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Review Article

A Clinical Review on Chronic Obstructive Pulmonary Disease

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Abstract

Chronic Obstructive Pulmonary Disease (COPD) is a prevalent and progressive respiratory disorder characterized by persistent airflow limitation, often associated with chronic bronchitis and emphysema. This abstract provides a comprehensive overview of COPD, emphasizing its clinical significance and impact on global health. COPD represents a significant public health concern, with escalating prevalence and mortality rates worldwide. Understanding epidemiological trends and risk factors is crucial for effective disease management and prevention strategies. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines serve as a compass in COPD management. It provides a comprehensive overview of the GOLD guidelines, elucidating their role in risk stratification, treatment escalation, and personalized care for individuals across varying disease severities. The management of COPD involves a multidimensional approach targeting symptom relief, improving lung function, and enhancing overall quality of life. Pharmacological interventions, such as bronchodilators and anti-inflammatory agents, play a pivotal role. Beyond conventional pharmacological treatments, various traditional therapies have gained attention in COPD management. These may include complementary and alternative medicine practices, such as acupuncture, herbal supplements, and yoga. While evidence supporting the efficacy of these interventions is still evolving, exploring their potential benefits. A comprehensive and integrative approach is crucial for optimizing COPD care and improving the lives of individuals affected by this intricate respiratory condition. This abstract concludes by encouraging continued collaboration among clinicians and patients to shape the future of COPD care. Ultimately fostering hope for improved outcomes and an enhanced prospect for those living with severe respiratory ailments.

Introduction

Chronic obstructive pulmonary disease (COPD) is a hypernym given to a class of persistent lung diseases, which increase the difficulty of breathing air out of the lungs.[1] The harmful chemicals in smoke can damage the lining of the lungs and airways, which increases mucus production and causes a productive cough. This productive cough may last for 3 months in a year and 2 years. Exposure to irritants and chemicals can result in overgrowth of bronchial mucous glands and goblet cells in bronchioles. The two most prevalent diseases causing COPD are emphysema and chronic bronchitis. These two ailments frequently coexist and can vary in severity among people with COPD.[2] Chronic bronchitis is an infection of the bronchial tubes, which transports air to and from the lungs' air sacs (alveoli). Emphysema is a disease in which the alveoli at the end of the bronchioles in the lungs are damaged due to harmful exposure to cigarette smoke and other irritating gaseous and particulate materials. It is characterized by daily coughing and mucus (sputum) production.[3] Most COPD patients can attain adequate symptom control, quality of life, and a decreased risk of other linked conditions, with the right care for their condition. The purpose of this exploration is to shed light on the complexities of COPD, ranging from its epidemiological significance to the intricacies of diagnosis, treatment, and traditional therapeutic approaches. The structure of this overview will follow a systematic progression, offering insights into the epidemiology of COPD, the diagnostic challenges, contemporary treatment modalities, the role of traditional therapies, and conclude with a reflection on the evolving landscape of COPD care.

Symptoms

Excessive mucus production during coughing affects the heart and lungs. Wheezing causes tightness in the chest, and coughing up clear, white, yellow, or greenish-colored mucus that often contains

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phlegm. Breathlessness, particularly during vigorous activity, and chest constriction are common symptoms that contribute to a lack of energy in patients suffering from unwelcome fatigue. Additionally, these symptoms may lead to weight loss in later phases.

Mechanism

A poorly controlled airflow restriction and an aberrant inflammatory response in the lungs cause COPD. The latter is an illustration of the innate and adaptive immunological reactions to repeated exposure to toxic gases and particles, particularly cigarette smoke. The natural course of the disease is indicated by the combination of structural and inflammatory alterations that characterize COPD both pathologically and mechanistically. The two classic prototypes are "the pink puffer" and "the blue bloater". Clinical manifestations of COPD's etiological characteristics and causes include a progressive decline in lung function and irreversible blockage of airflow. Small airway disease, a crucial component of COPD, is the primary cause of decreased lung function. Luminal blockage induced by mucus, peri-bronchial fibrosis, structural alterations in the airway epithelium, and immune system activation are characteristics of bronchiolar remodeling, serving as a structural synonym for small airway disease.

Epidemiology

Early death from COPD is associated with significant life costs for healthcare systems.[4] According to projections for 2020, COPD ranks third among all causes of mortality globally and fifth among all causes of death. The prevalence of this disease varies depending on the nation, encompassing several phenotypes that are currently under discussion.[5] COPD is also associated with consequential comorbidities. The main challenge in the upcoming years will be to mitigate the negative effects of smoking beyond early detection of sickness in the general population. A persistent breathing condition that consistently progresses, characterized by an obstructive ventilatory guide,[6] is commonly associated with cigarette use and can lead to enduring respiratory problems. Chronic bronchitis refers to a condition with persistent airway obstruction (forced expiratory volume in 1 second (FEV1) to forced vital capacity (FVC) ratio: 70%). Chronic obstructive bronchitis with hypoxemia is also termed chronic respiratory failure. Breathlessness is a symptom of the lung disease known as emphysema.

In individuals with emphysema, the alveoli, and the lungs' air sacs, suffer damage. The anatomical level of emphysema is explained by the destruction of alveolar sac/duct walls distant from the terminal bronchiole, which may result in abnormally large distal airways.[7]

COPD in India

Over 30 million persons are estimated to have this disease, with India accounting for a significant and increasing portion of cases. Morbidity is among the greatest globally, according to estimates.[8] In India, for those aged older than 64.7 years, conventional estimates indicate that there are approximately 556,000 deaths per 100,000 persons, or 7.4% (95% confidence interval: 5.0–9.8%).[9]

The first global report by lung experts, titled "Burden of Obstructive Lung Disease" (BOLD), is the most reliable method for estimating the impact of COPD and recommends everyone to estimate the disease burden.[10] The global burden of disease had access to the research data over the previous four to five years and used it to develop national estimates. Over 40 countries, including India, participated in BOLD when it first began in the United States approximately 10 to 15 years ago. Bangladesh had the highest estimated pooled prevalence of COPD (13.1%; 95% confidence interval: 12.1–14.0%),[11] followed by India (11.1%; 95% confidence interval: 3.5–18.7) and Nepal (8.5; 95% confidence interval: 7.2–10.0%).[12] In rural Srinagar in northern India, the overall prevalence of COPD was highest among people aged 40 or older (19.3% according to the fixed criteria; 16.1% according to the lower limit of normal standards),[13] and the lowest prevalence there was observed at 4.1% according to the fixed criteria. Furthermore, the prevalence rates for the lower limit of normal criteria-based COPD were higher in Kamlapur compared to the country of Bangladesh (22.0% vs 16.2%), a neighborhood of Kamlapur.[14,15] According to four investigations, men were more likely than women to have COPD,[16] according to fixed criteria in Delhi and Srinagar, as well as both spirometry criteria in Nepal and rural Matlab, Bangladesh.[17] The overall incidence of COPD was significantly higher in rural regions (17.0% by fixed criteria and 12.5% by lower limit of normal criteria) than in suburban areas (9.9% by fixed criteria and 8.0% by lower limit of normal criteria),[18] according to a single study from Bangladesh that contrasted samples from countryside and non-rural areas. As of 2019, nearly 393 million people worldwide, or 10.3% of those aged 30 to 79 years, had COPD. A ratio of 7.6% corresponding to 292 million individuals was affected (10.3%; 95% confidence interval: 8.2% to 12.8%).[19] The gender patterns of COPD passing rate among men decreased by 25%, from 57.4 per 100,000 individuals in 1999 to 42.9% in 2018, whereas the percentage among women has remained moderately comparable over this period.[20]

