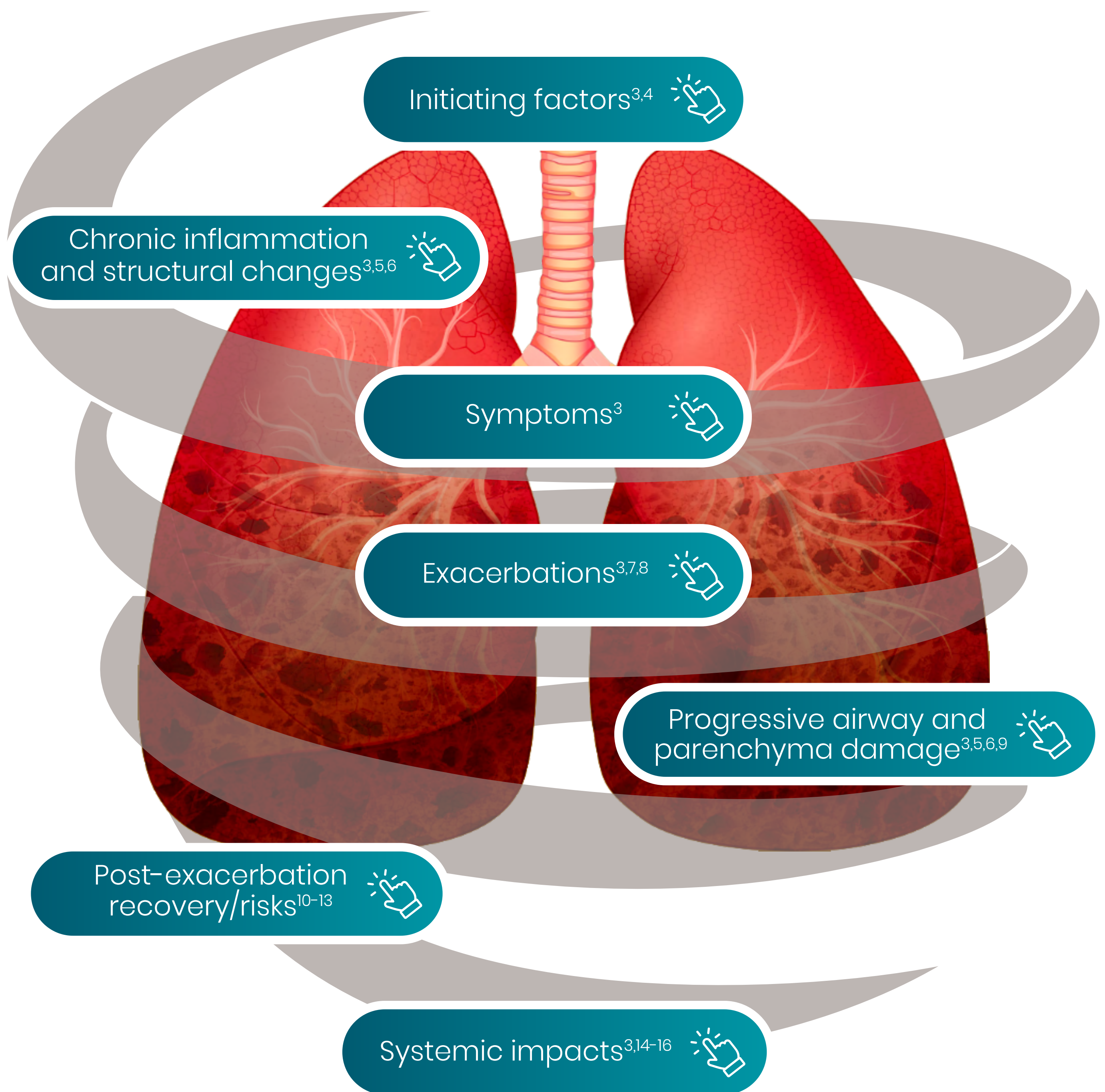


Worsening Disease Leads to a Vicious Cycle of COPD^{1,2}



1. Agusti AG. *Respir Med*. 2005;99(6):670-682. 2. Kardos P, Keenan J. *MedGenMed*. 2006;8(3):54. 3. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. Updated 2023. Accessed March 16, 2023. https://goldcopd.org/wp-content/uploads/2022/12/GOLD-2023-ver-11-2Dec2022_WMV.pdf. 4. Stolz D, et al. *Lancet*. 2022;400(10356):921-972. 5. Barnes PJ. *J Allergy Clin Immunol*. 2016;138(1):16-27. 6. Linden D, et al. *Eur Respir Rev*. 2019;28:180063. 7. Hogue SP, et al. *Clin Resp J*. 2020;14(3):183-197. 8. Jamieson DB, et al. *Am J Respir Crit Care Med*. 2013;188(2):187-192. 9. Higham A, et al. *Respir Res*. 2019;20(1):49. 10. Hansel TT, Barnes PJ. *Lancet*. 2009;374(9691):744-755. 11. Wageck B, et al. *COPD*. 2019;16(1):93-103. 12. Donaldson GC, et al. *Thorax*. 2002;57(10):847-852. 13. Garcia-Aymerich J, et al. *Thorax*. 2011;66(7):585-590. 14. Barnes PJ, Celli BR. *Eur Respir J*. 2009;33(5):1165-1185. 15. Dal Negro RW, et al. *Multidiscip Respir Med*. 2015;10(1):24. 16. Gaddam S, et al. *BMC Pulm Med*. 2016;16:158.



