

## Chronic pulmonary comorbidities increase the risk of severe COVID-19, but critical details remain undetermined

While most people infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) will have mild symptoms, up to 20% of those infected will require hospitalization and 2% will die.<sup>1</sup> Identifying which patients are most at risk of severe disease guides isolation advice, vaccine priority and clinical care. Age has been consistently identified as the most important risk factor for death, with those >80 years having a 20-fold risk of those aged 50–59 years.<sup>2</sup> Chronic respiratory illness was also identified early as a potential risk for severe illness. With a large number of observational studies published since the beginning of the epidemic, the recent publication by Gülsen et al. in *Respirology* quantifies existing knowledge about the risks posed by pre-existing respiratory disease.<sup>3</sup> For clinicians caring for patients with chronic respiratory illness, the results of this study are in keeping with a number of recently published meta-analyses that together provide essential data to guide our advice to patients and public health authorities.<sup>4,5</sup>

That underlying chronic obstructive pulmonary disease (COPD) is identified as a risk factor for severe coronavirus disease 2019 (COVID-19) will be unsurprising for respiratory physicians due to diminished respiratory reserve to withstand infection of the pulmonary parenchyma and a chronic inflammatory state. Gülsen et al. are able to confirm earlier reports of an approximately twofold increase in the risk of severe COVID-19 among patients with underlying COPD. The meta-analysis contains conflicting data from individual studies on the effect on COVID-19 severity of COPD. This likely indicates a weakness of retrospective study design to determine the impact of diseases, such as COPD, that may be under-diagnosed in routine clinical practice.<sup>6</sup> Patients with COPD have been very alert to the potential increased risk associated with COPD, and a report from the United Kingdom indicates increased symptoms of anxiety, as well as reduced social interactions and physical activity.<sup>7</sup> Further work is now needed to quantify the importance of COPD severity and the impact of common treatments on risk, and to identify ways in which people living with COPD can interact with others and engage in physical activity safely.

Chronic respiratory disease (CRD) includes a large number of conditions and disease severities. The finding that CRD is a risk factor for severe COVID-19 is merely the first step, and what is now urgently needed is a more detailed understanding of the role of key respiratory diseases including bronchiectasis, cystic fibrosis and interstitial lung

disease. It is plausible that some CRDs have a much greater impact on COVID-19 severity than others. As a respiratory research community, we need to ensure high-quality granular recording of respiratory comorbidities in primary data sets and publications to answer these questions. These research gaps are beginning to be filled. Emerging data indicate that interstitial lung disease increases the chance of death, particularly among the elderly, the obese and those with lower forced vital capacity.<sup>8</sup> Conversely, among patients with cystic fibrosis, outcomes have not been as severe as initially expected with a global registry report of four (2.7%) deaths from 149 patients with SARS-CoV-2 infection.

In reports of COVID-19, asthma has been frequently categorized separately from other respiratory illnesses, allowing Gülsen et al. to evaluate the risk of increased severity COVID-19 posed by asthma. The finding that in >12,000 patients with asthma there was no increased risk of severe COVID-19 will be reassuring to doctors and patients alike and is in keeping with other recent publications.<sup>10</sup> However, in many of the original publications, asthma severity was not reported and we must be cautious in our interpretation,<sup>11</sup> particularly among patients with more severe asthma, and those on immune-suppressing medication. While early data are encouraging that asthma biologic treatments do not represent a risk factor for severe COVID-19,<sup>12</sup> further data are needed and oral corticosteroid use has been highlighted in cohort studies as a risk factor for severe and fatal COVID-19.<sup>13</sup>

Systematic reviews rely on a comprehensive search that identifies all relevant literature to ensure robust findings. As such, it is notable that much of the data from the United Kingdom and substantial data published after the search date have not been included in the analysis.<sup>10,12,14</sup> While the absence of such data does not invalidate Gülsen et al.'s findings, it does highlight that this present study is not the final word on the role of lung disease as a risk factor for severe COVID-19. The current pandemic provides strong motivation to move towards living systematic reviews, where continual updates of relevant evidence are incorporated as soon as they become available.

### KEYWORDS

coronavirus disease, COVID-19, lung disease, prognosis, SARS-CoV-2

## CONFLICT OF INTEREST

The author declares that he has no conflicts of interest.

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