Course Content: Management of Chronic Obstructive Pulmonary Disease (COPD)

Abbreviations

BMI: Body Mass Index

BODE: BMI, Obstruction, Dyspnea, and Exercise

CAT™: COPD Assessment Test

CB: chronic bronchitis

CCQ©: The COPD Control Questionnaire

CI: confidence interval

COPD: Chronic Obstructive Pulmonary Disease

COVID-19: coronavirus disease

CT: computed tomography

CV: cardiovascular

DPI: dry powder inhaler

GOLD: Global Initiative for Chronic Obstructive Lung Disease

HFNT: high flow nasal therapy

HRCT: high-resolution CT

HR: hazard ratio

ICS: inhaled corticosteroid

FEV1: forced expiratory volume of air in 1 second

FVC: forced vital capacity (the total volume of air exhaled during FEV test)

HFA: hydrofluoroalkane

LABA: long-acting beta2 agonist

LAMA: long-acting muscarinic antagonist

LDCT: low-dose CT

LMIC: low-middle income countries

LTOT: long-term oxygen therapy

MDI: metered dose inhaler

mMRC: modified Medical Research Council

NNH: number needed to harm

NPPV: noninvasive positive pressure ventilation

OR: odds ratio

PaCO2: arterial carbon dioxide pressure

PaO2: arterial oxygen pressure

PRISm: Preserved Ratio Impaired Spirometry

NRT: nicotine replacement therapy

RR: relative risk

SARS-CoV-2: severe acute respiratory syndrome coronavirus 2

SABA: short-acting beta2 agonist

SAMA: short-acting muscarinic antagonist

SaO2: arterial oxygen saturation

SMI: soft mist inhaler

Tdap, dTaP, dTPa: tetanus, diphtheria, and pertussis

TR: trajectory

VA/Q: ventilation-perfusion

VHC: valved holding chamber

Background

COPD is a preventable and treatable heterogeneous lung condition.

COPD respiratory symptoms are caused by airway and/or alveoli abnormalities that cause persistent, often progressive, airflow obstruction.

Key risk factors include tobacco smoking, outdoor, occupational, and household air pollution (burning of wood and other biomass fuel).

Morbidity may be influenced by concomitant conditions (e.g., CV disease, musculoskeletal impairment, diabetes mellitus).

Statistics Overview

COPD is one of the leading cause of morbidity and mortality worldwide.

Specifically, COPD is the 3rd leading cause of death worldwide (3.23 million deaths in 2019).

90% of deaths occur in low- and middle-income countries.

Global prevalence is estimated at 10.3% (11.8% men, 8.5% women) with an estimated 3 million COPD-related deaths annually.

Tobacco smoking accounts > 70% of COPD cases in high-income countries.

The risk of mortality from COPD increases significantly in the first year after hospital readmission within 30 days [HR 2.48, 95% CI 1.10–5.59].

Introduction

Airway (bronchitis, bronchiolitis) and/or alveolar (emphysema) abnormalities

Non-fully reversible airflow limitation

- FEV1/FVC < 0.7 post-bronchodilation
- Measured by spirometry confirms diagnosis

Symptoms

- Dyspnea
- Cough
- Sputum production
- Exacerbations

In rare cases, patients may be found to have ?-1 antitrypsin deficiency.

Pre-COPD and PRISm

Pre-COPD

- Respiratory symptoms
- And/or structural lung lesions (e.g., emphysema)
- And/or physiological abnormalities (e.g., low-normal FEV1, gas trapping, hyperinflation, reduced lung diffusing capacity and/or rapid FEV1 decline)
- **Without** airflow obstruction (FEV1/FVC ≥ 0.7 post-bronchodilation)

PRISm (Preserved Ratio but Impaired Spirometry)

- Normal ratio but abnormal spirometry.
- There is currently no evidence on best treatment.

Pathological Changes

The normal response to chronic irritants is altered and may be partially genetically determined.

Increased inflammatory macrophages and other cells release mediators

- Attract inflammatory cells (chemotactic factors)
- Amplify inflammation (proinflammatory cytokines)
- Induce structural changes (growth factors)

Oxidative stress can also contribute.

Although increased eosinophils and type 2 innate lymphoid cells are more prevalent with asthma, some patients with COPD have a similar pattern.

Imbalance in the lungs between proteases (break down connective tissue components) and antiproteases.

Other possible changes

- Peribronchiolar fibrosis
- Interstitial opacities
- Excessive production of growth factors
- Altered lung vasculature

Pathophysiology

Airflow obstruction (measured by spirometry) is caused by

- Small airway disease (increases airway resistance)
- Parenchymal destruction (emphysema, decreased elastic recoil of lung parenchyma)

Decreased number of small airways is due to either loss or underdevelopment.

Lung changes

- Limit emptying of lungs during forced expiration
- Decrease FEV1 and FEV1/FVC ratio
- Contribute to gas trapping and lung hyperinflation

Static lung hyperinflation (loss of elastic recoil)

- Reduces inspiratory capacity
- Commonly associated with hyperinflation during exercise
- Results in airflow limitation, exertional dyspnea, and limited exercise capacity.

Lung hyperinflation can impair respiratory muscle contractility.

Exacerbations

Can be triggered by infections, pollutants, or unknown factors.

Increased airway and systemic inflammation, increased gas trapping, hyperinflation with reduced expiratory flow.

Increased dyspnea, worsening of VA/Q abnormalities.

Can result in arterial hypoxemia with or without hypercapnia.

Can coexist or be confused with other conditions (e.g., pneumonia, heart failure, pulmonary failure).

Other Abnormalities

Pulmonary gas exchange

- Structural abnormalities alter VA/Q distributions lead to arterial hypoxemia.
- Possible influence of reduced ventilatory drive (e.g., from sedative/hypnotic medications) leads to hypercapnic respiratory failure and acidosis.
- Parenchymal destruction leads to decreased lung diffusing capacity.

Pulmonary hypertension

- May develop late in COPD from loss of pulmonary capillary bed due to emphysema or hypoxic vasoconstriction of the small pulmonary arteries.
- May progress to right ventricular hypertrophy/right sided heart failure.

Comorbidities

- Airflow obstruction and hyperinflation can affect cardiac function.
- Inflammation can contribute to wasting, cachexia, ischemic heart disease, heart failure, osteoporosis, anemia, diabetes, and metabolic syndrome.

Risk Factors - Cigarette Smoking

In high income countries, tobacco smoking is the leading risk factor for COPD (accounting for > 70% of cases).

Individuals who smoke cigarettes have a greater rate of FEV1 decline and rate of COPD mortality than those who do not smoke.

Other types of tobacco (e.g., pipe, cigar, water pipe) and marijuana are also risk factors for COPD.

Passive smoke exposure can contribute to respiratory symptoms and COPD.

Worldwide, fewer than 50% of smokers develop COPD (it is estimated that half of COPD cases are due to risk factors other than tobacco).

A variety of environmental exposures influence COPD risk.

Risk Factors- Non-smoking COPD

May exhibit different clinical features/trajectories, may benefit from different treatment compared to smoking-associated COPD.

Currently, no randomized controlled trials have addressed non-smoking COPD.

Few studies reviewed non-smoking COPD characteristics (vs. smoking COPD):

- More common in females and younger age groups
- Similar or milder symptoms and quality of life
- Slower lung function decline over time
- Lower sputum neutrophils with a trend towards higher eosinophils
- Similar spirometry
- Greater small airway obstruction
- Less emphysema
- Similar effect on macrophage phagocytosis of pathogenic bacteria

Risk Factors - Biomass Exposure

In LMIC, smoking contributes to 30-40% of the total COPD burden.

Non-smoking factors comprise over 50% of the burden of COPD in LMIC.

Household air pollution exposure (wood, animal excrement, crop residues, and coal burned in open fires or poorly functioning stoves) is associated with an increased risk of developing COPD in LMIC.

Many of the environmental exposures in LMIC are unregulated. The risk for airway/lung damage is amplified combined with poverty and poor nutrition.

Risk Factors - Occupational Exposures

Include organic and inorganic dust, chemical agents and fumes.

Examples from studies of never smokers without asthma who developed COPD include occupations such as sculptors, gardeners, warehouse workers.

The American Thoracic Society concluded occupational exposures account for 10-20% of symptoms or functional impairment consistent with COPD.

Less regulated areas of the world are likely to have a much higher risk.

Risk Factors - Air Pollution

Particulate matter, ozone, nitrogen or sulfur oxides, heavy metals, other greenhouse gases.

Responsible for about 50% of COPD risk in LMICs.

In never smokers, air pollution is the leading risk factor for COPD.

There are "safer" thresholds; the more exposure, the higher the risk:

- Chronic exposure to particulate matter 2.5 and nitrogen oxides
- Significantly impairs lung growth in children
- Accelerates lung function decline in adults
- Increases risk for COPD in those without risk factors
- Increases risk of exacerbations, hospitalizations, and mortality from COPD

?-1 Antitrypsin Deficiency

The most relevant but rare genetic risk factor are mutations in Serpin Family A Member 1 gene that lead to ?-1 antitrypsin deficiency.

?-1 antitrypsin is a major circulating inhibitor of serine proteases.

Recent sibling studies indicate no increased risk in heterozygous patients in the absence of smoking.

Many other genetic variants have been found to be associated with increased COPD risk, but their effect size is estimated to be small and information regarding their association remains unclear.

Lung Function Trajectories

During adulthood, lung function plateaus and then declines mildly due to physiological lung aging.

"Young COPD" is defined as COPD in patients 20-50 years of age.

Pre-COPD: individuals of any age who have respiratory symptoms and/or structural/functional abnormalities, without airflow obstruction on forced spirometry. May or may not develop COPD over time.

PRISm: preserved ratio but impaired spirometry, can change to either normal or obstructed spirometry over time.

Early COPD: near the beginning of the process.

Mild COPD: describes severity of obstruction measured by spirometry (can occur at any age and progress at any rate).

Chronic Bronchitis

Cough with expectorated sputum during a defined timeframe (e.g. at least 3 months per year for 2 consecutive years) in the absence of other conditions

Primary risk is smoking, but 4-22% is found in never smokers (dust, biomass fuels, chemical fumes, domestic heating and cooking fumes may be important)

Gastroesophageal reflux is also associated with increased incidence

In young adults with normal lung function without asthma, chronic cough with sputum increases risk of developing COPD independently of smoking.

