Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Overall, the conclusion of the study by Brunwasser and colleagues reduces confidence in a causal effect of RSV-LRTI on the origin of chronic wheezing illnesses. However, it would be an unfortunate misunderstanding if this would also reduce enthusiasm of both policy makers and clinical researchers to develop and plan preventive and therapeutic interventions for RSV-LRTI. Besides the need to diminish the tremendous effect of the acute phase of RSV-LRTI on young children in both low-income and high-income countries, the nature of the association between RSV-LRTI and long-term respiratory dysfunction has still not been defined definitively. Several gaps in knowledge still exist, including possible explanations in which RSV-LRTI acts as a marker of respiratory disease susceptibility in addition to either a sufficient or contributory cause. Adding to the complexity, there might be a synergistic interaction between RSV-LRTI at a young age and genetic susceptibility or environmental exposure (eg, smoking), which increases the risk to develop a wheezing phenotype.[6,7] In the analytical strategy by Brunwasser and colleagues, such scenarios would be more difficult to grasp. Finally, part of the controversy on causal inference for wheezing illnesses might lie in the difficulty to discriminate whether we should focus on RSV per se or RSV-LRTI in conjunction with other viral and bacterial pathogens or (iatrogenic) treatments during hospital admission.

As such, it is ever more meaningful to integrate research programmes and clinical long-term follow-up after exposure to respiratory disease in early life. Hopefully, in the future, by this type of platform in combination with sophisticated data analysis as done by Brunwasser and colleagues,[4] we can help children to gain better protection against chronic diseases such as wheezing illnesses.

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Pulmonary fibrosis secondary to COVID-19: a call to arms?

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For more on **pulmonary fibrosis in COVID-19** see **Personal View** page 807

As of May 6, 2020, nearly 3·7 million people have been infected and around 260 000 people have died from coronavirus disease 2019 (COVID-19) worldwide.[1] Almost all COVID-19-related serious consequences feature pneumonia.[2] In the first large series of hospitalised patients (n=138) with COVID-19 in Wuhan, China, chest CT showed bilateral ground glass opacities with or without consolidation and with lower lobe predilection in all patients.[3] In this series, 36 (26%) patients required intensive care, of whom 22 (61%) developed acute respiratory distress syndrome (ARDS).[3] The mechanisms through which severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes lung damage are only partly known, but plausible contributors include a cytokine release syndrome triggered by the viral antigen, drug-induced pulmonary toxicity, and high airway pressure and hyperoxia-induced acute lung injury secondary to mechanical ventilation. To date, about 1·2 million people worldwide have recovered from COVID-19, but there remains concern that some organs, including the lungs, might have long-term impairment following infection (figure). No post-discharge imaging or functional data are available for patients with COVID-19.

Other strains of the coronavirus family, namely severe acute respiratory syndrome coronavirus (SARS-CoV; known as SARS) and Middle East respiratory syndrome coronavirus (MERS-CoV; known as MERS), are genetically similar to SARS-CoV-2 and cause pulmonary syndromes similar to COVID-19. At the end of the SARS epidemic in June, 2003, 8422 individuals were

affected and 916 died; whereas MERS, which was first identified in April, 2012, has infected 2519 individuals worldwide to date, including 866 deaths.[4] The predominant CT abnormalities in patients with SARS included rapidly progressive ground glass opacities sometimes with consolidation. Reticular changes were evident approximately 2 weeks after symptom onset and persisted in half of patients beyond 4 weeks.[5] However, a 15-year follow-up study of 71 patients with SARS showed that interstitial abnormalities and functional decline recovered over the first 2 years following infection and then remained stable. At 15 years, 4·6% (SD 6·4%) of the lungs showed interstitial abnormality in patients who had been infected with SARS.[6] In patients with MERS, typical CT abnormalities included bilateral ground glass opacities, predominantly in the basal and peripheral lung zones. Follow-up outcomes are less well described in patients with MERS. In a study of 36 patients who had recovered from MERS, chest x-rays taken a median of 43 (range 32–320) days after hospital discharge showed abnormalities described as lung fibrosis in about a third of the patients.[7] Longer-term follow-up of patients who recovered from MERS has not been reported.

Pulmonary fibrosis can develop either following chronic inflammation or as a primary, genetically influenced, and age-related fibroproliferative process, as in idiopathic pulmonary fibrosis (IPF). Pulmonary fibrosis is a recognised sequelae of ARDS. However, most follow-up studies—which have included both physiological measures and chest CT—have shown that persistent radiographic abnormalities after ARDS are of little clinical relevance and have become less common in the era of protective lung ventilation.[8] Available data indicate that about 40% of patients with COVID-19 develop ARDS, and 20% of ARDS cases are severe.[9] Of note, the average age of patients hospitalised with severe COVID-19 appears to be older than that seen with MERS or SARS, which is perhaps a consequence of wider community spread. In inflammatory lung disorders, such as those associated with autoimmune disease, advancing age is a risk factor for the development of pulmonary fibrosis. Given these observations, the burden of pulmonary fibrosis after COVID-19 recovery could be substantial.