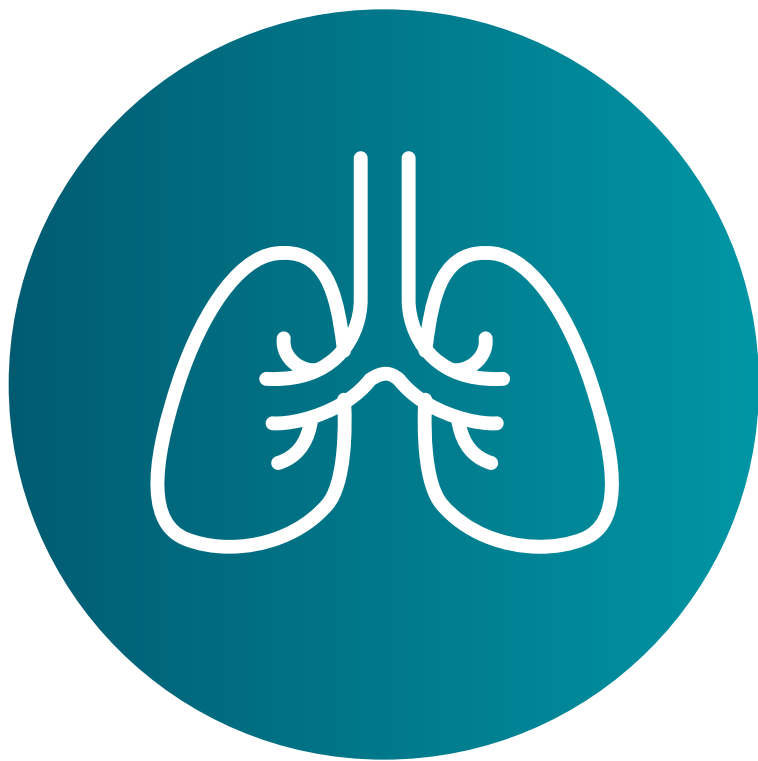
Initiating factors^{1,2}



Smoking



Pollutants and environmental/occupational exposure



Abnormal lung growth/development



Genetics and early life events

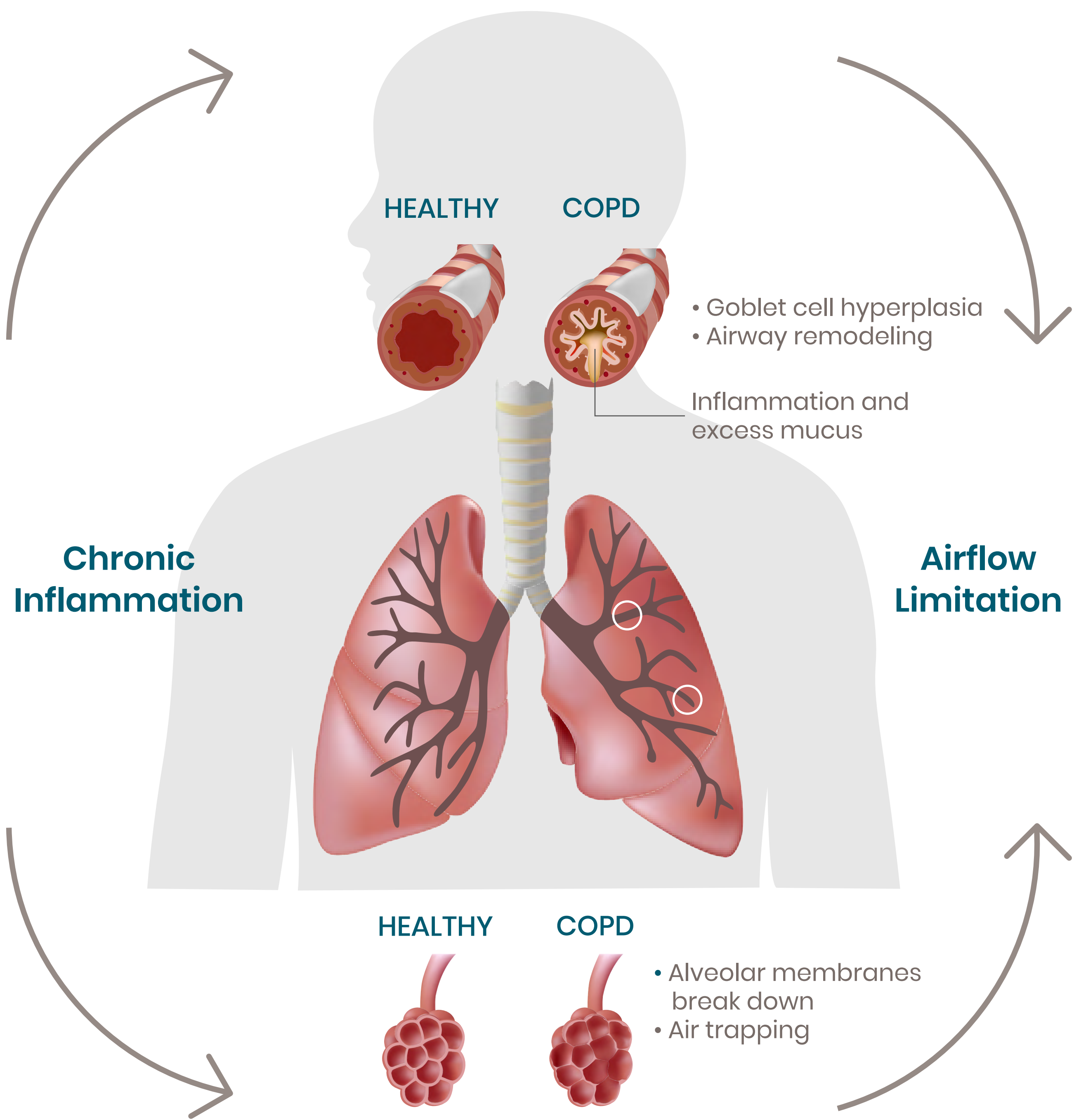
close

1. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. Updated 2023. Accessed March 16, 2023. https://goldcopd.org/wp-content/uploads/2022/12/GOLD-2023-ver-1.1-2Dec2022_WMV.pdf. 2. Stolz D, et al. *Lancet*. 2022;400(10356):921-972.