In adults younger than age 50, CB without airflow limitation increases susceptibility to long-term COPD risk and mortality.

The longer mucus hypersecretion is present, the greater the FEV1 reduction.

The strongest association has been seen with mucin polymer 5AC.

Proposed COPD Taxonomy

Criteria for COPD Diagnosis

Symptoms

- Dyspnea (progressive over time, worse with exercise, persistent)
- Recurrent wheezing
- Chronic cough (may be intermittent and unproductive, may eventually occur every day throughout the day)
- Sputum production
- Fatigue
- Weight loss, muscle mass loss, anorexia

History

- Recurrent lower respiratory tract infections
- Exposure to COPD risk factors

Spirometry: post-bronchodilator FEV1/FVC < 0.7 (mandatory for diagnosis)

Other Causes of Chronic Cough

Intrathoracic

- Asthma
- Lung cancer
- Tuberculosis
- Bronchiectasis
- Left heart failure
- Interstitial lung disease
- Cystic fibrosis
- Idiopathic cough

Extrathoracic

- Allergic rhinitis
- Postnasal drip

- Upper airway cough syndrome
- Gastroesophageal reflux
- Medication (e.g., angiotensin converting enzyme inhibitors)

Comorbidities

Assess for comorbidities which may influence COPD outcomes:

- CV disease
- Skeletal muscle dysfunction
- Metabolic dysfunction
- Osteoporosis
- Depression
- Anxiety
- Lung cancer
- Bronchiectasis
- Obstructive sleep apnea
- Gastroesophageal reflux disease
- Anemia

Differential Diagnosis

Spirometry

The most objective and reproducible measurement of airflow obstruction.

Role of spirometry in COPD

- Diagnosis
- Assessment of severity of airflow obstruction (for prognosis)
- Therapeutic decisions (pharmacological and non-pharmacological)
- Follow-up assessment
- Consideration of alternative or additional diagnoses
- Identification of rapid decline

Spirometry for Screening

Screening may be considered in patients with symptoms and/or risk factors, including but not limited to:

- Smoking > 20 pack-years
- Recurrent lung infections
- Early life events

Screening in patients with lower or other risk is less clear.

Data to support use of spirometry screening before onset of symptoms is weak.

Spirometry Process

1. **Have patient sit upright.**
2. **Place the clip on patient's nose.**
3. **Give patient plastic mouthpiece attached to spirometry machine.**
4. **Instruct patient to place lips tightly around the mouthpiece, then breathe in as big and as deep as possible, and then exhale as hard and fast as possible Continue to exhale until all breath is out.**
5. **Repeat 3 times**

Spirometry Recommendations

The administrator should be trained in technique and quality control and follow standard recommendations.

Patients should give maximal effort to avoid misdiagnosis.

The pause between inspiration and expiration should be less than 1 second.

The recording should continue until volume plateau, which can take > 15 seconds in severe disease.

FVC and FEV1 should be the largest values from 3 curves and should vary no more than 15% or 150 mL, whichever is greater.

Spirometry Considerations

Administer bronchodilator 10 to 15 minutes before spirometry

- 400 mcg short-acting beta2-agonist
- or 160 mcg short-acting anticholinergic
- or the 2 combined (check FEV1 30-45 minutes after)

Patients already on bronchodilator do not need to hold therapy.

Spirometry results are based on

- Age
- Height
- Sex
- Race

Postbronchodilator FEV1/FVC < 0.7 confirms non-fully reversible airflow obstruction.

Spirometry Cautions

Challenges using FEV1/FVC < 0.7

- May over-diagnose COPD in the elderly due to physical or other limitations
- May under-diagnose in young adults and patients with mild COPD

Lower limit of normal can be used, but no has yet to be validated by research.

Airflow obstruction that is not fully reversible is not specific for COPD (can also be found in asthma and other conditions). Consider clinical context and risk factors.

If FEV1/FVC 0.6-0.8, repeat spirometry on a separate occasion should be done to confirm presence or absence of airflow obstruction and COPD diagnosis.

Prospective Urban and Rural Epidemiological Study

International, community-based prospective study

Pre-bronchodilator spirometry study of 153,996 healthy people with < 5 pack-year histories in 17 countries

Not using relevant predicted values can over- or underestimate airflow obstruction severity.

Found lung function variation around the world. Compared to North America or Europe, FEV1 adjusted for height, age, and sex was:

- 31.3% (95% CI 30.8-31.8%) lower in south Asia
- 24.2% (23.5-24.9%) lower in southeast Asia
- 20.9% (19.9-22.0%) lower in sub-Saharan Africa
- 12.8% (12.4-13.4%) lower in east Asia
- 11.2% (10.6-11.8%) lower in the Middle East
- 5.7% (5.1-6.4%) lower in South America

Initial Assessment

Once COPD is diagnosed (FEV1/FVC < 0.7), assessment must combine:

- Airflow limitation severity (based on post-bronchodilator FEV1)
- Mild (GOLD 1): FEV1 ≥ 80% predicted
- Moderate (GOLD 2): 50% ≤ FEV1 < 80% predicted
- Severe (GOLD 3): 30% ≤ FEV1 < 50% predicted
- Very severe (GOLD 4): FEV1 < 30% predicted
- Current symptoms (nature and magnitude)
- Exacerbation risk: previous history of moderate and severe exacerbations
- Presence and type of risk factors and comorbidities

There is a weak correlation between airflow obstruction severity and symptoms or health status impairment. Therefore, formal symptom assessment with validated questionnaires is required.

Validated COPD Symptom Assessment Questionnaires

Dyspnea questionnaire (the mMRC scale): relates well to other multidimensional health status measures and predicts future mortality risk.

Multidimensional questionnaires:

- CAT™ and CCQ©: correlate closely to each other and suitable for clinic use
- Chronic Respiratory Questionnaire and St. George's Respiratory Questionnaire: important for research but too complex for practice

Cut-points (more severe COPD and/or treatment should be considered):

- mMRC ≥ 2
- CAT ≥ 10
- SGRQ ≥ 25

mMRC Scale

CHECK (ONE BOX ONLY) WHICH APPLIES TO YOU

qmMRC GRADE 0: I only get breathless with strenuous exercise

qmMRC Grade 1: I get short of breath when hurrying on the level or walking up a slight hill.

qmMRC 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.

qmMRC Grade 3: I stop for breath after walking about 100 meters or after a few minutes on the level.

qmMRC Grade 4: I am too breathless to leave the house or I am breathless when dressing or undressing.

CAT™

I never cough	0 1 2 3 4 5	I cough all the time
I have no phlegm (mucus) in my chest at all	0 1 2 3 4 5	My chest is completely full of phlegm (mucus)
My chest does not feel tight at all	0 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	0 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	0 1 2 3 4 5	I am very limited doing activities at home
I am confident leaving my home despite my lung condition	0 1 2 3 4 5	I am not at all confident leaving my home because of my lung condition
I sleep soundly	0 1 2 3 4 5	I don't sleep soundly because of my lung condition
I have lots of energy	0 1 2 3 4 5	I have no energy at all

GOLD ABE Assessment

- Used for initial pharmacologic treatment of COPD.
- The clinical relevance of exacerbations is independent of symptoms.
- Provides individualized assessment of symptoms plus exacerbation risk.
- Groups previously listed as C and D according to prior GOLD classification systems were combined into one Group E for 2023.

Additional Tests

More detailed evaluation may be needed

- Lung volumes
- Carbon monoxide diffusing capacity of the lungs
- Oximetry and arterial blood gas measurement
- Exercise testing and assessment of physical activity
- Chest x-ray
- CT
- ?-1 antitrypsin deficiency
- Composite score (e.g., BODE)
- Biomarkers (e.g., patients with blood eosinophil ≥ 300 cells/μL are at increased risk for exacerbations and are more likely to benefit from ICS)

Follow-up Clinical Assessments

Symptoms (using CAT and/or mMRC) and exacerbations since initial/last visit

Medication use and self-management progress

Smoking cessation / avoidance of irritants

Pulmonary rehabilitation

Comorbidities and risk factors

Vaccines

Other assessment

- History and physical exam
- Exercise capacity
- Health status and impact of breathlessness
- Inspiratory and expiratory muscle strength, lower limb strength
- Imaging if needed (e.g., worsening symptoms, purulent sputum)
- Patient goals and expectations
- LTOT if indicated
- Post-bronchodilator spirometry (at least yearly)

Pharmacologic Treatment Approaches

Smoking cessation

- Recommended for all patients with COPD (Evidence A)
- Pharmacotherapy plus counseling offers a high chance of success

COPD pharmacotherapy (bronchodilators, ICS, etc.) can improve

- Symptoms
- Exacerbations
- Lung function decline
- Mortality
- Health status
- Exercise tolerance

Vaccines should be administered as recommended for patients with COPD

- Reduce risk of serious illness
- Reduce risk of mortality

Non-pharmacologic Treatment Approaches

Pulmonary rehabilitation

- One of the most cost-effective strategies
- Improves dyspnea, health status, exercise capacity, anxiety and depression (Evidence A)
- Reduces hospitalization in those with recent exacerbation(s) (Evidence B).

Patient self-management

- Medication use, other treatments
- Managing risk factors
- Reducing exposure to irritants
- Stress management
- Lifestyle
- Breathing exercises/techniques
- Managing breathlessness
- Action plan

Additional Treatment Approaches

Other pharmacologic agents: roflumilast, azithromycin, mucolytics, theophylline, low-dose long-acting opioids, treatment of vitamin D deficiency

Individual patient factors should be evaluated for each patient's potential need for supplemental oxygen.

In some patients with ?-1 antitrypsin deficiency (esp. never or ex-smokers with FEV1 35%-60% predicted), intravenous augmentation therapy may slow the progression of emphysema.

In some patients with advanced refractory emphysema, surgery or bronchoscopic intervention may help.

In advanced COPD, palliative strategies can control symptoms.

