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.

health policy makers or payers, and could further cloud the diagnostic certainty of sarcoidosis, which is already a challenge in many situations. The introduction of the term parasarcoidosis would also affect sarcoidosis research by further obfuscating the goals of treatment. Should we research sarcoidosis and parasarcoidosis separately, or should they be considered as one disease? The implication of parasarcoidosis as a separate entity might undermine what little research investment is made in sarcoidosis. Moreover, individuals with sarcoidosis often have to face and struggle with the fact that their disease is not taken seriously.[1,9] If we, as professionals, speak about parasarcoidosis, this could send the wrong message that we do not believe these symptoms to be part of their disease. A complex condition such as sarcoidosis justifies a holistic approach in which the patient is taken seriously. In idiopathic pulmonary fibrosis, and other fibrotic lung diseases, fatigue has also been acknowledged as a substantial burden.[10] Will this fatigue be called parafibrosis? We should be careful about stigmatising symptoms in this way.

In summary, patients with sarcoidosis tend to be affected by specific organ-related symptoms with functional impairments and by less specific symptoms. Although some disease manifestations are hard to verify, it does not mean that they are not associated with or do not belong to sarcoidosis. What we need is a guideline to assess, quantify, and manage disability in sarcoidosis, and not a new confusing term to label what we, to date, do not completely understand. Because of its complexity, the care of sarcoidosis needs to be personalised and a multidisciplinary approach is recommended.

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COVID-19 vaccination in patients with α1-antitrypsin deficiency

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For **more details** on COVID-19 data see https://covid19.who.int/

COVID-19 is continuing its spread across the world, generating a wake of devastating health, economic, and social consequences. The urgency of the situation has simultaneously driven the development of COVID-19 vaccines to an astonishingly fast pace, with more than 2·1 billion doses administered worldwide). Despite the hugely successful vaccination campaign, the efficacy of COVID-19 vaccines in patients with genetic pulmonary diseases, such as α1-antitrypsin deficiency (AATD), have not been delineated. Inherited AATD is characterised by low concentrations of functional α1-antitrypsin in the blood, predisposing individuals to enzymatic tissue injury and inflammation, most notably in the lungs. Given the unclear timeline for an end to the ongoing pandemic, shedding light onto such issues that might

have potentially fatal consequences for the affected individuals is necessary.

The efficacy of COVID-19 vaccines in individuals with AATD might only be inferred from published studies on influenza and pneumococcal vaccination in this population. In an observational study of 939 participants with AATD, influenza vaccination rates were up to 81·6% in patients with AATD, yet this finding did not translate into a decrease in exacerbation rates of chronic obstructive pulmonary disease or decreased health-care use.[1] In another study, the magnitude of the antibody response to pneumococcal vaccination in patients with severe AATD was no less robust than in healthy volunteers.[2] The immune responses to antigen provocation in individuals with AATD appear to be far more complex, and protection from SARS-CoV-2 might not necessarily be afforded with vaccination alone.

We have hypothesised that individuals with AATD might derive limited benefit from the current COVID-19 vaccines for several reasons. First, even though vaccination has been prioritised to more vulnerable populations (such as people with AATD), individuals with AATD are usually not included in clinical trials (as reported in ClinicalTrials.gov), and thus the effectiveness and adverse event profile of vaccination in this population are unknown. Clinical scientists should include the AATD population in clinical trials of COVID-19 vaccines to better characterise the safety and efficacy for individuals with AATD. Second, Kueppers[3] has shown that the increase in trypsin-inhibiting capacity of serum after injection of typhoid vaccine is largely due to the increase of the α1-antitrypsin concentration. Consequently, AATD inhibits the quantitative response of the α1-antitrypsin to such a stimulus.[3] Emerging evidence has shown a strong correlation between concentrations of circulating α1-antitrypsin and the induction of trained immunity.[4] Data from previous studies of severe acute respiratory syndrome, Middle East respiratory syndrome, and other human respiratory viruses allude to a risk of antibody-dependent enhancement associated with SARS-CoV-2 vaccines and antibody-based interventions. Liu and colleagues[5] have recently reported that the concentrations of enhancing and neutralising antibodies were higher in patients with severe COVID-19 than in patients with non-severe COVID-19. For individuals with AATD, there is a possibility that the antibody-dependent enhancement effect might be amplified by SARS-CoV-2 infection or vaccination. Third, AATD eases virus spike protein activation by elastase, resulting in the faster spread of the SARS-CoV-2 subtype with spike 614Gly mutation, which is more virulent and results in greater host morbidity.[6] Fourth, COVID-19 vaccine efficacy might not reach 100%; governmental negligence, socioeconomic inequalities, personal values, and the looming spectre of a SARS-CoV-2 mutation all contribute to suboptimal vaccination rates, lower than that of the flu vaccination. Recent studies are raising concern that current COVID-19 vaccines might not have sufficient efficacy against the new SARS-CoV-2 variants B.1.1.7 and B.1.351.[7,8] In particular, the SARS-CoV-2 variant B.1.351 might decrease SARS-CoV-2 vaccine-derived neutralisation of SARS-CoV-2 by 6–86 times.[9] Finally, *Pi*MZ*, *Pi*SZ*, or unknown AATD genotype have been associated with a greater odds of unhealthy

