Ministry of Health
Republic of Maldives

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GUIDELINE FOR THE MANAGEMENT OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

2024

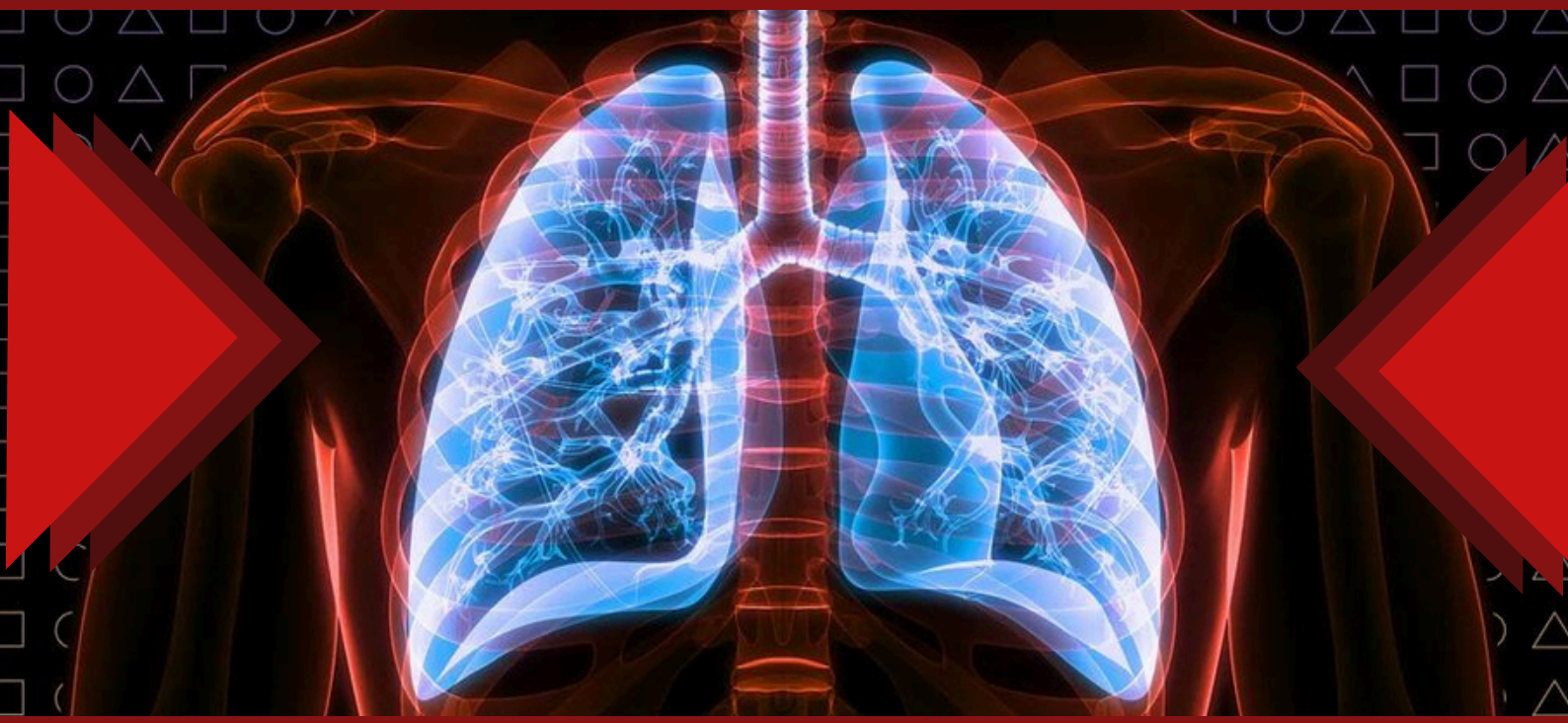

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Table of Contents

Abbreviations

AATD - alpha-1 antitrypsin deficiency

COPD – chronic obstructive pulmonary disease

CVD – cardiovascular disease

FEV1 – forced expiratory volume in 1 second

FVC – forced vital capacity

GOLD - Global initiative for chronic obstructive lung disease

ICS - Inhaled corticosteroids

LABA - long-acting beta 2 agonists

LAMA -long-acting muscarinic antagonists

mMRC - modified medical research council

NIV - non-invasive ventilation

OCS – oral corticosteroids

SABA -Short acting beta 2 agonists

SAMA - short acting muscarinic antagonists

CHRONIC OBSTRUCTIVE PULMONARY DISEASE

1.0 Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a major cause of chronic morbidity and mortality throughout the world. Many people suffer from this disease for years, with frequent doctors' visits and multiple hospitalizations due to exacerbations and dying prematurely from it or its complications.

In 2019, COPD was the third leading cause of death worldwide, causing 3.23 million deaths. Globally, the COPD burden is projected to increase in the coming decades because of continued exposure to COPD risk factors and aging of the population. Similarly, in the Maldives, the prevalence of risk factors, especially smoking is very high. According to the STEP survey conducted in Maldives in 2020-2021, 23 percent of the respondents were smokers. And, in those rural islands where fishing is the major source of income, women involved in making smoked fish have years of prolonged exposure to household smoke that increases the risk for COPD.

Chronic respiratory diseases including COPD are among the 4 prioritized diseases included in WHO Global Action Plan on non-communicable diseases. More focus on the disease has led to better understanding of the condition, thus improving pharmacological therapy as well as more recognition of other effective interventions like pulmonary rehabilitation. Hence there is a need to have an updated guideline, that provides an evidence-based framework for evaluation and management of COPD.

2.0 Scope of this guideline

There is no local guidance to manage COPD except for the adapted WHO PEN package for primary care, which also needs revision and updating based on new research and developments in COPD management. Hence it is important to have a guidance document for standardized and effective quality care to manage COPD. This Guideline is based on recent published clinical evidence and is intended to provide guidance on best evidence-based practices on the diagnosis, evaluation, and

management of COPD. As local treatment pathways for COPD management are guided by Global Initiative for Chronic Obstructive lung Disease (GOLD) guideline, management pathways in this guideline have been adapted from it.

This guideline is intended for use by health care providers, including general medical practitioners, physicians, respiratory physicians, nurses, and community health workers involved in the health care team providing care to COPD patients.

3.0 Background

3.1 What is COPD?

Chronic Obstructive Pulmonary Disease (COPD) is a heterogenous lung condition that is characterized by chronic respiratory symptoms (dyspnoea, cough, sputum production and/or exacerbations) due to and airflow limitation that is due to airway and/or alveolar abnormalities that cause persistent, often progressive, airflow limitation.

3.2 What causes COPD?

The most encountered risk factor for COPD is tobacco smoking. Non-smokers may also develop COPD as it is the result of a complex mix of long-term cumulative exposure to noxious gases and particles, combined with a variety of host factors including genetics, airway hyper-responsiveness and poor lung growth during childhood. The risk of developing COPD is related to the following factors:

- Tobacco smoke

  Cigarette smokers have a higher prevalence of respiratory symptoms and lung function abnormalities, a greater annual rate of decline in FEV1, and a greater COPD mortality rate than non- smokers. Other types of tobacco such as pipe, cigar, water pipe and marijuana are also risk factors for COPD. Passive exposure to environmental tobacco smoke and second-hand smoking may also lead to respiratory symptoms and COPD.

- Indoor air pollution

  Indoor air pollution resulting from burning of wood and other biomass fuels used for cooking and heating in poorly vented dwellings, is a risk factor that particularly affects women in developing countries. There is a lack of research about biomass related COPD, although there is limited evidence from an observational study that switching to cleaner cooking fuels or reducing exposure may reduce COPD risk in non-smokers.

- Occupational exposures

  Exposure to organic and inorganic dusts, chemical agents and fumes, are risk factors for COPD.

