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## COPD with COVID-19: An Overview



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### ABSTRACT

COPD patients have a higher risk of myocardial ischemia and other variables that put them at risk for COVID-19-related problems. The majority of covid 19 with COPD care is provided by primary care clinicians, who are critical in the diagnosis and management of COPD with covid 19. In this article, we'll take a closer look at how COVID-19 can affect you if you have COPD, with a focus on the management of COPD with covid 19 in the primary care setting. We discuss the COPD airway in COVID-19; describe COPD risk factors, signs, and symptoms and how dangerous is COPD with COVID-19 as well as treatment recommendations and epidemiology, is also discussed. Patients and families are important partners in COPD with COVID-19 management; therefore, we outline simple steps that may assist them in caring for those affected by COPD with COVID-19.



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## INTRODUCTION [1,2]

COPD, or chronic obstructive pulmonary illness, can increase the chance of contracting COVID-19, a novel coronavirus that causes respiratory disease. COPD can increase the risk of COVID-19 issues because it affects the respiratory system. Lung damage and loss of function associated with COPD can increase the risk of COVID-19 complications for individuals who live with it. It might also hurt one's health. Chronic bronchitis and emphysema are two lung disorders that fall within the COPD umbrella. The airways in your lungs can become persistently irritated as a result of COPD. This can block the airways, resulting in poor airflow and possibly the destruction of the gas-exchange section of your lungs. The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that causes Coronavirus Disease 2019 (COVID-19) has triggered a pandemic with significant morbidity and mortality. Asymptomatic infections to moderate self-limiting upper respiratory tract illness, severe pneumonia with respiratory failure, or death are all possible outcomes. Although comorbidities are major determinants impacting patient prognosis, there is a dearth of evidence and experience with COVID-19 treatment. Because of their poor underlying lung reserve and elevated expression of the angiotensin-converting enzyme 2 (ACE-2) receptor in the small airways, patients with chronic respiratory disorders, particularly chronic obstructive pulmonary disease (COPD), are at high risk for COVID-19 infection. Comprehensive assessments of the hazards, the severity of disease, and clinical course in COVID-19 COPD patients are, however, limited. By stratifying COVID-19 patients in China based on the number of comorbidities, researchers were able to assess the probability of major adverse outcomes. Having more comorbidities was linked to poorer clinical outcomes, with COPD patients having the greatest hazard ratio (2.68) for ICU admission, invasive ventilation, or mortality among patients with various chronic underlying disorders.



**FIGURE:1**

People with COPD are five times more likely to develop COVID-19 as a result of getting SARS-CoV-2, according to another meta-analysis. COPD patients are also more prone to have severe oxygenation problems, according to this study. COPD patients and current smokers are at a higher risk of developing severe illness. Furthermore, both COPD patients and smokers are at an increased risk of dying from COVID-19.

#### **How Harmful Is COVID-19 For COPD Sufferers?[3,6]**

COVID-19 affects the lungs. Existing lung damage makes it more difficult for the lungs to fight off an infection. People with severe COPD may be at a higher risk of COVID-19 problems.

The researchers determined that patients with COPD may have a considerably increased chance of having severe COVID-19 infections after a meta-analysis of seven studies.

The coronavirus outbreak in China was described in a case series published by the Chinese Center for Disease Control and Prevention in 2020.

The total case fatality rate (CFR) was 2.3 percent, meaning that 1,023 people died out of 44,672 confirmed COVID-19 cases. The CFR was 6.3 percent Trusted Source in persons with chronic respiratory illness.

According to the Centers for Disease Control and Prevention (CDC)Trusted Source, people with COPD should not stop taking their medications, especially corticosteroids.

### **Mechanisms of COPD patients' sensitivity to SARS-CoV-2[4-11]**

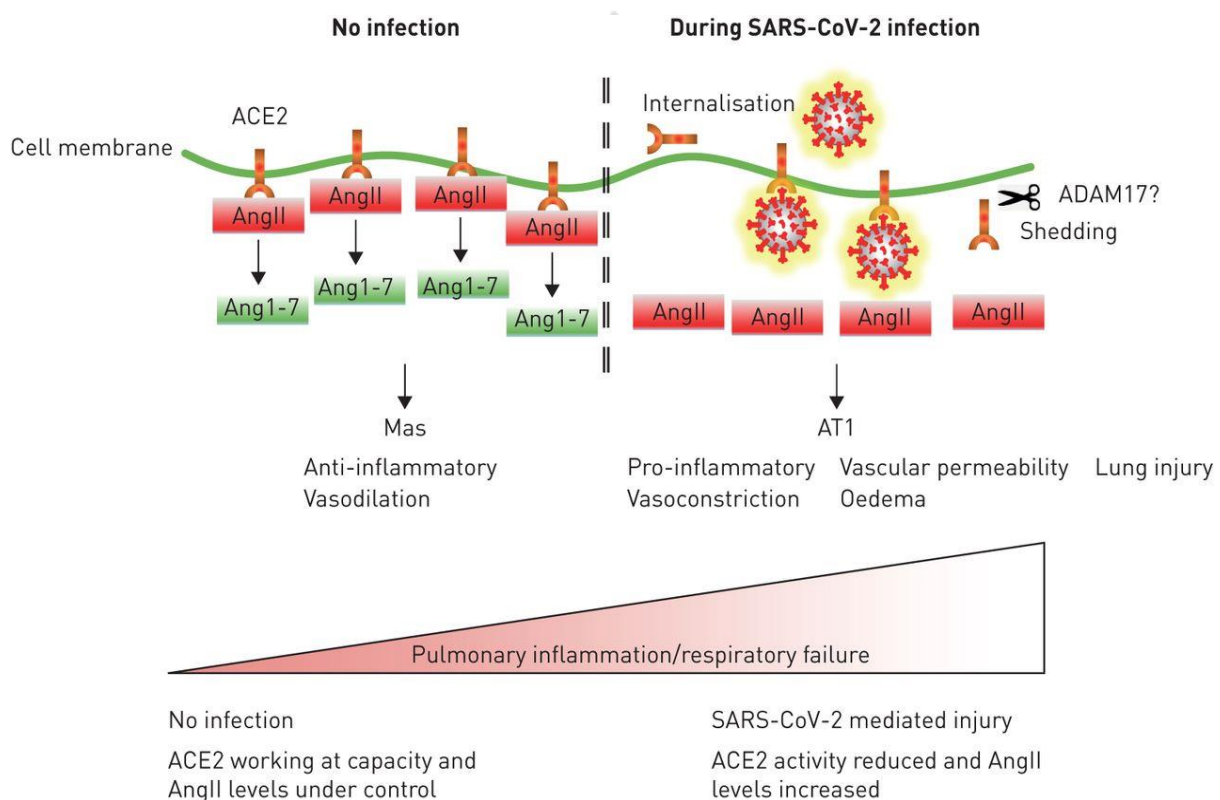
infectionSARS-CoV-2 enters host cells in a two-step process that includes cellular attachment and endocytosis. The membrane-bound viral spike protein, which comprises the S1 receptor binding subunit and the S2 membrane fusion component, is responsible for this. SARS-CoV-2, like other coronaviruses, uses angiotensin-converting enzyme 2 (ACE2) as a cellular attachment receptor (mediated by the S1 subunit). SARS-CoV-2 spike protein mutations are thought to allow for increased transmission This virus's affinity for attaching to ACE2 improves its capacity to acquire cellular entrance.