Panel: **Currently available therapeutic approaches to manage α1-antitrypsin deficiency during the COVID-19 pandemic**

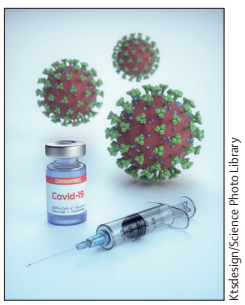
Lifestyle changes
- Avoid crowded places and mass gatherings
- Wear a medical mask in public spaces
- Patients should be counselled and receive assistance in smoking cessation
- Patients should be advised to avoid environmental risk exposures, such as smog, second-hand tobacco smoke, dusts, and fumes
- Maintain a healthy bodyweight and consume a balanced, vitamin-rich, and high-fibre diet

Pharmacotherapy
- Patients should receive general medical therapy for chronic obstructive pulmonary disease, including bronchodilators, steroids, and oxygen therapy, as per local chronic obstructive pulmonary disease guidelines

Vaccination
- Patients should receive the annual flu vaccine and pneumococcal vaccine as per guidelines
- Patients should also receive vaccination against SARS-CoV-2

Augmentation therapy
- Intravenous plasma-purified alpha$_1$-proteinase inhibitor should be considered for the treatment of α1-antitrypsin deficiency-related lung disease

Surgery
- Lung transplantation could be considered for patients with very severe disease refractory to pharmacotherapy



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behaviours, such as not obtaining the pneumococcal or influenza vaccine, adopting sedentary lifestyles, and smoking.[10] Individuals who do not know their genotype might require additional education and intervention to mitigate the risk of SARS-CoV-2 infection. As the advocacy for COVID-19 vaccination in people with AATD continues, studies need to elucidate a proven vaccine correlation with SARS-CoV-2 strains.

In the meantime, the protective roles of α1-antitrypsin on lung structure and function, on preventing acute lung injury and acute respiratory distress syndrome, and especially on inhibiting SARS-CoV-2 infection renders alpha$_1$-proteinase inhibitor a promising candidate for COVID-19 treatment in select populations.[11,12] For patients with AATD, alpha$_1$-proteinase inhibitor therapy might solve two problems with one single action because it is also the best candidate drug for the treatment of COVID-19. As the ongoing pandemic persists in the foreseeable future, we strongly advocate that public health officials and health-care professionals should encourage the population of people with AATD to adopt protective behaviours, including lifestyle changes, pharmacotherapy, alpha$_1$-proteinase inhibitor therapy, surgery, and other therapeutic approaches in addition to COVID-19 vaccine uptake (panel). Patient-centric educational messages for patients with AATD that emphasise the severity of COVID-19, particularly the potential long-term negative health sequelae, are needed. We must fight to ensure that all patients with AATD, regardless of race, ethnicity, immigration status, income, and insurance status, have access to essential medications and timely and high-quality care in this difficult time.

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Ongoing asthma management in children during the COVID-19 pandemic: to step down or not to step down?

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A substantial reduction in asthma exacerbations in both children and adults has been seen in many countries worldwide during the COVID-19 pandemic.[1,2] The cause of this reduction is likely to be multifactorial, but at least partly due to population-level public health measures, such as physical distancing, masking, and hand washing, which reduce broad viral transmission.[2] This improvement in asthma control poses an interesting clinical dilemma: should clinicians consider tapering asthma medications in children during the pandemic in the face of good asthma control? Furthermore, if medicines are reduced during the COVID-19 pandemic, should clinicians return to the pre-COVID-19 schedule as respiratory precautions are gradually relaxed?

Before the pandemic, the evidence strongly supported a step-down therapeutic approach in children (aged >5 years) with good asthma control. The Global Initiative for Asthma (GINA) strategy, under usual circumstances,