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.

Perspective of patients with autoimmune diseases on COVID-19 vaccination

Published Online
February 22, 2021
https://doi.org/10.1016/
S2665-9913(21)00037-0

The socioeconomic burden of COVID-19 and pressure on health-care systems can only be reduced by achieving herd immunity against SARS-CoV-2. For herd immunity to be achieved, it has been estimated that, depending on the efficacy of the vaccines employed, approximately 60–100% of the global population needs to be vaccinated.[1] Countries all over the world are developing vaccination strategies, and many have already started vaccinating their populations. However, the rapid development, approval, and release of vaccines against SARS-CoV-2 has led to uncertainties in the population, which might reduce willingness to get vaccinated.[2] These reservations might be especially apparent for patients with autoimmune diseases, such as rheumatic or neuroinflammatory diseases, because there is no data available about the balance between benefits and risks of the newly developed COVID-19 vaccines in this population. It is therefore relevant to evaluate considerations and concerns regarding vaccination of patients with autoimmune diseases and to identify if and how physicians can influence their patients' decision to get vaccinated.

This Comment reports the results of a questionnaire assessing the perspective of patients with autoimmune diseases on vaccination against SARS-CoV-2. We sent a questionnaire to patients with various rheumatic diseases or multiple sclerosis and controls who were enrolled in two ongoing prospective cohort studies (Netherlands Trial Register, trial ID NL8513 and NCT04498286). Between April 26 and Dec 1, 2020, all adult patients (18 years and older) with systemic autoimmune diseases from the Amsterdam Rheumatology & Immunology Center, Amsterdam, Netherlands; all adult patients with vasculitis from the Amsterdam UMC, Amsterdam, Netherlands; and all adult patients with multiple sclerosis from the Amsterdam Multiple Sclerosis Center of Amsterdam UMC, Amsterdam, Netherlands were invited to participate in these studies. In the first study (NL8513), patients needed to be diagnosed by their treating physician with a systemic autoimmune disease. In the second study (NCT04498286), patients needed to be diagnosed by their treating physician with multiple sclerosis. Our study did not have any exclusion criteria. Patients with rheumatic disease were asked (but not obliged) to register a control subject from their family or close network who did not have a rheumatic disease, were the same sex, and were a comparable age (an age difference of <5 years). Information on demographic data and medication use was collected at baseline (when patients were included into the study, rather than only at the start of the study) and information on patients' perspective on vaccination was collected between Dec 1 and Dec 24, 2020. At both timepoints, data were collected via online questionnaires, which were distributed via email. In the vaccination questionnaire, participants were asked to indicate which scenarios were most applicable, considering their behaviour, thoughts, and concerns regarding COVID-19 vaccination and COVID-19 in general. We included questions regarding a history of COVID-19, and participants were asked about their willingness to get vaccinated if they were to be invited in the first few months of the vaccination programme. There were additional disease related questions for patients with rheumatic diseases or multiple sclerosis.

All participants who completed the vaccination questionnaire before Dec 24, 2020, were included in the analyses. Multivariable logistic regression analyses were used to compare willingness to get a COVID-19 vaccine between patients and controls, patients treated with and without biological agents, all participants younger than and older than 60 years, and all male and female participants. When applicable, associations were adjusted for age, gender, presence of comorbidities, and presence of autoimmune diseases. To identify effect modifiers, a threshold of $p<0·05$ was used for interaction terms. Exploratory subgroup analyses within patients with rheumatoid arthritis, vasculitis or systemic lupus erythematosus (SLE), and multiple sclerosis were done. Data on the patient perspective on COVID-19 vaccinations were compared between patients with autoimmune diseases who were willing to, not willing to, and unsure about getting vaccinated. SPSS (version 23.0) was used for the analyses. The research protocols were approved by the medical

ethical committee of the VU University medical center (registration number 2020·169 and 2020·370). All participants gave informed consent.