Progressive, fibrotic irreversible interstitial lung disease, which is characterised by declining lung function, increasing extent of fibrosis on CT, worsening symptoms and quality of life, and early mortality,[10] arises, with varying degrees of frequency, in the context of a number of conditions including IPF, hypersensitivity pneumonitis, autoimmune disease, and drug-induced interstitial lung disease. Although the virus is eradicated in patients who have recovered from COVID-19, the removal of the cause of lung damage does not, in itself, preclude the development of progressive, fibrotic irreversible interstitial lung disease. Furthermore, even a relatively small degree of residual but non-progressive fibrosis could result in considerable morbidity and mortality in an older population of patients who had COVID-19, many of whom will have pre-existing pulmonary conditions.

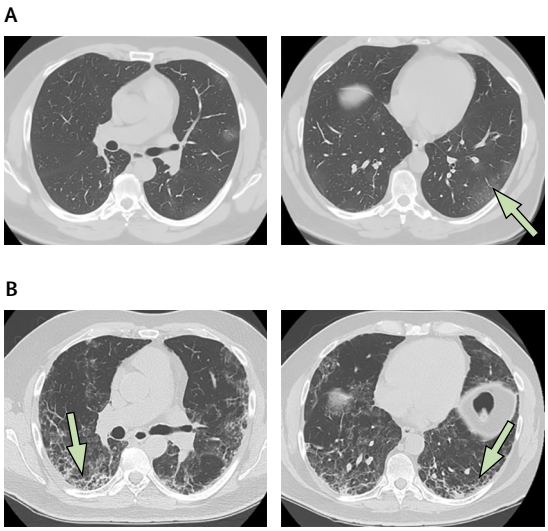

Figure: **Lung CT of a patient with coronavirus disease 2019**
(A) Images of peripheral mild ground glass opacities in the left lower lobe (arrow). (B) Three weeks later, at the same lung zones, the disease has rapidly progressed and fibrotic changes are now evident (arrows).

At present, the long-term pulmonary consequences of COVID-19 remains speculative and should not be assumed without appropriate prospective study. Nonetheless, given the huge numbers of individuals affected by COVID-19, even rare complications will have major health effects at the population level. It is important that plans are made now to rapidly identify whether the development of pulmonary fibrosis occurs in the survivor population. By doing this, we can hope to deliver appropriate clinical care and urgently design interventional trials to prevent a second wave of late mortality associated with this devastating pandemic.

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Identification of pathophysiological patterns for triage and respiratory support in COVID-19

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For more on the **ICNARC audit** see https://www.icnarc.org/Our-Audit/Audits/Cmp/Reports

In the UK, more than 279 392 cases of COVID-19 had been documented by June 3, 2020, and more than 39 500 patients had died with the disease, according to the COVID-19 web-based dashboard at Johns Hopkins University.[1] Data derived from the UK Intensive Care National Audit and Research Centre (ICNARC) Case Mix Programme Database show that, for the first 8062 patients admitted to the ICU across the UK with documented outcomes, by May 29, 2020, about 72% received advanced mechanical ventilation and the mortality rate was around 53%. This mortality far exceeds that of typical severe acute respiratory distress syndrome (ARDS).[2] The significant surge in the number of patients requiring ventilatory support has presented the UK National Health Service with unprecedented challenges, including pressures on critical care capacity, resources, and supplies, concerns about staff protection, as well as ethical issues associated with triage and resource allocation.[3] Debates about the way in which different modalities of ventilatory support should be provided to the largest number of patients, while controlling the number of critical care admissions and protecting staff, have at times generated adversarial positions at the extremes of the debate. The motivations behind these arguments are undoubtedly positive, but they do not necessarily help frontline clinicians who are caring for individuals with COVID-19.

To design triage systems and pathways of care, it is important to operate cautiously within models that best reflect evolving understanding of the pathophysiology and natural history of this new disease. COVID-19 pneumonia leads to hypoxaemic respiratory failure, initially due to the coexistence of interstitial oedema and altered pulmonary perfusion, in the absence of a significant loss of lung volume and compliance.[4] Although, on average, patients present with an oxygenation deficit[5] similar to that of moderate-to-severe ARDS (median PaO_2/FiO_2 of 20 kPa),[2] the cause of this deficit seems to be unlike that of classic ARDS, and the response to positive end-expiratory pressure (PEEP) or continuous positive airway pressure (CPAP) in terms