- Outdoor air pollution

  High levels of urban air pollution also contribute to the lungs' total burden of inhaled particles, although it appears to have a relatively small effect in causing COPD compared to smoking, it has shown to have a significant impact on lung maturation and development

- Genetic factors

  Severe hereditary deficiency of alpha-1 antitrypsin (AATD) is the best documented genetic risk factor for COPD. Single genes like the gene encoding matrix metalloproteinase 12 and glutathione S-transferase have also been related to a decline in lung function or risk of COPD.

- Age

  Aging is often listed as a risk factor for COPD. Most studies in the past showed COPD prevalence and mortality more in men than women but later data from developed countries has reported the prevalence of COPD to be now almost equal in men and women

- Lung growth and development

  Any factor that affects lung growth during gestation and childhood (low birth weight, respiratory infections, etc.) has the potential to increase an individual's risk of developing COPD.

- Socioeconomic status

  Poverty is consistently associated with airflow obstruction and lower socioeconomic status is associated with an increased risk of developing COPD. It is not clear, however, whether this pattern reflects exposures to indoor and outdoor air pollutants, crowding, poor nutrition, infections, or other factors related to low socioeconomic status.

- Asthma and airway hyper-reactivity

  Asthma may be a risk factor for the development of airflow limitation and COPD.

- Infections

  A history of severe childhood respiratory infection has been associated with reduced lung function and increased respiratory symptoms in adulthood.

4.0 Diagnosis and assessment of COPD

4.1 When to suspect COPD?

COPD should be considered in any patient especially over 40 years who has symptoms suggestive of COPD (chronic dyspnea, cough or sputum production, a history of recurrent lower respiratory tract infections) and/or a history of exposure to risk factors for the disease.

4.1.1 Symptoms suggestive of COPD

- Dyspnea that is progressive over time and /or worsens with exercise is the most characteristic symptom.
- Chronic Cough: often the first symptom, may be intermittent initially but subsequently may be present daily. It may be productive or unproductive.
- Chronic Sputum production
- Wheezing and chest tightness
- Recurrent lower respiratory infections
- Reduced exercise tolerance

- Other symptoms in severe COPD include, **fatigue**, **muscle loss**, **weight loss**, **anorexia**, **ankle swelling**, **depression** and **anxiety**. Syncope and rib fractures have also been reported during prolonged coughing spells

4.1.2 Risk factors for COPD

- Tobacco smoke
- Smoke from home cooking over wood fires and heating fuels
- Occupational dusts, vapors, fumes, gases and other chemicals
- Host factors such as genetic factors, congenital and developmental abnormalities

4.2 Role of Spirometry in diagnosis of COPD

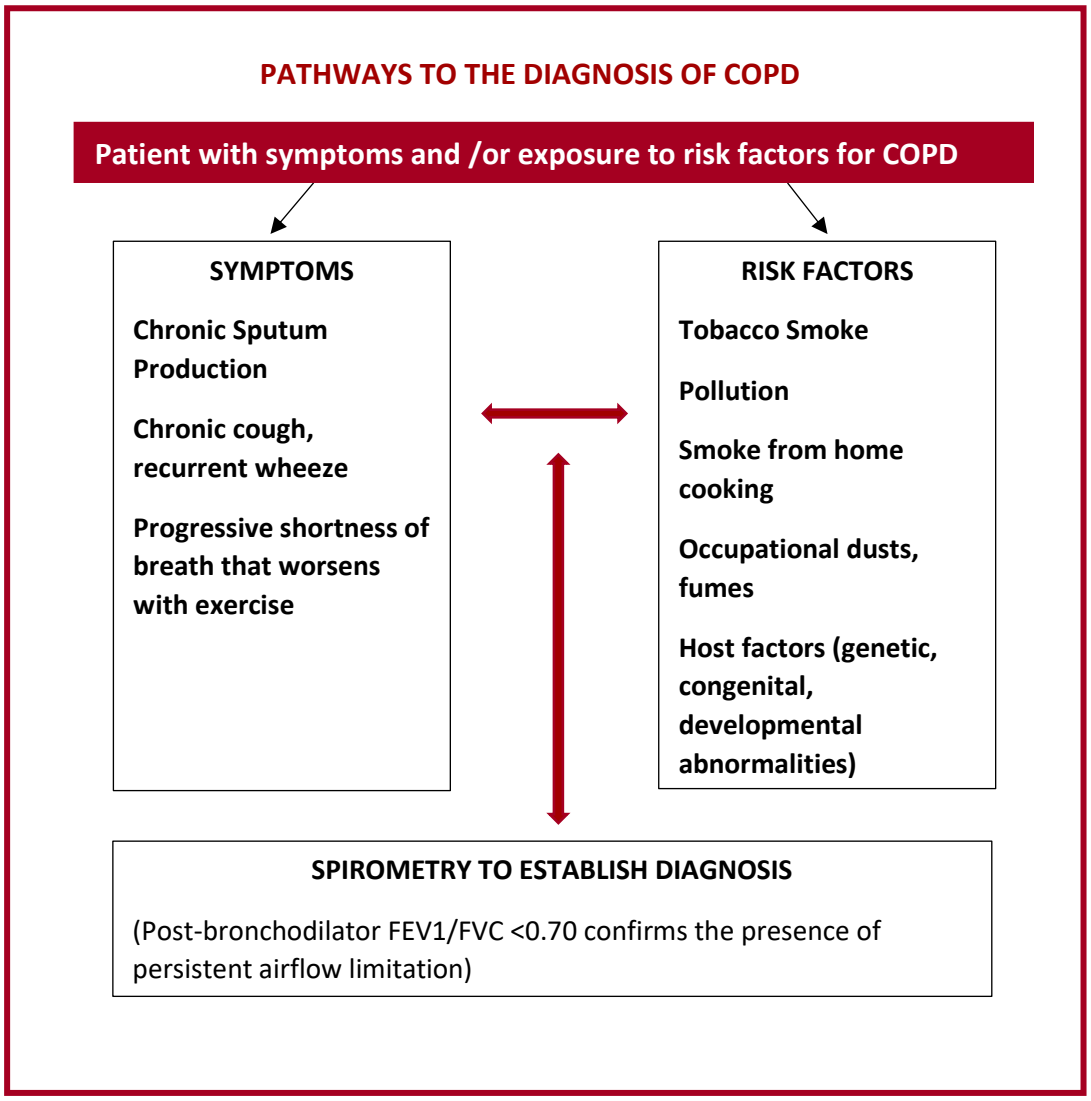
- All patients suspected of having COPD (based on symptoms and exposure to risk factors), should undergo spirometry to establish the diagnosis of COPD.

- In Health centers and Atoll hospitals, where Spirometry is unavailable: -
  - Commence treatment as COPD if there is a confident clinical diagnosis.
  - Offer prevention and risk reduction advice including smoking cessation and
  - Refer patient to do spirometry from a higher center where it is available.
  - Note that Peak expiratory flow measurement alone cannot be reliably used as the only diagnostic test because of its weak specificity in diagnosing COPD.

- Spirometry should be performed after the administration of an adequate dose of a short-acting inhaled bronchodilator, to minimize variability.
  Bronchodilator may include 400 mcg of salbutamol or 160mcg of Ipratropium or the two combined together.

- FEV1 should be measured 10-15 minutes after giving salbutamol or 30-45 minutes after ipratropium or a combination of both.

- Post-bronchodilator forced expiratory volume in first second (FEV_1)/forced vital capacity (FVC); FEV1/FVC < 0.70 on spirometry, defines persistent airflow limitation and diagnosis of COPD.



4.3 Differential Diagnosis

A major differential diagnosis of COPD that is commonly found in the population is asthma. In some patients with chronic asthma, a clear distinction from COPD is not always possible using current imaging and physiological testing techniques. In these patients, current management is similar to that of asthma.

