



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.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

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 (ZLEK, 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



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

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

See Online for appendix

the ethics review board of Strasbourg (#CE-2020-199), and respondents gave their consent to participate to the study. Full methods are detailed in the appendix (pp 4–5).

The study included 1531 participants (1291 [84.3%] women vs 240 [15.7%] men; median age 53 [40–64] years for men vs 48 [38–59] years for women), from 56 countries (appendix pp 1–2). Among the participants, 1266 (82.7%) were patients with systemic autoimmune or inflammatory rheumatic diseases and 265 (17.3%) were health-care professionals (including, 203 physicians). The most common inflammatory or autoimmune conditions were systemic lupus erythematosus (492 [38.9%] of 1266), spondyloarthritis (176 [13.9%]), and rheumatoid arthritis (160 [12.6%]; appendix p 1). On a 0 (not at all in agreement) to 10 (full agreement) scale, patients reported being afraid to get infected by SARS-CoV-2 with a median score of 8 (IQR 6–10) and to develop severe COVID-19 with a median score of 9 (7–10) whereas health-care professionals had median scores of 5 (3–8) and 5 (1–8), respectively (appendix p 1).

The proportion of patients with systemic autoimmune or inflammatory rheumatic diseases willing to get vaccinated against SARS-CoV-2 was 54.2% (686/1266; uncertainty was reported in 32.2% [408/1266] and unwillingness to get vaccinated in 13.6% [172/1266]; appendix p 1). Patients with systemic autoimmune or inflammatory rheumatic diseases reported wanting to get vaccinated against SARS-CoV-2 to protect themselves (850 [67.1%] of 1266 patients), their relatives (686 [54.2%] of 1266), and the general population (791 [62.5%] of 1266) in priority. The willingness to get vaccinated was slightly lower in women than in men (89 [71.2%] of 125 men vs 597 [52.3%] of 1141 women; relative risk [RR] 0.93 [95% CI 0.89–0.98], $p=0.02$) and increased significantly with age ($p<0.0001$). Also, vaccine willingness was strongly associated with the fear of being infected by SARS-CoV-2 ($p<0.0001$) and the fear to get severe COVID-19 ($p<0.0001$). The most trusted health-care professional regarding the recommendation to get vaccinated against COVID-19 for 855 (67.5%) of 1266 patients was their specialist (eg, rheumatologist or internist) and for 244 (19.3%) of 1266 patients was their general practitioner. The willingness to get vaccinated increased to 62.8% (795/1266; with uncertainty declining

to 28.4% [360/1266] and unwillingness to 8.8% [111/1266]) when vaccination was recommended by a physician. Importantly, the willingness to get vaccinated against SARS-CoV-2 was significantly higher in those who had been vaccinated against influenza at least once in the last 3 years than those who had not (593 [88.8%] of 668 for vaccination and 93 [48.9%] of 190 against vaccination; RR 1.98 [95%CI 1.67–2.36]; $p<0.0001$) or had received the pneumococcal vaccine in the last 5 years than those who had not (339 [84.8%] of 400 for vaccination and 289 [74.1%] of 390 against vaccination; RR 1.43 [1.16–1.77]; $p=0.0002$), but not with the presence of comorbidities additional to age and systemic autoimmune or inflammatory rheumatic diseases (330 [80.5%] of 410 for patients with at least an additional comorbidity vs 356 [79.5%] of 448 for those without additional comorbidity; RR 1.03 [0.87–1.24]; $p=0.71$) nor with the immunocompromised status (417 [80.0%] of 521 for immunocompromised patients vs 269 [79.8%] of 337 for non-immunocompromised patients; RR 1.01 [0.88–1.15]; $p=0.94$). Additional associations are shown in appendix (p 3).

The proportion of health-care professionals willing to get vaccinated against SARS-CoV-2 was 74.0% (196/265; uncertainty was reported in 18.1% [48/265] and unwillingness to get vaccinated in 7.9% [21/265]). Vaccine hesitancy was observed in 22.3% (59/265; appendix p 1). Health-care professionals willing to get vaccinated reported that they wanted to protect themselves (128 [48.3%] of 265) and people at-risk (110 [41.5%] of 265), but more importantly to protect their relatives (160 [60.4%] of 265) and the general population (161 [60.8%] of 265). The willingness to get vaccinated was significantly lower in women than in men (98 [86.0%] in 114 women vs 98 [95.1%] in 103 men; RR 0.66 [95% CI 0.50–0.87]; $p=0.02$) and increased significantly with age. Vaccine willingness in health-care professionals was associated with the fear of getting severe COVID-19 ($p=0.02$), but not with fear of being infected by SARS-CoV-2 ($p=0.25$) and was significantly increased in health-care professionals who had been vaccinated against influenza at least once in the last 3 years (177 [92.2%] of 192 for vaccination vs 19 [76.0%] of 25 against vaccination; RR 1.26 [0.96–1.66]; $p=0.01$).

