



Mind the Gap: Addressing Cardiovascular Disease in Chronic Obstructive Pulmonary Disease

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Over the past thirty years, age-adjusted death rates from cardiovascular disease (CVD) have declined by an astonishing 50% (Figure 1) (1). This dramatic improvement is multifactorial; however, identification and modification of population attributable risk factors have undoubtedly paved the way to success (2). Sadly, the reduction of mortality rates associated with chronic obstructive pulmonary disease (COPD) has been far less substantial, and it is still a leading cause of death worldwide (3). Interestingly, exacerbations of COPD dramatically increase the risk for future CVD events (4), underscoring the need to better understand this complex disease.

Therapies to modify atherosclerotic cardiovascular disease (ASCVD) have been increasingly available for the past 3 decades. Since the 1980s, statins have been known to reduce low-density lipoprotein (and subsequent ASCVD risk) by 40–50% (5), leading the United States Preventive Services Taskforce to recommend statins as primary

prevention through the age of 75 for ASCVD (6). Similarly, improving glycemic control using newer antidiabetic therapies such as liraglutide, a glucagon-like peptide-1 analog, has been shown to decrease the risk for cardiovascular death, myocardial infarction, and stroke (7). Similar approaches have already shown potential benefits for dapagliflozin, a sodium–glucose cotransporter-2 inhibitor used for the treatment of diabetes in patients with COPD. A subgroup analysis in the DAPA–HF (Dapagliflozin and Prevention of Adverse Outcomes in Heart Failure) study found that dapagliflozin improved outcomes of worsening heart failure or cardiovascular death in patients with COPD (8). Most importantly, targeted hypertension management, as observed in SPRINT (Systolic Blood Pressure Intervention Trial) (9), as well as modest weight loss (10), have been established as primary prevention for ASCVD.

Such success has even led to ongoing strategies combining preventative therapies (e.g., polypill) to reduce the risk of cardiovascular events in individuals at intermediate risk (11). Hence, proven therapies are readily available to mitigate comorbid CVD among patients with COPD.

In this issue of *AnnalsATS*, Hawkins and colleagues (pp. 1102–1111) did an elegant study assessing established cardiovascular risk factors among patients with COPD (12). Using classically defined modifiable ASCVD risk factors (hypertension, dyslipidemia, diabetes mellitus, obesity, and smoking), the authors conducted a repeated cross-sectional analysis of primary care electronic medical records for patients with COPD within a large national cohort with longitudinal follow-up from 2013 to 2018. With over 32,000 patients with COPD, the investigators compared primary care management of these key risk

**Age-Standardized Death Rate
United States, 1999–2016**

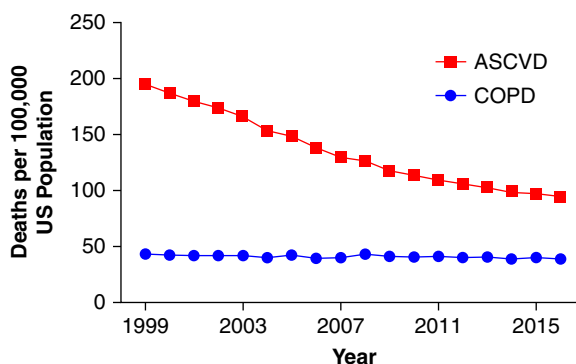


Figure 1. Age-standardized death rate—United States, 1999–2016. Age-adjusted death rates for ASCVD (shown in red) decreased by nearly 50%, and rates for COPD (shown in blue) decreased by 9% between 1999 and 2016. Figure created using the Centers for Disease Control and Prevention Compressed Mortality File 1999–2016 using the Wide-ranging Online Data for Epidemiologic Research online database (1). ASCVD = atherosclerotic cardiovascular disease; COPD = chronic obstructive pulmonary disease.

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DOI: 10.1513/AnnalsATS.202204-317ED

factors to a control cohort matched for age, sex, and rural residence. The results were both unexpected and alarming.

ASCVD risk factors were nearly twice as common among patients with COPD than in the control group in a primary care setting. Not surprisingly, Framingham Risk Scores were high (greater than 20%) in over half of the COPD cohort. Despite such high-risk features, patients with COPD had shockingly low rates of risk factor monitoring over the observed period. Most surprising, smoking status was only recorded in half of the patients with COPD at any time, with fewer than 8% having an active status recorded within the last year. As might be expected, guideline-recommended targets (i.e., blood pressure) were only achieved in a low proportion of individuals, whereas proven medical therapies were underused. Taken together, these findings suggest that primary prevention measures for cardiovascular disease were poor among patients with COPD. This is especially striking as patients with COPD were reported to use the primary healthcare system 1.5 times more frequently than control subjects (7.3 vs. 4.9 visits in the last year, respectively). If these findings are confirmed in other health systems, including those in the United States, it suggests that there is much work to be done.