Differential Diagnosis of COPD	
Diagnosis	Characteristic Features (*All features are not a must for e.g.: - asthma can be of adult onset or COPD may be present in a Nonsmoker*)
COPD	Onset in mid life Symptoms slowly progressive History of smoking or exposure to smoke and fumes from other sources
Asthma	Onset often in childhood Symptoms worse at night and early morning Variability in symptoms from day to day Family history of asthma History of allergy, atopy, eczema and rhinitis
Bronchiectasis	Associated with bacterial infection Marked purulent sputum production Clubbing Coarse crackles on auscultation CT shows bronchial wall thickening and irregularity and bronchial dilation
Tuberculosis	Microbiological confirmation / GeneXpert/sputum smear Lung infiltrates on chest X-Ray Can occur at any age
Congestive heart failure	Fine basilar crackles on auscultation Chest Xray shows dilated heart, pulmonary edema No airflow limitation on spirometry

Obliterative Bronchiolitis	Onset at younger age and most are male Ho chronic rhinitis almost in all Most are non -smokers HRCT chest show diffuse small centrilobular nodular opacities and hyperinflation

4.4 Additional Investigations

In addition to spirometry, additional investigations may be considered in the diagnosis and assessment of COPD severity and complications as well as to rule out other differential diagnosis.

Chest X-Ray	A chest X-ray helps to exclude alternative diagnoses and establish the presence of other diseases such as concomitant bronchiectasis, pleural diseases and cardiomegaly Chest Xray is not useful to establish the diagnosis of COPD. Signs of lung hyperinflation with increased lucency and rapid tapering of the vascular markings are some X-Ray changes associated with COPD
Full blood count	To identify anemia or polycythemia, assessment of eosinophils for guidance in use of corticosteroids
Sputum culture	To identify infective organism, if sputum persist and purulent and suggestive of bacterial infection
sputum smear for acid fast bacilli	All new COPD suspects with cough of more than 2 weeks to rule out pulmonary tuberculosis
Pulse Oximetry	Pulse oximetry should be used to assess all patients with clinical signs suggestive of respiratory failure to evaluate a patient's arterial oxygen saturation and need for supplemental oxygen therapy.
Arterial blood gases	If peripheral oxygen saturation is < 92%, arterial blood gases should be assessed
ECG	If there is history of CVD or hypertension or clinical signs of tachycardia, oedema or features of corpulmonale

Echocardiogram	To assess cardiac status If cardiac disease or pulmonary Hypertension are suspected
CT Scan of Chest	NOT recommended routinely. CT scan may be helpful in the differential diagnosis where concomitant other lung diseases such as bronchiectasis are present. CT scan is also necessary when a surgical procedure like lung volume reduction surgery is considered for feasibility of surgery and in those patients that meet the criteria for lung cancer risk assessment.
Exercise testing	Walking tests like the 6-minute walk test may be useful in assessing disability, risk of mortality and effectiveness of pulmonary rehabilitation
Serum alpha-1 antitrypsin	alpha-1 antitrypsin deficiency may be done if symptoms of early onset (young patients) with minimal or no smoking history and lower lobe emphysema

4.5 Assessment

Patient assessment is targeted not only to determine the presence and level of airflow limitation but also to know its effect on the health status of the patient and the risk of future events such as exacerbations to decide on the treatment.

No one single measure can adequately assess disease severity in an individual, hence the assessment should consider:

- Current symptoms and their severity and the impact on patients' life including activity and work.
- History of exacerbations or previous hospitalizations
- Presence and severity of airflow limitation on spirometry
- Concomitant presence of comorbidities
- Exposure to risk factors

4.5.1 Assessment of severity of Symptoms

Level of patient's disability due to symptoms should be assessed using modified Medical Research Council (mMRC) dyspnea questionnaire or the COPD assessment test (CAT) and recorded at each visit.

Modified British Medical Research Council (MRC) questionnaire grades breathlessness according to the level of exertion required to elicit it. The scale lacks assessment of other symptoms and a score ≥ 2 is used as a threshold for separating less breathlessness from more breathlessness.

MODIFIED MRC DYSPNOEA SCALE		
PLEASE TICK IN THE BOX THAT APPLIES TO YOU / one box only/ Grades 0-4		
mMRC Grade 0	I only get breathlessness with strenuous exercise	☐
mMRC Grade 1	I get Short of breath when hurrying on the level or walking up a slight hill	☐
mMRC Grade 2	I Walk slower than people of the same age on the level because of breathlessness, or I have to stop for breath when walking on my own pace on the level	☐
mMRC Grade 3	I Stop for breath after walking about 100 meters or after a few minutes on the level	☐
mMRC Grade 4	I am too breathless to leave the house, or I am breathless when dressing or undressing	☐
Adapted from Fletcher CM.BMJ:1960; 2:1662.		

The COPD Assessment Test (CAT™) is more comprehensive, taking other symptoms and their impact on the patients' health. Scores in CAT ranges from 0-40 and a cut point of CAT 10 is used as a threshold for considering regular treatment for symptoms.

CAT™ ASSESSMENT			
For each item below, place a mark (X) in the box that best describes you currently. *Be sure to only select one response for each question*			
EXAMPLE: I am very happy	1 2 **3** 4 5	I am very sad	SCORE
I never cough	1 2 3 4 5	I cough all the time	
I have no phlegm(mucus) In my chest at all	1 2 3 4 5	My chest is completely full of phlegm(mucus)	
My chest does not feel tight at all	1 2 3 4 5	My chest feels very tight	
When I walk up a hill or one flight of stairs I am not breathless	1 2 3 4 5	When I walk up a hill or one flight of stairs, I am very breathless	
I am not limited doing any activities at home	1 2 3 4 5	I am very limited doing activities at home	
I am confident leaving my home despite my lung condition	1 2 3 4 5	I am not at all confident leaving my home because of my lung condition	
I sleep soundly	1 2 3 4 5	I don't sleep soundly because of my lung condition	
I have lots of energy	1 2 3 4 5	I have no energy at all	
Reference: Jones et al.ERJ 2009; 34(3);648-54			TOTAL SCORE: ◯

4.5.2 Classification of severity of airflow limitation

Classification of severity of the disease should be done for all COPD patients based on the FEV_1 on spirometry. Specific spirometry cut points are used to classify severity of air flow limitation from mild to very severe.

GOLD- Classification of severity of airflow limitation in COPD (based on post bronchodilator FEV1)		
In patients with COPD, FEV1/FVC <0.7		
GOLD 1	Mild	FEV1 ≥ 80% predicted
GOLD 2	Moderate	50% ≤ FEV1 < 80% predicted
GOLD 3	Severe	30% ≤ FEV1 < 50% predicted
GOLD 4	Very Severe	FEV1 <30% predicted

