William Diez, DMSc, PA-C, RRT, AE-C
MSL – Respiratory & Immunology
AstraZeneca

Reevaluating the Approach to COPD Management

I have had the privilege to serve patients as a health care provider for almost 20 years: the first 12 as a respiratory care practitioner, 4 as an emergency medicine physician assistant, and the last 3 as a medical science liaison. In that time, there have been many great patient outcomes to celebrate. But with these victories come defeats and heartaches. One disease in particular that I have witnessed devastate patients and families is chronic obstructive pulmonary disease (COPD). Although significant strides have been made in the last few decades to improve the management of patients with COPD, there is still more work to be done to overcome the challenges associated with this debilitating condition.[1]

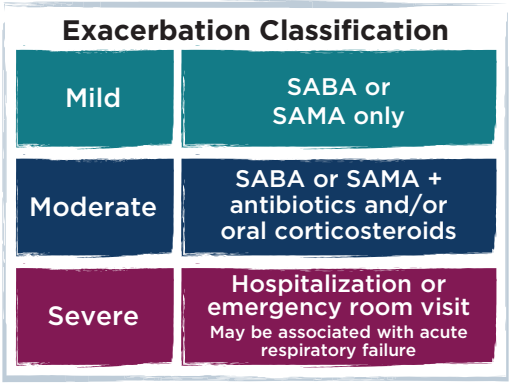

Figure 1: Exacerbation Severity is Defined by the Treatment Needed[1]

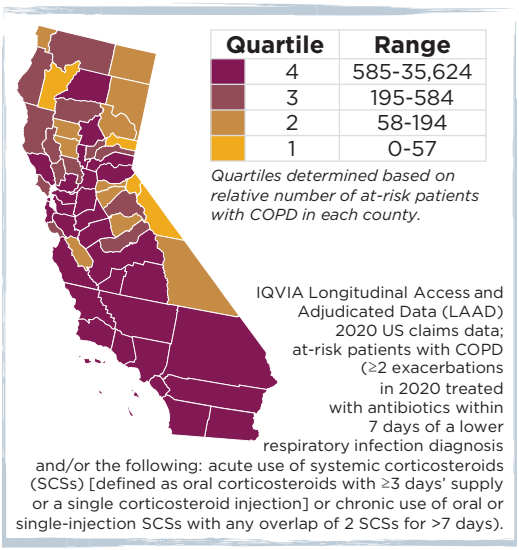

Figure 2: California Heatmap of At-risk Patients with COPD[5]

COPD is a leading cause of mortality in the United States[2] and a major healthcare burden, as evident by an alarming 4000+ emergency department visits and just over 1900 hospitalizations per day attributed to COPD.[3,4,*] A key contributor is COPD exacerbations, defined by the GOLD report as an acute worsening of respiratory symptoms lasting from 7 to 10 days, if not longer, and requiring additional therapy (**Figure 1**).[1] In 2020, an estimated 44% of patients with COPD in California were at risk for experiencing a future exacerbation, with just over half of the state's counties among the highest quartile nationally in concentration of at-risk patients with COPD (**Figure 2**).[5] Not only are exacerbations frequent in COPD,[6] they may also have life-changing consequences by driving a cascade of further exacerbations,[7,8] disease progression,[9,10] and increased mortality risk[8,11] (**Figure 3**). What cannot be overlooked is the impact that may occur beyond the lungs, particularly in patients with comorbid cardiovascular disease (CVD).[12] In addition to the heightened morbidity and mortality risks associated with these frequently comorbid diseases,[13-18] some patients with COPD and CVD showed an increased risk of cardiovascular events following an exacerbation[12] (**Figure 3**).

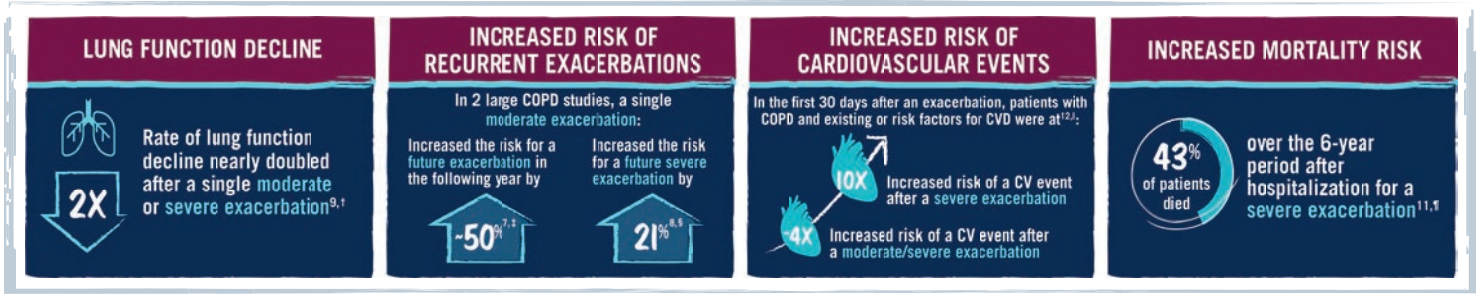

Figure 3: Exacerbations May Cause Life-changing Impacts

*Data from 2011 and 2010, respectively.

