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.

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1 Henderson LA, Canna SW, Schulert GS, et al. On the alert for cytokine storm: immunopathology in COVID-19. *Arthritis Rheumatol* 2020; **72:** 1059–63.

2 The RECOVERY Collaborative Group. Dexamethasone in hospitalized patients with COVID-19. *N Engl J Med* 2021; **384:** 693–704.

3 Shankar-Hari M, Vale CL, Godolphin PJ, et al. Association between administration of IL-6 antagonists and mortality among patients hospitalized for COVID-19: a meta-analysis. *JAMA* 2021; **326:** 499–518.

4 Kyriazopoulou E, Poulakou G, Milionis H, et al. Early treatment of COVID-19 with anakinra guided by soluble urokinase plasminogen receptor plasma levels: a double-blind, randomized controlled phase 3 trial. *Nat Med* 2021; **27:** 1752–60.

5 Tanaka Y, Luo Y, O'Shea JJ, Nakayamada S. Janus kinase-targeting therapies in rheumatology: a mechanisms-based approach. *Nat Rev Rheumatol* 2022; **18:** 133–45.

6 Han MK, Antila M, Ficker JH, et al. Ruxolitinib in addition to standard of care for the treatment of patients admitted to hospital with COVID-19 (RUXCOVID): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Rheumatol* 2022; published online March 29. https://doi.org/10.1016/S2665-9913(22)00044-3.

7 Kalil AC, Patterson TF, Mehta AK, et al. Baricitinib plus remdesivir for hospitalized adults with COVID-19. *N Engl J Med* 2021; **384:** 795–807.

8 Guimarães PO, Quirk D, Furtado RH, et al. Tofacitinib in patients hospitalized with COVID-19 pneumonia. *N Engl J Med* 2021; **385:** 406–15.

9 Kelmenson DA, Cron RQ. Who, what, and when—effective therapy for severe COVID-19. *Lancet Rheumatol* 2022; **4:** e2–3.

10 Keenan C, Nichols KE, Albeituni S. Use of the JAK inhibitor ruxolitinib in the treatment of hemophagocytic lymphohistiocytosis. *Front Immunol* 2021; **12:** 614704.

COVID-19 vaccine acceptance over time in patients with immune-mediated inflammatory rheumatic diseases

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Before the global distribution of COVID-19 vaccines, we observed substantial concerns among non-immunocompromised people about the lack of long-term research or the occurrence of adverse events after vaccination, and concerns among patients with immune-mediated inflammatory rheumatic diseases about interactions with their underlying autoimmune disease or immunosuppressive treatment regimens.[1] Our findings have since been replicated,[2,3] but there is as yet no data on how patients' thoughts and behaviour have evolved as vaccines were distributed, or data that compare COVID-19 vaccine coverage between patients with rheumatic immune-mediated inflammatory diseases and healthy controls.

In this Comment, we aim to describe the evolution of COVID-19 vaccination willingness over time in patients with immune-mediated inflammatory rheumatic diseases compared with controls, to evaluate motives for getting or not getting vaccinated against COVID-19, changes in psychosocial wellbeing after receiving a COVID-19 vaccination, and perspectives towards additional COVID-19 vaccinations. Questionnaires were sent to patients and controls included in an ongoing prospective cohort study (Netherlands Trial Register, trial ID NL8513) that was set up at the start of the COVID-19 pandemic to compare the severity of COVID-19 between patients with immune-mediated inflammatory rheumatic diseases and healthy controls. Between April 26, 2020, and March 1, 2021 all adult patients (aged ≥18 years) with an immune-mediated inflammatory rheumatic disease from the Amsterdam Rheumatology and Immunology Center (Amsterdam, Netherlands) were digitally invited to participate in the study.[4] Patients were asked, but not obliged, to recruit their own healthy control participant who was of the same sex and similar age (age difference <5 years). All participants provided written informed consent.

See **Online** for appendix

Data were collected via online questionnaires distributed via email.[4] Demographic data, including age, sex, height, weight, smoking status, disease type, ethnicity, and educational level, were collected at baseline. Information on patients' perspectives on COVID-19 vaccinations were collected in some, but not all, follow-up questionnaires of the study: in December, 2020, before the start of the Dutch vaccination programme; in April and May, 2021, shortly before the application of the COVID-19 vaccination passport; and in August and September, 2021, when the whole Dutch population had been given the chance to get a COVID-19 vaccination. A complete overview of the study surveys, including the content, is presented in the appendix (pp 12–17). Participants who completed at least two questionnaires that assessed their perspective on COVID-19 vaccination were included in the analyses.