ACE2 is a transmembrane peptidase that converts angiotensin II to angiotensin1-7. Angiotensin II causes cellular contraction and thus higher vascular tone by acting directly on vascular smooth muscle cells via the angiotensin type 1 (AT1) receptor. In human individuals, angiotensin II infusion increases pulmonary vascular pressure. Due to leakage from the single-cell thick capillary bed, sustained high pulmonary vascular pressures create hydrostatic edema. Angiotensin II also improves microvascular permeability; a study employing rat postcapillary venules found that angiotensin II caused enhanced fluid flow across the endothelial layer.

ACE2 is found in the trachea, large airway epithelium, small airway epithelium, type 2 pneumocytes, and endothelium, among other places in the body. In the lungs, ACE2 has a homeostatic protective role by decreasing the effects of angiotensin II activity on vascular tone and permeability while increasing the production of vasodilator angiotensin 1–7. Angiotensin II also causes the release of pro-inflammatory cytokines. In endotoxin-exposed rats, reduced ACE2 activity resulted in higher pulmonary cytokine levels and neutrophil influx, as well as increased vascular permeability and lung edema. Angiotensin 1–7, on the other hand, reduces experimental lung damage in rats. Loss of ACE2 function may thereby increase inflammatory responses in the host, resulting in vasoconstriction and vascular damage.

SARS-CoV-2 infection is prevented by a lack of ACE2 expression, according to in vitro investigations. Furthermore, the level of ACE2 expression is proportional to the degree of SARS-CoV infection of epithelial cells. According to new data from computational research, genetic variations of the ACE2 structure may affect the SARS-CoV-2 interaction, increasing infection susceptibility. However, it is unknown to what extent altered ACE2 expression levels or genetic variation leads to greater vulnerability to SARS-CoV-2 infection in humans or the development of severe COVID-19. The role of ACE2 in the disease process is likely part of a complex and multi-factorial sequence of pathophysiological mechanisms.

Following virus engagement, cell surface ACE2 activity may be diminished during SARS-CoV-2 infection due to internalization or shedding, as shown with SARS-CoV infection. In mouse models, SARS-CoV promotes ACE2 shedding and enhanced lung damage, but not HCoV NL63, with concomitant elevations in angiotensin II levels. Importantly, antagonism of the AT1 receptor reduced these effects. These findings point to a reduction in ACE2 activity in COVID-19 lung damage (figure 2).



**FIGURE 2:**

The consequences of angiotensin-converting enzyme (ACE2) malfunction during infection with the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). In the absence of

infection, ACE2 is fully functional, and angiotensin II (ang II) levels are carefully controlled through conversion to angiotensin 1–7 (and 1–7). The Mas receptor is activated by Ang 1–7, which regulates inflammation and vasomotor tone. Because of receptor occupancy, shedding, and internalization, ACE2 activity is lowered during SARS-CoV-2 infection, while ang II levels rise. Ang II stimulates the AT1 receptor, resulting in increased pro-inflammatory cytokine production, vasoconstriction, vascular permeability, edema, and other symptoms.

virus membranes, where the spike protein is proteolytically cleaved at the S1/S2 interface, allowing the virus and host membranes to fuse (initiated by Fusion between the host and the S2 subunit), and subsequent cell penetration is the second phase of SARS-CoV-2 cellular entry. During this process, the virus uses host proteases such as furin, transmembrane serine protease 2 (TMPRSS2), and cathepsins.

ACE2 expression was found to be higher in the bronchial epithelium and total lung tissue of COPD patients compared to controls in recent gene and protein expression investigations, with a connection between higher ACE2 expression levels and decreased lung function. Researchers employed bronchial brushing samples taken by bronchoscopy to show that COPD patients had higher ACE2 gene expression than controls, which included a mix of never-, former-, and current smokers. Current smokers showed greater levels of ACE2 gene expression in these samples. Immunohistochemistry was also used to show that COPD patients have higher ACE2 protein expression in the small airway epithelium than never-smokers but not current smokers. ACE2 gene expression was shown to be higher in COPD patients' bronchial brushing samples when compared to former smokers but not current smokers.

COPD patients had increased ACE2 protein expression in the small airway epithelium than never-smokers but not current smokers, according to immunohistochemistry. When compared to former smokers but not current smokers, ACE2 gene expression was shown to be greater in COPD patients' bronchial brushing samples.