†Based on 2000 patients from a cohort study that included 10,300 patients, with or without COPD, who were current or former smokers (smoking history ≥10 pack-years).

‡Retrospective study of ≈1.5 million patients with COPD ≥40: Data shown for Medicare FFS (96% of the study population).

§Population-based study of ≈100,000 patients (UK) with COPD (up to 10 years of follow-up). Moderate exacerbations were defined as those managed outside the hospital and severe exacerbations were defined as those requiring hospitalization.

‖Post-hoc analysis of 16,485 patients with moderate COPD with CVD or increased risk of CVD.

¶Retrospective cohort study of 17,450 patients (US) with COPD in the Intermountain Healthcare system from 2009 to 2014.

Despite these risks, exacerbations may be under-reported and under-treated, which can result in preventable burden.[19-21] Clinicians and health care organizations can help improve care and outcomes for patients with modifiable high risk of future exacerbations through implementation of quality care standards to encourage early identification aimed at optimizing COPD management (**Figure 4**).[22] These principles include a combination of approaches, designed to drive patient-centered, risk-based assessment and guide phenotype-specific selection of pharmacological and nonpharmacological interventions. To contribute to optimal care, it is important to consider earlier intervention and to more proactively diagnose and manage patients with COPD.[22] Real-world studies have shown that delaying initiation of guideline-recommended maintenance therapy more than 30 days following an exacerbation was associated with greater morbidity and economic burden.[23,24] One retrospective observational analysis of US healthcare claims from patients with COPD initiating triple therapy* following an exacerbation showed that these outcomes worsened with each 30-day delay, resulting in an 11% increase in odds of a future COPD exacerbation and ≈$616 increase in all-cause health care costs per month compared to patients who were initiated on triple therapy within 30 days during the 12 months after the index exacerbation.[23] Routine follow-up to assess a patient's disease status and review self-management techniques is essential to ensure that the quality of care is maintained long term.[1,22]

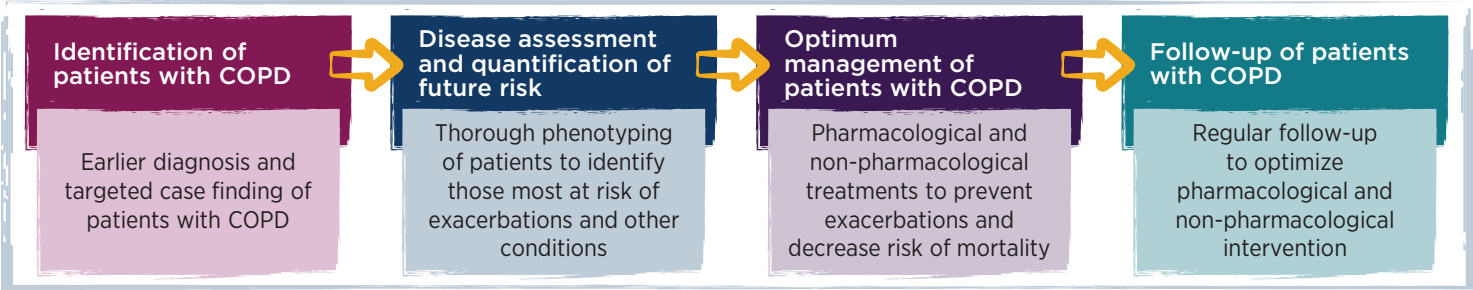

Figure 4: A Combination of Approaches for Optimal Management of COPD[1,22]

As we continue to make progress toward optimizing the management of COPD, it is important to remain cognizant of the challenges and concerns felt by the millions of patients who suffer from this chronic condition.[25] As a health care provider, my priority is always to help improve a patient's outcomes and quality of life, regardless of disease or ailment. I believe it is crucial to promote an open dialogue with patients to serve not only as a clinician, but as an educator and an ally. Collaboratively, we can help redefine what it means to be living with COPD.

*The index treatment window and the timing of closed triple therapy approval in the US resulted in ~3% of study patients receiving closed triple therapy as their index treatment.