Allergies and COPD

COPD is a progressive condition that presents challenges in exhaling. Allergies and susceptibility to environmental pollutants can exacerbate the symptoms of COPD. Individuals with COPD should be aware that potential irritants and triggers are likely to aggravate the symptoms. Inhaled steroids, such as fluticasone and mometasone furnace, may help reduce inflammation and mucus production, thereby decreasing symptoms of an allergic reaction or asthma attack and preventing COPD exacerbation. Medications, like pseudoephedrine (Sudafed), may relieve allergy symptoms, but they may not be optimal for daily.[21]

Diagnosis

Based on clinical symptoms, a specific test is called the pulmonary function test (PFT).[22] To identify the condition, doctors would evaluate people's signs, symptoms, and PFT.[23] PFT assesses the capacity for air inhalation and exhalation and determines whether the lungs can supply adequate oxygen to the blood.[24] For a thorough physical examination, medical professionals use various techniques to assess the patient's respiratory health. A physical examination might offer crucial tips, even though a final diagnosis of COPD usually requires a combination of clinical evaluation, medical history, pulmonary function testing, and imaging studies.

Physical examination

A medical professional performing a physical examination for COPD may make the following observations through sight, touch, and sound:

Sight

While observing a patient, a healthcare professional may watch for any indications of respiratory distress. These can include cyanosis,

blue staining of the lips or nails indicating insufficient oxygenation, rapid or laborious breathing, and the employment of accessory muscles (chest or neck muscles). The healthcare professional will also count the patient's respiratory rate, which can be elevated in COPD patients.

Touch

The medical professional may examine the patient's chest and back with their hands to check for soreness or abnormalities. The presence of a barrel chest appearance, caused by long-term lung hyperinflation and commonly found in patients with severe COPD, can be observed. Additionally, COPD patients might also be screened for hyperinflated lungs. Light palpation can be used to check for masses, crepitus (a crackling feeling beneath the skin), and any localized discomfort.

Sound

The healthcare professional will listen to breath sounds in different lung fields using a stethoscope. Specific findings in COPD may comprise decreased airflow in affected areas, as indicated by diminished breath sounds. A high-pitched whistling sound typically produced during expiration may indicate airway blockage, known as wheezing. Rales or crackles, usually audible during inspiration, may indicate fluid accumulation or tissue damage.[25]

Analyzing breathing patterns

The pace, rhythm, and depth of the patient's breathing will all be noted by medical professionals. Respiratory distress can be indicated by irregular or difficult breathing patterns.

Examining the shoulders and neck

Indications of increased usage of auxiliary muscles during breathing can be observed by checking the neck and shoulder regions. To aid with breathing, this may involve utilizing the scalene muscles in the neck and the trapezius muscles in the shoulders.

Auscultation of lung sounds

The healthcare professional will use a stethoscope to listen to lung sounds in various regions of the chest. Wheezing (high-pitched musical notes) and diminished breath sounds are two signs of COPD.

Assessment of general health

The medical professional will evaluate the patient's general health, considering any signs of muscle wasting or weight loss that may be related to severe COPD.

Medication evaluation

The evaluation frequently involves a discussion of the patient's current medications, including oral and inhalation treatments for COPD.

Functional assessment

The healthcare professional may assess the patient's capacity for performing activities of daily living, gauge exercise tolerance, and discuss any restrictions on physical activity, depending on their symptoms and functional limits.[26]

The six-minute walk test involves strolling at a regular pace for six minutes. This test is used to monitor the effectiveness of therapies for lung, heart, and other health issues. Individuals with COPD, pulmonary hypertension, interstitial lung disease, or other lung conditions often undergo this test.[27] Pulse oximetry, a non-invasive test, determines blood oxygen saturation by illuminating light at specific wavelengths into the tissue,[28] most frequently through the fingernail bed. A normal level is about 95% or more oxygen, while about 90% of patients with breathing problems or chronic lung illness may have normal levels.[29] The following techniques are also used to diagnose COPD.[30]

Spirometry

A painless test is used to identify and monitor specific lung problems by measuring the amount of air involved.[31] The first stage involves determining the test's validity. The next phase is categorized as either an obstructive or restrictive ventilatory pattern.[32] Depending on the severity, if a ventilatory pattern is identified, certain individuals may require additional tests such as static lung volumes, diffusing capacity of the lung for carbon monoxide, and bronchodilator challenge testing.[33]

Spirometric measurements

The FVC or Forced Vital Capacity, is the greatest amount of air that can be forcibly expelled. FEV1 is an abbreviation for Forced Expiratory Volume in one second, signifying the amount of air forcibly evacuated in the first second after a maximal inhalation.[34] The FEV1/FVC ratio indicates the proportion of FVC evacuated in one second.[35] FEV6 is an acronym for Forced Expiratory Volume in six seconds. An FEF of 25–75% is a shorthand for forced expiratory flow throughout the middle half of the FVC, representing the average flow from the point where 25% of the FVC has been expelled to the point when 75% of the FVC will be exhaled. MVV represents Maximum Voluntary Ventilation, and it is better correlated with different outcomes from physical activity in daily life than FEV1 and inspiratory capacity.[35]

Chest X-ray

Identifying signs such as persistent cough or shortness of breath helps recognize COPD manifestations in lung images. Images may reveal enlarged lungs, air pockets (bullae), and a flattened diaphragm. This device is primarily utilized for chest X-rays and comprises wall-mounted, box-like equipment storing X-ray images or a specialized plate that digitally records images.[36]

Blood test

Anemia, characterized by too little iron in the body, and polycythemia, involving an excess of red blood cells in the blood, can both exhibit symptoms similar to COPD. When there is a deficiency of alpha-1-antitrypsin, this may be assessed. The levels of oxygen and carbon dioxide in the blood are determined through an arterial blood gas test, indicating how effectively the lungs are operating.[37] The results of this test can assist in determining the severity of COPD and whether patients can benefit from oxygen therapy.

Computed tomography scan

It assesses an individual's lungs to aid in detecting emphysema and determining whether surgery for COPD would be beneficial. In comparison to a chest X-ray, computed tomography imaging may have the ability to detect emphysema earlier and identify additional COPD changes, including enlarged arteries in the lungs. This test involves a minimal amount of emission, but if a contrast dye is used, there may be some discomfort from the needle, a slight tingling sensation after the injection, or a metallic taste in the mouth. Although quite uncommon, the contrasting dye may cause allergic reactions in one or two individuals.[38]

Echocardiogram

Echocardiography is a rapid, noninvasive, portable, and accurate method for evaluating heart changes.[39] This is the least common echocardiographic finding in pulmonale, appearing in 62 % of the patients. Other echocardiographic outcomes include right atrium/right ventricle expansion, right ventricular hypertrophy, left ventricular diastolic dysfunction, right ventricular systolic dysfunction and left ventricular hypertrophy. The frequency of heart dysfunction also increases with the severity of COPD.[40]

Electrocardiogram

When used to diagnose individuals with COPD, the results of the electrocardiogram were shown to be 35.8% hypersensitive and 95.7% reliable, with most of the patients also experiencing respiratory issues.[41] The electrocardiogram captures an image of the heart's electrical functioning throughout the tracked period, including the pressure evaluation, holter monitor, event recording device, and loop recording. Suppose there are any indications that an electrocardiogram could be irregular. In that case, various conditions may be considered, such as a lack of blood flow, a larger heart, cardiac abnormalities, birth defects, irregular heartbeats, and difficulties with ions. Examples of conditions that may affect the electrocardiogram include blocked arteries, cardiovascular disease, chamber hypertrophy, chamber dilatation, and alterations in how power flows through the heart.[42]