4.5.3 Combined COPD Assessment

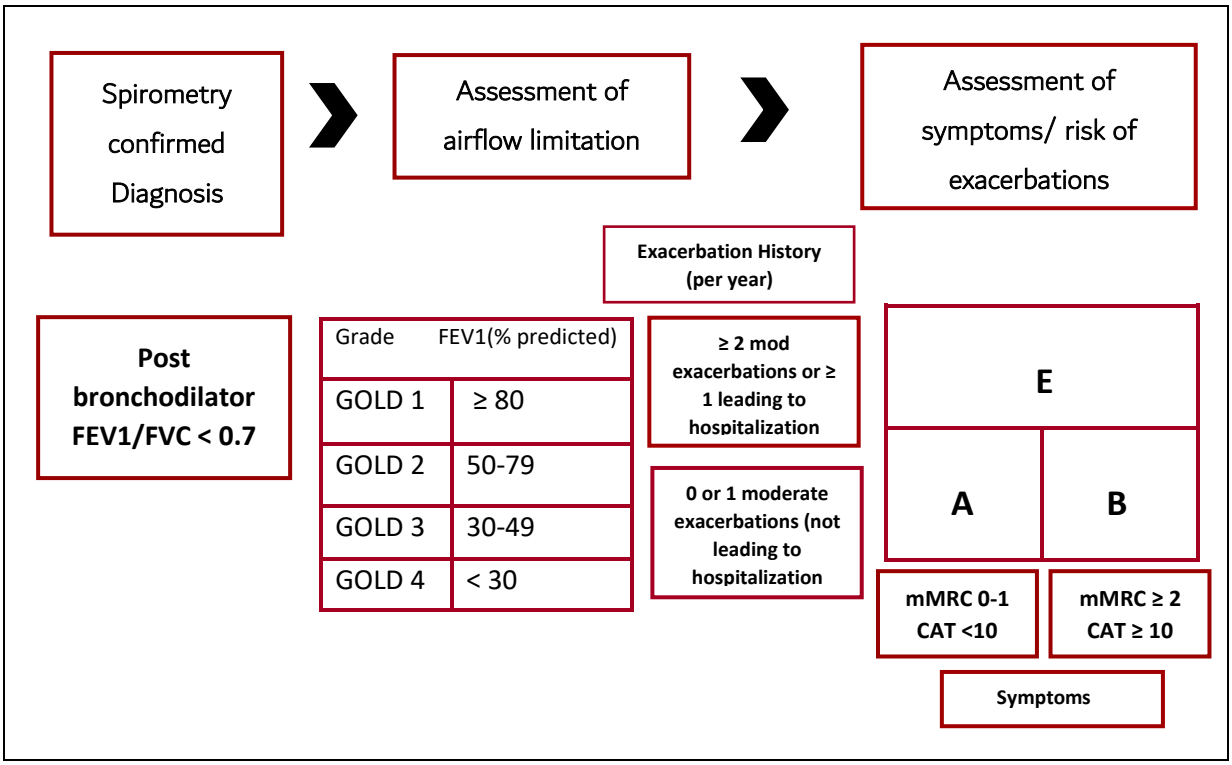
The health status of a COPD patient is understood by taking into consideration, the combination of symptomatic assessment, air flow limitation classification and the risk of exacerbations. This is vital, not only for diagnosis but for prognosis and adjustment of therapy.

Hence assessment should include:

- Spirometry to determine the severity of airflow limitation (spirometry grades 1 to 4)
- Assessment for symptom burden using modified MRC dyspnea scale and COPD Assessment Test (CAT).
- History of moderate and severe exacerbations, including prior hospitalizations
- Blood eosinophil count may also predict exacerbation rates (in patients treated with LABA without ICS).

The combined assessment strategy proposed by GOLD includes the level of symptoms, severity of air flow limitation and the frequency of previous exacerbations. The Refined ABCD assessment tool of 2021 GOLD guidelines have evolved in 2023 guidelines as GOLD ABE Assessment Tool where Cand D groups were merged, to highlight the importance of exacerbations. This tool is used to guide the initial pharmacological treatment.

THE ABE ASSESSMENT TOOL (GOLD 2023)



5.0 Management of COPD

- Management of COPD should be based on individualized assessment with the aim to:
  - reduce symptoms
  - improve exercise tolerance and overall health status
  - reduce future risks by preventing exacerbations, disease progression
  - reduce mortality

- Management strategies should include both pharmacological as well as appropriate non - pharmacological interventions that focus on identifying and reducing exposure to risk factors, vaccination and general advice on a healthy lifestyle

5.1 Smoking Cessation:

- Smoking cessation is a key component in the management of COPD and those patients who are smokers should be strongly advised to quit.

- Provide smoking cessation counselling with brief interventions using 5A's approach (Ask about tobacco use, advise to quit, assess willingness to quit, assist in quitting and arrange follow up) at each visit.

- For those smokers who are not ready to quit use 5Rs to motivate (Relevance to him to quit, Risks of tobacco use, Rewards, repetition, Roadblocks to quit).

- Unless contraindicated, pharmacotherapy for tobacco cessation and nicotine replacement therapy should be prescribed to people who want to quit and where available patient should be referred to cessation clinics.

- Reduction of exposure to occupational dusts, indoor and outdoor air pollutants, use of nonpolluting cooking stoves should be advised as well.

5.2 Vaccination:

- Influenza vaccination yearly to decrease incidence of lower respiratory infections leading to exacerbations and hospitalizations
- Pneumococcal vaccinations, PCV13 and PPSV23, are recommended for all COPD patients ≥ 65 years of age

5.3 Pharmacologic therapy

Treatment is targeted to reduce symptoms, including the frequency and severity of exacerbations, improve exercise tolerance and health status of the patient. Pharmacotherapy once started can be stepped up or stepped down based on the presence of the symptoms and continued occurrence of exacerbations. Treatment should be individualized and guided by:

- the severity of symptoms and risk of exacerbations
- side-effects
- comorbidities
- drug availability and cost and
- the patient's response and ability to use various drug delivery devices

MEDICATIONS USED TO TREAT COPD

5.3.1 Bronchodilators

- Inhaled bronchodilators are effective for symptom management and given on a regular basis to reduce symptoms.

- Inhaled LABA (eg: formoterol, salmeterol and indacaterol) and LAMA (eg: tiotropium and glycopyrronium) are preferred over short acting agents except for patients with occasional dyspnoea

- Regular and as needed SAMA or SABA also improves FEV1 and symptoms and combination of both are superior than either given alone and can be given for those with occasional dyspnoea

- Patients may be started on single (LAMA preferred) or dual Long-acting bronchodilator therapy (LABA+LAMA)

5.3.2 Anti-inflammatory Agents

- Long term treatment with ICS in combination with LABA + LAMA may be considered for patients with a history of exacerbations despite appropriate treatment with long-acting bronchodilators.

- Triple inhaled therapy of LABA+LAMA+ICS improves lung functions and reduces exacerbations and has a beneficial effect on mortality in those with frequent and severe exacerbations.

- Factors in strong support of initiating ICS in combination with LABA +LAMA are:
    - ≥2 moderate exacerbations per year
    - history of hospitalization
    - concomitant asthma
    - blood eosinophil count >300 cells /uL

- Long term monotherapy with ICS or oral corticosteroids (OCS) should not be given. OCS play a role in management of acute exacerbations.

- In patients with chronic bronchitis, severe COPD and history of exacerbations despite LABA+LAMA+ICS, the addition of a PDE4 inhibitor can be considered which improves lung function and decreases exacerbations.

5.3.3 Prophylactic Antibiotics

- In reformed smokers with frequent exacerbations resulting in hospitalizations, despite optimal therapy, macrolides in particular azithromycin, can be considered (usually 250 mg/ day or 500 mg 3 times a week) or erythromycin (250mg 2 times per day) for one year.

- Factors of bacterial resistance, prolonged QTc interval and impaired hearing should be considered with azithromycin.

- Before starting prophylactic antibiotic ensure that:

- the patient has had a sputum culture and sensitivity, including tuberculosis culture, to identify other possible causes infection that may need specific treatment (for example, antibiotic-resistant organisms, atypical mycobacteria or Pseudomonas aeruginosa)
- patient has training in airway clearance techniques to optimize sputum clearance
- a CT scan of the thorax to rule out bronchiectasis and other lung pathologies.

5.3.4 Methylxanthines

- Theophylline is the most used methylxanthine. It is not recommended as first line therapy in COPD. It has a dose related toxicity with a narrow therapeutic window and a wide range of toxic effects and most of the benefit occurs, when near toxic doses are given.

- Theophylline can be used:
    - as an alternative in patients noncompliant with inhalers for any reason
    - as an add-on therapy in patients continuing to have symptoms despite optimum inhaled therapy.

- Caution should be used when using theophylline in older people, because of differences in pharmacokinetics, the increased likelihood of comorbidities and interactions with other medications being used.

5.3.5 Mucolytics

- Routine use of mucolytic agents is not recommended but treatment with mucolytics such as carbocysteine and N-acetyl cysteine has shown to reduce risk of exacerbations in selected populations like those not on ICS.

5.3.6 Delivery systems

- Bronchodilator therapy is best administered using an inhaler. Provide an alternative inhaler if a person cannot use a particular one correctly or it is not suitable for them.