## Symptoms[12-14]

Symptoms of COPD Exacerbation vs. COVID-19 <sup>8,9</sup>	
COPD	COVID-19
More coughing, wheezing, or shortness of breath than usual	Cough, shortness of breath
Changes in the color, thickness, or amount of mucus	Fever or chills, body aches, headaches
Feeling tired for more than one day	Fatigue
Swelling of the legs or ankles	New loss of taste or smell
Feeling the need to increase your oxygen if you are on oxygen	Sore throat
	Congestion or runny nose

Dyspnea, or shortness of breath, is frequent in patients with COPD and COVID-19. COVID-19-related dyspnea and COPD exacerbation, on the other hand, can be distinguished in a few ways.

Though a fever may indicate COVID-19 infection, there's no way to tell if your symptoms are caused by COVID-19, COPD, or another infection. If you already have COPD, see your doctor if any of the following symptoms occur:

- Worsening breathing problems
- More coughing
- New types of coughing
- Changes in phlegm color or amount
- More wheezing
- Lower blood oxygen levels at rest
- Increased oxygen use

- More use of rescue inhaler

### **How to manage symptoms**

People must manage their COPD symptoms during the COVID-19 outbreak.

People can create a management plan with a healthcare team. This can help them keep track of medication, monitor COPD symptoms, and check that symptoms are not worsening. A person can call their doctor to discuss this over the phone if they do not already have a plan in place.

Eating a healthful diet and drinking plenty of water can also help to support the body and remove excess mucus from the lungs.

Some people may find that eating fewer carbohydrates and more healthful fats improve their breathing.

The American Lung Association has a selection of breathing exercises that may help ease shortness of breath and relax the airways.

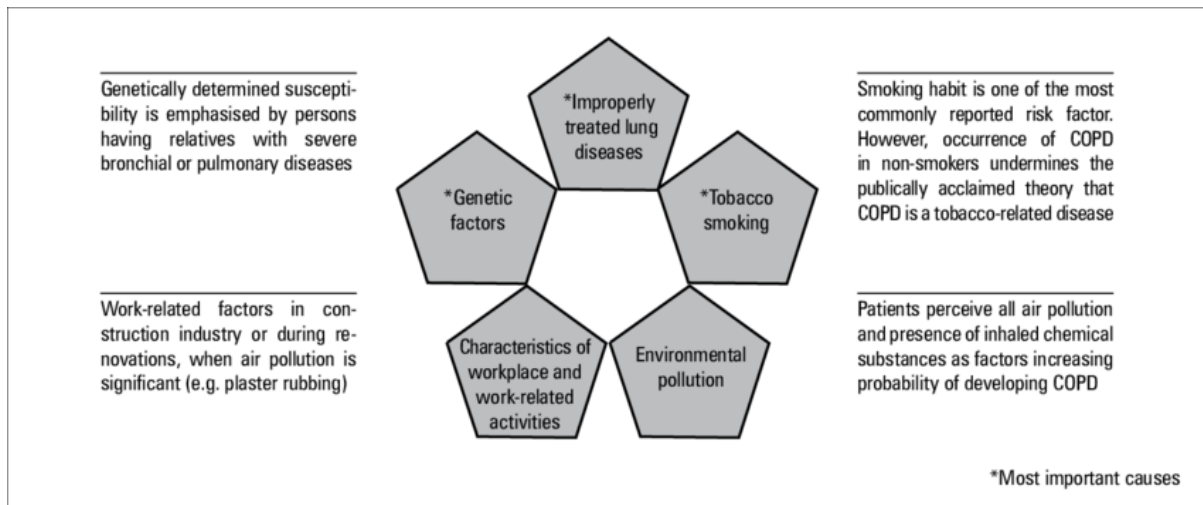
Asking others for help and talking with friends, family, or healthcare professionals can help maintain emotional and mental health.

### **Are patients with COPD at an increased risk for COVID-19?[5,33]**

Because COPD patients are susceptible to viral respiratory tract infections and COPD is typically a condition of the elderly, many people assumed that COPD patients would have a much higher chance of contracting COVID-19. However, studies have shown that only about 2% of patients treated to hospitals in China with COVID-19 infection had underlying COPD, even though COPD prevalence in China ranges from 5% to 13%. COPD was not the most commonly reported comorbidity in COVID-19 patients. While the low percentage shows that COPD is not a risk factor for COVID19, the pandemic's scope will nonetheless affect many COPD patients. Furthermore, as compared to individuals with other comorbidities, people with COPD and COVID-19 have a worse clinical outcome. : people with COPD who are also smokers are at a higher risk of developing severe disease. Furthermore, both COPD patients and smokers are at a higher risk of dying from COVID-19.