Exacerbation Management

- Oxygen if hypoxemic
- NPPV if increased work of breathing or impaired gas exchange
- Bronchodilators
- Systemic corticosteroids in moderate to severe exacerbations
- Antibiotics for duration of 5 days when indicated
- Long-acting bronchodilators initiated as maintenance therapy prior to/upon discharge (inhaled corticosteroids added depending on blood eosinophil levels, prior therapy, and exacerbation history)

Investigative Therapies

Interleukin-5 agents:

- Preliminary data suggests benefit in patients with severe COPD, recurrent exacerbations, and eosinophilic inflammation.
- Further research is needed to confirm these findings.

Icenticaftor (new mucolytic class)

- Cystic fibrosis transmembrane conductance regulator potentiator
- Small, double-blind placebo-controlled study saw improvements in FEV1 and sputum bacterial colonization vs placebo

New bronchoscopic interventions proposed to reduce mucus hypersecretion.

HFNT nasally administered mixtures of humidified air-oxygen blends

- Flow rates of 20-60 L/min
- For patients with severe COPD on LTOT undergoing exercise training, HFNT may reduce respiratory muscle load and respiratory rate while increasing expiratory time.

Tele-rehabilitation (pulmonary rehabilitation using remote delivery platforms)

- Videoconference, phone, website with phone support, mobile application with feedback, centralized “hub”
- Studies included in-person exercise test at the center prior to commencement, found to be safe with similar benefits thus far.

Phase III trials of cryospray, rheoplasty, and targeted lung denervation technology for patients with refractory exacerbations and CB.

C-reactive protein or procalcitonin to guide antibiotic reduction.

Treatments Not Currently Recommended

Oral glucocorticoids

- Utility is mainly for acute exacerbations
- Long-term use has numerous adverse effects (Evidence A), with no evidence of benefit (Evidence C)

Statins and/or beta blockers for prevention of exacerbations are not recommended, unless otherwise needed for CV indications (Evidence A).

Antitussives are not recommended for COPD (Evidence C).

Drugs for primary pulmonary hypertension are not recommended for patients with pulmonary hypertension secondary to COPD (Evidence B).

Nedocromil and leukotriene modifiers (e.g., montelukast) have not been adequately tested in COPD and available evidence does not support their use.

There was no benefit, but evidence of harm including malignancy and pneumonia with infliximab in studies of moderate to severe COPD.

Smoking Cessation Overview

Tobacco dependence is a chronic condition that warrants repeated treatment until long-term or permanent abstinence is achieved.

Despite knowing they have COPD, about 40% of patients continue smoking.

Long-term quit success rates of 25% can be achieved with dedication.

Individual approaches and legislative bans can increase quit rates and reduce harm from second-hand smoke.

The "5 A's" of Smoking Cessation: Ask, Advise, Assess, Assist, Arrange

Counseling by Health Professionals

Counseling by physicians and other health professionals significantly improves chances of success compared to self-initiated strategies.

Even brief (3-minute) counseling can improve smoking cessation rates.

There is a strong dose-response relationship between the intensity of tobacco dependence counseling and its effectiveness.

Chances of cessation success increase with treatment intensity:

- Increased length of counseling session
- Increased number of treatment sessions
- Increased number of weeks over which treatment is delivered

Behavioral support plus pharmacotherapy increases success rates.

Sustained quit rates of 10.9% over 6 months have been achieved when clinician tutorials and feedback are linked to counseling sessions.

Financial incentives were found to be more effective than usual care in increasing smoking cessation rates at 6 months.

3 types of counseling found to be especially effective:

- Practical counseling
- Social support of family and friends as part of treatment
- Social support arranged outside of treatment

Literature on Counseling by Health Professionals

Smoking cessation rates compared to placebo

- Simple advice from a physician (RR 1.66; 95% CI, 1.42-1.94)
- Health professional counseling (OR 1.56; 95% CI, 1.32-1.84)

The Lung Health Study

- Randomized controlled trial of heavy smokers who were asymptomatic or mildly symptomatic
- Intervention: strong physician message plus 12 group sessions and nicotine gum administered during 10 weeks
- 14.5-year follow-up compared with nonintervention group (n = 1,964)
- Those randomly assigned to a smoking cessation intervention (n = 3,923) experienced a 15% reduction in all-cause mortality (8.83 vs. 10.38 per 1,000 person-years; *P* = .03)

Smoking Triggers

Examples of triggers

Stressful situations

Social events

Drinking coffee

Finishing a meal

Drinking alcohol

Driving a car

Using the phone

Ideas for trigger management

Exercise or keep busy

Call or text someone

Use chewing gum, mint, toothpicks, or fake cigarettes

Go for a walk or jog

Practice deep breathing or other coping methods

Serve in the community, donate, or do a good deed for someone

The “5 A’s” of Smoking Cessation: Ask

At every visit: “Do you use tobacco products, for example cigarettes or e-cigarettes?”

Review the type and brand of tobacco used and the amount used each day

Assess start date or years of tobacco use

History of quit attempts

- What has helped in the past?
- What has hindered in the past?
- What may help today?

If patient recently quit, congratulate them and ask how they've been doing (any urges to use tobacco?)

The "5 A's" of Smoking Cessation: Advise

Advise patients to quit.

Personalize for each patient.

Remember, even brief (3-minute) counseling can improve success rates.

Example:

- "Quitting smoking is the most important thing you can do for your health"
- If they tried to quit in the past: "It can take several tries to quit successfully"
-

The "5 A's" of Smoking Cessation: Assess

Assess each patient's readiness to quit

Examples of questions to ask:

How do you feel about stopping smoking?"

"What are your motivators for quitting?

"Have you ever tried to stop before?" "What happened?"

"What are your triggers?"

"How can you overcome cravings?"

"What strategies do you think will be most helpful?"

If your patient is not ready to quit, leave the door open:

"I am here to support you. We can re-visit again the next time I see you."

The "5 A's" of Smoking Cessation: Assist

Provide tobacco cessation pharmacotherapy unless contraindicated.

STAR Quit Plan

- Set a quit date, ideally within 2 weeks
- Tell family, friends, coworkers and request understanding and support
- Anticipate challenges
- Remove tobacco products from your home, car, work

Refer to additional in-depth and free cessation help:

- State tobacco quitline (1-800-QUIT-NOW; 1-855-DÉJELO-YA)
- Tobacco cessation program in the community, clinic, or healthcare system
- Web: CDC.gov/quit; Smokefree.gov; becomeanex.org
- Text: Smokefree.gov/SmokefreeTXT
- App: Smokefree.gov/tools-tips/apps/quitstart

The "5 A's" of Smoking Cessation: Arrange

Arrange follow up within 1-2 weeks after quit date

Then every 1-2 months

- Assess progress
- Refill medications if needed
- Add or change methods if needed

Ongoing motivation

- Reminders of benefits of quitting and risks of continuing to smoke
- Recognition of accomplishments
- Serves as positive reinforcement

Tobacco Cessation Pharmacotherapy

Improved cessation rates over placebo after 6 months

- NRT, alone or in combination (RR 1.58; 95% CI, 1.50–1.66)
- Varenicline (RR, 2.33; 95% CI, 1.95–2.80)
- Sustained-release bupropion (OR, 1.94; 95% CI, 1.72–2.19)

Varenicline or bupropion may be combined with NRT (caution with increased risk of side effects), but further research is needed to determine the role of varenicline plus bupropion combination therapy.

Other medications used for smoking cessation: clonidine, nortriptyline

E-cigarettes remain controversial and contain harmful chemicals.

Nicotine Withdrawal

Can start within 24 hours of quitting and lasts 1-2 weeks

Symptoms

- Depressed mood
- Insomnia
- Irritability, frustration, anger
- Anxiety
- Difficulty concentrating
- Restlessness, impatience
- Increased appetite, weight gain

The weaning method can reduce amount severity of withdrawal symptoms

- Switching to cigarette brands that deliver less and less nicotine
- Cut down number of cigarettes smoked per day

Nicotine Replacement

First-line option and standard of care: long-acting NRT formulation combined with short-acting agent (even in patients with stable CV disease)

Long-acting NRT: to replace current nicotine intake and reduce cravings

Short-acting NRT: for breakthrough cravings and sensory substitute

All dosage forms are equally effective.

NRT can be continued for months if necessary.

Available as: patch, lozenge, gum, inhaler, nasal spray, oral mist (Canada)

Nicotine Patch

Long-acting NRT dosage form

Dose is based on number of cigarettes smoked per day

- ≥ 10 cigarettes per day: 21 mg patch
- < 10 cigarettes per day: 14 mg patch

Easy to use, may cause local skin irritation, insomnia, and vivid dreams.

- Rotate patch site to minimize skin irritation
- Remove patch at bedtime if insomnia or vivid dreams occur for several days

Treatment duration

- Usually used for 10-12 weeks, but can continue longer if needed
- Can consider tapering at 6 weeks (e.g., if on lower dose)

Short-acting NRT dosage form

Dose is based on time of day of first cigarette or # of cigarettes per day

- ≤ 30 minutes of waking, or > 25 cigarettes per day: 4 mg lozenge
- > 30 minutes of waking or ≤ 25 cigarettes per day: 2 mg lozenge
- Maximum 15-20 lozenges per day

Place lozenge between gum and cheek and allow to melt slowly.

- Takes about 10 minutes to completely dissolve.
- No food or drink within 15 minutes before or during use.
- Can move to opposite check to help reduce mouth irritation.

Possible side effects: mouth irritation, hiccups, heartburn, nausea.

Treatment duration: can be used ≥ 3 months, some experts use up to 6 months

Nicotine Gum

Short-acting NRT dosage form

Dose is based on time of day of first cigarette or # of cigarettes per day

- ≤ 30 minutes of waking, or > 25 cigarettes per day: 4 mg gum
- > 30 minutes of waking or ≤ 25 cigarettes per day: 2 mg gum
- Maximum 20-24 pieces per day

Possible side effects: mouth irritation, jaw soreness, heartburn, hiccups, nausea. Proper chewing is required to minimize side effects:

- Chew until tingling starts, then park between gum and cheek until tingling ends (usually 1 minute)
- Repeat chewing and parking process
- Spit gum out after 30 minutes
- No food or drink within 15 minutes before or during use.