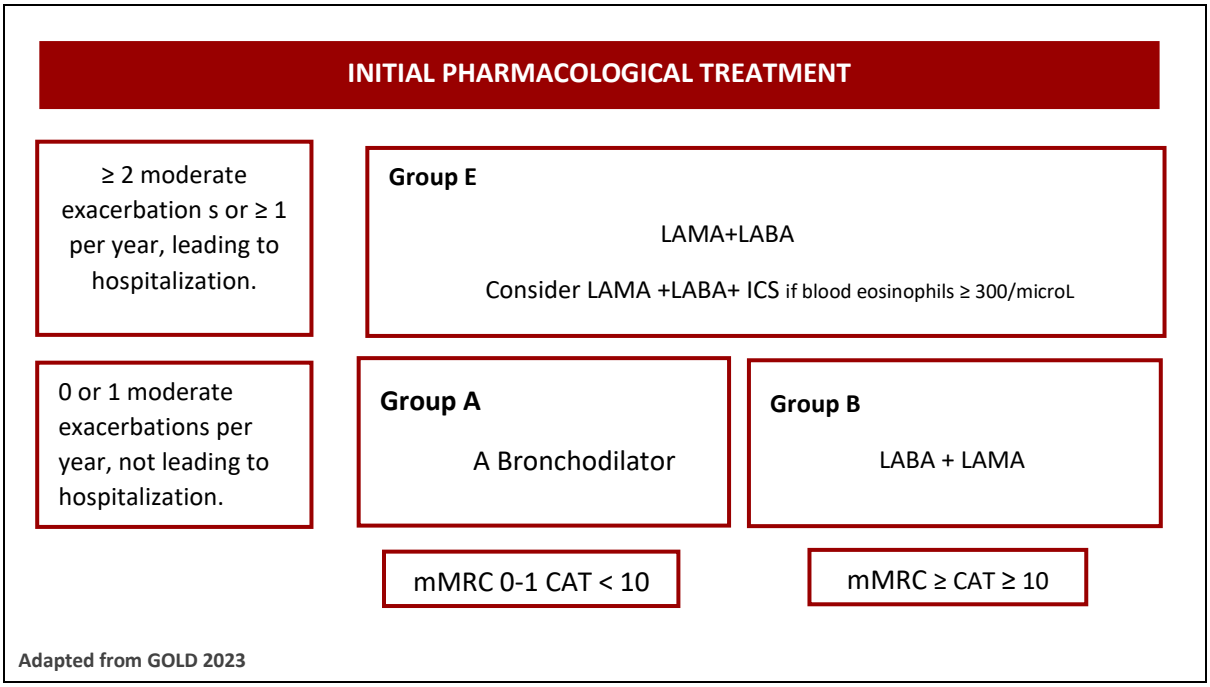
- Prescribe inhalers after patients have been trained to use them and can demonstrate correct technique. Inhaler technique should be regularly assessed at each visit and corrected if needed.

- Provide a spacer that is compatible with the person's metered-dose inhaler and advise people on how to use a spacer with a metered-dose inhaler.
  Teach to administer the drug by single actuations of the inhaler into the spacer, inhaling after each actuation and there should be minimal delay between inhaler actuation and inhalation.

<table>
<tr><th colspan="2">COMMONLY USED AND AVAILABLE MEDICATONS FOR COPD</th></tr>
<tr><td colspan="2">Drug Name</td></tr>
<tr><td colspan="2">BETA2 AGONISTS</td></tr>
<tr><td>SABA:
Salbutamol
Fenoterol
Levalbuterol
Terbutaline</td><td>LABA:
Formoterol
Salmeterol
Indacaterol</td></tr>
<tr><td>ANTI CHOLINERGIC</td><td></td></tr>
<tr><td>SAMA:
Ipratropium bromide</td><td>LAMA:
Tiotropium
Glycopyrronium bromide
Glycopyrrolate</td></tr>
<tr><td>Combination SABA/SAMA
Fenoterol/ipratropium
Salbutamol/Ipratropium</td><td>Combination LABA/LAMA
Indacaterol/glycopyrronium
Formoterol/glycopyrronium</td></tr>
<tr><td colspan="2">Methylxanthines
Aminophyline
Theophylline (SR)</td></tr>
<tr><td colspan="2">Combination LABA/ICS
Formoterol/beclomethasone
Formoterol/budenoside
Formoterol/mometasone
Salmeterol/fluticasone propionate</td></tr>
<tr><td colspan="2">Combination LABA/LAMA/ICS
Beclometasone/formoterol/glycopyrronium
Budenoside/formoterol/glycopyrrolate</td></tr>
<tr><td colspan="2">Phosphodiesterase-4 inhibitors
Roflumilast</td></tr>
<tr><td colspan="2">Mucolytic agents
N-acetylcysteine
carbocysteine</td></tr>
</table>

5.4 Initiation of therapy

Initial pharmacological treatment is to be based on the patients GOLD group based on the level of symptoms and risk of exacerbations following the ABE assessment tool.



Group A:

- Treatment should be initiated in all group A patients with either a short or long-acting bronchodilator (long acting preferred) based on its effect on breathlessness and to be continued

Group B:

- Initial therapy should be a combination LABA + LAMA.

Group E:

- Initial therapy of a combination of LAMA +LABA
- Use of LABA+ICS not encouraged in COPD and if there is an indication to use an ICS, then LABA+LAMA+ICS is preferred.
- In patients with eosinophil count ≥ 300 cells/uL, consider treatment with LABA+LAMA+ICS
- Treat COPD patients, with concomitant asthma like asthma and ICS should be used in these patients.