Peak flow test

A peak airflow meter calculates the volume of quick air that leaves the lungs as we forcibly breathe. Measurements from the meter might indicate whether children have asthma that is beginning to worsen. A peak expiratory flow rate of less than 80% is considered to be a good maximum flow reading for COPD and can identify over 90% of the population with the condition. This includes people with mild to moderate symptoms who are likely to benefit from the use of bronchodilators.[43]

Grades or stages

The phrase "stages" was used in the original Global Initiative for Chronic Obstructive Lung Disease (GOLD) system to describe the various COPD severity levels. They are now referred to as "grades". The initial stages only utilized FEV findings. The physician will grade the following four factors: the severity of the patient's present symptoms and the outcomes of the patient's spirometry.[44]

Grades of spirometry findings

The findings of spirometry are reviewed to determine how well the lungs are functioning. These outcomes are classified into four grades: GOLD-1 indicates mild, GOLD-2 indicates moderate, GOLD-3 indicates severe, and GOLD-4 indicates an extremely severe condition. The term "flare" is used if the spirometry result is GOLD-3 or GOLD-4, as individuals are more likely to experience these flare-ups.[45]

COPD Groups

Physicians categorize COPD into groups based on various factors, including symptoms, spirometry results, and exacerbation risk.

GOLD 1 or 2 in Group A: Relatively minor symptoms with FEV-1 is at least 80%. The symptoms didn't lead to hospitalization.

GOLD 1 or 2 in Group B: FEV-1 ranges from 50% to 80%, with more symptoms compared to Group A. Patients often visit their doctor for symptoms like coughing, wheezing, and shortness of breath.

GOLD 3 or 4 in Group C: The lungs' capacity to take in and expel air is significantly constrained. The FEV-1 ranges from 30% to 50%. The individuals have experienced at least one hospital admission or more than two flare-ups in the last year.

GOLD 3 or 4 in Group D: Breathing in and out is difficult. A minimum of two flare-ups or one hospitalization occurred within the last year. This condition is referred to as the "end-stage" of COPD.[46]

Comorbid diseases

The common conditions associated with COPD include the following:

Cardiovascular diseases

Coronary artery disease, heart failure, and hypertension are cardiovascular conditions associated with an elevated risk of COPD. Cardiovascular issues may be exacerbated by the systemic inflammation and decreased oxygenation from COPD.[47]

Osteoporosis

People with COPD are more likely to develop this disorder, which is characterized by weaker bones that are more likely to break. Reduced physical activity and corticosteroid use may contribute to this condition.

Type 2 diabetes

Type 2 diabetes is more prevalent in people with COPD, likely due to similar risk factors such as smoking and inflammation.[48]

Gastroesophageal reflux disease

People with COPD are more likely to have gastroesophageal reflux disease. It might be a factor in exacerbations and can worsen respiratory symptoms.

Muscle weakness and wasting (Cachexia)

COPD can cause muscle weakness and wasting, restricting physical activity, and impairing function.

Infections of the respiratory system

Infections that may cause pneumonia and bronchitis, are more common in people with COPD. Persistent infections can lead to exacerbations.[49]

Smoking

Smoking is a common risk factor for lung cancer and COPD. Lung cancer is more likely to develop in those with COPD.

Anemia

Some people with COPD may develop anemia, caused by chronic inflammation or other reasons.

Metabolic syndrome

People with COPD are more likely to suffer from this group of ailments, including obesity, high blood pressure, high blood sugar, and abnormal lipid profiles.

Obstructive sleep apnea

Linked to COPD, this disorder can lower quality of life, increase fatigue, and cause daytime sleepiness.[50]

Treatment of COPD

The current COPD management strategy focuses on a combination of symptom control and reducing exacerbation risk. The GOLD-ABCD (A, low risk, fewer symptoms; B, low risk, more symptoms; C, high risk, fewer symptoms, D, high risk, more symptoms) concept tool categorizes patients into "risk stratification" groups, guiding direct pharmacotherapy. This classification is based on symptom severity, determined by both the COPD Assessment Test score and the modified Medical Research Council scale, along with worsening risk identified by both spirometry-defined airflow restriction or past exacerbations.[51] COPD treatment involves managing related illnesses and providing additional oxygen for breathing.[52,53] The key for individuals with COPD is to utilize respiratory aids such as inhaler devices, and drugs including bronchodilators, aerosol steroids, and specific antibiotics.[54] Lung rehabilitation, a specialized fitness and respiratory program, as well as surgery or a lung transplant, are available options for a very small percentage of patients.

Nebulizer medicine

If inhaler devices fail to alleviate a severe case of COPD, a nebulizer device can be used. It serves to transform liquid medication into a fine spray that patients can inhale using a mouthpiece or a face mask. This method allows for the administration of multiple drugs simultaneously.[55] Typically, a nebulizer machine can be provided for home use.

Roflumilast

It is a novel drug that is effective in treating flare-ups. It is recommended for those who feel that they have experienced a sudden worsening at least twice over the past 12 months. The drug is available in tablet form, and it alleviates respiratory and lung irritation.[56]

Long-term oxygen therapy

COPD causes blood oxygen levels to drop, and hence individuals may be advised to use a mask or nasal tubes at home to receive oxygen. This may assist in preventing a decrease in blood oxygen levels. It is recommended to use oxygen for at least 16 hours a day. When using oxygen, it is crucial to avoid smoking. Due to the heightened flammability of increased oxygen levels, even a single cigarette could lead to an explosion or fire.[57]

Ambulatory oxygen therapy

Vascular air, which individuals with COPD use while walking or engaging in physical activity, can be beneficial for them. Instead of undergoing long-term oxygen therapy, individuals may be able to receive portable oxygen treatment if their blood oxygen levels are normal at rest but drop during exercise.[58]

Non-invasive ventilation

Non-invasive ventilation therapy is employed for individuals admitted to a hospital due to a severe flare-up. A portable machine is connected to a mask that covers the nose or face, supporting the pulmonary system and facilitating breathing through the nose.[59]

Colorful inhalers for COPD

A variety of anticholinergic inhalers are available, including aclidinium, glycopyrronium, ipratropium, tiotropium, and umeclidinium. It is recommended to use anticholinergic inhalers daily, even if asymptomatic.

Inhalation devices for beta-agonists include salmeterol, olodaterol, arformoterol, formoterol and indacaterol.

Gobbled corticosteroids include beclomethasone, fluticasone, ciclesonide, mometasone, budesonide, and flunisolide. While taking these medications, the patient must rinse the mouth, gargle and spit it out.