Treatment duration: can be used ≥ 3 months, some experts use up to 6 months

Nicotine Inhaler

Short-acting NRT dosage form

Dose is based on cravings

- Maximum 12-16 cartridges per day
- Change cartridge when nicotine taste disappears
- Each cartridge contains about 80 puffs

Puff until cravings stop (do not inhale into lungs)

Possible side effects: mouth and throat irritation, coughing

Treatment duration: can be used at least 3 months

Nicotine Nasal Spray

Short-acting NRT dosage form

Dose is standard

- One spray in each nostril every 1-2 hours
- Maximum dose is 80 sprays per day
- Patients should not sniff or inhale while spraying
- Patients should wait 2-3 minutes after use before blowing their nose

Associated with the most side effects of the NRT products: nasal and throat irritation, runny nose, sneezing, coughing, tearing

Regular use for 1 week may lead to diminishing side effects.

Treatment duration: can be used at least 3 months

Varenicline

Blocks nicotine binding to ?-4-β-2 nicotinic acetylcholine receptors and partially stimulates nicotinic receptors

- Blocks reward of smoking
- Reduces cravings and withdrawal

Start 1-4 weeks before quit date (some data suggest 3 months before quit date)

Dose based on titration schedule:

- Day 1-3: 0.5 mg **once** daily
- Day 4-7: 0.5 mg twice daily
- Day 8 onward: 1 mg twice daily (may continue 0.5 mg twice daily)

Treatment duration: typically, 12 weeks, can be used up to 12 months

Varenicline Adverse Effects

- Constipation, nausea (take with food and full glass of water), vomiting
- Vivid dreams, headache, seizures, depressed mood
- Caution in patients with acute coronary syndrome (wait until discharge and patient is stable)

- Similar potential for psychiatric side effects as other smoking cessation agents (increased risk for adverse effects if combined with other agents)

Sustained-release Bupropion

Second-line option after NRT or varenicline

Inhibits dopamine/norepinephrine reuptake, weak nicotinic receptor antagonist.

- Improves smoking cessation rates vs placebo
- Suppresses weight gain associated with smoking cessation

Start 1-2 weeks before quit date, dose based on titration schedule:

- Day 1-3: 150 mg once daily
- Day 4 onward: 150 mg **twice** daily

Treatment duration: 3 to 6 months

Consider for

- Patients with stable CV disease
- Patients with concomitant depression

Possible side effects (caution when combining with other agents)

- Insomnia
- Agitation
- Dry mouth
- Constipation
- Seizures
- Headache

Pharmacologic Treatment Overview

COPD pharmacotherapy consists primarily of inhalers (bronchodilators, ICS)

Roflumilast and azithromycin are outlined by GOLD guidelines in severe/advanced COPD.

Other pharmacologic agents which are not as commonly used for COPD management include **mucolytics, theophylline, low-dose long-acting opioids, treatment of vitamin D deficiency.**

Vaccines should be administered as recommended for patients with COPD.

Inhaler Device Introduction

Many different inhaler devices are available

- MDIs, breath-actuated MDIs
- SMIs
- VHCs/spacers
- DPIs: powder contained in reservoir or blisters
- Nebulizers

There is no evidence for superiority of one device, patients in clinical trials were given education/follow-up and mastered inhalation technique.

Smart inhalers incorporate sensors that detect date/time of use and some inspiratory flow/inspired volume.

Inhaler Device Considerations

MDIs, breath-actuated MDIs and SMIs

- Require slow, deep inspiration
- Consider adding VHC/spacer or switching devices if patient may be struggling with proper use

DPIs

- Require forceful inspiration
- If patient unable to inhale forcefully:
- Check inspiratory flow objectively using an inspiratory flow meter, or
- Switch to MDI (+/- VHC/spacer), SMI, or nebulizer

Bronchodilator Overview

Bronchodilators benefits

- Given to prevent or reduce symptoms (Evidence A)
- Improve FEV1 and can change other spirometry values (Evidence A)
- Alter smooth muscle tone and widening of the airways
- Reduce dynamic hyperinflation at rest and during activity
- Improve exercise performance
- Help with acute episodes but not necessarily stable disease

Cautions

- Dose-related adverse effects and toxicity
- Regular use of short-acting bronchodilators is not recommended

Bronchodilator Classes

β2 agonists (SABAs, LABAs)

- Relax airways by stimulating β2 receptors on bronchial smooth muscle

- Increase cyclic adenosine monophosphate and block bronchoconstriction

Antimuscarinic agents (SAMAs, LAMAs)

- Block acetylcholine on M3 antimuscarinic receptors in airways
- Block bronchoconstriction

Bronchodilator Adverse Effects

β2 agonists Adverse Effects

- Tachycardia, tremors, palpitations
- Hypokalemia
- Headache
- Nervousness

Antimuscarinic Adverse Effects

- Dry mouth
- Possible urinary symptoms, bitter metallic taste
- Unexpected small increase in CV events with regular ipratropium use
- In large, long-term trials, tiotropium did not increase CV risk
- Nebulizer solutions can precipitate acute glaucoma if the solution comes in contact with the eyes

Short-acting Bronchodilators

Regular and as-needed use of SAMA or SABA (Evidence A)

- Improves FEV1
- Reduces symptoms

SAMAs and SABAs are typically used as-needed for symptoms

Difficulty breathing

Wheezing

Shortness of breath

Coughing

Chest tightness

SAMA nebulizer solution (ipratropium) can be used either as-needed for symptoms, or for maintenance therapy (i.e., for patients who need LAMA nebulizer solution but have challenges with access).

Role of Short-acting Bronchodilators in COPD

Rescue short-acting bronchodilators should be prescribed for all patients with COPD for as-needed immediate symptom relief.

Monotherapy for patients with Group A COPD (long-acting bronchodilators are preferred, short-acting bronchodilators more suitable for occasional dyspnea)

- mMRC 0-1 and/or CAT <10
- 0 or 1 mild to moderate COPD exacerbation not requiring hospitalization

Added to a maintenance regimen (with long-acting bronchodilators, ICS, etc.), used as-needed for symptoms

SAMA vs SABA: in a systematic review, the SAMA ipratropium, vs SABA, showed benefits for:

- Lung function
- Health status
- Reduced need for oral steroids

Short-acting Beta2 Agonists

The effects of SABAs wear off in 4 to 6 hours.

Albuterol sulfate

- MDI: HFA inhaler (Proventil®, ProAir®, Ventolin®), 108 mcg per inhalation

1-2 inhalations every 4-6 hours

- DPI (ProAir® RespiClick® or ProAir® Digihaler™?), 117 mcg per dose

1-2 inhalations every 4-6 hours

- Nebulizer solution (AccuNeb®) 0.63-1.25 mg per 3 mL vial

1 vial inhaled via nebulizer 3-4 times daily as needed

Levalbuterol (Xopenex®)

- MDI: HFA inhaler 45 mcg per inhalation, 1-2 inhalations every 4-6 hours
- Nebulizer solution: 0.63 mg or 1.25 mg per 3 mL vial

1 vial inhaled via nebulizer 3-4 times daily

Short-acting Muscarinic Antagonists

In addition to M3, SAMAs block the M2 muscarinic receptor which can cause vagally-induced bronchoconstriction.

Ipratropium Bromide

- MDI: Atrovent® HFA, 17 mcg per inhalation
- 1-2 inhalations 4 times (up to 12 times) daily
- Used as-needed for symptoms
- Nebulizer solution 500 mcg per 2 mL vial
- 1 vial inhaled via nebulizer 3-4 times daily (6-8 hours apart)
- Used either as-needed for symptoms, or for maintenance

Long-acting Bronchodilators

LABAs and LAMAs are used for maintenance therapy

- Recommended for patients with Group B and Group E COPD
- Preferred over short-acting bronchodilators for Group A COPD

Duration of action of LABAs and LAMAs is 12 hours or more.

LAMA vs LABA: clinical trials demonstrate a greater effect of LAMAs compared to LABAs on

- COPD exacerbation rates (Evidence A)
- Hospitalizations (Evidence B)

Long-acting Beta2 Agonists

Formoterol and salmeterol are twice daily LABAs that significantly improve

- FEV1 and lung volumes
- Dyspnea
- Health status
- Exacerbation rate and hospitalizations

Indacaterol is a once daily LABA that significantly improves

- Breathlessness
- Health status
- Exacerbation rate

Olodaterol and vilanterol are once daily LABAs that improve

- FEV1
- COPD symptoms

LABA Agents

Once-daily

- DPI: indacaterol (Arcapta® Neohaler®) 75 mcg per dose

1 inhalation once daily

- SMI: olodaterol hydrochloride (Striverdi® Respimat®) 2.7 mcg per inhalation

2 inhalations once daily

Twice-daily

- DPI: salmeterol (Serevent® Diskus®) 50 mcg per dose

1 inhalation twice daily

- Nebulizer solutions
- Formoterol fumarate (Perforomist®) 20 mcg per 2 mL

1 vial inhaled via nebulizer every 12 hours

- Arformoterol tartrate (Brovana®) 15 mcg per 2 mL

1 vial inhaled via nebulizer every 12 hours

Long-acting Muscarinic Antagonists

LAMAs bind to the M3 muscarinic receptor for long duration, faster dissociation from M2, prolonging the duration of bronchodilation.

Significantly improve (Evidence A)

- Lung function
- Dyspnea
- Health status
- Exacerbation rates

Also improve cough, sputum and hospitalizations.

Tiotropium improves effectiveness of pulmonary rehabilitation in increased exercise performance (Evidence B).

Once-daily LAMA Agents

SMI: Tiotropium (Spiriva®) Respimat® 2.5 mcg per inhalation

2 inhalations once daily

DPI

- Tiotropium (Spiriva®) Handihaler® 18 mcg per capsule

2 inhalations from 1 capsule once daily

-

- Umeclidinium (Incruse® Ellipta®) 62.5 mg per dose

1 inhalation once daily

-
- Glycopyrrolate (Seebri® Breezhaler®) 50 mcg per capsule

Inhale powder contents of 1 capsule once daily

Nebulizer solution: revefenacin (Yupelri™?) 175 mcg per 3 mL vial

1 vial inhaled via nebulizer once daily

Twice-daily LAMA Agents

DPI

- Aclidinium (Tudorza® Pressair®) 400 mcg per dose

1 inhalation twice daily

- Glycopyrrolate (Seebri™? Neohaler®) 15.6 mcg per capsule

Inhale powder contents of 1 capsule twice daily

Nebulizer solution: glycopyrrolate (Lonhala® Magnair®), 25 mcg per 1 mL

1 vial inhaled via nebulizer twice daily

Bronchodilator Combinations

Compared to increasing the dose of individual agents, combining agents helps

- Promote bronchodilation
- Lower the risk of side effects

SABA + SAMA is superior to either agent alone at improving FEV1 and reducing symptoms (Evidence A).