Chronic inflammation and structural changes¹⁻³

Structural Changes of Airways



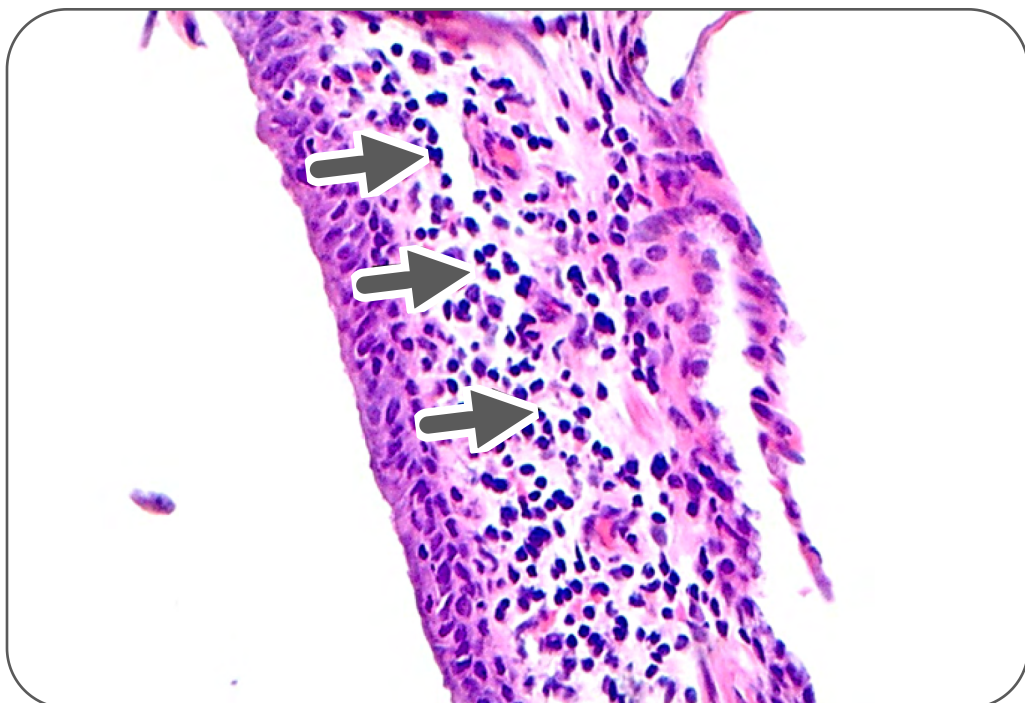
Parenchymal Destruction

close

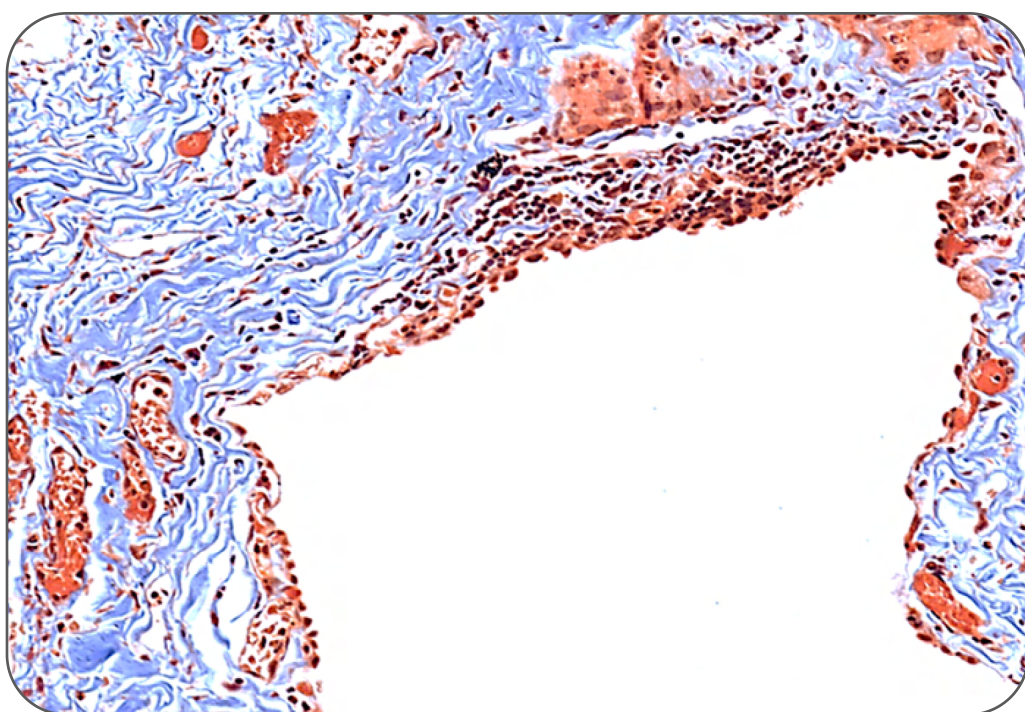
1. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. Updated 2023. Accessed March 16, 2023. https://goldcopd.org/wp-content/uploads/2022/12/GOLD-2023-ver-1.1-2Dec2022_WMV.pdf. 2. Barnes PJ. *J Allergy Clin Immunol*. 2016;138(1):16-27. 3. Linden D, et al. *Eur Respir Rev*. 2019;28:180063.