A combination of two drugs includes budesonide and formoterol, albuterol and ipratropium, fluticasone and salmeterol, fluticasone and vilanterol, formoterol and mometasone, and tiotropium and olodaterol. These combinations are swallowed.[60]

Exacerbation of COPD

Patients experiencing COPD exacerbation are sometimes referred to as having a flare-up, when they face a significant worsening of breathing problems due to the condition. Although reactions to flare-ups vary, there are potential warning signs, such as the sensation of being unable to exhale. Worsening may last for several weeks or even days, necessitating the use of oral corticosteroids and antibiotics. Exacerbations are more likely to occur as lung function declines in the later stages of COPD. These episodes are often caused by bacterial or viral lung infections, but they can also result from factors or situations that make breathing difficult. In addition to the typical COPD symptoms, there are other signs of exacerbation. Sometimes, people mistake them for other conditions, such as severe allergies, a severe cold, or a sinus infection. The most common warning signs of an imminent exacerbation include:

Coughing, wheezing, or shortness of breath that occurs more frequently than usual; changes in the tone, thickness, or amount of mucus; prolonged exhaustion lasting more than a day; swelling in the ankles or legs; increased difficulty with sleep; or the urge to take in more oxygen if the oxygen level drops.[61]

Prevalence and risk factors

COPD affects 300 million individuals worldwide, ranking as the third leading cause of mortality and affecting one in every ten persons globally. There are about 3.2 million annual deaths.[62] Among older age groups, significantly higher rates and numbers of COPD fatalities are observed.[63] About 86% of COPD fatalities occur in persons aged 65 years or older.[64] The age group between 75 to 84 years accounts for the majority of deaths, although 85 and older people experience the highest death rates. Except for those aged 85 and older, whose mortality rates increased by 0.5% each year from 1999 to 2018, death rates among people aged 55 and older are declining for each age group every 10 years.[65]

Traditional medicines and healing therapies for COPD

When exploring natural remedies for COPD or other respiratory illnesses, one might encounter thyme, echinacea, ginger, and curcumin, *etc*. Although there is some medical support for many of these herbs.

Echinacea

In earlier times, people have taken echinacea to aid in preventing the spread of upper respiratory illnesses related to influenza and the typical cold and it is typically well-tolerated. When adverse

Table 1. Location and efficacy of acupuncture points

Acupuncture points	Location	Efficacy
(Lung 1): LU1	On the upper chest, just below the collarbone.	Used to treat asthma, cough, and other respiratory symptoms, as well as to enhance lung function.
(Lung 5): LU5	On the forearm, in the depression at the elbow crease when the arm is bent.	Used frequently to clear the lungs and relieve cough, sore throat, and respiratory discomfort.
(Lung 7): LU7	On the wrist, in the crease of the inner wrist, in line with the thumb.	Used to be effective for problems including cough, asthma, and shortness of breath since it aids in promoting lung function and reducing inflammation.[76]
(Lung 9): LU9	On the wrist, between the tendon of the abductor pollicis longus muscle and the radial artery, in the depression at the lateral end of the transverse crease of the wrist.	Supports lung function, relieves respiratory symptoms, boosts the immune system, and promotes emotional well- being.
(Conception Vessel 17): CV17	In the center of the chest, in line with the nipples.	Supports emotional well- being and relaxation, potentially reducing stress and anxiety that can affect lung health.
(Lung 20): LU20	In the depression below the clavicle, approximately 6 inches lateral to the midline (away from the sternum).	Relieves cough, chest congestion, and respiratory discomfort; may also support emotional balance.
(Lung 10): LU10	On the palm, between the first and second metacarpal bones, at the midpoint of the second metacarpal bone.	Addresses sore throat, throat discomfort, and local pain in the throat area.[77]
(Lung 11): LU11	On the thumb, at the corner of the nail on the radial (thumb) side.	Particularly useful for throat conditions such as sore throat and difficulty swallowing.
(Ren 22): RN22	On the upper chest, between the collarbones	Opens the chest and promotes easier breathing, beneficial for cough, chest congestion, and throat discomfort.[78,79]

effects do occur, they frequently involve common gastrointestinal symptoms like nausea or stomach pain. A rash, worsened asthma symptoms, and anaphylaxis are just a few of the allergic reactions that echinacea has been linked to.[66]

Thyme

Thymus vulgaris, an expectorant and antioxidant frequently used in respiratory problem treatment, is a common culinary herb. In a laboratory model of a person's COPD airways, thyme essence was reported to increase the cilia beating frequency.[67] The small filaments known as cilia, which line the respiratory system and aid in clearing mucus from the airway, are frequently harmed in COPD instances.[68]

Curcumin

The main active molecule in turmeric (Curcuma longa), is a highly effective anti-inflammatory compound that may reduce inflammation of the airways.[69] Scientists discovered that people with COPD who included curcumin in their diet showed significantly fewer incidences of a particular colonizing bacteria, non-typeable Haemophilus influenzae.[70]

Ginger

It is believed that ginger contains potent antioxidants and natural antibiotics to aid the immune system in fighting off infection. Additionally, ginger may relieve sore throats and help clear congestion. A few minor adverse effects have been noted, such as flatulence, diarrhea, and stomach pain. The interaction of ginger with blood thinners is also a potential risk. Given that ginger might enhance bile flow, several specialists also advise against using it for those with gallstone disease.[71]

N-acetylcysteine (NAC)

A type of antioxidant that is derived from the amino acid L-cysteine, aids in thinning thickened mucus and may halt or stop the deterioration of COPD symptoms. Several researchers examined the effects of NAC at low and high doses on the incidence of exacerbations in thousands of COPD patients who received treatment for four to 36 months. The study's findings revealed that people who took NAC experienced significantly fewer flare-ups of COPD or chronic bronchitis.[72]

Acupuncture

While COPD is incurable, the symptoms of COPD may be alleviated, and the disease progression may be slowed by medications and alternative treatments such as acupuncture. Originating from traditional Chinese medicine, acupuncture entails the placement of tiny needles inside certain body parts. It can occasionally be used to treat conditions such as migraines and persistent pain. Acupuncture is believed to regulate the production of cytokines, which are pro-inflammatory chemicals. Lowering cytokine levels could potentially reduce inflammation in the respiratory system, alleviating symptoms of COPD such as loss of breath. Several investigations have discovered that acupuncture may enhance exercise effectiveness, immune response, and lifestyle quality.[73] Acupuncture needles are placed into the body at precise sites called acupoints during an acupuncture treatment.[74] The acupoint has unique therapeutic effects and can be used to treat a range of health issues.[75] Acupuncture points that are often used and their efficacy under various conditions are listed in Table 1.[76–79]

Yoga

Yoga can benefit those who have COPD in several ways, such as

encouraging conscious breathing, reducing anxiety, maintaining muscles, and increasing mobility. Additionally, practicing meditation will teach a person how to control breathing. Asanas and pranayama are both part of yoga. The breathing exercise known as pranayama can strengthen the diaphragm. Muscles are lengthened and strengthened through yogic postures known as asanas, maintaining flexibility and mobility.[80]

Future treatments for COPD

Researchers and medical professionals are continually striving to develop novel COPD treatments that will help patients breathe more easily. Anti-interleukin-5 medications benralizumab, mepolizumab, and reslizumab are the newer biological drugs designed to reduce exacerbations.[81,82] Benralizumab and mepolizumab are both licensed for patients aged 12 years and older, while reslizumab is only approved for those 18 years and older.[83,84] These medications exhibit outstanding safety and effectiveness profiles, significantly reducing asthma exacerbations and related healthcare consumption.

When combined with standard therapy, azithromycin, taken daily for a year, was found to reduce the frequency of exacerbations and improve the quality of life but was associated with hearing loss in a small number of participants.[85]

The lung flute, an innovative respiratory tool, increases mucous evacuation by emitting a low-frequency acoustic wave during a moderately powerful exhalation.

To achieve lung denervation and facilitate ventilation, a revolutionary bronchoscope treatment is used for COPD. The most recent COPD medication Fluticasone/Umeclidinium/Vilanterol (TRELEGY ELLIPTA), was the first triple inhaled therapy authorized for the condition.