Between April 26 and Dec 1, 2020, 2887 patients with rheumatic disease, 530 patients with multiple sclerosis, and 1050 controls were included in this study. The vaccination questionnaire was completed by 1727 patients (1361 patients with rheumatic disease and 366 patients with multiple sclerosis) and 682 controls, who were all included in the analyses. Individuals in the patient group had a mean age of 56 years (SD 13) and individuals in the control group had a mean age of 55 years (SD 13); the majority of participants were female (1113 [64%] of 1727 female *vs* 614 [36%] male in the patient group and 479 [70%] of 682 female *vs* 203 [30%] male in the control group; appendix p 1). Patients with rheumatoid arthritis, and patients with vasculitis or SLE, were older than were patients with multiple sclerosis (mean age 60 years [12] and 56 [13] years *vs* 48 [12] years; appendix p 1). Most patients received immunosuppressive treatment: 1325 (77%) of 1727 patients, 813 (99%) of 823 patients with rheumatoid arthritis, 45 (98%) of 46 patients with vasculitis or SLE, 184 (37%) of 492 patients with other rheumatic diseases, and 283 (77%) of 366 patients with multiple sclerosis. 710 (41%) of 1727 patients received biological agents, which predominantly consisted of tumour necrosis factor inhibitors in patients with rheumatoid arthritis (257 [73%] of 354 patients receiving biologics) and anti-CD20 therapies in patients with vasculitis or SLE (8 [40%] of 20 patients receiving biologics) and patients with multiple sclerosis (64 [55%] of 117 patients receiving biologics).

See Online for appendix

The proportion of patients and controls who would be willing to get vaccinated against SARS-CoV-2 was similar; 1060 (61%) individuals in the patient group and 441 (65%) in the control group (appendix p 2). Accordingly, multivariable regression analyses showed no significant difference between patients and controls. Odds ratios (ORs) for individuals in the rheumatoid arthritis group, vasculitis or SLE group, and multiple sclerosis group compared with individuals in the control group were similar, and they remained similar after adjusting for confounders (appendix p 3). Use of biological agents was not associated with willingness to get vaccinated in all patients or in the patient subgroups. Overall, male participants and individuals older than 60 years were both approximately twice as likely to be willing to get vaccinated than were female participants (930 [58%] of 1592 female participants *vs* 572 [70%] of 817 male participants; OR 1·7 [95% CI 1·4–2·0]) and individuals younger than 60 years (767 (55%) of 1391 people younger than 60 years *vs* 734 (72%) of 1018 people aged 60 years or older years; OR 2·0 [1·7–2·4]; appendix p 3).

The most common reasons for refusing or doubting vaccination in both patients and controls were concerns for adverse events and no long-term research (appendix p 4). Patients who were unsure about vaccination or who were not willing to get vaccinated were more concerned that the vaccine might aggravate their autoimmune disease than were patients who were willing to get vaccinated (164 [32%] of 515 patients and 53 [45%] of 118 patients *vs* 119 [11%] of 1060 patients; appendix p 4). Lastly, 392 (23%) of 1727 patients with autoimmune diseases indicated that a physicians' advice to get vaccinated would lead to a change in their preference regarding vaccination willingness; 356 [69%] of 515 patients who were uncertain about vaccination and 36 (31%) of 118 patients who would be unwilling to get vaccinated would change their minds following physicians' advice (appendix p 4).

A limitation of this study was that control participants were not a random sample of the general population, but often people with close ties to patients with autoimmune diseases (eg, friends or family). This limitation could contribute to an absence of differences between patients and controls regarding vaccination willingness, because people close to patients with autoimmune diseases might be more health conscious than people without close ties to these patients. However, a US study[2] reported similar proportions of vaccination willingness in the general population as compared with our own findings in the control group (60% *vs* 441 [65%] of 682). The effect of our method for recruiting healthy controls on our final results is therefore probably limited.

Altogether, our results indicate that willingness to get vaccinated against SARS-CoV-2 does not differ between patients with autoimmune diseases and controls, and that it is not influenced by autoimmune disease type or medication use. Additionally, we showed that approximately 1060 (61%) of 1727 patients with autoimmune diseases were willing to get vaccinated

against SARS-CoV-2, and that physicians have the potential to increase this number by more than 20% (392/1727 patients). Important causes of vaccine hesitancy in patients with autoimmune diseases are concerns about adverse events and aggravation of the underlying autoimmune disease, which has been reported by others as well.[3] However, although data are still scarce, results of previous studies on vaccines against other viruses are reassuring; few adverse events and disease flares in patients with autoimmune diseases have been described.[4] The possibility of the occurrence of adverse events should therefore not be a reason to not recommend vaccination against SARS-CoV-2 in patients with autoimmune diseases, especially because results of previous studies suggest that these patients can be at increased risk of severe COVID-19 disease.[5] Therefore, physicians of patients with autoimmune diseases should actively encourage their patients to get vaccinated against SARS-CoV-2, because this can contribute considerably to a reduction in COVID-19 related morbidity and mortality.

