noninvasive or invasive mechanical ventilation may be required for acute respiratory failure. In moderate to severe AECOPD, pharmacologic management includes adding regularly scheduled short-acting bronchodilators and systemic corticosteroids (i.e., oral prednisone 30–50 mg daily for 5–10 days) to ongoing long-acting bronchodilators. Consider antibiotic use in patients with two or more cardinal symptoms [1].Refer to local guidelines for choice of antibiotic therapy. In mild AECOPD, treatment involves an increase in SABD therapy.

Long-Term Complications

As the disease progresses, and if not managed, the patient may develop secondary pulmonary hypertension, which can result in cor pulmonale (right-sided heart failure). As this a progressive disease, patients can move on to respiratory failure and death [1].

Clinical Pearls

- Pharmacists play an important role in the identification and management of patients with COPD.
- Suspect COPD in smokers over 40 years of age and refer for diagnosis.
- As drugs within a class (i.e., LABA) have similar efficacy, patient factors such as ability to manage inhaler device, frequency of dosing, and cost should guide drug choice within a therapeutic class.
- Assessment at follow-up visits (refills) includes review of inhaler technique and use, evaluation of how well the therapy is managing the patient's symptoms and improving quality of life, frequency of exacerbations, and adverse effects.
- Ensure each COPD patient has an action plan and knows what to do in case of an exacerbation.

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