GOLD treatment guidelines for COPD

Reducing the adverse consequences of the present exacerbation and helping to avoid future episodes are preventive measures for managing a COPD exacerbation.[86] Short-acting beta2-agonists, either with or without short-acting anticholinergics, are the first line of therapy for mild exacerbations.[87] Based on the location of airflow constraint, the GOLD criteria categorize situations into four separate orders: GOLD-1 (mild), GOLD-2 (moderate), GOLD-3 (severe), or GOLD-4 (verifiably severe). This classification can be determined by evaluating the post-bronchodilator FEV1/FVC.

Non-pharmacologic and precautionary remedy of GOLD

Non-pharmacologic therapy for COPD includes smoking cessation, exercise, and immunization. According to the 2021 GOLD recommendations, discontinuation rates were much greater for this therapy compared to patient-initiated therapy. The most sophisticated method of quitting cigarettes is to take medicine for nicotine withdrawal, utilizing ingredients such as those found in nicotine chewing gum, inhalers, nasal spray, skin patches, lingual tablets, or pills. Numerous medications, such as varenicline, bupropion, and nortriptyline, have been shown to increase long-term cessation rates. Even though e-cigarettes have been available for over fifteen years, there is still debate over their safety and efficacy.[88,89] One of the most significant changes to the GOLD recommendations for 2021 is the inclusion of the Tdap immunization. Providing information on inhaler use, medication adherence, and proper technique is one important function a pharmacist can perform in helping COPD patients.[90] It may be helpful to have a well-supported written action plan that covers avoiding aggravating factors and treating or managing exacerbated symptoms.[91] Screening should check for increasing symptoms of COPD along with smoking status, the quantity, and regularity of flare-ups.[92]

Tips to stop COPD

The injury that has already occurred to the lungs cannot be repaired. However, the damage can be slowed down or prevented from worsening with certain alterations.[93] It is crucial to avoid lung irritates, such as dust, pollutants, secondhand smoke, and smog as much as possible. For individuals with COPD, even a simple cold could cause serious issues. Therefore, it is essential to clean their hands thoroughly and regularly, especially in cold weather. Breathing can be made easier with the help of medications, other treatments, and lifestyle modifications. To achieve worldwide goals aimed at reducing premature mortality by 25% by 2025, there must be a considerable increase in the number of smokers attempting to cease, as well as a significant improvement in the success rates of those attempts in low-, middle-, and higher-income countries.[94]

Conclusion

In India, the prevalence of COPD is relatively high, with notable regional variations. Smoking cigarettes and bidis, as well as nonsmokers' exposure to environmental tobacco smoke, are significant risk factors. COPD is not only caused by smoking but also by exposure to secondhand smoke. Additionally, prolonged exposure to air pollution may lead to COPD, as individuals inhale dust or fumes from fuel burned for cooking or heating. Severely ill patients may require more intensive treatment. Patients with severe disease may benefit from advanced care planning, palliative care, and non-invasive home ventilation. Hence it is crucial to establish a consistent technique for assessing the national burden of illness and implementing disease-surveillance programs. Medications may be administered or inhaled to alleviate symptoms and reduce flare-ups.

Perspectives on holistic care which include advancements in pharmacological and non-pharmacological treatments, have improved symptom management. Integrating mental health considerations, nutritional support, and patient education into COPD care could enhance overall well-being and resilience, providing a more comprehensive approach to managing this chronic condition. Empowering individuals with COPD through education, self-management strategies, and community support is an integral aspect of future directions. Promoting patient advocacy initiatives can not only enhance disease awareness but also foster a sense of community and resilience among those affected by COPD. In conclusion, by embracing a dynamic and inclusive approach to COPD care, we can strive towards a future where the burden of this respiratory condition is alleviated, and individuals affected by COPD experience enhanced quality of life and well-being.

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Conflict of interest

The authors declare that they have no competing interests.

Author contributions

Study impression and outline (SS, SR, RA and TV); review of literature, perusal and clarification (SR, SS and TV); draft of manuscript (SS and SR); manuscript writing (SR and SS); critical revision (SS, RA and TV); administrative support (RA, SS and TV). All the authors reviewed the literature, compiled the data and approved the final version of the manuscript.

References

[1] Matsunaga K, Harada M, Suizu J, Oishi K, Asami-Noyama M, Hirano T. Comorbid Conditions in Chronic Obstructive Pulmonary Disease: Potential Therapeutic Targets for Unmet Needs. J Clin Med 2020;9(10):3078. doi:10.3390/jcm9103078, PMID:32987778.

[2] World Health Organization. Chronic obstructive pulmonary disease. Geneva: World Health Organization; 2023.

[3] Tsutsumi A, Chubachi S, Irie H, Sasaki M, Yamada Y, Sugiura H, *et al*. Characteristics of chronic obstructive pulmonary disease patients with robust progression of emphysematous change. Sci Rep 2021;11(1):9548. doi:10.1038/s41598-021-87724-8, PMID:33953210.

[4] May SM, Li JT. Burden of chronic obstructive pulmonary disease: healthcare costs and beyond. Allergy Asthma Proc 2015;36(1):4–10. doi:10.2500/aap.2015.36.3812, PMID:25562549.

[5] Wang H, Ye X, Zhang Y, Ling S. Global, regional, and national burden of chronic obstructive pulmonary disease from 1990 to 2019. Front Physiol 2022;13:925132. doi:10.3389/fphys.2022.925132, PMID:36017339.

[6] Wheaton AG, Liu Y, Croft JB, VanFrank B, Croxton TL, Punturieri A, *et al*. Chronic Obstructive Pulmonary Disease and Smoking Status - United States, 2017. MMWR Morb Mortal Wkly Rep 2019;68(24):533–538. doi:10.15585/mmwr.mm6824a1, PMID:31220055.

[7] Szalontai K, Gémes N, Furák J, Varga T, Neuperger P, Balog JÁ, *et al*. Chronic Obstructive Pulmonary Disease: Epidemiology, Biomarkers, and Paving the Way to Lung Cancer. J Clin Med 2021;10(13):2889. doi:10.3390/jcm10132889, PMID:34209651.

[8] GBD Chronic Respiratory Disease Collaborators. Prevalence and attributable health burden of chronic respiratory diseases, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet Respir Med 2020;8(6):585–596. doi:10.1016/S2213-2600(20)30105-3, PMID:32526187.

[9] McKay AJ, Mahesh PA, Fordham JZ, Majeed A. Prevalence of COPD in India: a systematic review. Prim Care Respir J 2012;21(3):313–321. doi:10.4104/pcrj.2012.00055, PMID:22790612.

[10] Buist AS, McBurnie MA, Vollmer WM, Gillespie S, Burney P, Mannino DM, *et al*. International variation in the prevalence of COPD (the BOLD Study): a population-based prevalence study. Lancet 2007;370(9589):741–750. doi:10.1016/S0140-6736(07)61377-4, PMID:17765523.

[11] Alam DS, Chowdhury MA, Siddiquee AT, Ahmed S, Clemens JD. Prevalence and Determinants of Chronic Obstructive Pulmonary Disease (COPD) in Bangladesh. COPD 2015;12(6):658–667. doi:10.3109/15412555.2015.1041101, PMID:26263031.

[12] Adhikari TB, Acharya P, Högman M, Neupane D, Karki A, Drews A, *et al*. Prevalence of Chronic Obstructive Pulmonary Disease and its Associated Factors in Nepal: Findings from a Community-based Household Survey. Int J Chron Obstruct Pulmon Dis 2020;15:2319–2331. doi:10.2147/COPD.S268110, PMID:33061350.