One of the main findings of the VAXICOV study is that the proportion of patients with systemic autoimmune or inflammatory rheumatic diseases

willing to get vaccinated against COVID-19 was moderate in a generally at-risk population. Of note, uncertainty was reported by 402 (31.8%) of 1266 patients, which suggests that vaccine willingness could be increased using appropriate measures. Vaccine willingness increased significantly with age and was significantly associated with the fear, but not with the presence of additional comorbidities or with the immunocompromised status. These results show that a significant proportion of patients with systemic autoimmune or inflammatory rheumatic diseases who are at risk of severe COVID-19³ do not perceive themselves as such, and highlight the importance of increasing patient education in this context. Among the main concerns reported by patients were the scarcity of experience and background information regarding new COVID-19 vaccines, the use of a new technology (eg, mRNA vaccines) that has never been used before, the possible induction of a flare of their disease, and the risk to develop a local reaction or side-effects (appendix p 3). Importantly, the willingness to get vaccinated against SARS-CoV-2 increased when vaccination was recommended by a physician, and the most trusted health-care professionals was the specialist physician. These data show the crucial and timely role of rheumatologists in vaccination uptake. Although there could be a selection bias with regard to people who would be more likely to respond to such a questionnaire, overall the participation of more than 1200 patients worldwide is probably a reasonable reflection of the state of mind of patients with systemic autoimmune or inflammatory rheumatic diseases.

Another important finding of the VAXICOV study is that vaccine unwillingness was low among health-care professionals. Although patients with systemic autoimmune or inflammatory rheumatic diseases would like to get vaccinated primarily to protect themselves against COVID-19 before any other reason, health-care professionals would like to get vaccinated to protect the general population. Among the main concerns reported by health-care professionals was the scarcity of experience and background information regarding new COVID-19 vaccines suggesting the importance of communicating, largely about the results of ongoing phase 3 vaccine studies. The completion of this study in less than 2 weeks confirms the feasibility of using

social media for sampling large cohorts of patients with systemic autoimmune or inflammatory rheumatic diseases and real-time assessment of behaviours associated with important health issues in specific populations.

Data from the VAXICOV study are crucial to understand the main expectations and concerns regarding COVID-19 vaccination in patients with systemic autoimmune or inflammatory rheumatic diseases and health-care workers and to allow the identification of valuable strategies to increase vaccine coverage in those populations.

RF has received consultancy fees from Pfizer (unrelated to the VAXICOV study). MFU-G reports grants from Janssen and Pfizer (unrelated to the VAXICOV study). JS has received consultancy fees from Pfizer (unrelated to the VAXICOV study). J-EG has received consultancy fees from Pfizer & Astra-Zeneca (unrelated to the VAXICOV study). LA has received consultancy fees from Pfizer and Astra-Zeneca (unrelated to the VAXICOV study). All other authors declare no competing interests. RF, MD, MUG, AC, LK, HB, CC, LP, JF, EC, CS, RMJ, JEG, JS, YFS, and LA conceptualised the study. RF and LA curated the data. RF, MD, MUG, AC, LK, HB, CC, LP, JF, EC, CS, RMJ, JEG, JS, YFS, and LA did the investigation. RF, MD, MUG, JS, YFS, and LA did the methods. RF and LA drafted the original manuscript. RF, MD, MUG, AC, LK, HB, CC, LP, JF, EC, CS, RMJ, JEG, JS, YFS, and LA reviewed and edited the manuscript. We wish to acknowledge the crucial role of the following patient associations: LupusEurope, Agrupacion Lupus Chile, RarasInolvisibles, Lupus UK, Lupus France, SPONDYLASSO, Spondyl(O)action, AFL+, in the dissemination of the survey. We are indebted to Gonzalo Tobar Carrizo for the Spanish translation of the survey, all patients, families, and health-care professionals for their kind participation in our study. We wish to thank Sylvie Thuong for her invaluable assistance in the preparation of the manuscript.

*Renaud Felten, Maxime Dubois, Manuel F Ugarte-Gil, Aurore Chaudier, Lou Kawka, Hugo Bergier, Charlotte Costecalde, Luc Pijnenburg, Jérémy Fort, Emmanuel Chatelus, Christelle Sordet, Rose-Marie Javier, Jacques-Eric Gottenberg, Jean Sibilia, Yurilis Fuentes-Silva, *Laurent Arnaud*

Laurent.arnaud@chru-strasbourg.fr

Service de rhumatologie, Centre National de Référence des Maladies Auto-immunes Systémiques Rares Est Sud-Ouest, Hôpitaux Universitaires de Strasbourg, Strasbourg, France (RF, MD, AC, LK, CC, LP, JF, EC, CS, R-M), J-EG, JS, YF-S, LA); School of Medicine, Universidad Científica del Sur, Lima, Peru (MFU-G); Rheumatology Department, Hospital Nacional Guillermo Almenara Irigoyen, Lima, Peru (MFU-G); Division of Rheumatology, Complejo Hospitalario Universitario Ruiz y Páez, Universidad de Oriente, Ciudad Bolívar, Centro Nacional de Enfermedades Reumáticas, Venezuela (YF-S)

- 1 Figueroa-Parra G, Esquivel-Valerio JA, Santoyo-Fexas L, Moreno-Salinas A, Gamboa-Alonso CM, De Leon-Ibarra AL, et al. Knowledge and attitudes about influenza vaccination in rheumatic diseases patients. *Hum Vaccines Immunother* 2020; **16**: 1–6.
- 2 Loubet P, Kernéis S, Groh M, Loulergue P, Blanche P, Verger P, et al. Attitude, knowledge and factors associated with influenza and pneumococcal vaccine uptake in a large cohort of patients with secondary immune deficiency. *Vaccine* 2015; **33**: 3703–08.
- 3 Contributors F/SFR/SNFMI/SOFREMIP/CR/IMIDIATE consortium and contributors. Severity of COVID-19 and survival in patients with rheumatoid and inflammatory diseases: data from the French RMD COVID-19 cohort of 694 patients. *Ann Rheum Dis* 2020; published online Dec 2. <https://ard.bmj.com/content/early/2020/12/01/annrheumdis-2020-218310>.