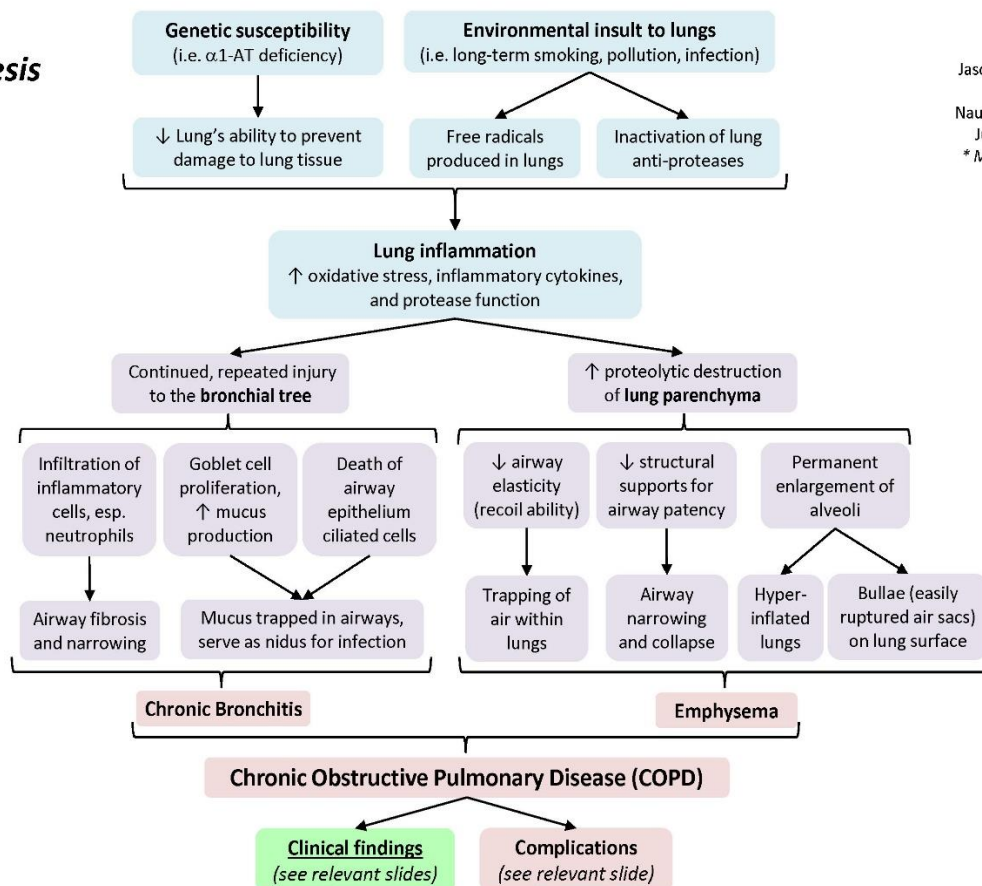


## CAUSES OF COPD



## PATHOPHYSIOLOGY OF COPD

### COPD: Pathogenesis



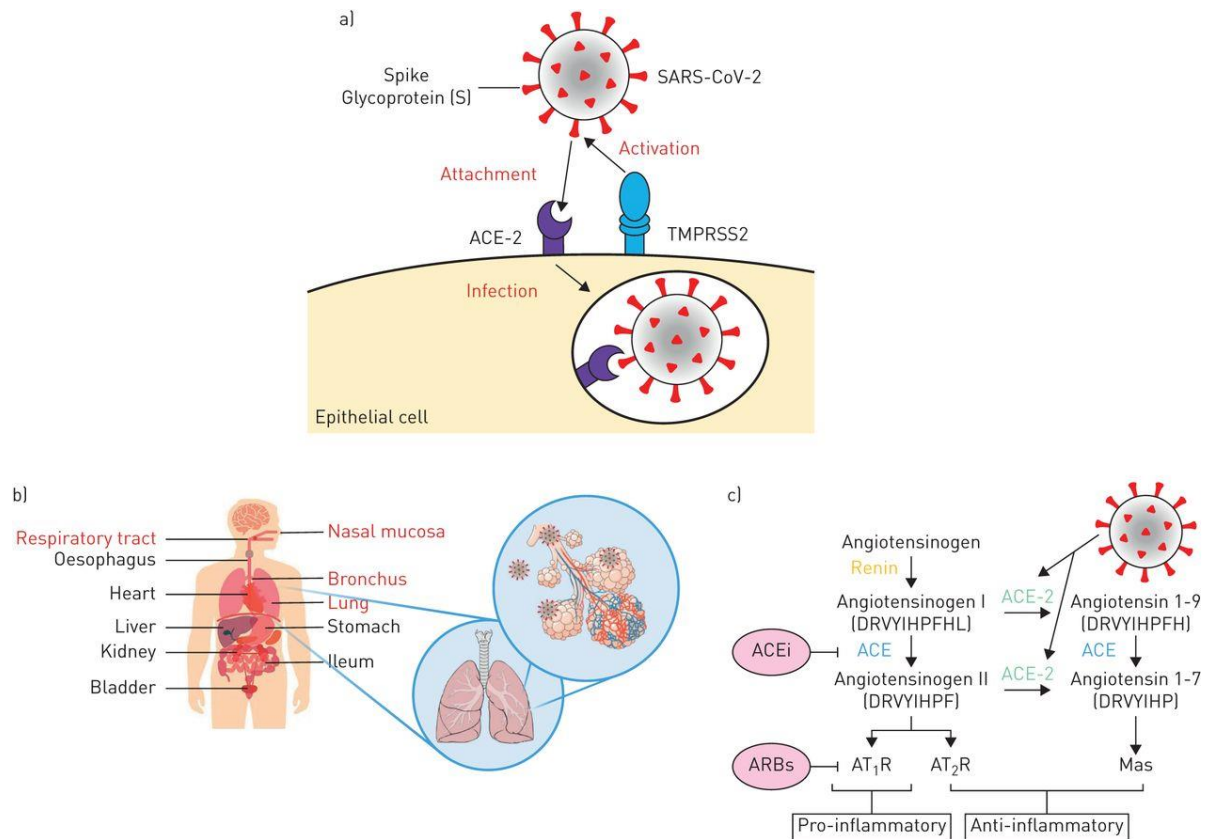
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Legend: Pathophysiology Mechanism Sign/Symptom/Lab Finding Complications Published January 7, 2013 on www.thecalgaryguide.com



### **The COPD airway in COVID-19 [15-23]**

It's interesting speculating why COPD individuals appear to have worse results after contracting COVID-19 (even if their likelihood of contracting was low, to begin with). First, new research suggests that COPD patients and smokers may have differing levels of the machinery required for SARS-CoV-2 cellular entrance. SARS-CoV-2 has an envelope spike protein that is primed by the cellular serine protease TMPRSS2 to allow fusion of the virus with the cell's angiotensin-converting enzyme 2 (ACE-2) receptor and subsequent cell entrance (figure 3), similar to SARS-CoV (which caused the 2002–2003 SARS epidemic). In three independent cohorts with available gene expression profiles from bronchial epithelial cells, our group recently demonstrated that ACE-2 expression was considerably higher in COPD patients compared to control people in three separate cohorts. Current smoking was also linked to higher ACE-2 expression in comparison to former and never smokers, a finding that has since been confirmed by other researchers in separate cohorts of lung tissue and airway epithelial samples, as well as by additional evidence linking ACE-2 expression to nicotine exposure. Our group recently demonstrated that ACE-2 expression was significantly greater in COPD patients compared to control participants in three separate cohorts with available gene expression profiles from bronchial epithelial cells. In comparison to former and never smokers, current smoking was also linked to higher ACE-2 expression, a finding that has since been confirmed by other researchers in separate cohorts of lung tissue and airway epithelial samples, as well as by additional evidence linking ACE-2 expression to nicotine exposure.



