

# COVID-19 and rheumatology: is shielding really necessary?

Rheumatology patients who are taking immunosuppressants are considered to be at 'high risk' from COVID-19, hence have been self-isolating or shielding. However, they may be protected from the features of hyperinflammation driven by a 'cytokine storm', so may have better clinical outcomes if infected. This editorial discusses whether it may not be necessary to advise these patients to shield.

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## Introduction

Shielding is a measure intended to protect the most vulnerable patients from being exposed to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and involves strict quarantine and minimal non-essential contact with other household members (NHS Inform, 2020). It is an extremely socially isolating measure, with the risk of adversely affecting people's mental health and making those who live alone at risk of psychosocial implications. The World Health Organization states that it is expecting to see an increase in depression, self-harm and suicidal behaviour as a result of quarantine. Some heavily affected populations in Italy are already having major concerns regarding people developing mental health conditions or those with pre-existing conditions worsening because of issues with service access and continuity (World Health Organization, 2020). Shielding renders the person completely dependent on others to cater for their food and medicinal needs (Healthwatch, 2020). Some household members have decided to temporarily live separately from a shielding family member in order to protect them, but with uncertainty surrounding the duration required to shield, social and financial concerns inevitably begin to surface (British Medical Association, 2020).

In the UK, Public Health England has deemed rheumatology patients who are immunosuppressed among the population who are believed to be at 'high risk' of severe illness from COVID-19 and are hence being asked to shield (NHS Inform, 2020).

It has been suggested that COVID-19 patients with the worst outcomes are those exhibiting features of hyperinflammation which is driven by a 'cytokine storm' (Mehta et al, 2020). This involves over-activation of the immune system and hence uncontrolled release of pro-inflammatory cytokines (Spezzani et al, 2020), which causes subsequent multi-organ manifestations and tissue damage. Severely ill COVID-19 patients admitted to intensive care units have higher levels of cytokines (tumour necrosis factor- $\alpha$ , granulocyte-colony stimulating factor, monocyte chemoattractant protein-1 and macrophage inflammatory protein-1 alpha) (Misra et al, 2020), indicating that the cytokine storm possibly correlates with disease severity. Macrophage activation syndrome is a life-threatening complication of rheumatic disorders in which there is excessive cellular activation and expansion of cytotoxic T cells and macrophages resulting in a hyperinflammatory state (Ravelli, 2002), similar to that seen in patients with severe COVID-19. As is the case in the management of macrophage activation syndrome, early recognition and intervention through the use of immunosuppressants is critical (Ravelli, 2002).

It has been postulated that immunosuppressed COVID-19 patients may have better clinical outcomes as a result of an attenuated cytokine response, leading to reduced intensive care unit admissions and mortality (Spezzani et al, 2020). The authors believe that shielding of rheumatology patients may be an unnecessary measure as these patients may not be more vulnerable to the effects of severe COVID-19 disease and, in fact, may be protected from the serious cytokine storm or even macrophage activation syndrome.

In a retrospective analysis of 450 patients with confirmed SARS-CoV-2 admitted to the authors' centre, only 11 (2.4%) had rheumatological conditions that were being treated with immunosuppressants (prednisolone, hydroxychloroquine, mycophenolate, methotrexate

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and rituximab), and none of these patients required intensive care support. Five of the 11 patients (45.5%) died but all had significant comorbidities and a mean age of 85.2 years vs 68.9 years in the non-immunosuppressed group. Of 414 non-immunosuppressed patients, 67 (16.2%) required intensive care unit admission because of their disease severity and 161 out of 414 (38.9%) died (Barnet Hospital, unpublished data, 2020). Similar findings are emerging globally with Wuhan, China disclosing data showing that of 1099 confirmed cases only two had an immunodeficiency (Guan et al, 2020). Italy has released similar data, showing that of 320 rheumatological immunosuppressed patients, only one required admission to hospital and none died (Monti et al, 2020).

## Discussion

These observations, supported by preliminary emerging global data, suggest that there are only a small number of rheumatology patients on immunosuppressants infected with COVID-19 who require hospital admission. Furthermore, this group appears to have reduced disease severity as none of them required intensive care admission. The authors hypothesise that the immunosuppression in these patients has blunted their immunological response. Therefore, the macrophage activation syndrome response and mounting of the cytokine storm is reduced, as are the consequent damaging hyperinflammatory effects, multi-organ damage and requirement for intensive care support.

This raises two key questions that need addressing:

1. Do we still need to advise rheumatology patients who are taking immunosuppressants to shield?
2. If infected with COVID-19, should rheumatology patients who are taking immunosuppressants stop their treatment or continue it?

In the authors' experience, the baseline use of immunosuppressants was not associated with a worse COVID-19 disease outcome. Similarly, patients with chronic rheumatological conditions on immunosuppressants, residing in regions of high incidence of SARS-CoV-2 in Italy, did not seem to be at higher risk of respiratory or serious complications from COVID-19 compared with the general population (D'Antiga, 2020; Monti et al, 2020).

It is also important to note that data from previous coronavirus outbreaks (SARS and Middle East respiratory syndrome) did not show increased fatality in immunosuppressed patients and hence immunosuppression is not deemed a risk factor for mortality (D'Antiga, 2020).

It appears that COVID-19 will be prevalent for an extended period of time with governments now planning for the years to come. It is not be feasible, or fair, to ask immunosuppressed rheumatology patients to shield indefinitely, and the authors' experience and global trends suggest that this measure is disproportionate and perhaps not required.

The authors believe that immunosuppressed rheumatological patients may not actually be more vulnerable to the effects of severe COVID-19 and hence asking these patients to shield may be an unnecessary and unjust measure. Rather, they should continue with self-isolation and social distancing measures, as advised for the general population. Furthermore, there may be an argument that it is not necessary to stop immunosuppressant medication if these patients are admitted with COVID-19 disease.

Time, experience and larger scale data from other centres will hopefully guide the creation of national guidelines about whether immunosuppressed patients require shielding, and also whether patients infected with COVID-19 should be advised to suspend their immunosuppressive therapies during admission.

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## Key points

- Immunosuppressed patients are deemed extremely vulnerable and are hence asked to shield to protect them from the severe effects of COVID-19.
- Severe COVID-19 patients exhibit features of hyperinflammation, which is driven by a 'cytokine storm'.
- Immunosuppressed patients may be protected from this cytokine storm as a result of a blunted immunological response.
- Global emerging data show that the baseline use of immunosuppressants in rheumatology patients is not associated with a worse outcome of COVID-19 disease.
- It may not be necessary to ask immunosuppressed patients to shield but instead to follow advice targeted to the general population.

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## Conflicts of interests

The authors declare no conflicts of interests.

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