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.

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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UK Biobank ethical approval was from the North West Multi-centre Research Ethics Committee. The current analysis was approved under the UKB application (Applicant Number: 69718).
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TABLE I. The infection rate, hospitalization rate, and mortality of COVID-19 among participants who used long-term medications (antihistamine, glucocorticoids, inhaled corticosteroids, and β_2-adrenoceptor agonists) to control allergic rhinitis (AR) or asthma

		COVID-19 infection (n = 2540/13,232)			COVID-19 hospitalization (n = 945/2624)			COVID-19 mortality (n = 122/2624)		
Medication	**Variable**	**Number**	**RR (95% CI)**	***P* value**	**Number**	**RR (95% CI)**	***P* value**	**Number**	**RR (95% CI)**	***P* value**
Antihistamine	No	11,732	Reference	.656	2309	Reference	.302	2309	Reference	.891
	Yes	847	1.04 (0.89-1.21)		172	1.14 (0.89-1.45)		172	0.95 (0.44-2.05)	
Systemic glucocorticoids	No	10,904	Reference	.922	2180	Reference	.685	2180	Reference	.726
	Yes	1675	0.99 (0.88-1.12)		301	0.96 (0.79-1.16)		301	0.91 (0.55-1.52)	
Inhaled corticosteroids	No	11,823	Reference	.649	2348	Reference	.328	2348	Reference	.23
	Yes	756	0.96 (0.81-1.14)		133	0.85 (0.62-1.18)		133	0.42 (0.1-1.72)	
β_2-Adrenoceptor agonists	No	11,689	Reference	.104	2294	Reference	.736	2294	Reference	.321
	Yes	890	1.13 (0.97-1.32)		187	0.96 (0.77-1.21)		187	1.31 (0.77-2.23)	

Adjusted for sex, age, Townsend deprivation index, education, body mass index, ethnic background, smoking status (smoking experience and pack-year), drinking status, and pre-existing comorbidities (eg, diabetes, circulatory diseases, fracture, lower respiratory disease, upper gastrointestinal diseases, renal diseases, and dementia). Note that β_2-adrenoceptor agonists were only prescribed for asthma, not AR.
CI, Confidence interval; *RR*, relative risk.

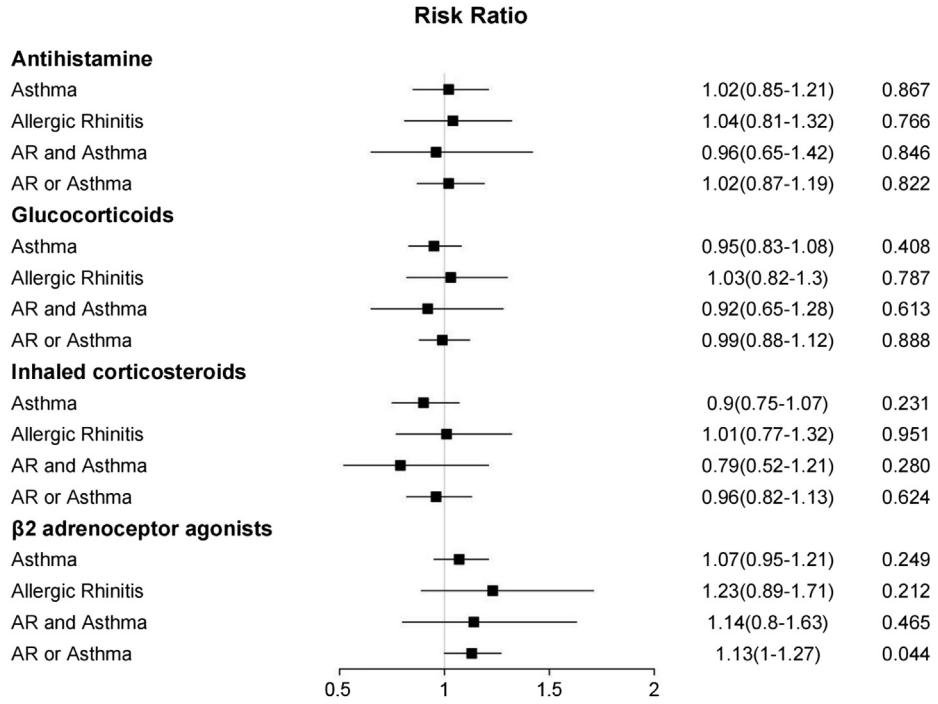

FIGURE 1. Association between long-term control of allergic rhinitis (AR)/asthma medications (antihistamine, systemic glucocorticoids, inhaled corticosteroids, and β_2-adrenoceptor agonists) and the infection of COVID-19 in patients with AR/asthma. Adjusted for sex, age, Townsend deprivation index, education, current employment status, body mass index, ethnic background, smoking status (pack-year) and drinking status, and pre-existing comorbidities (eg, diabetes, circulatory diseases, fracture, lower respiratory disease, upper gastrointestinal diseases, renal diseases, dementia, arthritis, and certain immune disorders). The *x*-axis indicates a log-scale.