**FIGURE 3:**

Schematic illustration of a) SARS-CoV-2 binding to the angiotensin-converting enzyme 2 (ACE-2) receptor after activation of the spike protein (s) by transmembrane serine protease 2 (TMPRSS2), which leads to endocytosis and infection. b) Human organs that demonstrate ACE2 expression, as described by ZOU et al. [105], with the respiratory system marked in red. b) The putative SARS-CoV-2 action and the renin-angiotensin system (RAS). Through the binding of angiotensin II receptor type 1 (AT<sub>1</sub>R), the production of angiotensin II from angiotensin I by angiotensin-converting enzyme (ACE) causes vasoconstriction of blood vessels and pro-inflammatory effects, whereas the receptor type 2 (AT<sub>2</sub>R) may inhibit this process. Angiotensin-converting enzyme inhibitors (ACEi) and angiotensin II receptor blockers (ARBs) are effective antihypertensives because they cause blood vessels to dilate. By converting angiotensin I to angiotensin 1–9 and angiotensin II to angiotensin 1–7, ACE-2 suppresses the activity of angiotensin II, which binds to the MAS1 proto-oncogene (Mas) receptor and has anti-inflammatory effects. When SARS-CoV-2 binds to ACE-2, the ACE/ACE-2 balance shifts in favor of ACE, causing enhanced pro-inflammatory effects and tissue destruction.

## COPD patient management during the COVID-19 pandemic [15,24-32]

During this pandemic, two clinical difficulties have emerged: 1) whether the standard COPD pharmaceutical treatment algorithms still apply, and 2) how to weather the huge reductions in non-pharmaceutical therapies that this epidemic has inflicted. Even though our understanding of COVID-19 has improved dramatically in a short period, these issues have primarily been the domain of expert opinion rather than scientific evidence. Two clinical issues have arisen as a result of this pandemic: 1) whether normal COPD pharmaceutical therapy algorithms still apply, and 2) how to cope with the massive decreases in non-pharmaceutical therapies that this epidemic has wrought. Even though our understanding of COVID-19 has grown considerably in a relatively short amount of time, these difficulties have mostly been a matter of expert opinion rather than scientific data. The same association has not yet been proven in the COPD airway, where the tendency to pneumonia following ICS therapy is well-documented. For the time being, in the absence of conclusive evidence, Spike Glycoprotein of SARS-CoV-2 (S) a) TMPRSS2 Activation Infection with ACE-2 Respiratory tract epithelial cell b) Oesophagus Heart Liver Kidney Bladder Nasal mucosa Bronchus Lung Stomach Angiotensinogen c) Renin ACE ACE-2 ACE-2 Angiotensinogen I (DRVYIHPFHL) Angiotensinogen II (DRVYIHPF) ARBs AT1R ACEi Pro-inflammatory Anti-inflammatory AT2R Mas Ileum Attachment osa II L ng ACE Angiotensin 1-9 (DRVYIHPFH) Angiotensin 1-7 (DRVYIHP) FIGURE 2 Schematic representation of a) severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) binding to the angiotensin-converting enzyme 2 (ACE-2) receptor following activation of the spike protein (s) by transmembrane serine protease 2 (TMPRSS2), which leads to endocytosis and infection. b) Human organs that demonstrate ACE2 expression, as described by ZOU et al., with the respiratory system indicated in red. b) The putative SARS-CoV-2 action and the renin-angiotensin system (RAS). Angiotensin II is produced when the angiotensin-converting enzyme (ACE) converts angiotensin I to angiotensin II. Angiotensin II receptor type 1 (AT1R) binding causes blood vessel constriction and pro-inflammatory effects, whereas receptor type 2 (AT2R) binding may inhibit this pathway. Angiotensin-converting enzyme inhibitors (ACEi) and angiotensin II receptor blockers (ARBs) are effective antihypertensives because they cause blood vessels to dilate. By converting angiotensin I to angiotensin 1–9 and angiotensin II to angiotensin 1–7, ACE-2 suppresses the activity of angiotensin II, which binds to the MAS1 proto-oncogene (Mas) receptor and has anti-inflammatory effects. When SARS-CoV-2 binds to ACE-2, the ACE/ACE-2 balance shifts towards a positive. Blood artery constriction and pro-