[13] Park J, Kim HJ, Lee CH, Lee CH, Lee HW. Impact of long-term exposure to ambient air pollution on the incidence of chronic obstructive pulmonary disease: A systematic review and meta-analysis. Environ Res 2021;194:110703. doi:10.1016/j.envres.2020.110703, PMID:33417909.

[14] Varmaghani M, Dehghani M, Heidari E, Sharifi F, Moghaddam SS, Farzadfar F. Global prevalence of chronic obstructive pulmonary disease: systematic review and meta-analysis. East Mediterr Health J 2019;25(1):47–57. doi:10.26719/emhj.18.014, PMID:30919925.

[15] Islam MS, Hossain MM, Pasha MM, Azad AK, Murshed KM. Prevalence and risk factors of chronic obstructive pulmonary disease (COPD) in Dhaka city population. Mymensingh Med J 2013;22(3):547–551. PMID:23982547.

[16] GBD 2017 Risk Factor Collaborators. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet 2018;392(10159):1923–1994. doi:10.1016/S0140-6736(18)32225-6, PMID:30496105.

[17] Jarhyan P, Hutchinson A, Khaw D, Prabhakaran D, Mohan S. Prevalence of chronic obstructive pulmonary disease and chronic bronchitis in eight countries: a systematic review and meta-analysis. Bull World Health Organ 2022;100(3):216–230. doi:10.2471/BLT.21.286870, PMID:35261410.

[18] Lee HW, Park J, Jo J, Jang EJ, Lee CH. Comparisons of exacerbations and mortality among regular inhaled therapies for patients with stable chronic obstructive pulmonary disease: Systematic review and Bayesian network meta-analysis. PLoS Med 2019;16(11):e1002958. doi:10.1371/journal.pmed.1002958, PMID:31730642.

[19] Verma A, Gudi N, Yadav UN, Roy MP, Mahmood A, Nagaraja R, *et al*. Prevalence of COPD among population above 30 years in India: A systematic review and meta-analysis. J Glob Health 2021;11:04038. doi:10.7189/jogh.11.04038, PMID:34484706.

[20] Gudi N, Mahmood A, Roy MP, Ravishankar, Nayak P, Verma A. Burden of COPD among population above 30 years in India: protocol for a systematic review and proposed meta-analysis. Can J Respir Ther 2021;57:14–17. doi:10.29390/cjrt-2020-040, PMID:33542948.

[21] Millard E. Are Allergies Making Your COPD Worse? Health Central; 2023.

[22] Ruppel GL, Enright PL. Pulmonary function testing. Respir Care 2012;57(1):165–175. doi:10.4187/respcare.01640, PMID:22222135.

[23] Hopkinson NS, Molyneux A, Pink J, Harrisingh MC, Guideline Committee (GC). Chronic obstructive pulmonary disease: diagnosis and management: summary of updated NICE guidance. BMJ 2019;366:l4486. doi:10.1136/bmj.l4486, PMID:31358491.

[24] George MD, Shah R, Kreider M, Miller WT Jr, Merkel PA, Werth VP. Pulmonary function tests, interstitial lung disease and lung function decline in outpatients with classic and clinically amyopathic dermatomyositis. Br J Dermatol 2017;176(1):262–264. doi:10.1111/bjd.14771, PMID:27229750.

[25] Kim Y, Hyon Y, Jung SS, Lee S, Yoo G, Chung C, Ha T. Respiratory sound classificationfor crackles, wheezes, and rhonchi in the clinical field using deep learning. Sci Rep 2021;11(1):17186. doi:10.1038/s41598-021-96724-7, PMID:34433880.

[26] Lynch DA. Functional imaging of COPD by CT and MRI. Br J Radiol 2022;95(1132):20201005. doi:10.1259/bjr.20201005, PMID:34541865.

[27] Li F, Huang ZW, Wang XF, Xu HW, Yu H, Chen YB, *et al*. Safety and use of pulmonary function tests: a retrospective study from a single center over seven years' clinical practice. BMC Pulm Med 2019;19(1):259. doi:10.1186/s12890-019-1019-z, PMID:31864318.

[28] Stephanie W. What Is Pulse Oximetry? WebMD; 2023.

[29] Amalakanti S, Pentakota MR. Pulse Oximetry Overestimates Oxygen Saturation in COPD. Respir Care 2016;61(4):423–427. doi:10.4187/respcare.04435, PMID:26715772.

[30] Bhatt SP, Sieren JC, Dransfield MT, Washko GR, Newell JD Jr, Stinson DS, *et al*. Comparison of spirometric thresholds in diagnosing smoking-related airflow obstruction. Thorax 2014;69(5):409–414. doi:10.1136/thoraxjnl-2012-202810, PMID:23525095.

[31] Christopher DJ, Oommen AM, George K, Shankar D, Agrawal A, Thangakunam B. Prevalence of Airflow Obstruction as Measured by Spirometry, in Rural Southern Indian Adults. COPD 2020;17(2):128–135. doi:10.1080/15412555.2020.1723074, PMID:32020813.