COPD shares similar disease mediators with CVDs, including inflammation, aging, and smoking. Given the high burden of disease for both conditions, therapeutic interventions have long sought to achieve primary prevention as well as ameliorate secondary complications. The record of accomplishment in CVD has proven that intervention on modifiable risk factors can reduce the risk of developing ASCVD and subsequently lower the risk of death. Regarding COPD, smoking cessation has long been an established means of primary prevention and secondary reduction of COPD mortality (13). Recently, several trials

have attempted to ameliorate COPD severity and/or progression by employing classic cardiovascular therapies. Specifically, Beta-Blockers for the Prevention of Acute Exacerbations of Chronic Obstructive Pulmonary Disease (BLOCK COPD) used β -blockers to reduce exacerbations (14), STATCOPE (Simvastatin Therapy for Moderate and Severe COPD) used simvastatin to reduce exacerbations (15), and most recently, Losartan Effects on Emphysema Progression (LEEP) used losartan to decrease the rate of emphysema progression (16). Despite strong scientific premise and observational studies that supported the potential efficacy of these interventions, BLOCK COPD and STATCOPE, unfortunately, failed to meet their primary endpoints. The results of LEEP are not yet available.

The results from Hawkins and colleagues highlight that the total burden of cardiovascular risk among patients with COPD is very high and undertreated. Considering our continued shortcomings, the current observations call attention to two glaring areas of need. First, unified statements from leading international associations and expert groups (i.e., GOLD [Global Initiative for Chronic Obstructive Lung Disease], American Heart Association, and American College of Cardiology) are needed to highlight the ongoing disparity in ASCVD management among patients with COPD. Although protocolized interventions are unlikely to suit all clinical environments, it is imperative that attention be drawn to this underrecognized paradigm. Further research is also needed to better understand what accounts for these differences in practice. Albeit speculative, these observations should be seen as an opportunity to revisit the shared partnership between primary care and subspecialists in an effort to untangle any potential obstacles to care. Second, we must ask whether

incremental treatment of comorbid cardiovascular risk will ever be sufficient to meaningfully reduce COPD morbidity and mortality. Should we instead focus on holistic risk factor modification for ASCVD among patients with COPD? Results from Hawkins and colleagues suggest that we have been somewhat myopic in our approach to disease modifications by singularly focusing on COPD and/or emphysema instead of the patient as a whole. Overall, this study uncovers the significant opportunity for prospective studies aimed at targeting extra modifiable ASCVD risk factors in COPD.

Limitations

Limitations to the current study include the role of the Canadian Primary Care Sentinel Surveillance Network on data reporting from primary care providers. This could lead to an underrepresentation of disease monitoring for intervention. In addition, this study only focused on the reporting of modifiable risk factors for cardiovascular disease, which may not give the complete picture for assessing comorbid conditions. Calculation of ASCVD risk by other variables may provide additional perspective on the total risk among patients with COPD.

Conclusions

Despite any limitations, these findings serve as a warning to “mind the gap” in ASCVD prevention among patients with COPD. Primary care providers, subspecialty cardiologists, and pulmonologists will all need to be aware of the ongoing disparity in best practices when caring for patients with COPD. If we truly desire to reduce the morbidity and mortality of COPD, then we must intervene on these readily apparent risk factors for cardiovascular disease. ■

Author disclosures are available with the text of this article at www.atsjournals.org.

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Works in Progress: Using Administrative Data to Estimate the Prevalence of Progressive Fibrosing Interstitial Lung Disease

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The world of interstitial lung disease (ILD) is undergoing a paradigm shift in the way it conceptualizes and treats patients with progressive fibrosing ILD (1). Rather than focusing solely on the underlying etiology of a patient's ILD, recent evidence

highlights the importance of also considering the shared pathophysiology across the progressive fibrotic disease spectrum (2), as well as the common benefits provided by antifibrotic therapy when used in patients with varying causes of pulmonary fibrosis (3, 4). Yet, in part because progressive fibrosing ILD is a novel concept for which treatment was only recently approved, and also because it is a phenotype that can affect any of a heterogeneous group of distinct lung diseases, data regarding the prevalence of progressive fibrotic ILD (outside of idiopathic pulmonary fibrosis [IPF]) are scarce and highly variable (5).

In this issue of *AnnalsATS*, Singer and colleagues (pp. 1112–1121) report the observations of a retrospective review of administrative claims data that attempts to provide a real-world estimate of the prevalence of non-IPF fibrosing ILD (6). The authors assumed the great challenge of identifying patients with progressive fibrosis using *International Classification of Diseases, Tenth Revision* (ICD-10) codes

that are based on specific ILD diagnoses rather than disease behavior. To do this, they designed a multistep algorithm to characterize patients as having chronic fibrosing ILD using ICD-10 codes and then used procedural and pharmacy claims to identify several proxies for disease progression, such as pulmonary function testing claims within 3 months, computed tomography chest claims in a year, and oral corticosteroid prescriptions. The authors methodically included multiple definitions of disease progression that provide differing degrees of diagnostic stringency to account for the variation in estimating fibrosing ILD prevalence on the basis of administrative claims. After applying their carefully crafted algorithm, Singer and colleagues estimated a prevalence range for non-IPF progressive fibrosing ILD of 12.14–29.05 per 10,000 among Medicare Part D enrollees between 2015 and 2019. This estimate is significantly higher than those obtained in previous analyses in Europe and the United States (1.94–7.8 per 10,000) (5) and

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DOI: 10.1513/AnnalsATS.202203-276ED