Should COPD stand for "comorbidity-related obstructive pulmonary disease"?

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There is a pressing need to diagnose and effectively treat comorbidities of COPD
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The burden of chronic obstructive pulmonary disease (COPD) is enormous and growing. Currently, COPD affects 300 million people worldwide and kills more than 3 million people each year [1]. COPD exacts a large financial toll on society because it is the leading cause of hospitalisation in many jurisdictions in the Western world. In the USA, for example, which has a very robust population-based data, COPD accounts for 650 000 hospital admissions and 1.7 million emergency visits per year [2]. Because hospital-based care is very expensive, the costs of COPD care are staggering, estimated to be $101 billion per year in the USA [3]. These costs are expected to double over the next 10 years, owing largely to the ageing population. Regrettably, the current treatments for COPD are suboptimal and woefully inadequate to reduce the burden of COPD-related hospitalisations. Indeed, even with the "best" available therapies, one in 10 patients hospitalised with an acute exacerbation will die during their hospital stay and even among the "lucky" ones who survive, a majority will experience adverse effects related to corticosteroids, including hyperglycaemia, insomnia, hypertension and weight gain, and one in three patients will relapse, requiring another hospitalisation within 6 months of discharge [4]. These observations beg the question: why are COPD hospitalisations so difficult to treat and manage, and why are they associated with such poor health outcomes?

In this issue of the *European Respiratory Journal*, Faner *et al.* [5] offer a novel insight that, at least in part, answers these questions with one word: "comorbidities". Using a chart audit, which notoriously underestimates the burden of comorbidities, the authors of the study evaluated 5447 patients who were hospitalised for COPD exacerbations and discovered that nearly two-thirds of these patients had at least one major comorbidity that impacted their underlying COPD. Predictably, the most common comorbidities were diabetes, heart failure, peripheral vascular disease and ischaemic heart disease as previously described [6]. They then made a clever use of publically available databases, including Cytoscape (www.cytoscape.org), DisGeNet (www.disgenet.org) and HIPPIE (Human Integrated Protein–Protein Interaction Reference) (http://cbdm.mdc-berlin.de/tools/hippie), to unravel the potential molecular and pathway interactions of these comorbidities with COPD. Interestingly, their analysis revealed that although some comorbidities, such as connective tissue diseases, cancer and liver disease, were largely disconnected and occurred in isolation, many others, such as heart failure, diabetes, renal disease and myocardial infarction, clustered together as related clinical and molecular entities, reflecting shared pathophysiologies (most likely) in the "vascular" pathways.

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Why are vascular comorbidities relevant for patients with COPD? Mannino *et al.* [6] have shown that COPD patients with cardiovascular comorbidities have nearly six times the risk of hospitalisation than those without any comorbidity. Not surprisingly, the total healthcare costs of COPD patients relate exponentially to the number of comorbidities they have. For example, COPD patients with four or more comorbidities incur direct costs that are four times higher than COPD patients without any comorbidities. These excess costs are driven largely by hospitalisations, which are increased 26-fold in patients with multimorbidities compared with those without comorbidities. These data are also consistent with costs estimates of Ford *et al.* [3]. While the total direct costs of COPD care are beyond $100 billion per year in the USA, adjustments for the excess costs related to the management of multimorbidities and other features lead to a >90% reduction in costs to a (more modest) total of $7 billion per year [3].

These data highlight the pressing need to diagnose and effectively treat comorbidities of COPD. Cardiovascular comorbidities, such as heart failure and ischaemic heart disease, deserve special emphasis as they are the most common comorbidities and are, most importantly, modifiable with treatment. For instance, the appropriate use of β-blockers can reduce total mortality of patients with congestive heart failure by 30%, even in those with COPD [7]. Despite a large body of data demonstrating the safety of β-blockers (especially cardioselective ones), there is still great hesitancy to using these medications in COPD patients with concomitant heart failure. Provocatively, there are emerging data that cardiovascular therapies, such as β-blockers, aspirin and statins, may be effective in improving COPD end-points, such as exacerbations [8–10]. Reciprocally, there is also an interest in using airway medications, such as inhaled corticosteroids and long-acting bronchodilators, by themselves or in combination, to reduce morbidity and mortality associated with cardiovascular disease in COPD patients [11]. Towards this end, there is a growing number of clinical trials targeting combined cardiovascular and COPD end-points, and within the next few years, we will have high-quality data to determine the clinical impact of using cardiovascular drugs for COPD patients. Until then, clinicians should aggressively "seek and treat" comorbidities of COPD, which undoubtedly will reduce the burden of morbidity and mortality of our COPD patients.

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