Progressive airway and parenchyma damage¹⁻⁴



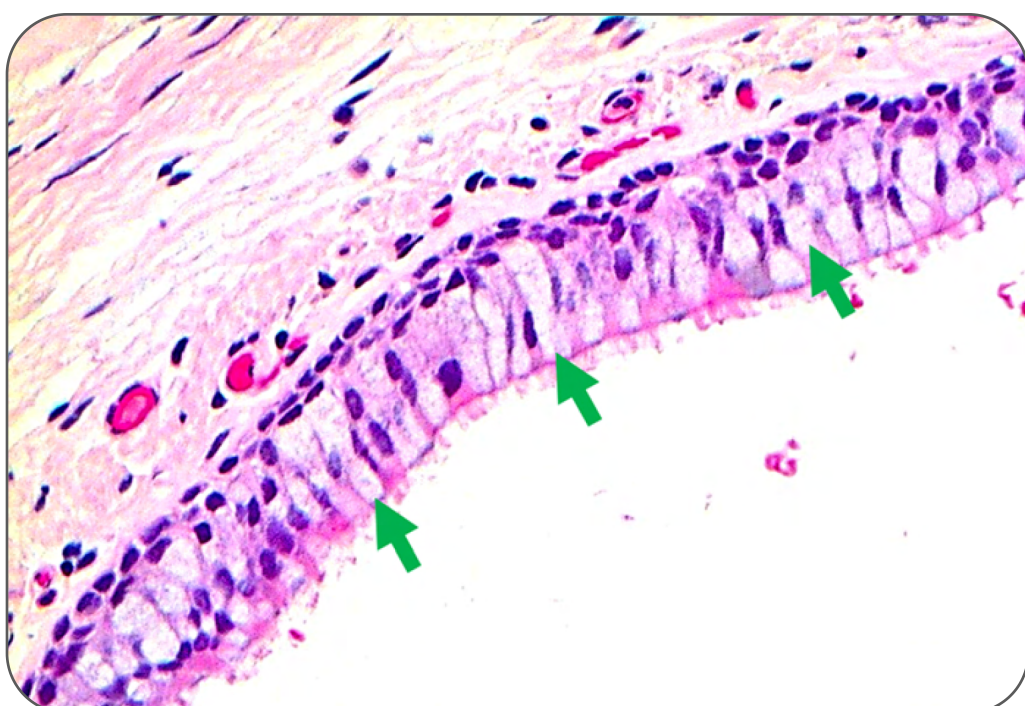
Inflammatory cell infiltration
(eg, neutrophils, macrophages, T cells)¹



Increased airway
wall thickness¹



Mucus overproduction
and plugging¹



Goblet cell hyperplasia¹

close

1. Higham A, et al. *Respir Res*. 2019;20(1):49. 2. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. Updated 2023. Accessed March 16, 2023. https://goldcopd.org/wp-content/uploads/2022/12/GOLD-2023-ver-11-2Dec2022_WMV.pdf. 3. Barnes PJ. *J Allergy Clin Immunol*. 2016;138(1):16-27. 4. Linden D, et al. *Eur Respir Rev*. 2019;28:180063.



