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Global Spotlights

Exacerbating the burden of cardiovascular disease: how can we address cardiopulmonary risk in individuals with chronic obstructive pulmonary disease?

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Cardiovascular disease (CVD) and chronic obstructive pulmonary disease (COPD) often co-exist.^{1,2} This is not surprising given their shared risk factors including, but not limited to, smoking, hypertension, dyslipidaemias, atrial fibrillation, physical inactivity, and air pollution. Evidence from the EURObservational Research Programme Heart Failure Long-Term Registry showed that prevalence of diagnosed COPD amongst individuals admitted with heart failure may be up to 19%, based on analysis of 6920 individuals hospitalized with heart failure.¹ Similarly, there is a reciprocal association with CVD in individuals with COPD. Data from the Julius General Practitioners' Network, a collaboration of nearly 70 general practices in the Netherlands with ~370 000 registered patients, demonstrated a 3-fold increased incidence of heart failure and 1.7-fold increased incidence of ischaemic heart disease in individuals with COPD.² In reality, these figures are likely to be underestimated because in the UK alone, reports estimate that there could be up to 2 million individuals with undiagnosed COPD,³ suggesting that many patients with potentially high CVD risk remain undetected and untreated.

In individuals with coexisting CVD and COPD, the risk of adverse clinical events is increased above that of each comorbidity in isolation. Mortality risk among those with both conditions is increased by up to 90% compared with those who have COPD alone,⁴ and approximately one-third of all COPD deaths could be cardiovascular in origin. It is well documented that acute exacerbations of COPD (AECOPDs) accelerate lung function decline and increase the risk of further acute events and premature mortality. An AECOPD also increases the risk of major

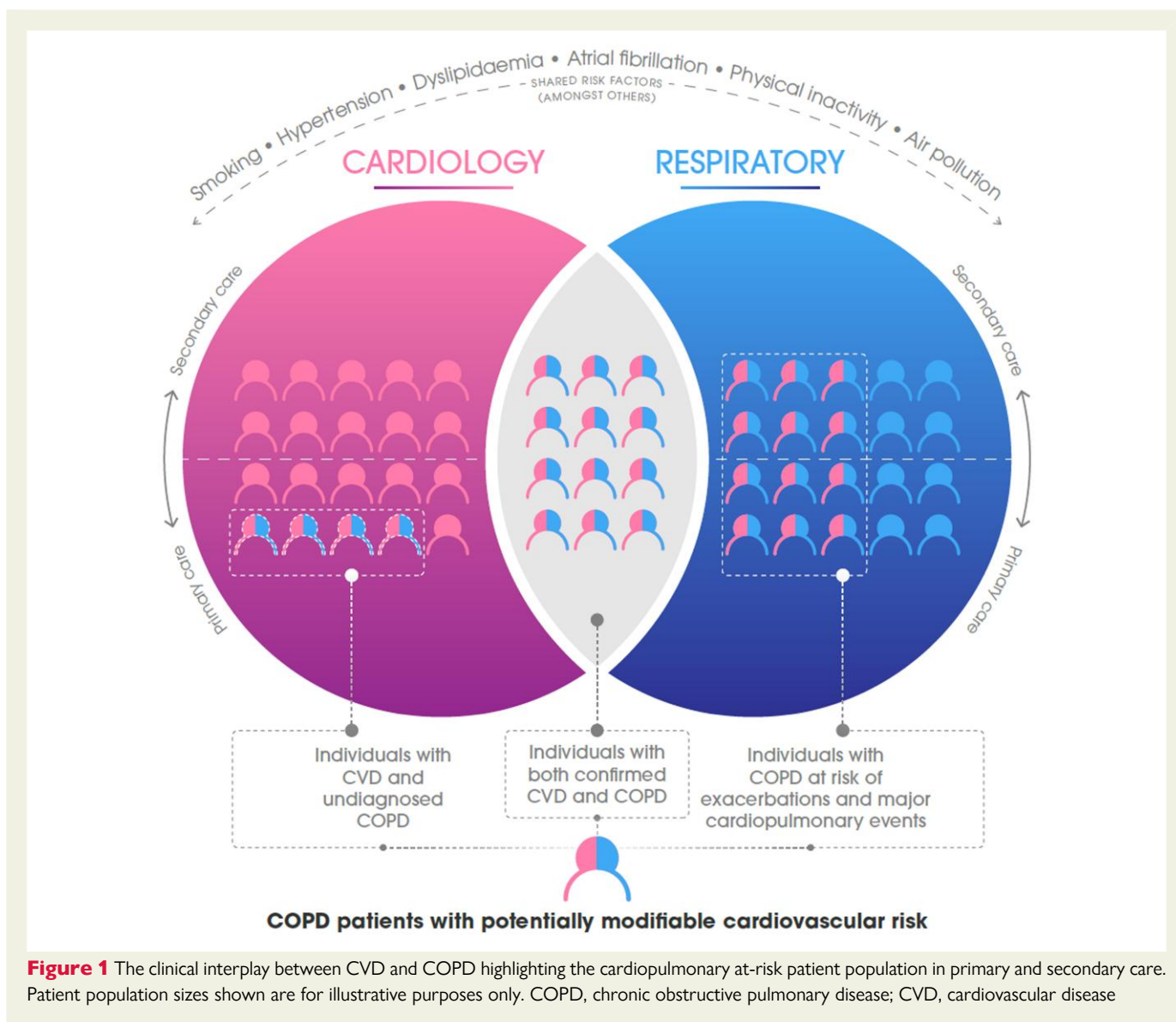
cardiovascular events in patients; up to 5 days following a moderate AECOPD, the risk of myocardial infarction (MI) is doubled, and at 6–10 days, the risk of stroke is reported to be increased by 40%.⁵ Moreover, it is estimated that in the first 30 days following a moderate or severe AECOPD, the risk of any cardiovascular event may be increased by up to four times and persists for a year, albeit attenuating over time.⁶ Recent data from the retrospective EXAcerbations of COPD and their OutcomeS on CardioVascular diseases (EXACOS-CV) US healthcare claims database of individuals with COPD ($n = 355\,978$), found that the risk of acute cardiovascular events in the first 30 days following an AECOPD of any severity may be increased by over 30% compared with those who did not have an AECOPD.⁷ Whilst the mechanisms underpinning how an AECOPD contributes to elevated cardiovascular risk require further research, it is clear that exacerbating individuals are at significant risk of both major pulmonary and cardiovascular events (cardiopulmonary risk). Optimized management of this group presents an important opportunity to improve COPD outcomes and reduce cardiovascular morbidity and mortality at a population level.