REFERENCES

1. GOLD. Global Strategy for the Diagnosis, Management, and Prevention of COPD. 2021 Report. https://goldcopd.org/wp-content/uploads/2020/11/GOLD-REPORT-2021-v1.1-25Nov20_WMV.pdf Accessed October 10, 2022.
2. Murphy SL, Kochanek KD, Xu JQ, Arias E. Mortality in the United States, 2020. NCHS Data Brief, no 427. Hyattsville, MD: National Center for Health Statistics. 2021.
3. Ford ES. Hospital discharges, readmissions, and ED visits for COPD or bronchiectasis among US adults: findings from the nationwide inpatient sample 2001-2012 and Nationwide Emergency Department Sample 2006-2011. *Chest.* 2015;147(4):989-998.
4. Ford ES, Croft JB, Mannino DM, et al. COPD Surveillance-United States, 1999-2011. *Chest.* 2013;144(1):284-305..
5. Data on file, REF-153806, AZPLP.
6. Hurst JR, Vestbo J, Anzueto A, et al. Susceptibility to exacerbation in chronic obstructive pulmonary disease. *N Engl J Med.* 2010;363(12):1128-1138.
7. Dreyfus J, Moretz C, Kumar S, et al. Does baseline exacerbation history in COPD predict future exacerbation frequency? Real world insights from multiple US insurers [abstract]. *Am J Respir Crit Care Med.* 2021;203:A2297.
8. Rothnie KJ, Müllerová H, Smeeth L, Quint JK. Natural history of chronic obstructive pulmonary disease exacerbations in a general practice-based population with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med.* 2018;198(4):464-471.
9. Dransfield MT, Kunisaki KM, Strand MJ, et al. Acute exacerbations and lung function loss in smokers with and without chronic obstructive pulmonary disease. *Am J Respir Crit Care Med.* 2017;195(3):324-330.
10. Watz H, Tetzlaff K, Magnussen H, et al. Spirometric changes during exacerbations of COPD: a post hoc analysis of the WISDOM trial. *Respir* Res. 2018;19(1):251.
11. Blagev DP, Collingridge DS, Rea S, et al. Stability of frequency of severe chronic obstructive pulmonary disease exacerbations and health care utilization in clinical populations. *Chronic Obstr Pulm Dis.* 2018;5(3):208-220.
12. Kunisaki KM, Dransfield MT, Anderson JA, et al. Exacerbations of chronic obstructive pulmonary disease and cardiac events. *Am J Respir Crit Care Med.* 2018;198:51-57.
13. Divo M, Cote C, de Torres JP, et al. Comorbidities and risk of mortality in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med.* 2012;186(2):155-161.
14. Miller J, Edwards LD, Agustí A, et al. Comorbidity, systemic inflammation and outcomes in the ECLIPSE cohort. *Respir Med.* 2013;107(9):1376-1384.
15. Mannino DM, Thorn D, Swensen A, Holguin F. Prevalence and outcomes of diabetes, hypertension and cardiovascular disease in COPD. *Eur Respir J.* 2008;32(4):962-969.
16. Rabe K, Hurst JR, Suissa S. Cardiovascular disease and COPD: dangerous liaisons? *Eur Respir Rev.* 2018;27:180057.
17. Morgan AD, Zakeri R, Quint JK. Defining the relationship between COPD and CVD: what are the implications for clinical practice?. *Ther Adv Respir Dis.* 2018;12:1753465817750524.
18. Chen W, Thomas J, Sadatsafavi M, FitzGerald JM. Risk of cardiovascular comorbidity in patients with chronic obstructive pulmonary disease: a systematic review and meta-analysis. *Lancet Respir Med.* 2015;3(8):631-639.
19. Leidy NK, Murray LT, Jones P, Sethi S. Performance of the EXAcerbations of chronic pulmonary disease tool patient-reported outcome measure in three clinical trials of chronic obstructive pulmonary disease. *Ann Am Thorac Soc.* 2014;11(3):316-325.
20. Dalal AA, Shah MB, D'Souza AO, Lunacsek OE, Nagar SP, Crater GD. Observational study of the outcomes and costs of initiating maintenance therapies in patients with moderate exacerbations of COPD. *Respir Res.* 2012;13(1):41.
21. Diette GB, Dalal AA, D'Souza AO, Lunacsek OE, Nagar SP. Treatment patterns of chronic obstructive pulmonary disease in employed adults in the United States. *Int J Chron Obstruct Pulmon Di*s. 2015;10:415-422.
22. Pullen R, Miravitlles M, Sharma A, et al. CONQUEST Quality Standards: For the Collaboration on Quality Improvement Initiative for Achieving Excellence in Standards of COPD Care. *Int J Chron Obstruct Pulmon Dis.* 2021;16:2301-2322.
23. Tkacz J, Evans KA, Touchette DR, et al. PRIMUS – prompt initiation of maintenance therapy in the US: A real-world analysis of clinical and economic outcomes among patients initiating triple therapy following a COPD exacerbation. *Int J Chron Obstruct Pulmon Dis.* 2022;17:329–342.
24. Coutinho AD, Lokhandwala T, Boggs RL, et al. Prompt initiation of maintenance treatment following a COPD exacerbation: outcomes in a large insured population. *Int J Chron Obstruct Pulmon Dis.* 2016;11:1223-1231.
25. American Lung Association. COPD Prevalence. https://www.lung.org/research/trends-in-lung-disease/copd-trends-brief/copd-prevalence. Accessed October 10, 2022.