LABA + LAMA combinations have demonstrated (vs placebo or monotherapy)

- Improved lung function and symptoms (Evidence A)
- Reduced risk for exacerbations (Evidence B)
- Increased quality of life

Can be given in separate inhalers, but a single-entity combination (e.g. 2-in-1 inhaler, 2-in-1 nebulizer solution) is preferred if accessible for patient.

LABA + LAMA is preferred for Group E COPD, but if blood eosinophils ≥ 300 cells/μL and/or concomitant asthma, LABA + LAMA + ICS is recommended.

SAMA+SABA Single Entity Combinations

SMI: ipratropium bromide 21 mcg + albuterol sulfate 120 mcg (Combivent® Respimat®) 1-2 inhalations 4 times (up to 12 times) daily

Nebulizer solution

Ipratropium bromide 0.5 mg + albuterol sulfate 2.5 mg (Duoneb®) inhalation via nebulizer 4-6 times daily

LAMA+LABA Single Entity Combinations

SMI: Tiotropium bromide 2.5 mcg + olodaterol hydrochloride 2.5 mcg (Stiolto® Respimat®), 2 inhalations once daily

Pressurized MDI: glycopyrrolate 9 mcg + formoterol fumarate 4.8 mcg (Bevespi® Aerosphere™?), 2 inhalations twice daily

DPIs

- Umeclidinium 62.5 mcg + vilanterol 25 mcg (Anoro® Ellipta®)

1 inhalation once daily

- Glycopyrrolate 15.6 mcg + indacaterol 27.5 mcg (Utibron® Neohaler®)

Inhale powder contents of 1 capsule twice daily

- Aclidinium bromide 400 mcg + formoterol fumarate 12 mcg (Duaklir® Pressair®), 1 inhalation twice daily

Inhaled Corticosteroids

COPD-associated inflammation has limited response to corticosteroids.

Most studies found ICS alone doesn't modify FEV1 decline or mortality.

Some drugs (e.g., beta2-agonista, theophylline, macrolides) may facilitate glucocorticoid sensitivity.

In patients with exacerbations and moderate to severe COPD, ICS combined with LABA is more effective than the individual components in (Evidence A):

- Improving lung function
- Improving health status
- Reducing exacerbations

Prescribing information for ICS are typically dosed for asthma.

ICS can be added to a regimen via a separate inhaler, but combination single-inhalers (ICS+LABA, LABA+LAMA+ICS) are preferred in COPD.

When to Add ICS to Long-acting Bronchodilators

ICS Agents

MDIs

- Beclamethasone dipropionate (Qvar® Redihaler™? HFA), 40 mcg or 80 mcg

1-4 inhalations twice daily

- Fluticasone propionate (Flovent® HFA), 44 mcg, 110 mcg, or 220 mcg

1-2 inhalations twice daily

- Mometasone furoate (Asmanex® HFA), 100 mcg or 200 mcg

2 inhalations every 12 hours

Nebulizer solution

Budesonide (Pulmicort ® Respules®), 0.25 mg, 0.5 mg, or 1 mg

1-2 mg every 6 hours inhaled via nebulizer for exacerbations

DPIs

- Budesonide (Pulmcort® Flexhaler™?), 180 mcg or 360 mcg

1 inhalation twice daily

- Fluticasone propionate (Flovent® Diskus®), 100 mcg or 250 mcg

1 inhalation twice daily

- Fluticasone propionate (Armonair® Digihaler®), 55 mcg, 113 mcg, 232 mcg

1 inhalation twice daily

- Fluticasone furoate (Arnuity® Ellipta®)

100 mcg 1-2 inhalations once daily; 200 mcg 1 inhalation once daily

- Mometasone furoate (Asmanex® Twisthaler®) 220 mcg (200 mcg mometasone furoate), 1 inhalation once daily (in the evening) to twice daily

ICS+LABA Agents

MDI

- Fluticasone propionate (45 mcg, 115 mcg, or 230 mcg) + salmeterol (21 mcg): Advair® HFA, 2 inhalations twice daily
- Budesonide (80 mcg indicated for asthma or 160 mcg for COPD or asthma) + formoterol (4.5 mcg): Symbicort® HFA, 2 inhalations twice daily
- Mometasone furoate (100 mcg or 200 mcg) + formoterol dihydrate (5 mcg)

Dulera® HFA: 2 inhalations twice daily

DPI

- Fluticasone propionate (100 mcg, 250 mcg, or 500 mcg) + salmeterol (50 mcg): Advair® Diskus®, 1 inhalation twice daily
- Fluticasone furoate (100 mcg indicated for COPD or asthma; 200 mcg for asthma) + vilanterol 25 mcg: Breo® Ellipta®, 1 inhalation once daily

LAMA+LABA+ICS is preferred over and superior to LABA+ICS for COPD

Triple Therapy LABA+LAMA+ICS

Improves lung function, symptoms, health status, and reduces exacerbations compared to LABA+ICS, LABA+LAMA, or LAMA monotherapy (Evidence A).

Recent evidence suggests lower risk of mortality with triple therapy compared to LABA+LAMA in patients with symptomatic COPD (CAT ≥ 10) and a history of frequent (≥ 2 moderate exacerbations) and/or severe exacerbations (≥ 1 exacerbation requiring hospitalization).

Single-inhaler triple therapy may be more convenient and effective than multiple separate inhalers.

LABA+LAMA+ICS Agents

DPI: vilanterol 25 mcg + umeclidinium 62.5 mcg + fluticasone 100 mcg

Trelegy ® Ellipta®: 1 inhalation once daily

Pressurized MDI (available outside of United States)

Beclamethasone dipropionate 100 mcg + formoterol fumarate 6 mcg + glycopyrronium bromide 12.5 mcg: Trimbow®, 2 inhalations twice daily

ICS Pneumonia Risk

Regular treatment with ICS increases risk of pneumonia (Evidence A)

- Especially in patients with severe COPD
- Lower blood and sputum eosinophils increases risk of bacterial infections (esp. proteobacteria *Haemophilus)* and pneumonia
- Blood eosinophil count < 2% increases pneumonia risk (Evidence C)

Patients at higher risk of pneumonia:

- Those who currently smoke
- Age ≥ 55 years
- History of prior exacerbations or pneumonia
- BMI < 25 kg/m2
- Poor mMRC dyspnea grade
- Severe airflow obstruction
- Blood eosinophil count < 2%

Other ICS Adverse Effects

Oral candidiasis (thrush): prevention strategies include

- Rinsing mouth and/or brush teeth and tongue after each use
- Using VHC/spacers with inhaler

Others: hoarse voice, sore throat, coughing, bruising

Possible side effects if taken as a high-dose for long-term

- Growth suppression
- Bone thinning
- Diabetes
- Cataracts
- Mycobacterial infection

Carefully consider the dose of ICS used to reduce the potential of ICS-related side-effects which are more likely to occur at higher doses.

Balancing Risks vs Benefits of ICS in COPD

ICS Withdrawal

Consider discontinuing ICS

- If pneumonia or other concerning side-effects develop
- When de-escalating therapy in stable patients.

Caution: abrupt withdrawal may lead to worse outcomes in COPD patients

- Some studies have shown an increase in exacerbations, symptoms, and decrease in FEV1, while others have not.
- The greatest FEV1 loss and increase in exacerbations are associated with ICS withdrawal in patients with blood eosinophils ≥ 300 cells/μL at baseline.

If feasible, slow, gradual dose reduction is preferred over abrupt discontinuation.

Additional Therapies

Phosphodiesterase 4 inhibitor, roflumilast

In patients with CB, severe COPD, and prior exacerbations, roflumilast

- Improves lung function and reduces moderate to severe exacerbations treated with systemic corticosteroids (Evidence A)
- Improves lung function and reduces exacerbations in patients on fixed-dose LABA+ICS combination (Evidence A)

Macrolide antibiotics

- In patients prone to exacerbations, long-term azithromycin or erythromycin were found to reduce exacerbations over one year (Evidence A)
- Especially for patients who are not current smokers
- The best evidence exists for azithromycin
- Azithromycin does not interact with roflumilast (erythromycin drug interaction with roflumilast)

Roflumilast

Dose (500 mcg tablet): 1 tablet by mouth once daily, with or without food

Place in therapy: for patients with COPD, CB, and FEV1 < 50% who are still experiencing exacerbations and are

- On a current regimen of LABA+LAMA+ICS, or
- On a current regimen of LABA+LAMA with blood eosinophils < 100 cells/μL
- Requiring therapy escalation to ICS but unable to take ICS

Adverse effects: diarrhea, nausea, reduced appetite, weight loss (average of 2 kg), abdominal pain, sleep disturbance, headache

Adverse effects tend to occur early in treatment and are reversible/diminish over time with continued treatment.

Other considerations

- Use caution in patients with depression.
- Patient weight should be monitored during treatment; roflumilast should be avoided in underweight patients.

Azithromycin

Place in therapy: for patients with COPD who are not current smokers and still experiencing exacerbations despite

- On a current regimen of LABA+LAMA+ICS, or
- On a current regimen of LABA+LAMA with blood eosinophils < 100 cells/μL
- Requiring therapy escalation to ICS but unable to take ICS

Associated with bacterial resistance (Evidence A), hearing test impairment (Evidence B), and prolongation of QTc interval.

Dose (can be taken with or without food)

- 250 mg tablet: 1 tablet by mouth once daily
- 500 mg tablet: 1 tablet by mouth three times per week

Duration of treatment: up to one year

Also available as oral suspension (100 mg per 5 mL or 200 mg per 5 mL)

Does not interact with roflumilast (erythromycin interacts with roflumilast)

Theophylline

Theophylline is not recommended unless other long-term treatment bronchodilators are unavailable, unaffordable, or contraindicated (Evidence B).