Symptoms¹

Respiratory symptoms



Cough



Dyspnea



Wheeze



Chest tightness

Other symptoms



Fatigue



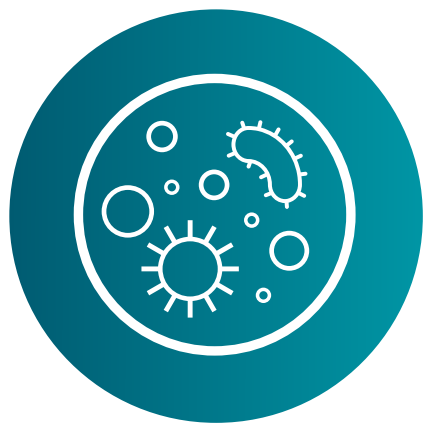
Sleep disturbance

close

1. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. Updated 2023. Accessed March 16, 2023. https://goldcopd.org/wp-content/uploads/2022/12/GOLD-2023-ver-1.1-2Dec2022_WMV.pdf



Exacerbations can be triggered by¹⁻⁴:



Respiratory Infections^{1,2}

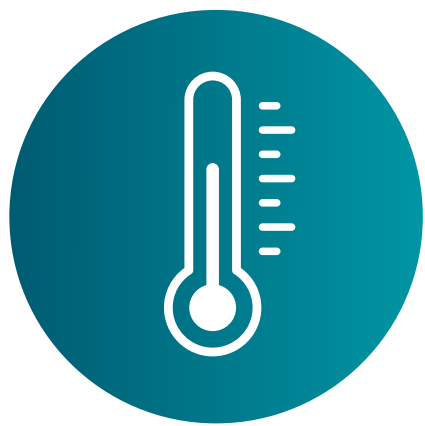
Most common causes of acute exacerbations of COPD

- Viral: rhinovirus, influenza, parainfluenza, pneumovirus^{1,2}
- Bacterial: *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catharralis*²



Pollution and Allergens^{1,3}

- Smoking
- Ozone
- Carbon monoxide
- Particulate matter (PM2.5, PM10)
- Sulfur dioxide
- Allergic phenotype (ie, hay fever or allergic response to pollen, house dust, or animals)³



Seasonal Variation¹

A few published studies show more common severe exacerbations during winter months

