



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.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Available online at  
**ScienceDirect**  
 www.sciencedirect.com

Elsevier Masson France  
**EM|consulte**  
 www.em-consulte.com



Letter to the Editor

## Severe forms of COVID-19 among patients with chronic respiratory diseases: be attentive to the severity of the underlying respiratory impairment



Dear Editor, we appreciate Ausset *et al.*, consideration of our study in their letter reminding us of the very recent literature related to a protective role of chronic respiratory diseases, especially asthma and chronic obstructive pulmonary disease (COPD). As stated in the letter, the meta-analysis by Rogliani *et al.*, included 8476 hospitalized patients for SARS-CoV-2 infection and found that patients with asthma and COPD were at reduced risk of hospitalization [1]. Another meta-analysis showed opposite results [2]. These data should be interpreted with great caution as they do not consider the severity of the underlying respiratory disease. Indeed and as well explained in the letter by Ausset *et al.*, it is now clear that patients with the most severe form of asthma and COPD have a high risk of developing a severe form of COVID-19 (*i.e.*, requiring invasive mechanical ventilation) [3]. Our results are consistent with this since, as mentioned in our article, our population did not include patients with severe asthma and only three patients with COPD had long-term oxygen therapy.

The letter by Ausset *et al.*, also has the merit of summarizing the literature in favor of a protective role for inhaled corticosteroids (ICS) in SARS-CoV-2 pneumonia. Most of the quoted articles only included outpatients without specifically addressing patients with chronic respiratory diseases. The novelty of our study is to have included patients hospitalized in the COVID-19 ward and accurately characterize patients with COPD or asthma. As stated by Ausset *et al.* in their letter, a randomized controlled and multicentric trial included 4700 outpatients at high risk of complications with a recent COVID-19 infection and revealed that ICS improved time to recovery [4]. A recent meta-analysis supported the benefit of ICS in resolving clinical symptoms in non-hospitalized patients with COVID-19 [5]. In contrast, in a post-hoc analysis of over 8 million patients, two or more prescriptions of ICS led to a slightly higher risk of severe COVID-19 [6]. As hypothesized in our article, ICS may have potential clinical effect in SARS-CoV-2 infection through various pathophysiological mechanisms. For example, Milne *et al.* demonstrated a downregulation of the expression of genes involved in SARS-CoV-2 infection in bronchial epithelial cells of patients with COPD by budesonide [7]. However, the clinical relevance of these *in vitro* findings remains to be clarified.

In conclusion, on the one hand, asthma and COPD seem to protect against COVID-19 depending on the severity of the underlying chronic respiratory disease. On the other hand, ICS could have a protective role but only the results of ongoing randomized controlled trials will confirm this hypothesis.

### Declaration of Competing Interest

None.

### References

- [1] Rogliani P, Lauro D, Di Daniele N, Chetta A, Calzetta L. Reduced risk of COVID-19 hospitalization in asthmatic and COPD patients: a benefit of inhaled corticosteroids? *Expert Rev Respir Med* 2021;1–8. doi: [10.1080/17476348.2021.1850275](https://doi.org/10.1080/17476348.2021.1850275).
- [2] Lippi G, Henry BM. Chronic obstructive pulmonary disease is associated with severe coronavirus disease 2019 (COVID-19). *Respir Med* 2020;167:105941. doi: [10.1016/j.rmed.2020.105941](https://doi.org/10.1016/j.rmed.2020.105941).
- [3] Bloom CI, Cullinan P, Wedzicha JA. Asthma phenotypes and COVID-19 risk: a population-based observational study. *Am J Respir Crit Care Med* 2022;205:36–45. doi: [10.1164/rccm.202107-1704OC](https://doi.org/10.1164/rccm.202107-1704OC).
- [4] Yu L-M, Bafadhel M, Dorward J, Hayward G, Saville BR, Gbinigie O, et al. Inhaled budesonide for COVID-19 in people at high risk of complications in the community in the UK (PRINCIPLE): a randomised, controlled, open-label, adaptive platform trial. *Lancet Lond Engl* 2021;398:843–55. doi: [10.1016/S0140-6736\(21\)01744-X](https://doi.org/10.1016/S0140-6736(21)01744-X).
- [5] Lee TC, Bortolussi-Courval É, Belga S, Daneman N, Chan AK, Hanula R, et al. Inhaled corticosteroids for outpatients with Covid-19: a meta-analysis. *Eur Respir J* 2022;2102921. doi: [10.1183/13993003.02921-2021](https://doi.org/10.1183/13993003.02921-2021).
- [6] Aveyard P, Gao M, Lindson N, Hartmann-Boyce J, Watkinson P, Young D, et al. Association between pre-existing respiratory disease and its treatment, and severe COVID-19: a population cohort study. *Lancet Respir Med* 2021;9:909–23. doi: [10.1016/S2213-2600\(21\)00095-3](https://doi.org/10.1016/S2213-2600(21)00095-3).
- [7] Milne S, Li X, Yang CX, Leitao Filho FS, Hernández Cordero AI, Yang CWT, et al. Inhaled corticosteroids downregulate SARS-CoV-2-related genes in COPD: results from a randomised controlled trial. *Eur Respir J* 2021;58:2100130. doi: [10.1183/13993003.00130-2021](https://doi.org/10.1183/13993003.00130-2021).

S. Valentin\*

S. Basin

A. Chaouat

Université de Lorraine, CHRU-Nancy, Pôle des spécialités médicales/  
 département de pneumologie, F-54000 Nancy, France  
 Université de Lorraine, Faculté de Médecine de Nancy, Inserm  
 UMR\_S1116, Vandœuvre-Lès-Nancy, France

\*Corresponding author.

Received 23 February 2022

Accepted 23 February 2022

Available online 15 March 2022