Sustained-released preparations were used in COPD studies.

Theophylline demonstrated a small bronchodilator effect vs placebo for COPD (Evidence A), as well as modest symptom benefits (Evidence B)

Improves FEV1 and breathlessness when added to salmeterol.

Additional Therapies

Mucolytics: agents such as N-acetylcysteine produces a small reduction in exacerbations (Evidence B) and modestly improves health status.

Low-dose long-acting opioids may be used for dyspnea in severe COPD (Evidence B).

In one meta-analysis, vitamin D supplementation reduced exacerbation rates in patients with low baseline vitamin D levels.

Narrow therapeutic window, dose-related toxicity can occur

Adverse effects: arrhythmias, convulsions, headaches, insomnia, nausea, heartburn, significant drug interactions (e.g., erythromycin, ciprofloxacin, allopurinol, cimetidine, fluvoxamine, zileuton)

Pneumococcal Vaccine in COPD

Has been shown to reduce incidence of community-acquired pneumonia and exacerbations (Evidence B)

Pneumococcal vaccine is recommended for adults aged 19-64 years with COPD.

Recommendations

- One dose of 15-valent conjugate vaccine followed by 23-valent polysaccharide vaccine ≥ 8 weeks later (Evidence B)
- One dose of 20-valent conjugate vaccine, or
- Adults who have only received 23-valent polysaccharide vaccine may receive either 20-valent or 15-valent conjugate vaccine ≥ 1 year after their 23-valent polysaccharide dose.

Annual influenza vaccination (Evidence B)

SARS-CoV-2 (COVID-19) vaccination (Evidence B)

Tetanus, diphtheria, pertussis (Tdap, dTaP, or dTPa) vaccination to protect against pertussis (whooping cough) for patients who were not vaccinated in adolescence (Evidence B)

Zoster vaccination against shingles for people over 50 years (Evidence B)

Others as recommended by the Centers for Disease Control and Prevention

Non-pharmacologic and Other Therapies

Self-Management

Structured, personalized, multi-component

Goals

- Motivate and engage patients
- Support patients to positively adapt their health behaviors
- Develop skills to better manage their disease

Behavior change techniques elicit motivation, confidence, and competence

Literacy-sensitive approaches are used for patient understanding

Self-Management Components

Medication use

- Dose, inhaler technique, adherence
- Report accessibility issues
- Monitor and report side effects

Managing COPD risk and aggravating factors (smoking, irritants, stress etc.) and comorbidities

Lifestyle: diet, exercise, sleep

Other treatments: pulmonary rehabilitation, oxygen and ventilatory support

Breathing

- Breathing exercises/techniques
- Managing breathlessness and action plan

Staying up-to-date on vaccines

Breathing Exercises

Can be taught by pulmonary rehabilitation specialists.

Breathing exercises can help expel stale air, improve diaphragm functionality, and increase oxygen levels.

Pursed-lip breathing

1.Breathe in through your nose

2.Breathe out at least twice as long through your mouth, with pursed lips.

Belly (diaphragmatic) breathing:

1.Breathe in through your nose.

2.Pay attention to how your belly fills up with air.

3.Breathe out through your mouth at least 2-3 times as long as your inhale.

4.Relax your neck and shoulders as you retrain your diaphragm to take on the work of helping to fill and empty your lungs.

Prescribing Inhalation Devices

Physicians should only prescribe devices they/their care team are familiar with.

DPIs require the patient can inhale forcefully and deeply. If unsure or patient is unable, consider objective assessment or switch devices.

MDIs require patients to inhale slowly and deeply. If there is concern or the patient is unable, consider adding a VHC/spacer or switching devices.

For patients unable to use DPIs, MDIs, or SMIs, nebulized medication should be considered.

Smart inhalers may be helpful with adherence/persistence or technique

Other Device Factors to Consider

Availability of the medication in the device (e.g. not all are available via nebulizer solution)

Patient accessibility (e.g. affordability, insurance coverage, ability of patient to travel to pharmacy or have medication delivered)

If > 1 medication is needed, minimize the number of devices used (e.g. single-inhaler combinations)

Consider patient's cognition, dexterity, and strength

Consider size and portability of device

Undergo shared decision-making with patient/family/caregiver

Inhaler Technique

- May be incorrect in 70-80% of patients.
- Individualize selection of device according to each patient.
- Demonstrate and check patient technique regularly.
- Teach-back (ask patient to show how the device is used) can be effective.
- Pharmacist, physician, physiotherapist, nurse, and lay health coach interventions can improve inhalation technique and adherence.
- Spacers improve MDI delivery and reduce thrush and dysphonia risk.
- Rinse and spit after ICS use.
- If multiple inhalers, try to use the same or similar device.

Inhaler Adherence

In a systematic review, 22%-93% of patients were non-adherent to COPD medication per pharmacy claims data (most were in high-income countries)

Non-adherence to COPD medication has been associated with

- Poor symptom control
- Increased risk of exacerbation
- Healthcare utilization and costs
- Decreased quality of life
- Higher mortality risk.

Adherence is complex

- Social
- Environmental
- Patient-related
- Treatment-related

Inhaler Adherence Interventions

Tailor to each patient, considering various factors including, but not limited to:

- Comorbidities
- Smoking status

- Schooling level
- Disease severity
- Drug regimen complexity, polypharmacy, side effects
- Living status (alone vs with family/caregiver)

Monitor dispensing records + patient interview

Adherence interventions examples:

- Medication dose reminders
- Automatic refills
- Counseling
- Regimen simplification
- Digital inhalers
- Minimizing adverse effects

Patients with COPD should be advised to avoid ongoing exposure to potential irritants

- Dust
- Fumes
- Gases

Infection prevention measures are also recommended

- Mask-wearing
- Minimizing social contact
- Hand washing and/or sanitization
- Vaccines

Exercise in COPD

Physical activity is a strong predictor of mortality in COPD (Evidence A).

Exercise tolerance tests

- Cycle ergometry or treadmill
- Maximal oxygen consumption
- Heart rate
- Work performed
- Self-paced, timed walking test (e.g. 6-minute walking distance)
- Shuttle walking test

Exercise Training Recommendations in COPD

Exercise training alone or with counseling significantly improves physical activity levels in COPD.

When possible, training to 60-80% of maximal work or heart rate is preferred, or to a Borg-rated dyspnea or fatigue score of 4 to 6 (moderate to severe).

Can be accomplished through either continuous or interval (dividing exercise into brief periods of high-intensity) exercise programs.

Exercise training can be enhanced by optimizing bronchodilators (LAMAs and LABAs have been shown to reduce resting and dynamic hyperinflation).

Nutrition in COPD

Patients should be advised to maintain a healthy dietary intake.

Weight loss and malnutrition indicate a poor prognosis.

Malnutrition in COPD is associated with impaired lung function, increased hospitalizations & mortality, worsened exercise tolerance and quality of life.

Imbalance of decreased oral intake and increased energy expenditure

- In COPD, decrease in appetite and oral intake often coincide with elevated systemic levels of pro-inflammatory cytokines and leptin (appetite suppressant hormone)
- Ventilator inefficiency increases daily energy requirements
- Can lead to a negative nitrogen balance and decreased skeletal muscle mass and function

Nutrition Supplementation in COPD

Nutritional supplementation should be considered in all malnourished patients with COPD (Evidence B).

Dietary advice and oral supplementation can improve

- Body weight and BMI
- Fat-free mass
- Quality of life
- Respiratory muscle strength
- 6-minute walking distance
- Exercise performance

Among hospitalized patients with malnutrition, 90 days after hospital discharge, protein enriched supplement has been found to:

- Decrease mortality
- Improve handgrip strength
- Improve body weight
- Improve nutrition biomarkers

Pulmonary Rehabilitation Overview

Comprehensive intervention to

- Improve the physiologic and psychological condition of people with chronic respiratory disease
- Promote long-term adherence to health-enhancing behaviors

Thorough patient assessment with tailored therapies, including:

- Exercise training
- Education
- Self-management
- Intervention aiming at behavior change

Recommended for patients with COPD Group B or Group E.

Pulmonary Rehabilitation Recommendations

At least twice weekly

Supervised exercise training, including:

- Endurance training
- Interval training
- Resistance/strength training
- Upper and lower limbs with walking exercise

Can also incorporate

- Flexibility
- Inspiratory muscle training
- Neuromuscular electrical stimulation

Should be integrated into the patient care plan.

Optimal benefits around 6-8 weeks (less added benefits if > 12 weeks)

Challenges with Pulmonary Rehabilitation

Evidence indicates that physical activity is decreased in patients with COPD.

In COPD, there can be a downward spiral of inactivity predisposing patients to

- Reduced quality of life
- Increased rates of hospitalization
- Increased risk of mortality

Providers or patients may be unaware of benefits of pulmonary rehabilitation.

Access to pulmonary rehabilitation be a challenge.

Behavior change and long-term implementation

- Inertia (e.g. patient continuing to smoke or be non-adherent to treatment)
- Benefits can wane over time

Oxygen and Ventilatory Support Overview

Individual patient factors should be evaluated for each patient's potential need for supplemental oxygen.

In patients with severe resting chronic hypoxemia, LTOT improves survival (Evidence A).

In stable COPD and moderate resting or exercise-induced arterial desaturation, LTOT does not lengthen time to death or hospitalization, or improve health status, lung-function or 6-minute walk distance (Evidence A)

In patients with severe chronic hypercapnia ($PaCO_2$ > 53 mmHg) and history of acute respiratory failure hospitalization, long-term NIV may decrease mortality/prevent readmission (Evidence B).

LTOT is indicated for stable patients who have

- PaO_2 ≤ 55 mmHg or SaO_2 ≤ 88%, with or without hypercapnia confirmed twice over a three-week period
-
- PaO_2 55-60 mmHg, or SaO_2 88%, if there is evidence of
- Pulmonary hypertension
- Peripheral edema suggesting congestive heart failure, or
- Polycythemia (hematocrit > 55%)

Once placed on LTOT, the patient should be re-evaluated:

- After 60-90 days
- Repeat arterial blood gas or SaO_2 while inspiring room air and the level of oxygen flow that had been prescribed to determine efficacy and continued need for LTOT.
- Titrate oxygen to keep SaO_2 ≥ 90% **Overview of COPD Exacerbations**

Increased symptoms which worsen in < 14 days

- Dyspnea
- Sputum (purulence and volume)
- And/or coughing and wheezing

May be accompanied by tachypnea and/or tachycardia, and often associated with increased local and systemic inflammation.