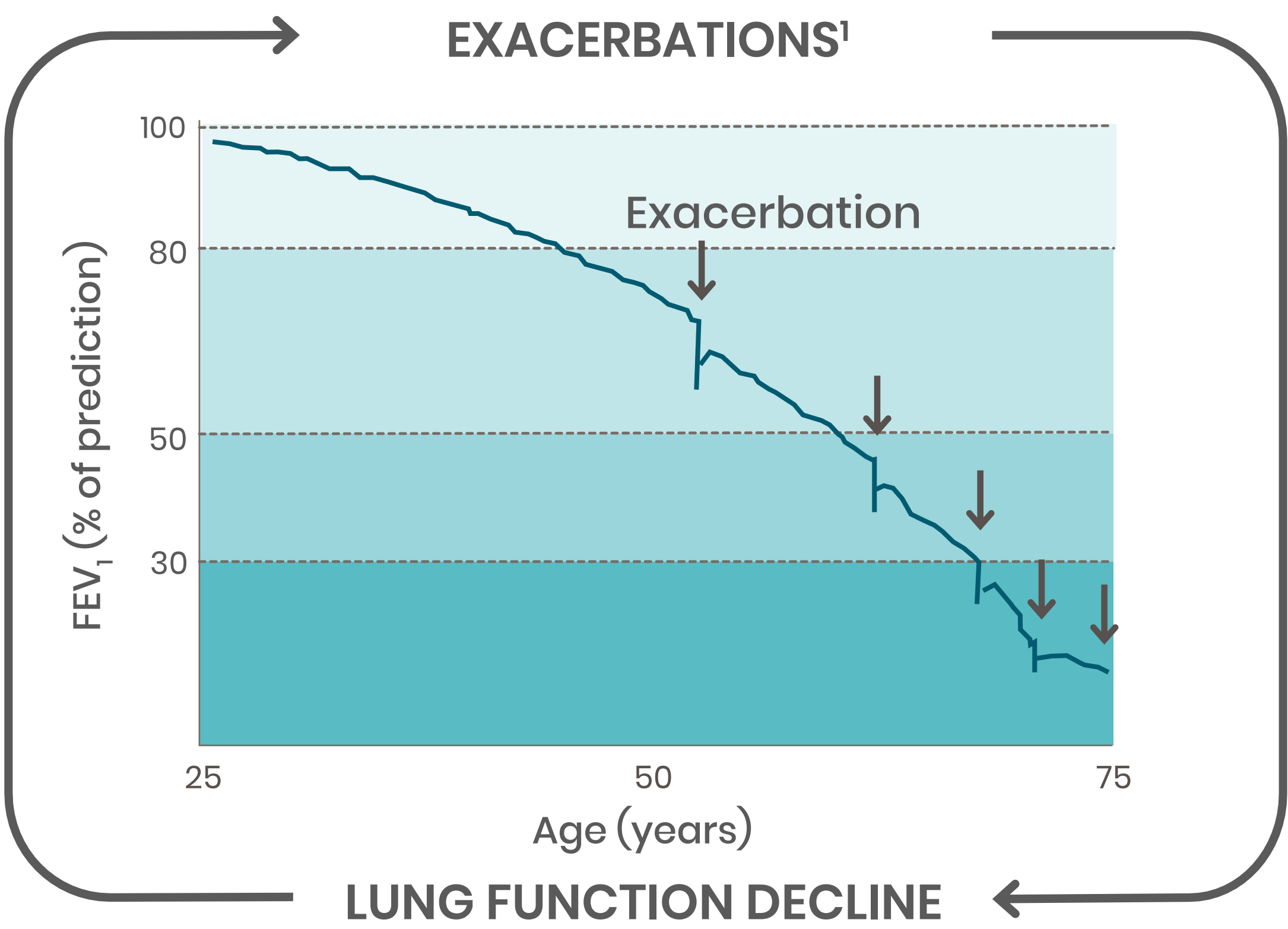
History of previous exacerbations is the most consistent predictor of COPD exacerbations¹

close

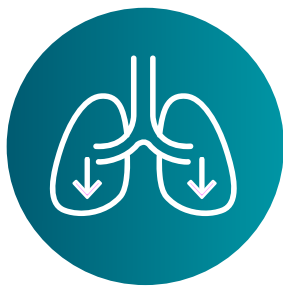
1. Hoge SP, et al. *Clin Resp J*. 2020;14(3):183-197. 2. Global Initiative for Chronic Obstructive Lung Disease (GOLD) Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. Updated 2023. Accessed March 16, 2023. https://goldcopd.org/wp-content/uploads/2022/12/GOLD-2023-ver-1.1-2Dec2022_WMV.pdf. 3. Jamieson DB, et al. *Am J Respir Crit Care Med*. 2013;188(2):187-192.



Post-exacerbation recovery/risks¹⁻⁶



Trajectory is based on a hypothetical COPD patient experiencing exacerbations and is reflective of published evidence demonstrating that exacerbations contribute to greater lung function decline¹⁻⁴



Following an exacerbation, FEV₁ often returns to baseline within several months, but for a small fraction of patients, FEV₁ does not return to pre-exacerbation levels⁵



Patients who experience frequent exacerbations show a significantly faster decline in FEV₁²



