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.

However, long-term use of short-acting β-agonists (SABAs) can produce these deleterious effects and has been linked to proinflammatory cytokine release in the airway epithelium[5]; therefore, it could contribute to AHR.

A variety of treatment options may be considered for women with premenstrual asthma. We agree that ICS are important for attenuating type 2 inflammation and associated AHR, they can upregulate B2R (which may be important when given with LABA or a SABA reliever), and that a flexible ICS–formoterol maintenance and reliever therapy (MART) strategy is attractive. To date, however, evidence for this regimen comes from studies in a general asthma population and lacks clinical data specific to premenstrual asthma.

In patients with mild asthma, ICS–formoterol on demand (anti-inflammatory reliever strategy) is preferable to as-needed SABA alone, particularly for lowering rates of severe exacerbation.[6] However, for more severe asthma, this strategy may not provide the symptom control of regular ICS maintenance therapy in patients with good adherence to therapy. Most clinical evidence supporting flexible anti-inflammatory reliever or MART regimens is from studies evaluating low-dose budesonide–formoterol in mild asthma (eg, SYGMA 1 and 2, Novel START, PRACTICAL). Nevertheless, patients with premenstrual asthma tend to have more severe disease[1] and are not a directly comparable population.

Robust data support once-daily maintenance with medium- or high-dose ICS/LABA,[7] and these regimens should be considered treatment options for some patients with premenstrual asthma, especially those with good adherence. When considering treatment options for women with premenstrual asthma, as with any patient, a personalized approach is preferred. The patient's preferences, adherence, inhaler technique, characteristics, comorbidities, and modifiable risk factors should be considered.

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Different effect of inhaled and systemic corticosteroids on the outcome of COVID-19 among patients with asthma

To the Editor:

We read with great interest the study by Ren et al,[1] which investigated the effect of allergic rhinitis (AR) and/or asthma on the risk of COVID-19 infection, severity, and mortality, and also assessed the impact of long-term AR and/or asthma medications on the outcomes of COVID-19. On the basis of the analysis of 770,557 adult participants who completed SARS-CoV-2 testing between March 16 and December 31, 2020, in the UK, they found that asthma would be a protective factor of SARS-CoV-2 infection among patients aged <65; however, asthma would be associated with a higher risk of COVID-19 hospitalization.[1] However, we have serious concerns about several important residual confounding factors, which might influence the results of this study.

First, the authors assessed the effect of several long-term medications for AR or asthma, including antihistamine, β_2-adrenoceptor agonists, and corticosteroid, but none of them showed association with COVID-19 infection or severity.[1] A previous study showed that the recent use of systemic corticosteroid was significantly associated with increased risk of both moderate-to-severe COVID-19 and all-cause mortality.[2,3] In contrast, several randomized controlled trials demonstrated the positive impact of inhaled budesonide on the outcome of COVID-19 among patients with asthma.[4,5] Therefore, we wonder whether the effect of systemic and inhaled corticosteroids (ICS) could differ. However, we only see that the number of events was lower in the ICS users than those

receiving systemic corticosteroids in Table E4. Further subgroup analysis according to the use of inhaled corticosteroids similar to the ones in Figure 2 is warranted to clarify this issue, and additional evaluation about a dose-response relationship is needed.

Second, the severity of asthma is another confounding factor affecting the outcome of COVID-19. One study using Swedish National Airway Register showed that patients with uncontrolled asthma and high disease burden, including increased asthma medication intensity, would be associated with an increased risk of severe COVID-19.[6] Similar findings were demonstrated in another national incident cohort study in Scotland.[3]

In conclusion, although Ren et al's study provided useful information, further analysis according to the use of corticosteroid and the severity of asthma is needed.

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Reply to "Different effect of inhaled and systemic corticosteroids on the outcome of COVID-19 among patients with asthma"

To the Editor:

We sincerely appreciate the interest of Hsu and Lai[1] in our recent publication in *The Journal of Allergy and Clinical Immunology*: *In Practice* titled "Impact of allergic rhinitis and asthma on COVID-19 infection, hospitalization, and mortality."[2] For the 2 main concerns raised in their correspondence, our clarifications are as follows.

In terms of the first concern regarding whether the effect of systemic and inhaled corticosteroids on COVID-19 could differ, in fact, we had initially analyzed the association between inhaled corticosteroids and the infection, severity, and mortality of COVID-19 among patients with allergic rhinitis and/or asthma, and the results were not significant (Table I and Figures 1-3). Because inhaled corticosteroids actually included oral inhaled corticosteroids and intranasal corticosteroids, we separated them in the subgroup analysis. Because the number of oral inhaled corticosteroid patients (n = 251) was significantly smaller than that in the nasal spray group (n = 12,579), we ultimately presented the results of corticosteroid nasal sprays instead of the inhaled corticosteroids. In addition, regarding the dose-response relationship, no detailed data on dose or duration information were collected in the UK Biobank, so no further analysis of these medications could be performed.

Second, Hsu and Lai also highlighted the potential role of asthma severity in confounding or modifying the association between asthma and the outcome of COVID-19, as other studies[3,4] have shown that patients with uncontrolled asthma had an increased risk of severe COVID-19 compared with those without asthma or with well-controlled asthma. We also agree that the confounding effects of asthma severity cannot be ignored, but, unfortunately, there are no relevant data on asthma severity in the UK Biobank, thus limiting the analysis of the impact of asthma severity on COVID-19 infection, hospitalization, and mortality in this study.

In conclusion, we concur that further research with more comprehensive data on medications and the severity of asthma is needed to reduce the confounding effects and better elucidate the relationship between asthma and COVID-19.

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