inflammatory effects are caused by angiotensin II receptor type 1 (AT1R) binding, but AT2R binding may block this pathway. Because they induce blood arteries to dilate, angiotensin-converting enzyme inhibitors (ACEi) and angiotensin II receptor blockers (ARBs) are efficient antihypertensives. ACE-2 reduces the function of angiotensin II, which binds to the MAS1 proto-oncogene (Mas) receptor and has anti-inflammatory properties, by converting angiotensin I to angiotensin 1–9 and angiotensin II to angiotensin 1–7. The ACE/ACE-2 balance flips to the positive when SARS-CoV-2 binds to ACE-2. Angiotensin II receptor type 1 (AT1R) binding causes blood vessel constriction and pro-inflammatory effects, but AT2R binding may block this pathway. Angiotensin-converting enzyme inhibitors (ACEi) and angiotensin II receptor blockers (ARBs) are effective antihypertensives because they cause blood vessels to dilate. By converting angiotensin I to angiotensin 1–9 and angiotensin II to angiotensin 1–7, ACE-2 inhibits the function of angiotensin II, which binds to the MAS1 proto-oncogene (Mas) receptor and has anti-inflammatory properties. When SARS-CoV-2 binds to ACE-2, the ACE/ACE-2 balance shifts to the positive. The SARS and the Middle East respiratory syndrome (MERS) pandemics have taught us that there is a risk of injury. While the bulk of studies on SARS was inconclusive, four studies did reveal harm, such as delayed virus clearance and higher rates of psychosis. Corticosteroid use has been linked to an increase in mortality and a delay in virus clearance in MERS patients. The most promising preliminary data on corticosteroids and COVID-19 thus far comes from a UK-based randomized controlled study of dexamethasone (RECOVERY), which showed a one-third reduction in mortality. However, published data are based on small retrospective studies and appear to be equivocal, with two studies showing no benefit and two studies showing improvements in death rates and care escalation. However, based on the findings of the RECOVERY study, dexamethasone is likely to become the standard of care treatment for COVID-19 patients, including those with COPD. COPD patients have felt the effects of the pandemic in a variety of ways. Face-to-face clinic visits with their doctors, as well as pulmonary rehabilitation sessions and COPD home visit programs, have been reduced. Patients who would typically present to the hospital during an exacerbation may prefer to stay at home for fear of being exposed, causing care to be delayed, as has happened in other illnesses such as myocardial infarction. The long-term consequences of this interruption in basic care are still unknown. For the time being, healthcare systems have had to adjust to these circumstances by increasing the use of telehealth and virtual visits. Fortunately, several randomized controlled trials evaluating telehealth for COPD patients have shown that it is feasible and, at the very least, non-inferior to standard care in terms of exacerbations,

hospitalizations, and quality of life. Furthermore, it appears that online pulmonary rehabilitation programs are as successful as in-person sessions. We advocate for the implementation of these virtual programs if social distancing measures remain in place for many more months so that our patient group can continue to receive excellent care.

## **TREATMENT**

### **Antibiotics [33-36]**

Not all AECOPDs should be treated with antibiotics outside of the context of COVID-19, and current guidelines suggest saving antibiotics for AECOPDs that require hospitalization or ventilatory support. Bacterial coinfections are uncommon in COVID-19, according to a recent meta-analysis, with just 8% of patients having a bacterial/fungal coinfection. Coinfections become more likely as COVID-19 becomes more severe: a cohort research on risk factors for COVID-19 in-hospital death indicated that 50% of non-survivors had secondary infections, with ventilatory-associated pneumonia seen in 31% of non-survivors. 9 We recommend treating hospitalized patients with COPD and COVID-19 and respiratory symptoms with broad-spectrum antibiotics, guided by local/national guidelines for treating pneumonia, because it may be difficult to distinguish SARS-CoV-2 infections from bacterial pneumonia, and because patients with COPD are at risk for bacterial (super)infections. This is following the current WHO COVID-19 therapy guidelines. In the absence of a coinfection, microbiological tests, such as sputum culture, should be conducted on admission, and antibiotics may be stopped.

### **Bronchodilators and nebulization [37-39]**

In hospitalized COPD patients, bronchodilators are usually administered through a nebulizer. The British Thoracic Society (BTS) guideline for treating COPD and COVID-19 patients recommends the use of nebulizers, saying that there is no indication of an increased risk of viral transmission and, second, that the aerosols around the nebulizer come from the nebulizer, not from individuals. However, there are some methodological issues with the meta-analysis that claims nebulizers do not promote viral transmission. It is based on one study with limited sample size, a second study that looked at a variety of therapies, and a third study that looked at infections that started before nebulization. The BTS guidance was also based on a methodological study that showed nebulizers primarily produce aerosols rather than droplets, which was used to support the idea that nebulization was safe. This study



did not look into the viral transmission, and since it's still unclear whether droplets or aerosols can carry SARS-CoV-2, we don't think these findings should be taken as proof that there's no risk of transmission. There are other options for inhalation, including pressurized metered-dose inhalers (pMDI) with a spacer. pMDIs are not inferior to nebulizers in AECOPD. Long-acting dual bronchodilators may be recommended; some have a quick onset of action and are more effective over time. Two long-acting pMDI combinations can be employed with a spacer right now. For nebulized short-acting bronchodilators, no maximum dosing has been established, and very large doses are frequently used to treat AECOPD. The maximum maintenance dose of long-acting bronchodilators should be doubled, reflecting the high doses of short-acting bronchodilators commonly used in clinical practice. We propose bronchodilators administered by pMDI and spacer over nebulizer treatment in symptomatic individuals with COPD and COVID-19 since the safety of nebulizers is debatable and there is a good alternative. Patients with severe, life-threatening diseases or those who are unable to utilize a pMDI should use nebulized treatment only when a pMDI with spacer is not practicable. During aerosol-generating treatments such as nebulizers, healthcare staff should wear breathing masks (FFP-3 or similar) and other persons protection equipment.

#### **Systemic corticosteroids [36,40-42]**

It is acknowledged that systemic corticosteroids are not required for all AECOPDs. Although eosinophil-based steroid treatment has been supported for both stable COPD and AECOPD, it has not been studied in individuals with COPD and COVID-19. Until recently, there was no definitive evidence that corticosteroids were effective in treating COVID-19, while a cohort study suggested that steroids would enhance clinical outcomes in COVID-19 patients. Dexamethasone decreases mortality in COVID-19 patients who require respiratory assistance, according to preliminary results from the Randomized Evaluation of COVID-19 Therapy (RECOVERY) trial. Previously, the WHO advised against using steroids, but it is now modifying treatment guidelines to allow dexamethasone or other corticosteroids. Patients with severe AECOPD benefit from corticosteroids, particularly those who require ventilatory support, as steroids reduce ventilation days and NIV failure. As a result, it is fair to treat patients with COPD and severe COVID-19 with a course of corticosteroids. Until additional information is available to guide treatment in people with COPD with covid 19, the RECOVERY regimen of 6 mg once daily could be utilized.