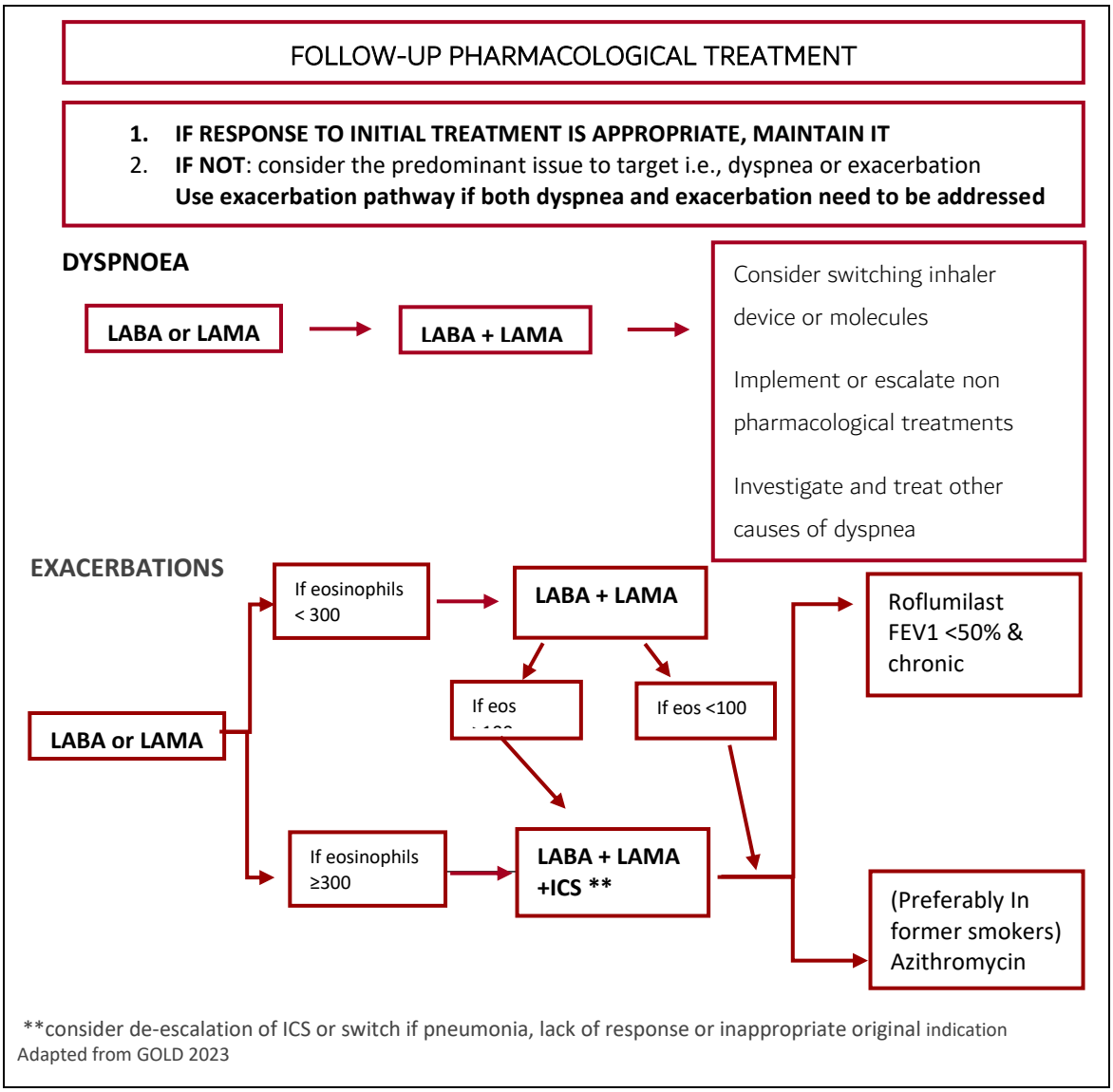
5.5 Follow-up pharmacological treatment

After initiation of therapy, patients should be:

- Reviewed for response to treatment ie symptom control.
- All patients should be assessed for adherence to treatment and the inhaler technique.
- Adjustments in medication, treatment escalation or switching the inhaler device or medicine may be needed after assessing the patient. De-escalation should be considered if there are side effects of therapy or if no clinical benefit or resolution of symptoms requiring less therapy. Following these, the patient should again be reviewed.

The follow up treatment pathway is separate from the initial one and facilitates management of patients on maintenance therapy addressing the predominant issues ie dyspnoea and exacerbations. Once reviewed and assessed, then the corresponding pathway for dyspnoea and/ 0or exacerbations in the follow up pathway should be used.

For those who patients who require a change in treatment due to both dyspnoea and exacerbation, the exacerbation pathway in the algorithm should be selected.



Patients with predominant or persistent Dyspnoea

- For those patients on long-acting bronchodilator (LABA or LAMA) monotherapy, Use two long-acting bronchodilators (LABA +LAMA)
- If addition of a 2nd bronchodilator does not improve symptoms, consider switching inhaler device or molecules.
- In all cases, investigate for other causes of dyspnoea and treat accordingly.

Patients with predominant Exacerbations

- In patients on long-acting bronchodilator monotherapy (LAMA or LABA), escalate to LABA+LAMA.
- In patients with exacerbations on LABA +LAMA therapy, escalate to LABA+LAMA+ICS therapy. Benefits of ICS treatment can be observed if blood eosinophil counts ≥ 100 cells/μL

Patients on LABA+LAMA+ICS with exacerbations, or those with blood eosinophils < 100 cells/μL:

- Add roflumilast: Consider in COPD patients with FEV_1 < 50% predicted and chronic bronchitis, particularly if at least one hospitalization for an exacerbation in the previous year despite triple inhaled therapy. Treatment with roflumilast should be started by a specialist in respiratory medicine.

- Add macrolide. The best available evidence exists for the use of azithromycin, especially in those who are not current smokers.

- Stopping ICS: Consider withdrawing ICS if there are no exacerbations over a year. In addition, ICS should be withdrawn if there are adverse effects or recurrent pneumonia. A blood eosinophil count ≥ 300 cells /μL identifies patients with the greatest likelihood of experiencing more exacerbations after ICS withdrawal and who subsequently should be followed closely for relapse of exacerbations.

If a COPD patient with no features of asthma is on LABA+ICS for whatever reason, if symptoms are well controlled, continuation of it is an option. If patient has major symptoms switching to LABA+ LAMA should be considered.

But if the patient has further exacerbations, treatment should be escalated to LABA+ LAMA +ICS if blood eosinophil count ≥ 100 cells /μL or change to LABA +LAMA if blood eosinophil count < 100 cells /μL

5.6 Other Non-Pharmacological Therapy

5.6.1 Oxygen therapy and Ventilatory support in stable COPD

- Be aware that inappropriate oxygen therapy in people with COPD may cause respiratory depression.

- Assess for need of long-term oxygen therapy by measuring arterial blood gases on 2 occasions at least 3 weeks apart, in people who have a confident diagnosis of COPD, and are receiving optimum medical management and whose COPD is stable.

- Assess the need for oxygen therapy in people with:
    - very severe airflow obstruction (FEV1 < 30% predicted)
    - cyanosis
    - polycythemia
    - peripheral oedema
    - raised jugular venous pressure
    - oxygen saturations of 92% or less breathing air
    - Also consider assessment for people with severe airflow obstruction (FEV1 30–49% predicted

- Long-term oxygen therapy is indicated for stable patients with severe resting hypoxemia who have:
    - PaO_2 ≤ 7.3 kPa (55 mmHg) or SaO_2 ≤ 88%, with or without hypercapnia confirmed twice over a three-week period or
    - PaO_2 between 7.3 kPa (55 mmHg) and 8.0 kPa (60 mmHg), or SaO_2 of 88%, if there is evidence of pulmonary hypertension, peripheral oedema suggesting congestive cardiac failure, or polycythaemia (haematocrit > 55%).

- Advise people who are on long-term oxygen therapy that they should breathe supplemental oxygen for a minimum of 16 hours per day and titrate to keep SaO2 ≥ 90%

- Once placed on long-term oxygen therapy (LTOT) the patient should be re-evaluated after 60 to 90 days with repeat arterial blood gas (ABG) or oxygen saturation while inspiring the same level of oxygen or room air to determine if oxygen is still indicated
- People who are having long-term oxygen therapy should be reviewed at least once per year by healthcare professionals familiar with long-term oxygen therapy

- In patients with stable COPD and resting or exercise induced moderate desaturation, LTOT should not be routinely prescribed

- NIV may be considered for decreasing morbidity and mortality in patients with severe chronic hypercapnia with a history of recurrent hospitalization for acute respiratory failure requiring NIV during the acute episode. The choice of the machine for NIV depends on the presence of coexistent sleep apnea syndromes. Patient should be referred to Pulmonology for management.

5.6.2 Education and self-management

- Health education including self-management should be a part of COPD management to motivate and engage patients to take greater responsibility for their health and increase ability to better cope with illness.

- Patients should receive information/education on:
    - aspects of medical treatment, strategies to minimize symptoms, advice on when to seek help and making decisions in exacerbations
    - Risks of smoking and benefits of quitting and cessation strategies
    - Nutrition and physical activity
    - Breathing strategies
    - Inhaler Use
    - Palliative care

5.6.3 End-of-life and palliative care

- The goal of palliative care is to relieve the suffering of patients and their families by the comprehensive assessment and treatment of physical and psychosocial symptoms experienced by patients.

- When appropriate, use opioids, benzodiazepines, tricyclic anti-depressants and oxygen to relieve breathlessness in end stage COPD

- Clinicians should help patients and their families to make informed choices that are consistent with patients' values and end of life care discussions with patients and their families should include their views on intensive care, resuscitation and invasive ventilation

5.6.4 Interventional Bronchoscopy and surgery in stable COPD

- In selected patients with a large bulla, occupying at least one third of the hemi thorax surgical bullectomy may be considered.

- In appropriately selected patients with very severe COPD and breathlessness that affects their quality of life despite optimal medical treatment and without relevant contraindications, lung transplantation may be considered.

- In selected patients with severe emphysema and significant hyperinflation refractory to optimized medical care, bronchoscopy modes of lung volume reduction (e.g., endobronchial one-way valves, lung coils or thermal ablation) may be considered but these therapies are not widely available in many countries.