COPD exacerbations have a negative impact on

- Health status
- Rates of hospitalization and readmission
- Disease progression

Other Impact of COPD Exacerbations

Increases risk of other events which may contribute to or confound diagnosis of COPD exacerbation, such as:

- Decompensated heart failure
- Pneumonia
- Pulmonary embolism

Long-term prognosis after hospitalization for exacerbation is poor

- Five-year mortality rate 50%
- Factors associated with poor outcome
- Older age
- Lower BMI
- Comorbidities
- Prior exacerbation hospitalizations
- Clinical severity
- Need for long-term oxygen therapy at discharge

Exacerbation Causes and Risk Factors

Commonly due to:

- Infection
- Pollution, or
- Other insult to airways

Commonly caused by viral infections which are often severe

- Human rhinovirus
- Influenza
- Para-influenza
- Metapneumovirus

If sputum is purulent, they are more likely due to bacterial infection.

The strongest predictor of future exacerbations is the number of exacerbations in the prior year.

Vitamin D levels tend to be lower in patients with COPD

- All patients hospitalized for COPD exacerbation should be assessed for vitamin D deficiency (especially if < 10 ng/mL).
- If vitamin D deficiency is identified, patients should be supplemented or treated accordingly.
- Increased ratio of pulmonary artery to aorta cross sectional dimension (i.e. > 1)
- Greater percentage of emphysema or airway wall thickness
- Chronic bronchitis

Exacerbation Differentials and Contributors

Pneumonia: chest radiograph

Pulmonary embolism

- Clinical probability assessment (e.g. hemoptysis, surgery, fracture, history of cancer, deep vein thrombosis)
- D-dimer, CT angiography for pulmonary embolism

Heart failure

- Chest radiograph, echocardiography
- NT Pro-Brain Natriuretic Peptide (Pro-BNP) and BNP

Pneumothorax, pleural effusion

- Chest radiograph
- Ultrasound

Myocardial infarction and/or cardiac arrhythmias

- Electrocardiography
- Troponin

COPD Exacerbation Classification

GOLD defines exacerbations based on the treatment given.

Mild: patient recovers outpatient with short-acting bronchodilator treatment (does not meet criteria for hospitalization.

Moderate: patient requires oral corticosteroids with or without antibiotics but can still be treated outpatient (does not meet criteria for hospitalization)

Severe: patient requires hospitalization (and requires oral corticosteroids with or without antibiotics)

COPD Exacerbation Assessment for Hospitalization

Severe symptoms

- Worsening of resting dyspnea
- High respiratory rate
- Decreased SaO2
- Confusion, drowsiness

Acute respiratory failure

New physical signs (e.g. cyanosis, peripheral edema)

Failure to respond to initial medical management

Presence of serious comorbidities (e.g. heart failure, new arrhythmias)

Inadequate home support

COPD Exacerbation Management

Pharmacotherapy is based on severity of the exacerbation.

Care coordination

- Mild to moderate exacerbations may be treated outpatient.
- Severe exacerbation: requires emergency room visit and/or hospitalization
- Oxygen if hypoxemic
- NPPV if acute respiratory failure (Evidence A)
- Improves gas exchange
- Reduces work of breathing
- Reduces need for intubation
- Decreases hospitalization duration
- Improves survival
- Pharmacologic treatment
- Transitions of care strategies

Exacerbation Pharmacologic Treatment

Acute treatment

- Mild exacerbation: SABAs with or without SAMAs
- Moderate to severe exacerbation:
- SABAs with or without SAMAs
- Oral corticosteroids (for ≤ 5 days)
- Antibiotics if indicated

Prior to or during hospital discharge

- Long-acting bronchodilators should be initiated as maintenance therapy
- ICS should be considered, especially for patients with:
- Blood eosinophil levels ≥ 300 cells/μL
- 2 or more previous exacerbation hospitalizations
- Already on (and adherent to) LABA+LAMA prior to admission
- Asthma or features of asthma

Corticosteroids for COPD Exacerbations

Should only be given to patients with moderate to severe exacerbations.

Prednisone 40 mg daily for 5 days is recommended (longer courses are associated with pneumonia and mortality risk).

Corticosteroids for COPD exacerbations can improve (Evidence A)

- FEV1
- Oxygenation
- Recovery time

- Duration of hospitalization

They also reduce risk of early relapse and treatment failure.

Nebulized budesonide may be an alternative in some patients depending on accessibility concerns.

Antibiotic Indications for COPD Exacerbations

When indicated, antibiotics can (Evidence B)

- Shorten recovery time
- Reduce risk of early relapse
- Reduce risk of treatment failure
- Shorten hospitalization duration

Antibiotics are recommended for moderate to severe exacerbations with:

- 3 of 3 cardinal symptoms
- Increased dyspnea
- Increased sputum volume
- Increased sputum purulence
- 2 of the 3 cardinal symptoms, one being increased purulence, or
- Mechanical ventilation requirement

Antibiotic Prescribing for COPD Exacerbations

Short duration

- As effective as longer treatment in outpatients
- Decreases the risk of antimicrobial resistance and complications
- Recommended treatment duration: 5-7 days (≤ 5 days for outpatient)

Initial empiric therapy (choose based on local bacteria resistance patterns and patient-specific factors)

- Amoxicillin + clavulanic acid (875 mg/125 mg twice daily)
- Azithromycin: 500 mg (1 dose), then 250 mg daily for 4 days, or 500 mg once daily for 3 days
- Doxycycline 100 mg, 1 tablet every 12 hours

For patients with frequent exacerbations, severe airflow obstruction, or requiring mechanical ventilation, sputum culture is recommended.

Oral is the preferred route of administration, but intravenous can be considered (e.g. patient inability to eat, pharmacokinetics)

Respiratory Support for COPD Exacerbations

- Oxygen should be titrated to a target saturation of 88% to 92%.

- Venturi masks provide more accurate and controlled oxygen delivery than nasal prongs.
- Blood gases should be monitored frequently.
- NIV is preferred over invasive mechanical ventilation (intubation and positive pressure ventilation) for initial treatment of acute respiratory failure in COPD exacerbation hospitalizations.
- Once patients improve (≥ 4 hours of unassisted breathing) NIV can be stopped.

Patient treatment wishes help with invasive mechanical ventilation decisions

- Advance directive or living will
- Risk of ventilator-acquired pneumonia, barotrauma, volutrauma, tracheostomy and prolonged ventilation

Indications for Respiratory or Medical Intensive Unit

- Severe dyspnea with inadequate response to initial emergency therapy
- Mental status changes (confusion, lethargy, coma)
- Persistent, worsening, or severe despite supplemental oxygen and NIV

Hypoxemia ($PaCO_2$ < 5.3 kPa or 40 mmHg)

And/or respiratory acidosis (pH < 7.25)

- Need for invasive mechanical ventilation
- Hemodynamic instability (need for vasopressors)

Indications for Mechanical Ventilation

Indications for NIV

- Respiratory acidosis ($PaCO_2$ ≤ 6.0 kPa or 45 mmHg, arterial pH ≤ 7.35)
- Severe dyspnea with signs of respiratory muscle fatigue and/or increased work of breathing
- Persistent hypoxemia despite supplemental oxygen

Indications for invasive mechanical ventilation

- NIV failure or unable to tolerate NIV
- Status post respiratory or cardiac arrest
- Diminished consciousness or psychomotor agitation despite sedation
- Massive aspiration or persistent vomiting
- Persistent inability to remove respiratory secretions
- Severe hemodynamic instability with inadequate response to fluids and vasoactive drugs
- Severe ventricular or supraventricular arrhythmias
- Life-threatening hypoxemia in patients unable to tolerate NIV

Exacerbation Hospitalization Statistics

For patients readmitted to the hospital for COPD within 30 days, the estimated absolute increase in mortality risk is

- 4% at 30 days (NNH, 25)
- 17% at 6 months (NNH, 6)
- 19% at 1 year (NNH, 6)
- 24% at 3 years (NNH, 5)

The 5-year mortality rate is 40%-70% depending on COPD severity. For patients with severe disease, the 2-year mortality rate is about 50%.

Two or more prior acute COPD exacerbations is independently associated with 30-day readmission (HR 2.47; 95% CI 1.51-4.05).

Significant risk factors for 30- and 90-day all-cause readmission:

- Comorbidities
- Previous exacerbations and hospitalizations
- Increased length of stay

Hospital Readmissions Reduction Program

In 2012, the Centers for Medicare and Medicaid Services (CMS) implemented the Hospital Readmissions Reduction Program to improve quality of care for patients hospitalized for certain high-risk conditions.

By 2015, COPD was added to the list of indications targeted by CMS.

Failure to improve care (reduce readmissions) for these conditions led to financial penalties from CMS.

- Hospitals were penalized 1% of payments in 2012
- Penalties increased to 3% by 2015

Good transitions of care and follow-up post hospital discharge are essential to reduce risk for re-exacerbations, readmissions, and mortality.

COPD Transitions of Care

Good clinical practice covers essential areas prior to hospital discharge.

Discharge planning:

- Education
- Medication and inhaler regimen, technique, adherence and accessibility
- Long-acting bronchodilators initiated as maintenance therapy
- ICS added depending on blood eosinophils, history of exacerbations, previous therapy, concomitant asthma or features of asthma
- Assess need for ongoing oxygen therapy
- Comorbidity management
- Early pulmonary rehabilitation (< 4 weeks post discharge)
- Telemonitoring and continued patient contact
- Motivational interview-based health coaching

Discharge Plans

Medication reconciliation

- Patient's medications must be cross-checked
- No chronic medications stopped unnecessarily
- Ensure safety of new prescriptions
- Prescriptions for new or changed medications should be filled and reviewed with the patient and family at or before discharge

Structured discharge communication

- Medication changes, pending tests/studies, and follow up needs must be accurately and promptly communicated to outpatient physicians.
- Discharge summaries should be shared with primary care provider as soon as possible after discharge.
- Follow-up appointments scheduled before discharge increases the likelihood of patient attendance.