In total, 1927 consecutive patients with immune-mediated inflammatory rheumatic diseases and 811 controls were included for analyses. The questionnaires sent in December, 2020, were completed

by 1515 (79%) patients and 646 (80%) controls; those sent in April, 2021, were completed by 1804 (94%) and 790 (97%) controls; and those sent in August, 2021, were completed by 1489 (77%) patients and 575 (71%) controls. The mean age was 58 years (SD 13; appendix p 5). The majority of participants were female (1831 [67%] of 2738 participants) and of White ethnicity (2164 [89%] of 2435 participants; some data were missing for ethnicity). The prevalence of chronic pulmonary disease, cardiovascular diseases, diabetes, and obesity was higher in patients than in controls. The most common rheumatic diagnosis was rheumatoid arthritis (996 [52%] of 1927 patients), and 1506 (78%) of 1927 patients received immunosuppressive treatment.

The proportion of participants who would be willing to get vaccinated against COVID-19 or who had already received a COVID-19 vaccination was similar between patients and controls, and increased with time: 936 (62%) of 1515 patients and 418 (65%) of 646 controls in December, 2020; 1649 (91%) of 1804 patients and 710 (90%) of 790 controls in April, 2021; and 1419 (95%) of 1489 patients and 551 (96%) of 575 controls in August, 2021 (appendix p 2). Patients and controls who were not willing to get a COVID-19 vaccination were younger than patients and controls who chose to get vaccinated (appendix p 6). A larger proportion of patients than controls consulted a physician before COVID-19 vaccination (540 [36%] of 1480 patients and 37 [6%] of 573 controls), mostly because of safety concerns (table). In addition, a considerable proportion of patients indicated that they would not have taken a COVID-19 vaccination without the advice of their rheumatologist; 185 (34%) of 540 patients, which corresponds to 12% of all patients. This finding emphasises the importance of vaccination-specific counselling to improve vaccine coverage, which might not only be relevant for COVID-19 vaccinations, but also for influenza or pneumococcal vaccinations for which vaccine uptake has been shown to be low among patients with autoimmune diseases.[5]

A lack of long-term research remained the most important reason for doubting or refusing vaccination in both patients and controls over time (appendix p 3). However, concerns about interactions with immunosuppressive treatment regimens or the underlying immune-mediated inflammatory disease became a more prominent reason for doubt or refusal among patients over time, whereas a feeling of not being at risk for severe COVID-19 disease became more prominent for controls. The most important reasons to accept vaccination included concerns for personal health among patients, and wanting to contribute to herd immunity among controls (appendix p 4). Only a small proportion of patients and controls were vaccinated because of the advantages of a COVID-19 vaccination passport (44 [3%] of 1419 patients and 25 [5%] of 551 controls).

Most patients and controls who had received two vaccinations by the end of August, 2021, indicated that they would be willing to get an additional vaccine dose (1085 [80%] of 1350 patients and 374 [75%] of

	Patients with rheumatic immune-mediated inflammatory disease	Healthy controls
Vaccination status in August, 2021		
n	1489	575
Vaccinated once	69 (5%)	50 (9%)
Vaccinated twice	1350 (91%)	501 (87%)
Not vaccinated	70 (5%)	24 (4%)
Contact with physician before COVID-19 vaccination*		
n	1480	573
Yes	540 (36%)	37 (6%)
No	940 (64%)	536 (94%)
Reasons for contact with physician before vaccination*		
n	540	37
Concerned about safety of the vaccine	344 (64%)	20 (54%)
Rheumatic treatment at the time of vaccination	195 (36%)	NA
Concerned about effectiveness of the vaccine	108 (20%)	3 (8%)
To discuss whether there is a preference for a particular vaccine type	152 (28%)	7 (19%)
Other	55 (10%)	10 (27%)
Impact of contact with physician on vaccination willingness*		
n	540	37
No impact (vaccinated, but would have been vaccinated regardless of advice)	355 (66%)	24 (65%)
Positive influence (vaccinated, and would not have been vaccinated without advice)	185 (34%)	13 (35%)

Data are n or n (%). Percentages might not add to 100% due to rounding. NA=not applicable. *Data based on questionnaires sent in April and August, 2021 (responses were combined).

