∂ Reply to Chen et al.

From the Authors:

We appreciate comments and questions raised by Chen and colleagues for our paper about associations between air pollution exposure and coronavirus disease (COVID-19)-related severity and mortality (1). For the first question regarding residual confounding, we went back and extracted information from our electronic medical records on whether the patients had each of the following diseases by International Classification of Diseases codes before the COVID-19 diagnosis: diabetes, hypertension, cancer or metastatic carcinoma, renal disease, asthma, chronic obstructive pulmonary disease, myocardial infarction, and congestive heart disease. We replaced Charlson Comorbidity Index by these diseases' indicators (yes vs. no for each) in the model as covariates. This alternative analysis resulted in similar estimates of the associations between air pollution and COVID-19 severity and mortality and did not change our study conclusions. The corresponding multipollutant adjusted odds ratios (95% confidence intervals [CIs]) associated with a 1-SD increase in 1-year particulate matter $\leq 2.5 \,\mu\text{m}$ in aerodynamic diameter (PM_{2.5}) (SD, 1.5 µg/m³) were 1.24 (1.16–1.32) for COVID-19–related hospitalization, 1.32 (1.19-1.47) for intensive respiratory support (IRS), and 1.31 (1.15-1.50) for ICU admission; the odds ratios (95% CIs) associated with 1-month NO₂ (SD, 3.3 ppb) were 1.12 (1.06-1.17) for hospitalization, 1.18 (1.10-1.27) for IRS, and 1.21 (1.11–1.33) for ICU. The hazard ratios (95% CIs) for mortality were 1.14 (1.02-1.27) for 1-year PM_{2.5} and 1.08 (0.99-1.17) for 1-month NO₂.

For the second question regarding interaction with patients' age, we have already tested the interactions and presented stratified results by age groups, sex, and race/ethnicity in our published paper in supplementary Tables E5–E7 (1). We did not find statistically significant interactions between age and 1-month NO₂ and 1-year PM_{2.5} exposures. However, the effect sizes of the associations were generally larger for hospitalization, IRS, and ICU for age \geq 65 years (supplemental Table E5 in Reference 1).

For the third question regarding mortality, we restricted the time window within 60 days after COVID-19 diagnosis to minimize the potential misclassification of the death due to other health issues or

The project protocol has been reviewed and approved by the Institutional Review Bord at Kaiser Permanente Southern California and the University of Southern California.

Author Contributions: Z.C., M.A.S., F.D.G., and A.H.X. were responsible for the data analysis and content of the letter.

life-threatening accidents. Causes of death were generally not recorded in electronic medical records and claim-based records; thus, we would not be able to specifically restrict the mortality due to COVID-19. Determining whether a patient died of or with COVID-19 requires in-depth medical record review and adjudication of cause of death. Adjudication review was outside the scope of this study. However, all these patients had COVID-19 diagnosis within 60 days before death, and we have adjusted for major preexisting comorbidities as mentioned above.

<u>Author disclosures</u> are available with the text of this letter at www.atsjournals.org.

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Reference

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Susceptibility of Patients with Asthma to a Poor Outcome of COVID-19

To the Editor:

In their lucid review, Conway and colleagues (1) imply inconsistent cell mechanisms, virus receptors, and T2 inflammation as regards coronavirus disease (COVID-19) occurrence in asthma, including effects of corticosteroids. Observations with rhinovirus,

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