Low FEV₁ is a risk factor for COPD exacerbations and hospitalizations⁶

close

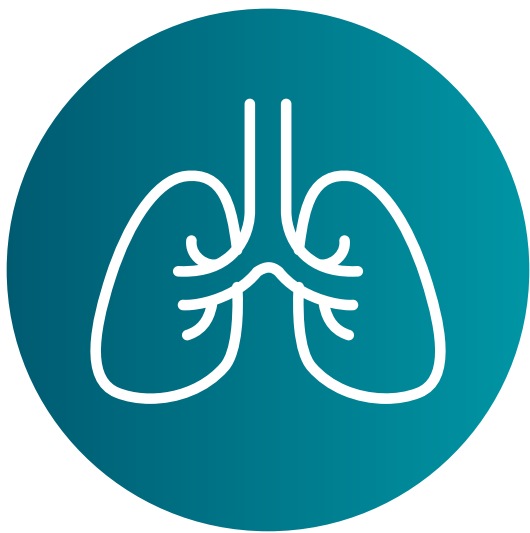
FEV₁, forced expiratory volume in 1 second.
1. Hansel TT, Barnes PJ. *Lancet*. 2009;374(9691):744-755. 2. Donaldson GC, et al. *Thorax*. 2002;57(10):847-852. 3. Wedzicha JA, Seemungal TAR. *Lancet*. 2007;370(9589):786-796. 4. Dransfield MT, et al. *Am J Respir Crit Care Med*. 2017;195(3):324-330. 5. Wageck B, et al. *COPD*. 2019;16(1):93-103. 6. Garcia-Aymerich J, et al. *Thorax*. 2011;66(7):585-590.



Multimorbidities associated with COPD

COPD is associated with high rates of comorbid conditions, some of which can contribute to increased mortality^{1,2}

Pulmonary



- Lung cancer¹⁻³
- Bronchiectasis^{1,3}
- Asthma³
- Pulmonary arterial hypertension^{1,2}

Extrapulmonary



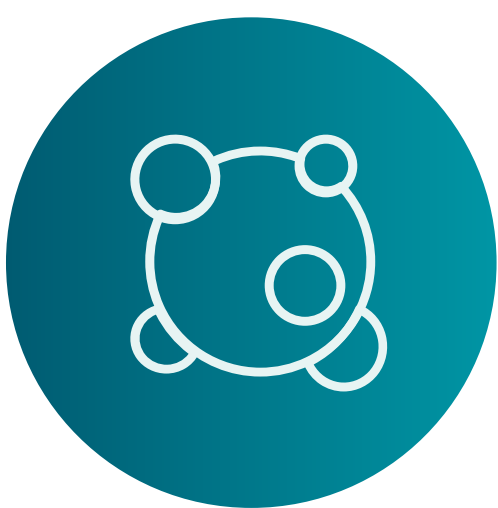
Cardiovascular¹⁻³



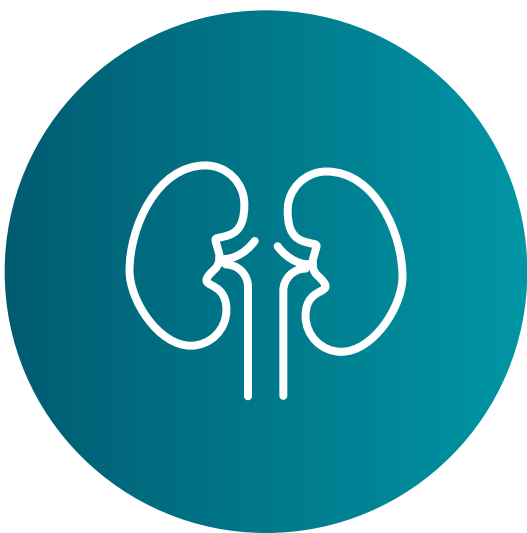
Musculoskeletal/
Osteoporosis¹⁻³



Neurologic¹⁻³



Metabolic^{1,2}



Renal⁴



Gastrointestinal^{1,3}

close

1. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. Updated 2023. Accessed March 16, 2023. https://goldcopd.org/wp-content/uploads/2022/12/GOLD-2023-ver-11-2Dec2022_WMV.pdf. 2. Barnes PJ, Celli BR. *Eur Respir J*. 2009;33(5):1165–1185. 3. Dal Negro RW, et al. *Multidiscip Respir Med*. 2015;10(1):24. 4. Gaddam S, et al. *BMC Pulm Med*. 2016;16:158.

