

SARS-CoV-2 vaccine hesitancy among patients with rheumatic and musculoskeletal diseases: a message for rheumatologists

SARS-CoV-2 vaccines appear to be the most promising strategy for fighting the virus and protecting also those who might be at higher risk of severe COVID-19, such as patients with rheumatic and musculoskeletal diseases (RMDs). However, vaccine hesitancy might greatly impair the possibility to reach herd immunity and curtail the virus.^{1,2} As underlined by some studies performed before vaccine availability, a non-negligible proportion of subjects among the general population would have refused vaccination against COVID-19.^{3,4}

During the first weeks of the ongoing vaccination campaign, we proposed an online survey to adult patients with RMDs residing in the Lazio region followed up at our tertiary referral centre in Rome, Italy. Healthy controls (HCs) were recruited using the 'best friend' system. Participants had to report on eight different domains with two possible answers: 'yes' or 'no' (table 1).

Only for the item 'Willingness to receive COVID-19 vaccination', answers were 'yes' or 'no/don't know', with the possibility to give an explanation in case of a negative answer.

For statistical analyses, Mann-Whitney test, χ^2 test and multivariable logistic regression models, also with interaction terms, were used (two-sided, significance level <0.05). Covariates were selected according to a clinical criterion. The analysis was performed by RStudio software.

In all, 626 (75%) of 830 patients with RMDs and 345 (93%) of 370 HCs completed the survey. RMDs included rheumatoid arthritis, psoriatic arthritis, systemic lupus erythematosus, ankylosing spondylitis, systemic sclerosis, Sjögren's syndrome, fibromyalgia, undifferentiated connective tissue

diseases, vasculitis, myositis, antiphospholipid syndrome, and miscellaneous rare diseases including mixed connective tissue disease, Behçet's disease, adult-onset Still's disease and IgG4-related disease (online supplemental figure 1). Clinical and demographic features as well as willingness to receive COVID-19 vaccine according to specific RMDs are shown in online supplemental table 1. Acceptance to receive COVID-19 vaccine was reported by 284 (82.3%) of 345 HCs and 344 (54.9%) of 626 patients with RMDs, which is a lower proportion in comparison with a smaller RMD cohort from Lombardy, a region more severely affected by SARS-CoV-2 pandemic compared with Lazio.⁵ Multivariable analysis confirmed that patients with RMDs were less willing to receive COVID-19 vaccine compared with HCs (table 1), although they were more likely to perceive themselves at risk of becoming infected with SARS-CoV-2 and developing a severe COVID-19. No differences emerged concerning fear of adverse events (AEs) or distrust for vaccines. Patients with RMDs did not show a generalised hostility to immunisation practices as they had mostly received vaccines against pneumococcus and influenza in the past. Of note, patients with RMDs refusing vaccination would be significantly more willing than HCs to reconsider their decision if more medical education was provided (table 1).

Among patients with RMDs, individual variables significantly associated with willingness to receive the COVID-19 vaccine included older age ($p=0.0009$) and male sex ($p=0.0009$), a finding not unexpected because the risk of developing severe COVID-19 is higher for elderly men who might consequently be more inclined to vaccinate.⁶ As previously reported,⁵ acceptance of vaccination was associated with higher levels of education, whereas neither comorbidities nor ongoing immune suppressive therapy had any effect (online supplemental table 1). Interaction tests did not reveal a more pronounced willingness in specific subgroups of patients with

Table 1 Multivariable models predicting willingness to receive COVID-19 vaccination and other SARS-CoV-2 and/or vaccine-related outcomes in patients with RMDs and healthy controls

	Domain 1 Willingness to receive COVID-19 vaccination		Domain 2 Perceive oneself at risk of becoming infected with SARS-CoV-2		Domain 3 Perceive oneself at risk of developing severe COVID-19		Domain 4 Fear of COVID-19 vaccine-related AEs	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Patients								
Rheumatologic Patients	0.24 (0.17 to 0.34)	<0.0001	11.3 (8.0 to 15.9)	<0.0001	11.06 (7.8 to 15.6)	<0.0001	0.95 (0.52 to 1.7)	0.865
Healthy controls	Ref.	–	Ref.	–	Ref.	–	Ref.	–
Age	1.01 (1.00 to 1.02)	<0.001	1.04 (1.03 to 1.05)	<0.0001	1.04 (1.03 to 1.06)	<0.0001	1.00 (0.98 to 1.02)	0.880
Sex								
Female	0.67 (0.47 to 0.95)	<0.01	1.74 (1.18 to 2.56)	<0.001	1.61 (1.1 to 2.36)	<0.1	2.25 (1.04 to 4.86)	0.039
Male	Ref.	–	Ref.	–	Ref.	–	Ref.	–
	Domain 5 Distrust of COVID-19 vaccine		Domain 6 Willingness to reconsider decision pending more information		Domain 7 Influenza vaccination received in 2020		Domain 8 Pneumococcal vaccination received in 2020	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Patients								
Rheumatologic Patients	1.29 (0.20 to 8.15)	0.781	3.08 (2.19 to 4.34)	<0.0001	1.60 (1.18 to 2.16)	0.002	2.23 (1.34 to 3.73)	0.002
Healthy controls	Ref.	–	Ref.	–	Ref.	–	Ref.	–
Age	0.99 (0.94 to 1.05)	0.930	0.99 (0.98 to 1.00)	0.250	1.05 (1.04 to 1.06)	<0.0001	1.06 (1.04 to 1.08)	<0.0001
Sex								
Female	0.30 (0.05 to 1.57)	0.155	1.37 (0.96 to 1.95)	0.078	1.04 (0.75 to 1.45)	0.778	0.89 (0.56 to 1.41)	0.630
Male	Ref.	–	Ref.	–	Ref.	–	Ref.	–

AEs, adverse events; RMD, rheumatic and musculoskeletal disease.

