Response to: 'COVID-19 in patients with rheumatic diseases: what is the real mortality risk?' by Marques *et al*

We appreciate the comments by Marques *et al* in response to our manuscript.[1] Their description of a cohort of patients with rheumatic disease and COVID-19 is another important contribution to the literature during this quickly evolving pandemic. In this report of 130 patients with rheumatic diseases, the authors estimated a mortality rate of 9.2%, higher than the 4.7% mortality rate reported in the general population in Brazil.[1] It is important to note that one must be cautious when comparing these two rates because the composition of these cohorts according to demographics and other confounding features likely differs but was unable to be accounted for in the analysis. However, there were several important features in this cohort which may explain the higher mortality rate including a large comorbidity burden among the deceased, frequent use of glucocorticoids and less frequent use of biologic disease-modifying antirheumatic drugs (DMARD).[2] The authors hypothesise that factors other than the underlying rheumatic disease explain the higher mortality rate.

We agree that there are scant data to explain why some patients with rheumatic diseases may have worse outcomes compared with the general population. Potential explanations for reported differences may include differences in the distribution of comorbidities, use of immunosuppressive medications or the underlying diseases themselves. The COVID-19 Global Rheumatology Alliance observed a lower hospitalisation rate among patients receiving biologic and targeted synthetic DMARDs,[2] and Marques *et al* reported that none of the deceased patients in their registry were on biologic DMARDs.[1] In our study of a cohort in Boston, MA, USA, we observed a higher risk of mechanical ventilation and intensive care unit admission in patients with rheumatic disease after adjusting for several relevant covariates including demographic features and key comorbidities, although residual confounding is still possible.[3] We did not have sufficient power to adjust for differences in immunosuppressive medications as they relate to differences in outcomes within our cohort of patients with rheumatic diseases.

When interpreting reports of outcomes in patients with rheumatic diseases during the COVID-19 pandemic, it is important to consider how cohorts are assembled. It is not clear how patients were identified and enrolled in the registry that Marques *et al* describe.[1] If patients with COVID-19 were not systematically obtained (eg, from administrative databases containing data from patients in hospitals, clinics or healthcare systems), there is potential for selection bias since more severe cases are more likely to present for care and be reported by their providers, which may lead to an overestimation of the mortality rate. Selection bias may explain why the mortality rates reported by the COVID-19 Global Rheumatology Alliance[2] and Marques *et al*[1] are higher than those observed in our cohort which was assembled from the population of patients with positive PCR testing within a large healthcare system.[3] The mortality in our rheumatic disease cohort was slightly higher numerically than that of the control population though this difference was not statistically significant (6% vs 4%, respectively; p=0.69).[3]

We thank Marques *et al*[1] for their contribution to help us all better understand the impact of COVID-19 on patients with rheumatic diseases. Additional studies of larger cohorts with appropriate comparators identified systematically from the same data set are necessary to clarify any association between rheumatic disease and outcomes of COVID-19 infection.

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REFERENCES

1 Marques C, Pinheiro M, Reis Neto E, *et al*. COVID-19 in patients with rheumatic diseases: what is the real mortality risk? *Ann Rheum Dis* 2020. doi: 10.1136/annrheumdis-2020-218388.
2 Gianfrancesco M, Hyrich KL, Al-Adely S, *et al*. Characteristics associated with hospitalisation for COVID-19 in people with rheumatic disease: data from the COVID-19 global rheumatology alliance physician-reported registry. *Ann Rheum Dis* 2020;79:859–66.
3 D'Silva KM, Serling-Boyd N, Wallwork R, *et al*. Clinical characteristics and outcomes of patients with Coronavirus Disease 2019 (COVID-19) and rheumatic disease: A comparative cohort study from a United States "hot spot". *Ann Rheum Dis* 2020;0:1–7.