  Lung volume reduction surgery can be considered in selected patients with upper lobe emphysema,

6.0 Monitoring and Follow up.

COPD patients require regular follow up and at each follow up visit, the patient should be assessed for:

- the smoking status and should encourage smoking cessation
- Symptoms including activity limitation and sleep
- Exacerbations, frequency, severity and likely cause of exacerbation
- Doses and effectiveness of the current medication
- Any side effects of medication
- Adherence to medicines
- Inhaler technique

If there is clear and significant worsening of symptoms a chest Xray may be indicated. Patient should also be monitored for comorbid conditions like heart failure and anxiety.

7.0 Referral for Specialist advice

When clinically indicated, patients should be referred for specialist advice. Referral may be appropriate at all stages of the disease and not solely in the most severely disabled patients.

Indications for specialist referral may include

- Spirometry – All suspected COPD patients should be offered Spirometry
- Diagnostic uncertainty
- Onset of corpulmonale
- Severe advanced COPD
- Assessment for oxygen therapy
- Bullous lung disease
- A rapid decline in FEV1
- Assessment for pulmonary rehabilitation
- Assessment for lung transplantation
- Symptoms disproportionate to lung function deficit
- Hemoptysis

8.0 Exacerbation of COPD

- An exacerbation of COPD is defined as an acute event characterized by sustained worsening of the patient's respiratory symptoms from their usual stable state that requires additional therapy.
- Exacerbations can be precipitated by several factors of which the most common are respiratory tract infections. COPD exacerbations are classified as:

    - Mild: treated with short acting bronchodilators only, SABDs
    - Moderate: treated with SABDs plus antibiotics and/or oral corticosteroids
    - Severe: patient requires emergency care and /or hospitalization and may also be associated with acute respiratory failure.

- The severity of the exacerbation during hospitalization is based on the clinical presentation of the patient. Patients may have:
    - No respiratory failure:
        - Respiratory rate of 20-30 breaths/minute
        - No use of accessory respiratory muscles
        - Hypoxemia improves with supplemental oxygen given via venturi mask 28-35% inspired oxygen (FiO2), with no increase in PaCO2 and
        - No changes in mental status

    - Acute respiratory failure but non-life-threatening:
        - Respiratory rate> 30 breaths/minute
        - Use of accessory respiratory muscles
        - No change in mental status
        - Hypoxemia improved with supplemental oxygen via Venturi mask 24-30% FiO_2; hypercarbia i.e., $PaCO_2$ increased compared with baseline or elevated 50-60 mmHg.

    - Acute life-threatening respiratory failure:
        - Respiratory rate > 30 breaths per minute

- Use of accessory respiratory muscles
- Acute changes in mental status

-Hypoxemia not improved with supplemental O2 via Venturi mask or requiring FiO2> 40%; hypercarbia i.e., PaCO2 increased compared with baseline or elevated > 60 mmHg or

- the presence of acidosis (pH ≤ 7.25)

8.1 Potential indications for hospitalization in exacerbation of COPD

- Severe symptoms such as sudden worsening of resting dyspnea, high respiratory rate >30/min and use of accessory respiratory muscle
- Decreased oxygen saturation <90%
- Systolic BP <90mmHg
- Altered sensorium including confusion or drowsiness
- Acute respiratory failure
- Onset of new physical signs e.g.: cyanosis, peripheral edema
- Failure of the exacerbation to respond to initial management
- Presence of serious comorbidities such as heart failure, arrhythmia
- Social reasons such as insufficient home care and support

8.2 Management of COPD exacerbations

- Assess severity of symptoms, perform pulse oximetry and administer supplemental oxygen therapy to correct hypoxemia with a target saturation of 88-92%

- Obtain serial blood gases where available, to ensure oxygenation, without CO2 retention and worsening acidosis.

- Administer SABA (salbutamol) with or without SAMA (Ipratropium) via air driven nebulizer or inhaler with spacer. Nebulized salbutamol at a dose of 2.5mg every 20 minutes or MDI

100mcg every 20 minutes for 1 hour. Further dosing will be based on the clinical response, generally every 4-6hours.

- If additional bronchodilatation is required, a combination of ipratropium (500mcg nebulized or 20 mcg 2-4 puffs with MDI) and salbutamol (2.5 mg nebulized or salbutamol MDI 100 mcg 2-4 puffs) every 4-6 hours can be used.

- A short course of systemic corticosteroids, a dose of 40mg prednisone or equivalent per day for 5-7 days. Nebulized budesonide is an alternative.
  Intravenous steroids should be given in patients who are being mechanically ventilated or cannot tolerate oral medication.

- Consider Antibiotics, when indicated such as signs of bacterial infection as increase in sputum volume and sputum purulence or require ventilation. The duration of therapy should be 5-7 days.
  Usual initial empirical treatment can be with amoxicillin/clavulanate or macrolide or doxycycline or second-generation cephalosporin or guided by most recent sputum culture susceptibilities.

- Send investigations including chest radiograph, blood count, Urea and electrolytes and send a blood culture if the person is febrile. Record an ECG to exclude cardiac comorbidities

- Sputum cultures should be sent, especially in those with frequent exacerbations and/or those requiring ventilation as resistant organisms to empirical antibiotics or gram-negative bacteria like pseudomonas may be present.

- At all times monitor fluid balance and treat associated conditions/ comorbidities

- Consider Subcutaneous heparin or LMWH for thromboembolism prophylaxis

- Maintenance therapy with long-acting bronchodilators should be initiated as soon as possible before hospital discharge.

- Use of routine Intravenous theophylline are not recommended due to increased side effect profiles

- Some patients may require immediate admission to ICU and may require ventilatory support for respiratory failure.

  Non-invasive mechanical ventilation (NIV) should be the first mode of ventilation if needed and should be used early in the management of respiratory failure It improves gas exchange, reduces the need for intubation, decreases hospitalization duration and improves survival. Once patients can tolerate 4 hours of unassisted breathing, NIV can be directly discontinued without any weaning period.

8.2.1 Indications for ICU Admission

- Severe dyspnoea that responds inadequately to initial emergency therapy
- Persistent or worsening hypoxemia PaO2 40mmHg and /or severe worsening of respiratory acidosis pH<7.25 despite supplemental oxygen and NIV
- Changes in mental status
- Need for invasive ventilation
- Hemodynamic instability

8.2.2 Indications for NIV

- Respiratory acidosis ($PaCO_2 \geq 6.0kPa$ or 45mmHg and arterial $pH \leq 7.35$)
- Severe dyspnoea with clinical signs of respiratory muscle fatigue, increased work of breathing or both
- Persistent hypoxemia despite supplemental oxygen therapy

8.2.3 Indications for invasive mechanical ventilation

With the availably of NIV, the need for invasive ventilation has significantly decreased. Invasive ventilation us indicated in:

- Unable to tolerate NIV or NIV failure
- Status post respiratory or cardiac arrest
- Massive aspiration or persistent vomiting
- Life threatening hypoxemia in patients unable to tolerate NIV
- Severe ventricular or supra ventricular arrhythmias
- Persistent inability to remove respiratory secretions
- Diminished consciousness, psychomotor agitation inadequately controlled by sedation

8.2.4 Discharge planning and follow up

In general, patient should be clinically stable for at least 24-48 hours, eat and sleep well with minimal requirements for SABA. The patient should be discharged after:

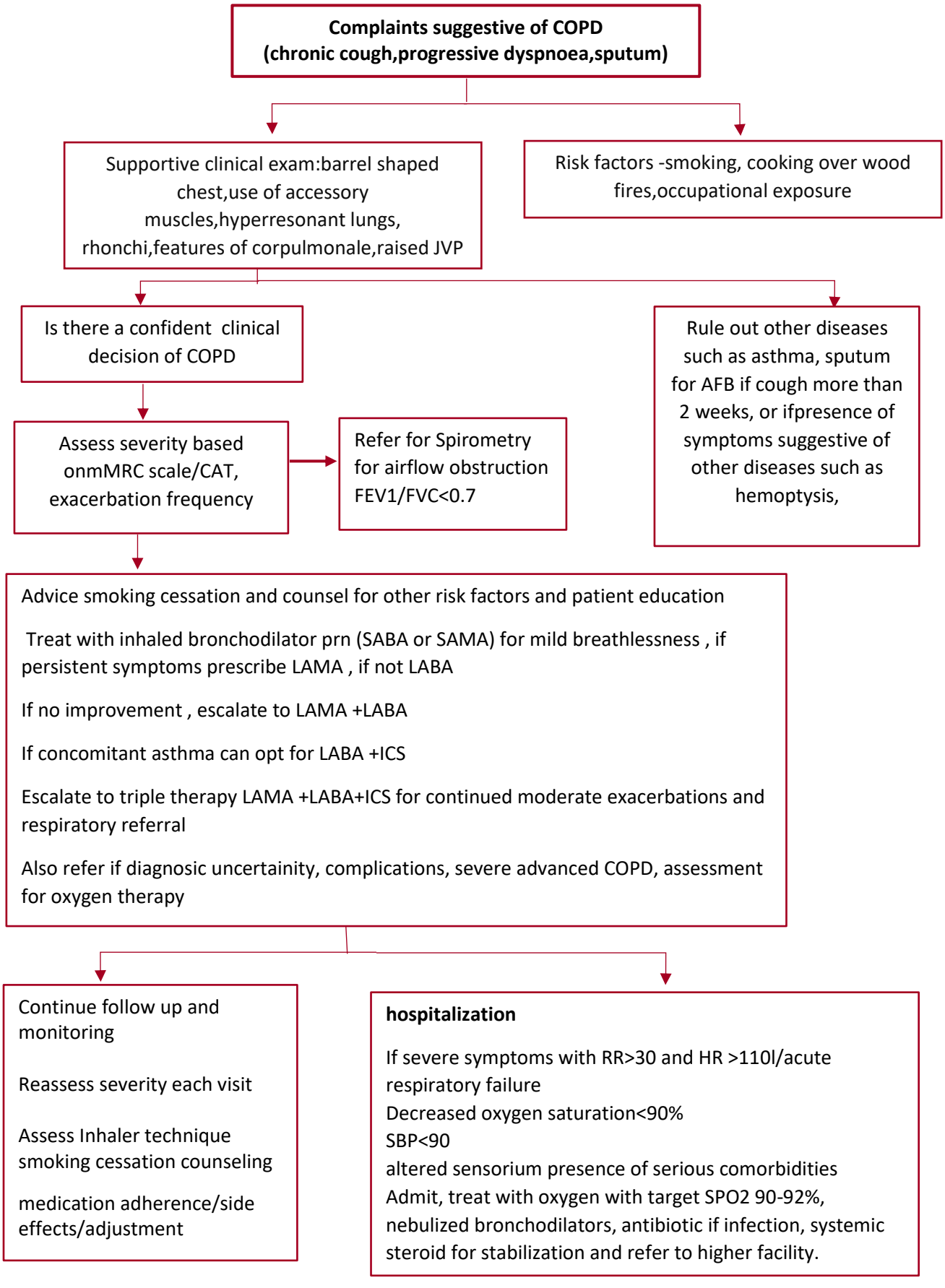
- Full review of all clinical and laboratory data done prior to discharge
- All clinical and investigation abnormalities have been identified and addressed
- Assessed for any need of continuing any oxygen therapy.
- Reassessed inhaler technique
- Withdrawal of acute medicines and optimization of maintenance medicines
- Provide a management plan for comorbidities and follow up.
- Ensure follow up arrangements, early follow up 4-6 weeks.

At Follow up:

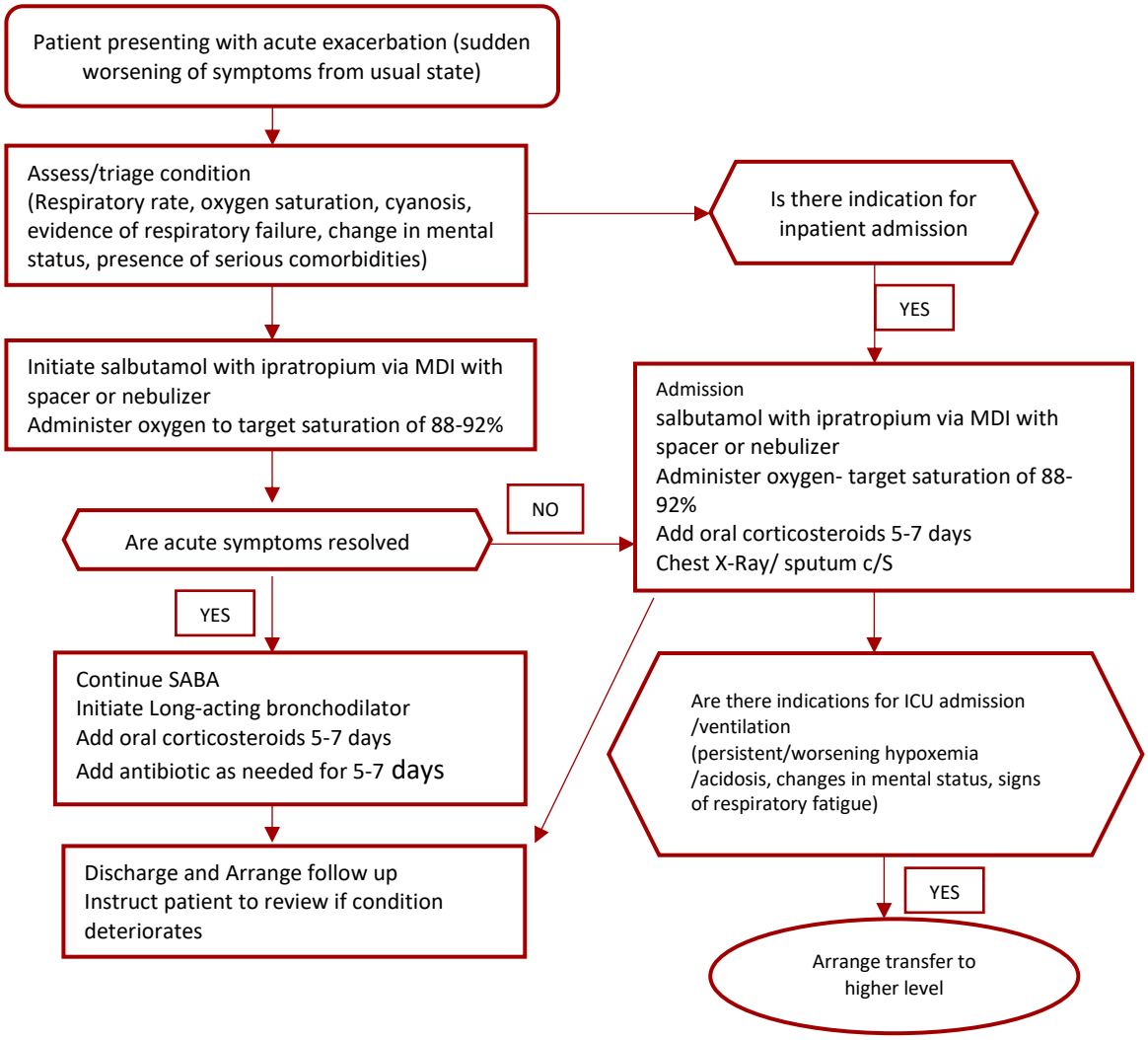
- Evaluate ability to cope in the patient's usual environment
- Document symptoms (MMRC /CAT)
- Review the treatment regimen
- Re assess inhaler technique
- Emphasis on smoking cessation
- Reassess need for long term oxygen
- Evaluate status of comorbidities

9.0 Algorithms

9.1 Management of COPD in primary care



9.2 Management of COPD exacerbation in primary care



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