Despite the burden of COPD and impact of even a single moderate AECOPD on short- and long-term outcomes, current COPD care remains suboptimal with care pathways that are often reactive rather than proactive in approach. Less than a quarter of patients in the UK receive all five of the National Institute for Health and Care Excellence fundamentals of COPD care (smoking cessation, vaccination, pulmonary rehabilitation, personalized self-management planning and optimized

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comorbidity treatment).³ Additionally, over a third of patients hospitalized with a first severe AECOPD are discharged without appropriate maintenance treatment.⁸ This is concerning given that two recent randomized clinical trials have demonstrated improvement in cardiopulmonary risk in individuals with COPD with a history of AECOPDs, reporting a reduction in mortality in those allocated to single-inhaler triple therapy with an inhaled corticosteroid (ICS), long-acting beta agonist (LABA) and long-acting muscarinic antagonist (LAMA) vs. dual therapy with a LABA/LAMA.^{9,10} Of note, data from the ETHOS trial suggested that this mortality reduction may be driven by a decline in cardiovascular deaths.⁹ Post hoc analysis also showed a lower major adverse cardiac event (MACE) incidence with ICS-containing therapy (1.4%) vs. therapy without ICS (2.1%). This difference in MACE rates on fatal cardiovascular events and non-fatal MI was more pronounced with a higher baseline eosinophil count.¹¹ Post hoc analysis of the IMPACT trial has also demonstrated a reduced risk of cardiopulmonary composite events (including exacerbations, pneumonia, cardiovascular events, and death) in individuals allocated to single-inhaler triple therapy vs. LABA/LAMA.¹⁰ Notably, this growing body of evidence has been reflected in the 2023

international consensus from the Global Initiative for Chronic Obstructive Lung Disease that recommends targeting mortality reduction in individuals with COPD.

The recent Lancet Commission on COPD outlined objectives to eliminate the disease and argued for a 'fundamental change' in thinking about COPD.¹² Notwithstanding the importance of treating tobacco dependency and other contributing pulmonary and cardiovascular risk factors in COPD, increased prioritization and treatment optimization to prevent AECOPDs and associated cardiopulmonary risk presents an important target for healthcare improvement (Figure 1). More evidence from real-world and randomized clinical trials could reinforce existing findings and generate new insights into how cardiovascular events may be reduced in AECOPDs.

Strategies to achieve this may include increased awareness and advocacy for treatment optimization for individuals with confirmed comorbid disease; identifying and investigating individuals with CVD who are suspected to have comorbid COPD; and proactive identification and treatment of individuals with COPD at risk of an AECOPD. Enhanced interdisciplinary working between cardiovascular,

respiratory, and integrated primary care services is also key to transforming COPD care pathways. Collaborative working has already seen success across cardiovascular, renal, and metabolic disciplines, and a similar partnership approach should be adopted across cardiology and respiratory care. This could improve patient outcomes with shared-goal treatment pathways across COPD and CVD.

Acknowledgement of this unmet need has inspired partnership working in the UK (The UK Cardiopulmonary Taskforce) to develop collaborative links between a multidisciplinary group of cardiac and respiratory healthcare professionals from primary and secondary care to understand and manage cardiopulmonary risk in COPD. This approach will help inform future clinical, academic, and policy approaches to improve cardiovascular care and outcomes for people with COPD—setting the scene for European initiatives to reduce premature deaths from cardiovascular disease.

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