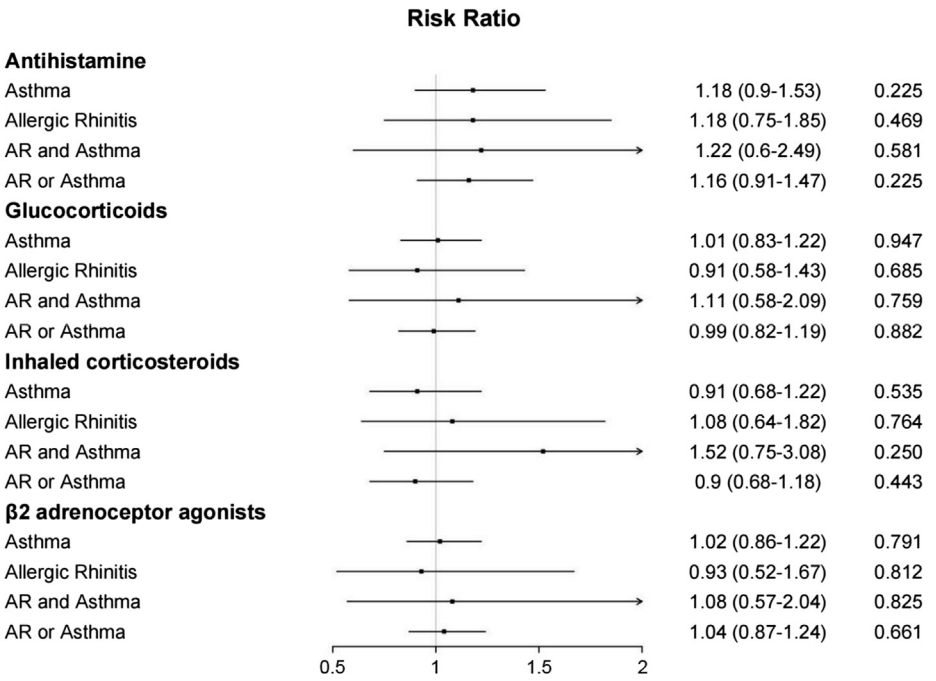

FIGURE 2. Association between long-term control of allergic rhinitis (AR)/asthma medications (antihistamine, systemic glucocorticoids, inhaled corticosteroids, and β_2-adrenoceptor agonists) and the hospitalization of COVID-19 in patients with AR/asthma. Adjusted for sex, age, Townsend deprivation index, education, current employment status, body mass index, ethnic background, smoking status (pack-year) and drinking status, and pre-existing comorbidities (eg, diabetes, circulatory diseases, fracture, lower respiratory disease, upper gastrointestinal diseases, renal diseases, dementia, arthritis, and certain immune disorders). The *x*-axis indicates a log-scale.

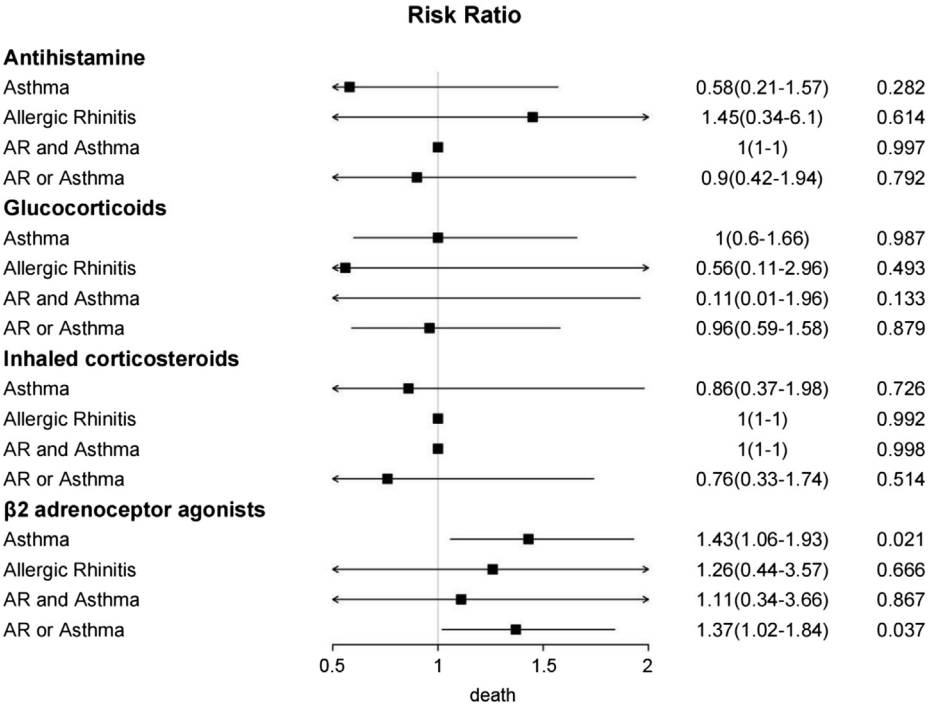

FIGURE 3. Association between long-term control of allergic rhinitis (AR)/asthma medications (antihistamine, systemic glucocorticoids, inhaled corticosteroids, and β_2-adrenoceptor agonists) and the mortality of COVID-19 in patients with AR/asthma. Adjusted for sex, age, Townsend deprivation index, education, current employment status, body mass index, ethnic background, smoking status (pack-year) and drinking status, and pre-existing comorbidities (eg, diabetes, circulatory diseases, fracture, lower respiratory disease, upper gastrointestinal diseases, renal diseases, dementia, arthritis, and certain immune disorders). The *x*-axis indicates a log-scale.

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