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factor α that are better predictors of mortality in different severity groups.⁴

Nevertheless, mortality in the low IL-6 group of patients is significantly lower than in the high IL-6 group of patients (appendix), suggesting that IL-6 inhibitors should be given only to patients with high IL-6. Indeed, a retrospective analysis of tocilizumab therapy as a function of baseline IL-6 concentrations showed a large reduction in mortality (from 36% to 16%) in patients with high-baseline IL-6, but no reduction in mortality in low-baseline IL-6 patients.⁵

In conclusion, clinical trials of IL-6 antagonist therapy, such as RECOVERY¹ and sarilumab COVID-19 global studies,² should consider reanalysis of their results as a function of IL-6 baseline concentrations. More generally, clinical trials of personalised precision medicine, based on cytokine profiling, are needed for optimisation of COVID-19 therapy.

We declare no competing interests.

*Avidan U Neumann,
Mehmet Goekkaya, Karim Dorgham,
Claudia Traidl-Hoffmann, Guy Gorochov
avidan.neumann@uni-a.de

Department of Environmental Medicine, Faculty of Medicine, Universitätsklinikum Augsburg, Augsburg, Germany (AUN, MG, CT-H); Institute of Environmental Medicine, Helmholtz Center Munich, Augsburg, Germany (AUN, CT-H); Environmental Medicine, Technical University Munich, Munich, Germany (MG, CT-H); Sorbonne Université, INSERM, Centre d'Immunologie et des Maladies Infectieuses, Paris, France. (KD, GG); Département d'Immunologie, Assistance Publique Hôpitaux de Paris, Hôpital Pitié-Salpêtrière, Paris, France (GG)

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Authors' reply

We thank Chengliang Yang and Hedi Zhao for their interest in the thrombotic event rate in the RECOVERY trial of tocilizumab in patients hospitalised with COVID-19.¹ Data on thrombotic events were only collected on follow-up forms from Nov 1, 2020, so these data are only available for about 60% of participants. Nevertheless, we observed no difference in the thrombotic event rate between patients allocated to tocilizumab or usual care alone (appendix).

Avidan Neumann and colleagues have suggested a post-hoc analysis of outcomes stratified by baseline levels of inflammatory biomarkers, to examine the hypothesis that a larger therapeutic response to interleukin (IL)-6 inhibition might be observed in patients with higher levels of inflammatory biomarkers. In the RECOVERY trial,¹ all patients included in the tocilizumab comparison were required to have a C-reactive protein (CRP) concentration of 75 mg/L or more; therefore, the trial already restricted the comparison with a patient subgroup selected on a biomarker. Although we did not collect data on baseline IL-6 concentrations, CRP data were collected because CRP is associated with IL-6 concentrations and clinical severity, and is globally a more affordable and available biomarker than IL-6.² In a post-hoc analysis of the primary outcome of 28-day mortality based on approximate tertiles of CRP there was no evidence of heterogeneity of effect by baseline CRP concentration of 75 mg/L or more ($p=0.30$; appendix). These data do not, therefore, support the hypothesis of restricting treatment with tocilizumab to those patients with the highest levels of CRP or other biomarkers of inflammation. On the contrary, these data raise the question of whether even more COVID-19 patients could benefit from IL-6 inhibition if a lower threshold (CRP <75 mg/L) were used to initiate treatment.

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*Peter Horby, Natalie Staplin,
Richard Haynes, Martin Landray
peter.horby@ndm.ox.ac.uk

Nuffield Department of Medicine, University of Oxford, Oxford OX3 7BN, UK

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The nutrition agenda must include tobacco control

The Lancet's Series on progress in maternal and child undernutrition reminds us that malnutrition and stunting, and the double burden of obesity and malnutrition, remain important priorities for achieving Sustainable Development Goal 3 and other goals for child health. However, although recognising the importance of the environment and commercial determinants of food availability, the nutrition agenda continues to ignore the importance of tobacco control in achieving nutritional goals.

Adult tobacco users consume significant calorie equivalents, and adult smoking is associated with hunger and food insecurity for household children and adults in high-income^{1,2} and low-income^{3,4} countries. Second-hand smoke exposure is associated with overweight and obesity, and the inflammatory effects of smoke can cause metabolic syndrome, dyslipidaemia, insulin resistance and diabetes, and premature atherosclerotic heart disease.⁵ Strong evidence-based interventions for comprehensive tobacco control are described in the Tobacco Free Initiative MPOWER package of interventions,⁶ which have been recognised and endorsed by WHO and the 22 other UN agencies that participate in the UN Interagency Task Force on Tobacco.

See Online for appendix

For the **Series on progress in maternal and child undernutrition** see <https://www.thelancet.com/series/maternal-child-undernutrition-progress>