[32] Ranu H, Wilde M, Madden B. Pulmonary function tests. Ulster Med J 2011;80(2):84–90. PMID:22347750.
[33] Centers for Disease Control and Prevention. Respiratory Health - Bronchodilator Procedures Manual 2008;AtlantaCDC.
[34] Whittaker HR, Jarvis D, Sheikh MR, Kiddle SJ, Quint JK. Inhaled corticosteroids and FEV(1) decline in chronic obstructive pulmonary disease: a systematic review. Respir Res 2019;20(1):277. doi:10.1186/s12931-019-1249-x, PMID:31801539.
[35] Mohamed Hoesein FA, Zanen P, Lammers JW. Lower limit of normal or FEV1/FVC < 0.70 in diagnosing COPD: an evidence-based review. Respir Med 2011;105(6):907–915. doi:10.1016/j.rmed.2011.01.008, PMID:21295958.
[36] James R. How Do X-Rays Help Diagnose COPD? Healthline; 2023.
[37] Khatib S, Sabobeh T, Jaber F, Abdalla K, Singh S, Salzman G. Use of Laboratory Tests and Their Prognostic Value in Patients with Stable Chronic Obstructive Pulmonary Disease. Mo Med 2022;119(6):545–552. PMID:36588649.
[38] Newell JD Jr, Fuld MK, Allmendinger T, Sieren JP, Chan KS, Guo J, *et al*. Very low-dose (0.15 mGy) chest CT protocols using the COPDGene 2 test object and a third-generation dual-source CT scanner with corresponding third-generation iterative reconstruction software. Invest Radiol 2015;50(1):40–45. doi:10.1097/RLI.0000000000000093, PMID:25198834.
[39] Levy PT, Patel MD, Choudhry S, Hamvas A, Singh GK. Evidence of Echocardiographic Markers of Pulmonary Vascular Disease in Asymptomatic Infants Born Preterm at One Year of Age. J Pediatr 2018;197:48–56.e2. doi:10.1016/j.jpeds.2018.02.006, PMID:29625733.
[40] Gupta NK, Agrawal RK, Srivastav AB, Ved ML. Echocardiographic evaluation of heart in chronic obstructive pulmonary disease patient and its co-relation with the severity of disease. Lung India 2011;28(2):105–109. doi:10.4103/0970-2113.80321, PMID:21712919.
[41] Warnier MJ, Rutten FH, Numans ME, Kors JA, Tan HL, de Boer A, *et al*. Electrocardiographic characteristics of patients with chronic obstructive pulmonary disease. COPD 2013;10(1):62–71. doi:10.3109/15412555.2012.727918, PMID:23413894.
[42] Sattar Y, Chhabra L. Electrocardiogram. StatPearls. Treasure Island (FL): StatPearls Publishing; 2023.
[43] Obaseki DO, Akanbi MO, Onyedum CC, Ozoh OB, Jumbo J, Akor AA, *et al*. Peak expiratory flow as a surrogate for health related quality of life in chronic obstructive pulmonary disease: a preliminary cross sectional study. Ghana Med J 2014;48(2):85–90. doi:10.4314/gmj.v48i2.5, PMID:25667555.
[44] Moore VC. Spirometry: step by step. Breathe (Sheff) 2012;8:232–240. doi:10.1183/20734735.0021711.
[45] Brat K, Svoboda M, Zatloukal J, Plutinsky M, Volakova E, Popelkova P, *et al*. Prognostic Properties of the GOLD 2023 Classification System. Int J Chron Obstruct Pulmon Dis 2023;18:661–667. doi:10.2147/COPD.S410372, PMID:37114105.
[46] Turan PA, Turan O, Güldaval F, Anar C, Polat G, Büyükşirin M. Transitions between COPD groups: A cross-sectional study in Turkey. Respir Med 2021;178:106310. doi:10.1016/j.rmed.2021.106310, PMID:33529994.
[47] Cavaillès A, Brinchault-Rabin G, Dixmier A, Goupil F, Gut-Gobert C, Marchand-Adam S, *et al*. Comorbidities of COPD. Eur Respir Rev 2013;22(130):454–475. doi:10.1183/09059180.00008612, PMID:24293462.
[48] Putcha N, Drummond MB, Wise RA, Hansel NN. Comorbidities and Chronic Obstructive Pulmonary Disease: Prevalence, Influence on Outcomes, and Management. Semin Respir Crit Care Med 2015;36(4):575–591. doi:10.1055/s-0035-1556063, PMID:26238643.
[49] Raherison C, Ouaalaya EH, Bernady A, Casteigt J, Nocent-Eijnani C, Falque L, *et al*. Comorbidities and COPD severity in a clinic-based cohort. BMC Pulm Med 2018;18(1):117. doi:10.1186/s12890-018-0684-7, PMID:30012144.
[50] Chetty U, McLean G, Morrison D, Agur K, Guthrie B, Mercer SW. Chronic obstructive pulmonary disease and comorbidities: a large cross-sectional study in primary care. Br J Gen Pract 2017;67(658):e321–e328. doi:10.3399/bjgp17X690605, PMID:28450344.
[51] Bollmeier SG, Hartmann AP. Management of chronic obstructive pulmonary disease: A review focusing on exacerbations. Am J Health Syst Pharm 2020;77(4):259–268. doi:10.1093/ajhp/zxz306, PMID:31930287.
[52] Wang MT, Lai JH, Huang YL, Kuo FC, Wang YH, Tsai CL, *et al*. Use of antidiabetic medications and risk of chronic obstructive pulmonary disease exacerbation requiring hospitalization: a disease risk score-matched nested case-control study. Respir Res 2020;21(1):319. doi:10.1186/s12931-020-01547-1, PMID:33267895.
[53] Rhee CK, Yoshisue H, Lad R. Fixed-Dose Combinations of Long-Acting Bronchodilators for the Management of COPD: Global and Asian Perspectives. Adv Ther 2019;36(3):495–519. doi:10.1007/s12325-019-0893-3, PMID:30742242.
[54] Wang MT, Liou JT, Lin CW, Tsai CL, Wang YH, Hsu YJ, *et al*. Association of Cardiovascular Risk With Inhaled Long-Acting Bronchodilators in Patients With Chronic Obstructive Pulmonary Disease: A Nested Case-Control Study. JAMA Intern Med 2018;178(2):229–238. doi:10.1001/jamainternmed.2017.7720, PMID:29297057.
[55] Barjaktarevic IZ, Milstone AP. Nebulized Therapies in COPD: Past, Present, and the Future. Int J Chron Obstruct Pulmon Dis 2020;15:1665–1677. doi:10.2147/COPD.S252435, PMID:32764912.
[56] Wedzicha JA, Calverley PM, Rabe KF. Roflumilast: a review of its use in the treatment of COPD. Int J Chron Obstruct Pulmon Dis 2016;11:81–90. doi:10.2147/COPD.S89849, PMID:26792988.
[57] Koczulla AR, Schneeberger T, Jarosch I, Kenn K, Gloeckl R. Long-Term Oxygen Therapy. Dtsch Arztebl Int 2018;115(51-52):871–877. doi:10.3238/arztebl.2018.0871, PMID:30765024.
[58] Kim Y, Park HY, Rhee CK, Min KH, Yoo KH, Lim SY, *et al*. Ambulatory oxygen therapy with documented self-monitoring of oxygen use improves health status among patients with chronic obstructive pulmonary disease. J Thorac Dis 2022;14(5):1353–1359. doi:10.21037/jtd-21-1878, PMID:35693613.
[59] Shah NM, D'Cruz RF, Murphy PB. Update: non-invasive ventilation in chronic obstructive pulmonary disease. J Thorac Dis 2018;10(Suppl 1):S71–S79. doi:10.21037/jtd.2017.10.44, PMID:29445530.
[60] Fletcher M, Scullion J, White J, Thompson B, Capstick T. Is the 'blue' colour convention for inhaled reliever medications important? A UK-based survey of healthcare professionals and patients with airways disease. NPJ Prim Care Respir Med 2016;26:16081. doi:10.1038/npjpcrm.2016.81, PMID:27808097.
[61] Mathioudakis AG, Janssens W, Sivapalan P, Singanayagam A, Dransfield MT, Jensen JS, *et al*. Acute exacerbations of chronic obstructive pulmonary disease: in search of diagnostic biomarkers and treatable traits. Thorax 2020;75(6):520–527. doi:10.1136/thoraxjnl-2019-214484, PMID:32217784.
[62] GBD 2015 Chronic Respiratory Disease Collaborators. Global, regional, and national deaths, prevalence, disability-adjusted life years, and years lived with disability for chronic obstructive pulmonary disease and asthma, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet Respir Med 2017;5(9):691–706. doi:10.1016/S2213-2600(17)30293-X, PMID:28822787.
[63] Rugbjerg M, Iepsen UW, Jørgensen KJ, Lange P. Effectiveness of pulmonary rehabilitation in COPD with mild symptoms: a systematic review with meta-analyses. Int J Chron Obstruct Pulmon Dis 2015;10:791–801. doi:10.2147/COPD.S78607, PMID:25945044.
[64] Sun Y, Milne S, Jaw JE, Yang CX, Xu F, Li X, *et al*. BMI is associated with FEV(1) decline in chronic obstructive pulmonary disease: a meta-analysis of clinical trials. Respir Res 2019;20(1):236. doi:10.1186/s12931-019-1209-5, PMID:31665000.
[65] Sikjær MG, Hilberg O, Ibsen R, Løkke A. Trends in COPD mortality from 1983 to 2018: protocol for a population-based cohort study in Denmark. BMJ Open 2024;14(1):e076936. doi:10.1136/bmjopen-2023-076936, PMID:38184314.
[66] Mary JD. Complementary and Alternative Therapies for COPD. WebMD; 2023.
[67] Dale K, Alyssa N. Herbs and Supplements for COPD. Healthline; 2023.
[68] Lyu YR, Lee SW, Kim SY, Han HB, Yang WK, Kim SH, *et al*. Herbal Medicines for the Treatment of Chronic Obstructive Airway Diseases (Asthma or Chronic Obstructive Pulmonary Disease): A Prospective Observational Study. Evid Based Complement Alternat Med 2022;2022:3485757. doi:10.1155/2022/3485757, PMID:35677382.
[69] Safari S, Davoodi P, Soltani A, Fadavipour M, Rezaeian A, Heydari F, *et al*. Curcumin effects on chronic obstructive pulmonary disease:

A systematic review. Health Sci Rep 2023;6(3):e1145. doi:10.1002/hsr2.1145, PMID:36890804.
[70] Clarke R, Lundy FT, McGarvey L. Herbal treatment in asthma and COPD - current evidence. Clin Phytosci 2015;1:4. doi:10.1186/s40816-015-0005-0.
[71] Zhang Q, Shi Y. Therapeutic effect on chronic obstructive pulmonary disease of lung qi deficiency at the stable stage treated with ginger-separated moxibustion and Chinese herbal medicine atomization (in Chinese). Zhongguo Zhen Jiu 2020;40(9):933–8. doi:10.13703/j.0255-2930.20190903-0002, PMID:32959586.
[72] Huang C, Kuo S, Lin L, Yang Y. The efficacy of N-acetylcysteine in chronic obstructive pulmonary disease patients: a meta-analysis. Ther Adv Respir Dis 2023;17:17534666231158563. doi:10.1177/17534666231158563, PMID:36927162.
[73] Fernández-Jané C, Vilaró J, Fei Y, Wang C, Liu J, Huang N, *et al*. Acupuncture techniques for COPD: a systematic review. BMC Complement Med Ther 2020;20(1):138. doi:10.1186/s12906-020-02899-3, PMID:32375775.
[74] Daniel Y. Acupuncture for COPD: Can It Be Helpful? Healthline; 2022.
[75] Yue JH, Golianu B, Zeng XX, Yuming W. Acupuncture for urinary retention after stroke: a protocol for systematic review. Eur J Bio Med Res 2015;1:7–11. doi:10.18088/ejbmr.1.2.2015.pp7-11.
[76] Feng J, Wang X, Li X, Zhao D, Xu J. Acupuncture for chronic obstructive pulmonary disease (COPD): A multicenter, randomized, sham-controlled trial. Medicine (Baltimore) 2016;95(40):e4879. doi:10.1097/MD.0000000000004879, PMID:27749542.
[77] Shih CC, Liao CC, Sun MF, Su YC, Wen CP, Morisky DE, *et al*. A Retrospective Cohort Study Comparing Stroke Recurrence Rate in Ischemic Stroke Patients With and Without Acupuncture Treatment. Medicine (Baltimore) 2015;94(39):e1572. doi:10.1097/MD.0000000000001572, PMID:26426630.
[78] Gao J, Ouyang B, Sun G, Dejun Z, Jinquan X. The effect of warm acupuncture on lung function and quality of life for stable COPD patients. Chin Acupunct Moxibustion 2011;31:893–897.
[79] Ngai SP, Jones AY, Cheng EK. Lung meridian acupuncture point skin impedance in asthma and description of a mathematical relationship with FEV1. Respir Physiol Neurobiol 2011;179(2-3):187–191. doi:10.1016/j.resp.2011.08.004, PMID:21856454.
[80] Carly Werner, RD.10 Yoga Practices to Help You Breathe Better with COPD. Healthline; 2024.
[81] Benralizumab (Fasenra) for Severe Eosinophilic Asthma. JAMA 2018;319(14):1501–1502. doi:10.1001/jama.2018.3609, PMID:29634828.
[82] Ortega HG, Liu MC, Pavord ID, Brusselle GG, FitzGerald JM, Chetta A, *et al*. Mepolizumab treatment in patients with severe eosinophilic asthma. N Engl J Med 2014;371(13):1198–1207. doi:10.1056/NEJMoa1403290, PMID:25199059.
[83] Reslizumab (Cinqair) for severe eosinophilic asthma. Med Lett Drugs Ther. 2016;58(1497):81–82. PMID:27305070.
[84] Albert RK, Connett J, Bailey WC, Casaburi R, Cooper JA Jr, Criner GJ, *et al*. Azithromycin for prevention of exacerbations of COPD. N Engl J Med 2011;365(8):689–698. doi:10.1056/NEJMoa1104623, PMID:21864166.
[85] Jithoo A, Enright PL, Burney P, Buist AS, Bateman ED, Tan WC, *et al*. Case-finding options for COPD: results from the Burden of Obstructive Lung Disease study. Eur Respir J 2013;41(3):548–555. doi:10.1183/09031936.00132011, PMID:22743668.
[86] Vogelmeier C, Hederer B, Glaab T, Schmidt H, Rutten-van Mölken MP, Beeh KM, *et al*. Tiotropium versus salmeterol for the prevention of exacerbations of COPD. N Engl J Med 2011;364(12):1093–1103. doi:10.1056/NEJMoa1008378, PMID:21428765.
[87] Gershon AS, Newman AM, Fischer HD, Austin PC, Daneman N, Bell CM, *et al*. Inhaled Long-acting Anticholinergics and Urinary Tract Infection in Individuals with COPD. COPD 2017;14(1):105–112. doi:10.1080/15412555.2016.1202912, PMID:27732117.
[88] Hajek P, Phillips-Waller A, Przulj D, Pesola F, Smith KM, Bisal N, *et al*. E-cigarettes compared with nicotine replacement therapy within the UK Stop Smoking Services: the TEC RCT. Health Technol Assess 2019;23(43):1–82. doi:10.3310/hta23430, PMID:31434605.
[89] Vestbo J, Hurd SS, Agustí AG, Jones PW, Vogelmeier C, Anzueto A, *et al*. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. Am J Respir Crit Care Med 2013;187(4):347–365. doi:10.1164/rccm.201204-0596PP, PMID:22878278.
[90] Agusti A, Böhm M, Celli B, Criner GJ, Garcia-Alvarez A, Martinez F, *et al*. GOLD COPD DOCUMENT 2023: a brief update for practicing cardiologists. Clin Res Cardiol 2024;113(2):195–204. doi:10.1007/s00392-023-02217-0, PMID:37233751.
[91] Davis KJ, Landis SH, Oh YM, Mannino DM, Han MK, van der Molen T, *et al*. Continuing to Confront COPD International Physician Survey: physician knowledge and application of COPD management guidelines in 12 countries. Int J Chron Obstruct Pulmon Dis 2015;10:39–55. doi:10.2147/COPD.S70162, PMID:25565799.
[92] Bullen C, Howe C, Laugesen M, McRobbie H, Parag V, Williman J, *et al*. Electronic cigarettes for smoking cessation: a randomised controlled trial. Lancet 2013;382(9905):1629–1637. doi:10.1016/S0140-6736(13)61842-5, PMID:24029165.
[93] Kristeen C. 12 Tips for Preventing COPD and Avoiding Flare-Ups. Healthline 2022;.
[94] Van Schayck OCP, Williams S, Barchilon V, Baxter N, Jawad M, Katsaounou PA, *et al*. Treating tobacco dependence: guidance for primary care on life-saving interventions. Position statement of the IPCRG. NPJ Prim Care Respir Med 2017;27(1):38. doi:10.1038/s41533-017-0039-5, PMID:28600490.