RMDs (online supplemental table 2). In more than half of the cases, the reason for refusal was disease-linked (28.4%, fear of AEs related to disease; 25.6%, fear of disease worsening; 43.5%, fear of AEs regardless of the disease; 2.7%, distrust in COVID-19 vaccine).

In conclusion, patients with RMDs may change their attitude to COVID-19 vaccination if properly informed about risks and benefits by their trusted specialist. Hence, rheumatologists should inform their patients transparently considering their doubts and concerns during follow-up visits or organise dedicated online patient meetings to influence the patient's health-related choices. Patient associations might be involved to give evidence-based advice to patients with RMDs.

Roberta Priori ^{1,2}, Greta Pellegrino ¹, Serena Colafrancesco ¹, Cristiano Alessandri ¹, Fulvia Ceccarelli ¹, Manuela Di Franco,¹ Valeria Ricciari ¹, Rossana Scrivo ¹, Antonio Sili Scavalli,¹ Francesca Romana Spinelli ¹, Fabrizio Conti ¹

¹Dipartimento di Scienze Cliniche, Internistiche, Anestesiologiche e Cardiovascolari-Reumatologia, Sapienza Università di Roma, Rome, Lazio, Italy

²UniCamillus, Saint Camillus International University of Health Sciences, Rome, Lazio, Italy

Correspondence to Dr Greta Pellegrino, Dipartimento di Scienze Cliniche, Internistiche, Anestesiologiche e Cardiovascolari- Reumatologia, Sapienza Università di Roma, Rome, Lazio, Italy; greta.pellegrino@uniroma1.it

Handling editor Josef S Smolen

Contributors RP and GP contributed to the design of the project, and drafted and revised the paper. SC was responsible for data analysis, and drafted and revised the paper. FC, VR, RS and FRS collected the data and revised the paper. CA, MDF, ASS and CF revised the paper.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; internally peer reviewed.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

This article is made freely available for use in accordance with BMJ's website terms and conditions for the duration of the covid-19 pandemic or until otherwise determined by BMJ. You may use, download and print the article for any lawful, non-commercial purpose (including text and data mining) provided that all copyright notices and trade marks are retained.

© Author(s) (or their employer(s)) 2021. No commercial re-use. See rights and permissions. Published by BMJ.



To cite Priori R, Pellegrino G, Colafrancesco S, et al. *Ann Rheum Dis* 2021;**80**:953–954.

Received 1 February 2021

Revised 5 February 2021

Accepted 8 February 2021

Published Online First 23 February 2021

Ann Rheum Dis 2021;**80**:953–954. doi:10.1136/annrheumdis-2021-220059

ORCID iDs

Roberta Priori <http://orcid.org/0000-0002-6695-1445>

Greta Pellegrino <http://orcid.org/0000-0002-1762-0770>

Serena Colafrancesco <http://orcid.org/0000-0001-7802-1192>

Cristiano Alessandri <http://orcid.org/0000-0003-4149-5321>

Fulvia Ceccarelli <http://orcid.org/0000-0001-5026-8783>

Valeria Ricciari <http://orcid.org/0000-0002-7507-5483>

Rossana Scrivo <http://orcid.org/0000-0002-2889-8962>

Francesca Romana Spinelli <http://orcid.org/0000-0003-1969-2097>

Fabrizio Conti <http://orcid.org/0000-0002-1897-049X>

REFERENCES

- Frederiksen LSF, Zhang Y, Foged C, et al. The long road toward COVID-19 herd immunity: vaccine platform technologies and mass immunization strategies. *Front Immunol* 2020;1817:11.
- 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 US 'hot spot'. *Ann Rheum Dis* 2020;79:1156–62.
- Akarsu B, Canbay Özdemir D, Ayhan Baser D, et al. While studies on COVID-19 vaccine is ongoing, the public's thoughts and attitudes to the future COVID-19 vaccine. *Int J Clin Pract* 2020:e13891.
- La Vecchia C, Negri E, Alicandro G, et al. Attitudes towards influenza vaccine and a potential COVID-19 vaccine in Italy and differences across occupational groups, September 2020. *Med Lav* 2020;111:445–8.
- Campochiaro C, Trignani G, Tomelleri A, et al. Potential acceptance of COVID-19 vaccine in rheumatological patients: a monocentric comparative survey. *Ann Rheum Dis* 2021. doi:10.1136/annrheumdis-2020-219811
- Grasselli G, Zangrillo A, Zanella A, et al. Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy region, Italy. *JAMA* 2020;323:1574–81.