Table: **Perspectives on COVID-19 vaccination among patients with rheumatic immune-mediated inflammatory disease and healthy controls**

501 controls; appendix p 8), and ten patients had already received an additional dose. However, the majority of both groups agreed that all people in low-income countries should have had access to at least the first COVID-19 vaccine dose before the national rollout of additional doses, and also that there should be clear scientific evidence on the additional value of vaccine doses in reducing COVID-19 related morbidity and mortality. Similarly, these statements were the most frequently reported factors that would influence the decision to get an additional vaccination; 679 (50%) of 1350 patients and 296 (59%) of 501 controls indicated that the availability of scientific evidence about additional vaccinations would influence their decision, and 314 (23%) of 1350 patients and 182 (36%) of 501 controls indicated that a fair worldwide distribution of COVID-19 vaccines would influence their decision. In addition, 352 (26%) of 1350 patients and 14 (3%) of 501 controls indicated that the advice of a physician would be important for their decision regarding an additional COVID-19 vaccination. Adverse events of previous COVID-19 vaccinations were only relevant in a small proportion of participants (95 [7%] of 1350 patients and 15 [3%] of 501 controls), which is consistent with our previous observation that adverse events were mostly mild and self-limiting in both patients and controls.[6]

Lastly, vaccination against COVID-19 had a favourable effect on the psychosocial wellbeing of both patients and controls; people felt safer, had more social contacts, and visited more public spaces. In addition, in a considerable number of patients and controls (546 [38%] of 1419 patients and 225 [41%] of 551 controls) experienced an increase in their quality of life after getting vaccinated (appendix p 7). These findings, combined with the focus in the scientific and public media reporting on waning of protective immunity against COVID-19, might explain the high willingness of patients and controls to get an additional COVID-19 vaccination. However, it is still unknown to what extent laboratory findings (eg, a diminished humoral or cellular immune response) are predictive of reduced protection against severe COVID-19 disease. Given the unknowns on the waning of actual protection, the emphasis on this topic going forward could therefore negatively affect patients' psychosocial wellbeing, because it might cause them to re-adhere to inappropriately strict social distancing measures for fear of severe illness.[7–9]

A limitation of this research is that clinical diagnoses and medication use were self-reported and not verified in health-care records. However, these data were only used to compare characteristics between study groups (eg, the prevalence of cardiovascular disease) rather than with other study cohorts, which minimises the bias introduced by this limitation. Moreover, a nationwide study showed concordance rates for self-reported diseases and medication use of over 90%.[10]

In conclusion, our data show that COVID-19 vaccine hesitancy largely subsided during the first 6 months after the start of global distribution of COVID-19 vaccinations in both patients with immune-mediated inflammatory rheumatic diseases and healthy controls, due to increased confidence in the safety and efficacy of COVID-19 vaccinations. Rheumatologists played an important role in this process, highlighting the relevance of vaccination-specific counselling in patients with rheumatic immune-mediated inflammatory diseases, which might also go beyond COVID-19 vaccination.

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1 Boekel L, Hooijberg F, van Kempen ZLE, et al. Perspective of patients with autoimmune diseases on COVID-19 vaccination. *Lancet Rheumatol* 2021; **3:** e241–43.
2 Ko T, Dendle C, Woolley I, Morand E, Antony A. SARS-CoV-2 vaccine acceptance in patients with rheumatic diseases: a cross-sectional study. *Hum Vaccin Immunother* 2021; **17:** 4048–56.
3 Gaur P, Agrawat H, Shukla A. COVID-19 vaccine hesitancy in patients with systemic autoimmune rheumatic disease: an interview-based survey. *Rheumatol Int* 2021; **41:** 1601–05.

4 Boekel L, Hooijberg F, Vogelzang EH, et al. Spinning straw into gold: description of a disruptive rheumatology research platform inspired by the COVID-19 pandemic. *Arthritis Res Ther* 2021; **23:** 207.

5 Lejri-El Euchi H, Chirpaz E, Foucher A, et al. Vaccination against influenza and pneumococcal infections in patients with autoimmune disorders under biological therapy: coverage and attitudes in patients and physicians. *Eur J Intern Med* 2019; **69:** 25–31.