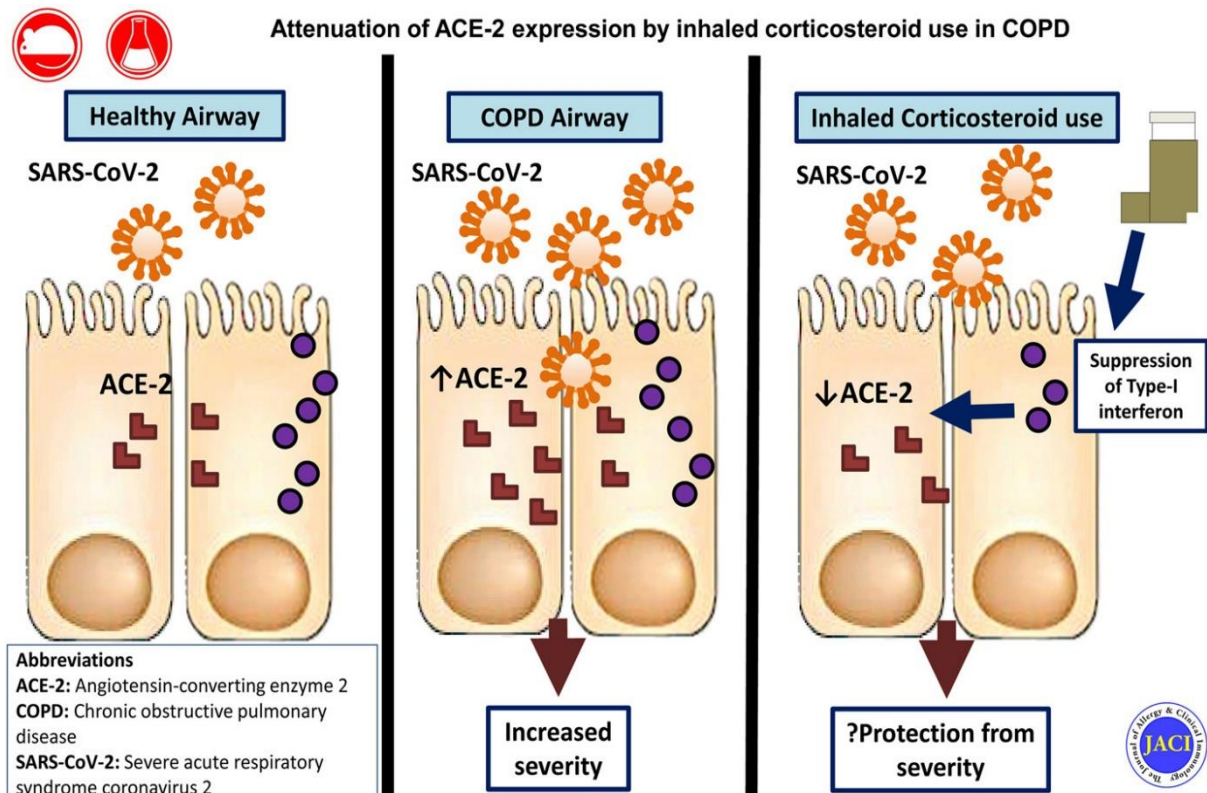


FIGURE:4

#### Ensifentrine and Covid-19 [43]

Because ensifentrine has “demonstrated substantial bronchodilator effects in healthy people and patients with COPD or asthma,” Verona believes it could be useful in improving outcomes for hospitalized Covid-19 patients.

According to Zaccardelli, ensifentrine has been demonstrated to improve lung function while also helping to “decrease lung inflammation by a reduction in local inflammatory cell counts like macrophages, neutrophils, eosinophils, and lymphocytes.” A cytokine storm, or an overactive inflammatory response, has been discovered to be a primary cause of illness severity and death in Covid-19 patients.

Furthermore, as a PDE4 inhibitor, ensifentrine is known to “reduce pro-inflammatory mediators, such as TNF $\alpha$  and IL-6,” which contribute to the severity of the cytokine storm and Covid-19, according to Zaccardelli.

**Other supportive treatments should be offered to patients with COPD and COVID-19 [40,44-45]**

SARS-CoV-2 infections can have a wide range of negative consequences for individuals. The enforced extreme isolation may heighten emotions of loneliness and despondency. In addition, SARS-CoV-2 patients frequently report a loss of taste and appetite, which increases the risk of unintended weight loss. Keeping up with regular exercise, let alone rehabilitation, is challenging while in the hospital. As a result, food, as well as mental and spiritual assistance, should be included in in-hospital therapy. Recent COVID-19-specific physiotherapy guidelines advocate early mobilization, although airway clearance procedures should be used with caution due to the potential of aerosol dissemination. Discharge packages should be continued after discharge to facilitate a smooth transition from hospital to home care and to lower the risk of readmission. Although pulmonary rehabilitation (PR) is suggested for persons with COPD, all patients with COVID-19 should receive rehabilitation, especially following ICU admission. Prolonged ICU stays are known to have a negative influence on both physical and emotional well-being, and patients may experience posttraumatic stress disorder symptoms as a result. Center-based PR and physiotherapy may be limited due to social distance and worries about viral transmission. In these times of social isolation, unsupervised, home-based public relations may be a viable option. Exercise-induced desaturation and cardiac arrhythmias linked to COVID-19, on the other hand, may make unsupervised training impossible to ensure. Patients should flow back into such supervised programs as soon as center-based PR is possible for maximum benefit.