Post Discharge Follow-up

Early follow-up (< 1 months) after discharge has been associated with less exacerbation-related readmissions.

Additional follow-up at 3 months can ensure return to clinical stability

- Patient self-management
- Review patient symptoms (CAT and/or mMRC)
- Reassess treatment regimen and medication use
- Spirometry
- Prognosis assessment (e.g. BODE)
- SaO2 and blood gas assessment to guide LTOT
- Review progress with or eligibility for pulmonary rehabilitation

Repeat follow-up 12-16 weeks post discharge

In patients with recurrent exacerbations and/or hospitalizations, CT assessment should be done to determine the presence of bronchiectasis and emphysema.

Comorbidities Overview

Comorbidities may pre-exist or arise due to COPD and its characteristics (e.g. breathlessness, difficulty exercising).

Comorbidities may worsen COPD and/or vice versa.

Comorbidities may be overlooked because symptoms can mimic COPD.

Patients should be assessed and treated for comorbidities.

Especially if untreated or inadequately treated, comorbidities are associated with poor prognosis and mortality.

Generally, comorbidities should not alter COPD treatment, and comorbidities should be treated according to their respective guidelines regardless of COPD.

COPD Comorbidities

CV disease (use smoking cessation agents & β2 agonists with caution)

- Heart failure: selective β1-blockers are recommended
- Ischemic heart disease: treat according to guidelines
- Arrhythmias: caution with SABAs and theophylline
- Peripheral vascular disease: consider patient risk for vascular events
- Hypertension: treat according to guidelines

Metabolic syndrome and diabetes: treat according to guidelines

Lung cancer

- Annual LDCT screening is recommended in smoking-related COPD
- Annual LDCT is not recommended for COPD not due to smoking

Bronchiectasis

- Patients may require more aggressive and/or prolonged antibiotics
- ICS may not be indicated in patients with bacterial colonization or recurrent lower respiratory tract infections

Obstructive sleep apnea: clear benefits with continuous positive airway pressure to improve survival and reduce risk of hospital admissions

Depression, anxiety

- Treat according to guidelines
- The Hospital Anxiety and Depression Scale and the Primary Care Evaluation of Mental Disorders Patient Questionnaire may help with identification and treatment

Gastroesophageal reflux disease: treat according to guidelines

Periodontitis: encourage dental hygiene practices

Osteoporosis

- Treat osteoporosis and COPD according to guidelines
- Avoid repeated use of systemic steroids if possible

Asthma & COPD

Asthma and COPD are different disorders which may coexist in a patient.

No longer referred to as asthma & COPD overlap

Some common features may be shared (e.g. eosinophilia)

Likely to see bronchodilator responsiveness with asthma vs COPD.

In patients with COPD who have concomitant asthma

- Pharmacotherapy should primarily follow asthma guidelines (e.g. ICS for initial maintenance therapy, SABA rescue inhaler)
- Secondarily follow COPD treatment guidelines
- Address differences such as treatment of allergies and avoidance of allergens which may be more common or applicable in asthma

Anemia

- Mainly related to chronic inflammation and impaired iron utilization
- Treat according to guidelines

Polycythemia

- Correct hypoxemia
- Treat comorbidities that may require intervention (e.g. obstructive sleep apnea, pulmonary hypertension, venous thromboembolism)

Vitamin D deficiency: assess for and treat vitamin D deficiency

Other comorbidities which may affect management (e.g. cognitive impairment, frailty, multiple comorbidities)

COVID-19 Considerations

In patients with COPD, factors which may predict severe COVID-19 include

- Decreased lung function
- Higher CAT score
- Underweight
- Depression
- Prior COPD treated inpatient or in secondary care

Avoid nebulizers

- SARS-CoV-2 may be viable in aerosol for up to 3 hours and lead to transmission of virus to other people
- MDI with spacer mouthpiece or mask preferred

- DPI and SMI are also options instead of nebulizers
- For critically-ill patients with COVID-19 receiving ventilatory support, nebulizer circuits should be kept intact (mesh nebulizer can be used)

Avoid spirometry if patient has suspected or confirmed COVID-19, or at times of high community prevalence, unless urgent or essential (i.e. procedures).

Delay elective bronchoscopy until patients have a negative COVID-19 test.

COVID-19 Testing Recommendations

Symptomatic patients should be tested for COVID-19.

- Differentiating COVID-19 symptoms from COPD may be challenging.
- Rapid deterioration of lung function may occur with COVID-19, as well as fever, impaired taste or smell, and gastrointestinal complaints.
- There is a distinct pattern of vascular injury, pneumonitis, hypoxemia, coagulopathy, high levels of systemic inflammation, lymphopenia, and multi-organ involvement in COVID-19.

Chest radiography is indicated for patients with COPD who have moderate to severe COVID-19 symptoms and those with worsening respiratory status.

Point-of-care ultrasound can detect COVID-19 pulmonary manifestations.

CT results may show pneumonia in asymptomatic patients with SARS-CoV-2.

If pulmonary embolism is suspected, perform chest CT angiography.

COVID-19 Treatment in COPD

Patients with COPD and COVID-19 should get the same standard of care as others with COVID-19 (antivirals, corticosteroids, thromboprophylaxis, interleukin-6 receptor blockers, baricitinib, antibiotics if severe COVID-19 or mild COVID-19 with clinical suspicion of bacterial infection)

Antibiotics for COPD exacerbation with 2 of 3 cardinal symptoms (1 being increased sputum purulence), or if mechanical ventilation is required.

Continue medications as prescribed and resume non-pharmacologic treatment for COPD as soon as possible

Follow strict infection control procedures.

As indicated: HFNT, NIV, or invasive mechanical ventilation for respiratory failure.

COVID-19 Follow-up in COPD

More frequent monitoring for patients with moderate to severe COVID-19:

- Need for oxygen therapy
- If chest X-ray abnormalities not resolved at hospital discharge, a chest X-ray and possibly CT should be considered at 6-12 months

Prioritize in-person visits (e.g. severe COPD, significant comorbidities, changes in symptoms, living home alone).

Consider remote follow up (phone/virtual/online) as appropriate.

Patients should receive the COVID-19 vaccine and other vaccines as recommended.

Patients should practice infection prevention, social distancing, and wear facial coverings during times when COVID-19 prevalence is high.

Follow up should include review of symptoms, spirometry, treatment (medications, oxygen, pulmonary rehabilitation) and self-management.

Conclusions

COPD is a characterized by airflow obstruction, exposure to risk factors, and symptoms (dyspnea, wheezing, cough, sputum, fatigue, weight loss).

Tobacco smoking accounts for most COPD cases in high-income countries, although other irritants (household, occupational, air pollution) are heavily implicated globally.

Patients may present with other COPD risk factors to consider when managing: ?-1 antitrypsin deficiency, CB, structural/functional abnormalities, asthma and/or airway hyperreactivity, infections, poverty, and female (may be more susceptible to effects of smoking).

Comorbidities which may influence outcomes should also be considered when managing COPD: CV disease, skeletal or metabolic dysfunction, osteoporosis, depression, anxiety, lung cancer, bronchiectasis, obstructive sleep apnea, gastroesophageal reflux disease, anemia, polycythemia.

Initial COPD assessment should include post-bronchodilator spirometry, symptom assessment using formal questionnaires, exacerbation history, and review of risk factors and comorbidities.

For all patients with COPD, smoking cessation is recommended as well as an as-needed SABA or SAMA for immediate relief of symptoms.

Smoking cessation success is optimized with counseling + pharmacotherapy.

COPD pharmacotherapy recommendations are provided by GOLD ABE Assessment and Follow-up Treatment Pathway.

- Start with a bronchodilator LABA or LAMA preferred, or an as-needed SABA or SAMA, for patients with minor symptoms (e.g. occasional breathlessness).
- For patients with more persistent or severe symptoms exacerbations, LABA+LAMA is recommended.

The addition of ICS to LABA+LAMA is strongly favored in patients with a history of hospitalization for COPD exacerbation, 2 moderate COPD exacerbations in the past year, blood eosinophils ≥ 300 cells/μL, or asthma/features of asthma.

ICS should be used cautiously (or carefully de-escalated if possible) due to risk for pneumonia and other adverse effects, and lack of evidence for added benefit unless favored as stated above.

COPD management follow-up should include assessment of symptoms, exacerbations, other outcomes as indicated (e.g. exercise capacity, quality of life, LTOT monitoring), medication use, self-management, smoking cessation and avoidance of irritants, physical assessment, pulmonary rehabilitation, comorbidities and risk factors, spirometry (annually) and vaccines.

For patients who are having exacerbations despite LABA+LAMA therapy (with blood eosinophils < 100 cells/μL or unable to take ICS) or despite therapy with LABA+LAMA+ICS, roflumilast is recommended for those with FEV1 < 50% and CB, while azithromycin for up to 1 year is recommended for non-smokers.

Other treatments depend on patient-specific factors: mucolytics, theophylline, low-dose long-acting opioids, treatment of vitamin D deficiency, supplemental oxygen, ventilatory support, ?-1 antitrypsin deficiency augmentation

All patients with advanced COPD should be considered for advance directives, end-of-life and palliative care support.

In some patients with advanced refractory emphysema, surgery or bronchoscopic intervention may help.

Prevention and treatment of COPD exacerbations prevents further exacerbations, delays disease progression, and reduces mortality risk.

Mild exacerbations can be treated outpatient with SABA +/- SAMA.

Moderate exacerbations may be treated outpatient, while severe exacerbations require emergency room or hospital treatment, with SABA +/- SAMA, corticosteroids for up to 5 days, and a short course of antibiotics if 2-3 cardinal symptoms, one being increased sputum purulence, or mechanical ventilation.

Effective transitions of care and follow-up post hospital discharge prevents the risk of exacerbation-related readmission.

Appropriate management of key comorbidities can help to optimize COPD outcomes, and vice versa.

In patients with COPD, risk of severe COVID-19 may be increased depending on risk factors, and those with COVID-19 should receive standard of care with monitoring and follow-up (more frequent if moderate to severe COVID-19).