6 Boekel L, Kummer LY, van Dam KPJ, et al. Adverse events after first COVID-19 vaccination in patients with autoimmune diseases. *Lancet Rheumatol* 2021; **3:** e542–45.

7 Hooijberg F, Boekel L, Vogelzang EH, et al. Patients with rheumatic diseases adhere to COVID-19 isolation measures more strictly than the general population. *Lancet Rheumatol* 2020; **2:** e583–85.

8 Glintborg B, Jensen DV, Engel S, et al. Self-protection strategies and health behaviour in patients with inflammatory rheumatic diseases during the COVID-19 pandemic: results and predictors in more than 12 000 patients with inflammatory rheumatic diseases followed in the Danish DANBIO registry. *RMD Open* 2021; **7:** e001505.

9 Krause PR, Fleming TR, Peto R, et al. Considerations in boosting COVID-19 vaccine immune responses. *Lancet* 2021; **398:** 1377–80.

10 Wu CS, Lai MS, Gau SS, Wang SC, Tsai HJ. Concordance between patient self-reports and claims data on clinical diagnoses, medication use, and health system utilization in Taiwan. *PLoS One* 2014; **9:** e112257.

The changing face of psoriatic arthritis

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The management of psoriatic arthritis and other inflammatory arthritides has progressed significantly in the past two decades. Improved screening methods, advanced diagnostic tests, and imaging tools facilitate earlier diagnosis, with highly efficacious advanced therapies and treatment strategies leading to excellent control of disease activity and improved outcomes for affected individuals. However, there is a growing perception among rheumatologists that the clinical phenotype of new psoriatic arthritis cases presenting to early arthritis clinics is evolving, posing challenges to clinical trial recruitment. Here, we discuss how current knowledge could guide future research.

The psoriatic arthritis paradigm is starting to shift. With symptom remission and halting of structural progression now a reality in rheumatoid arthritis, research efforts are increasingly focused on disease prevention. Rheumatoid arthritis studies have shown that B-cell depletion therapy can delay the onset of arthritis in patients positive for anti-cyclic citrullinated peptide (anti-CCP) while on therapy.[1] If proven of value, the prevention approach will require the treatment of asymptomatic patients based on their risk of developing rheumatoid arthritis, which will pose substantial challenges to the susceptible individuals' willingness to accept treatment and to the long-term safety and cost-effectiveness of such strategies. Similar to the value of anti-CCP in rheumatoid arthritis, the presence of skin psoriasis is an important predictor of psoriatic arthritis, since 70–90% of people with psoriatic arthritis have psoriasis at least 10 years before the development of arthritis. The question is whether the development of psoriatic arthritis could potentially be prevented in patients with psoriasis who are at risk of progression to psoriatic arthritis, with the important advantage that in comparison with rheumatoid arthritis, any potential preventive therapy is given to treat existing skin psoriasis (figure). In rheumatoid arthritis, prevention studies started two decades after the introduction of advanced therapies in standard care. In contrast, treatment changes in routine clinical practice for psoriasis might already have started to modify the development of psoriatic arthritis and perhaps even to prevent it.

A number of retrospective studies have looked at the possible preventive role of systemic treatment for psoriasis. In a study of 203 patients with psoriasis, new symptoms and signs leading to a diagnosis of psoriatic arthritis were found less often in patients receiving biologic therapies than in patients receiving topical treatment or no therapy (12% *vs* 37%).[2] In another study of 464 patients with psoriasis, biological therapies were associated with a lower risk of incident psoriatic arthritis compared with phototherapy (adjusted hazard ratio [HR] 0·27, 95% CI 0·11–0·66).[3] In a single-arm, prospective, phase-4 trial using ultrasound, ustekinumab (anti-Interleukin-12 and 23) therapy given for psoriasis also suppressed subclinical enthesopathy.[4] With increasing evidence of the role of enthesitis in psoriatic arthritis, the arrest of inflammation within the enthesis before expanding through the synovio-entheseal complex could explain a reduced incidence of psoriatic arthritis among at-risk patients with psoriasis receiving biologics. If confirmed in larger, longitudinal datasets, these results suggest a potential impact of psoriasis treatment in the prevention of psoriatic arthritis. However, although this appears to be a plausible theory, it is not entirely substantiated, with reports of an increased risk of psoriatic arthritis among patients on biologic treatment for psoriasis,[5] or a higher