**EPIDEMIOLOGY [47-49]**

Because the majority of COPD patients are older and have multiple concomitant diseases, individuals identified with COVID19 have worse outcomes, including a greater rate of hospitalization, ICU admission, and mortality. However, it is unclear how preexisting chronic inflammatory airway illnesses, such as COPD, and their treatment affect the risk of SARS-CoV-2 infection and COVID-19 development. Several cohort studies in mainland China and around the world found that COVID-19 patients had a lower percentage of active smokers than expected based on gender and age. It's unclear if this is due to missing or erroneous information about smoking habits as a result of substantial methodological flaws, such as small sample numbers and ascertainment bias. Similarly, data on COPD among COVID-19 patients demonstrated a wide range of COPD prevalence (1.1–38 percent) among COVID-19

patients hospitalized. Since reporting has focused on hospitalized and ICU patients rather than milder (e.g., outpatient settings) cases, estimating the COPD patient excess risk for developing COVID-19 has been difficult. Furthermore, because hospitals were overcrowded during the peak of the epidemic, not all COPD patients with COVID-19 sought medical treatment in a hospital setting. As a result, COVID-19-related AECOPD may have influenced mortality data without affecting hospitalization or ICU-related statistics. Because pulmonary function tests are not performed before or after hospitalization in COVID19 patients, airflow limitation may have been underestimated. A meta-analysis of 15 studies that looked at the presence of COPD in 2,473 verified COVID-19 patients found that the overall prevalence of COPD diagnosis in COVID-19 patients was low [2% [95 %CI, 1%-3%]. It's unclear whether this effect is attributable to COPD patients' self-isolation, which results in lesser representation in various COVID cohorts. COPD patients, on the other hand, had a considerably increased probability of more severe disease burden and mortality than controls (calculated RR, 1.88). Another cohort study utilizing multivariate logistic regression with covariate adjustment found no significant differences in SARS-CoV-2 positive rates between COPD and non-COPD patients. When compared to non-COPD patients, COPD patients infected with the virus had considerably higher rates of hospitalization [adjusted odds ratio [OR] of 1.36], ICU admissions (adjusted OR of 1.20), and invasive mechanical ventilation (adjusted OR of 1.49). If published studies reveal a varied frequency of COPD among COVID-19 patients, they also consistently show a worse clinical result in the same cohort when taken collectively. More research is needed to rule out potential ascertainment biases in profiling the COPD COVID19 population and to determine whether the worsening outcome in COPD patients is due to their underlying lung disease, the nature of immune responses, the underlying pharmacologic COPD treatment (e.g., chronic steroid use), or a combination of these factors.

### Caring for patients with COPD and COVID-19

1	There is no evidence that COPD is a risk factor for SARS-CoV-2 infection.
2	COPD is linked to a higher risk of poor outcomes in patients with COVID-19.
3	A COVID-19 chest infection in a person with underlying COPD is most likely not the same as an acute COPD exacerbation. However, a diagnosis of COVID-19 does not rule

	out the possibility of AECOPD. Furthermore, COVID-19 treatment should take into account the underlying COPD.
4	Antibiotics are recommended for COPD patients who require hospitalization for a SARS-CoV-2 chest infection, particularly if ventilatory assistance is required.
5	In patients with COPD and COVID-19 and respiratory symptoms, bronchodilators delivered by pMDI and spacer are preferred to nebulizer treatment. If needed, we recommend administering long-acting bronchodilators twice as often as maintenance treatment.
6	Patients with life-threatening diseases or those who are unable to utilize a pMDI and a spacer should use a nebulizer. In such instances, special attention should be taken to preventing airborne transmission.
7	Patients with COPD and AECOPD who require hospitalization for a SARS-CoV-2 chest infection should get a course of systemic corticosteroids.
8	When it comes to ventilatory support, patients' wishes and decisions about ventilatory support and/or ICU admission and intubation must be understood.
9	Patients with COPD, COVID-19, and acute (on chronic) hypercapnic respiratory acidosis should be given NIV. Use non-vented masks with exhaled air passing through a bacterial/virus filter before entering the room to reduce viral spread.
10	When patients with COPD on home NIV present with COVID-19, chronic NIV should be continued. It's possible that you'll be able to receive treatment at home.
11	If oxygen therapy fails, we recommend HFNC or CPAP with a high FiO <sub>2</sub> in patients with COPD and COVID-19, as well as acute hypoxaemic respiratory failure. Surgical masks should be worn over nasal cannulas to reduce virus dissemination. Exhaled air can be filtered before entering the room with CPAP.

12	If patients do not respond adequately to non-invasive assistance, rapid intubation and invasive mechanical ventilation should be performed, depending on previous talks and decisions about treatment escalation.
13	Hospitalized patients with COPD and COVID-19 should be monitored for unintentional weight loss and dietary support should be offered accordingly.
14	To limit the potential of viral transmission, airway clearing procedures should be used with caution in patients with COPD and COVID-19.
15	Early mobilization in patients with COPD and COVID-19 is very important.
16	Providing psychological and spiritual care to patients with COPD and COVID-19 during hospitalization and follow-up is critical.
17	After discharge from the hospital, all patients with COPD and COVID-19 should be offered pulmonary rehabilitation, maybe in a modified form as long as social separation is still required.
18	We recommend that all patients be screened with COVID-19 for emotional and functional difficulties, especially following an ICU stay, and that rehabilitation is offered as needed.
19	Patients with COPD should get timely advance care planning, which includes patient-physician dialogue about their values, goals, and preferences for life-sustaining medications, as well as concerns about the dying phase and palliative therapy alternatives. During this time of the COVID-19 pandemic, timeliness and diligence are especially more vital and demanding.
20	Appropriate symptom management at the end of life in COPD and COVID-19 patients is critical, including anxiety, dyspnea, and palliative sedation as needed.
21	We recommend that loved ones of dead COPD and COVID-19 patients explore



bereavement care since they may be at a higher risk of experiencing difficult sorrow.

- AECOPD, acute exacerbations of COPD; HFNC, high-flow nasal cannula; ICU, intensive care unit; NIV, non-invasive ventilation; pMDI, pressurized metered-dose inhaler.

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