TR reports grants from ZonMw during the conduct of the study. JK reports grants from Biogen Idec, Novartis, TEVA, Bayer Schering Pharma, Glaxo Smith Kline, Merck Serono, Genzyme, and Roche, all outside the submitted work. LB and FH did the analyses and wrote the manuscript. ZLEK, EHV, SWT, JK, MTN, MB, TWK, SMH, FE, LW, TR, and GJW helped revise the manuscript for important intellectual content. GJW supervised the manuscript. LB and FH did the analyses and wrote the manuscript. ZLEK, EHV, SWT, JK, MTN, MB, TWK, SMH, FE, LW, TR and GJW helped revise the manuscript for important intellectual content. GJW supervised the manuscript. All other authors declare no competing interests.

*Laura Boekel, Femke Hooijberg, Zoé L E van Kempen, Erik H Vogelzang, Sander W Tas, Joep Killestein, Michael T Nurmohamed, Maarten Boers, Taco W Kuijpers, S Marieke van Ham, Filip Eftimov, Luuk Wieske, Theo Rispens, Gertjan J Wolbink
l.boekel@reade.nl

Department of Rheumatology, Amsterdam Rheumatology and Immunology Center, Amsterdam 1056 AB, Netherlands (LB, FH, MTN, GJW, MB); Department of Neurology (ZLEvK, JK), Department of Epidemiology and Data Science (EHV, MB), Department of Pediatric Immunology (TWK), Vrije Universiteit, Amsterdam UMC, Amsterdam, Netherlands; Amsterdam Rheumatology and Immunology Center, Department of Rheumatology and Clinical Immunology (SWT, MTN), Department of Neurology and Neurophysiology, Amsterdam Neuroscience (FE, LW), Swammerdam Institute for Life Sciences (SMvH), University of Amsterdam, Amsterdam, Netherlands; Department of Immunopathology, Sanquin Research and Landsteiner Laboratory Academic Medical Center, Amsterdam, Netherlands (SMvH, TR, GJW)

1 Anderson RM, Vegvari C, Truscott J, Collyer BS. Challenges in creating herd immunity to SARS-CoV-2 infection by mass vaccination. *Lancet* 2020; **396:** 1614–16.
2 Guidry JPD, Laestadius LI, Vraga EK, Miller CA, Perrin PB, Burton CW, et al. Willingness to get the COVID-19 vaccine with and without emergency use authorization. *Am J Infect Control* 2021; **49:** 137–42.
3 Doornekamp L, van Leeuwen L, van Gorp E, Voeten H, Goeijenbier M. Determinants of vaccination uptake in risk populations: a comprehensive literature review. *Vaccines* 2020; **8:** 480.
4 Westra J, Rondaan C, van Assen S, Bijl M. Vaccination of patients with autoimmune inflammatory rheumatic diseases. *Nat Rev Rheumatol* 2015; **11:** 135–45.
5 Akiyama S, Hamdeh S, Micic D, Sakuraba A. Prevalence and clinical outcomes of COVID-19 in patients with autoimmune diseases: a systematic review and meta-analysis. *Ann Rheum Dis* 2021; **80:** 384–91.

Vaccination against COVID-19: expectations and concerns of patients with autoimmune and rheumatic diseases

Published **Online**
February 22, 2021
https://doi.org/10.1016/S2665-9913(21)00039-4

Vaccination is an important and effective tool to prevent infections in the general population, as well as in patients with autoimmune and inflammatory rheumatic diseases. It has been well established that influenza and pneumococcal vaccination rates do not reach recommended levels in this target population, despite specific guidelines.[1,2] Vaccine uptake has been negatively associated with low knowledge of vaccines and unfavorable attitudes towards vaccination in general.[2] We did an international study (VAccinations against COVid-19 [VAXICOV]) to explore the feelings of patients and health-care professionals regarding COVID-19 vaccination. Our main objective was to describe the expectations and potential concerns related to COVID-19 vaccination of patients with systemic autoimmune or inflammatory rheumatic diseases and health-care professionals.

The study consisted of 57 web-based questions that addressed epidemiological, socio-demographic, and therapeutic elements associated with expectations and potential concerns regarding COVID-19 vaccination. The study targeted patients with a self-reported diagnosis of systemic autoimmune or inflammatory rheumatic diseases and health-care professionals. Health-care professionals were the control group and had no systemic autoimmune or inflammatory rheumatic diseases. Dissemination of the study was ensured through social media and mailings via patient associations and various medical societies (not only limited to rheumatologists) between Dec 12 and Dec 21, 2020. The study was approved by