Arthritis & Rheumatology
Vol. 74, No. 5, May 2022, pp e21–e36
DOI 10.1002/art.42109

American College of Rheumatology
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American College of Rheumatology Guidance for COVID-19 Vaccination in Patients With Rheumatic and Musculoskeletal Diseases: Version 4

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Due to the rapidly expanding information and evolving evidence related to COVID-19, which may lead to modification of some guidance statements over time, it is anticipated that updated versions of this article will be published, with the version number included in the title. Readers should ensure that they are consulting the most current version.

However, because of publication timelines, there may be more updated recommendations online at the ACR website that are pending journal peer review and full manuscript publication. Readers should check the ACR website at https://www.rheumatology.org/Practice-Quality/Clinical-Support/COVID-19-Guidance to confirm the ACR's most recent recommendations. The online version of the tables as they were originally published, as well as a summary of revisions over time and their location, are included in Supplementary Tables 2–6.

Guidance developed and/or endorsed by the American College of Rheumatology (ACR) is intended to inform particular patterns of practice and not to dictate the care of a particular patient. The ACR considers adherence to this guidance to be voluntary, with the ultimate determination regarding its application to be made by the physician in light of each patient's individual circumstances. Guidance statements are intended to promote beneficial or desirable outcomes but cannot guarantee any specific outcome. Guidance developed or endorsed by the ACR is subject to periodic revision as warranted by the evolution of medical knowledge, technology, and practice.

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Objective. To provide guidance to rheumatology providers on the use of COVID-19 vaccines for patients with rheumatic and musculoskeletal diseases (RMDs).

Methods. A task force was assembled that included 9 rheumatologists/immunologists, 2 infectious disease specialists, and 2 public health physicians. After agreeing on scoping questions, an evidence report was created that summarized the published literature and publicly available data regarding COVID-19 vaccine efficacy and safety, as well as literature for other vaccines in RMD patients. Task force members rated their agreement with draft consensus statements on a 9-point numerical scoring system, using a modified Delphi process and the RAND/University of California Los Angeles Appropriateness Method, with refinement and iteration over 2 sessions. Consensus was determined based on the distribution of ratings.

Results. Despite a paucity of direct evidence, statements were developed by the task force and agreed upon with consensus to provide guidance for use of the COVID-19 vaccines, including supplemental/booster dosing, in RMD patients and to offer recommendations regarding the use and timing of immunomodulatory therapies around the time of vaccination.

Conclusion. These guidance statements are intended to provide direction to rheumatology health care providers on how to best use COVID-19 vaccines and to facilitate implementation of vaccination strategies for RMD patients.

INTRODUCTION

The global pandemic caused by SARS–CoV-2 has caused untold disruption to nearly all aspects of human health globally. The substantial morbidity and excess mortality attributed to COVID-19 has had a major impact on health and the delivery of health care. Given the role that rheumatology providers have in serving patients with rheumatic and musculoskeletal diseases (RMDs) (1), particularly those with autoimmune and inflammatory rheumatic diseases (AIIRDs), there is an urgent need to optimize strategies to curb the incidence of COVID-19. In addition to preventive measures such as physical distancing, mask-wearing, handwashing, and shelter-in-place orders, available COVID-19 vaccines provide a powerful tool to mitigate the burgeoning growth of adverse outcomes resulting from COVID-19.

Given the leadership role of the American College of Rheumatology (ACR) in facilitating dissemination of high-quality evidence and promoting best practices for the care of RMD patients, the ACR periodically convenes task forces charged with developing methodologically rigorous clinical practice guidelines and guidance documents. Previous ACR guidelines developed for the management of rheumatoid arthritis (RA) and psoriatic arthritis (PsA) have included some information regarding optimal use of vaccines for patients with those conditions. However, because the immunologic principles related to the use of vaccines and the impact of vaccine-preventable illnesses on patients cross a broad range of RMDs, the ACR altered its approach in 2020 and convened a new guideline development group to focus exclusively on vaccination. This cross-cutting team was charged with developing encompassing vaccination considerations for all disease and treatment-related areas within rheumatology, rather than embedding them into narrower, disease-specific clinical practice guidelines.

The development process of ACR guidelines follows a rigorous and formal methodology, is based on a reproducible and transparent systematic literature review, incorporates panelist expertise from rheumatology health care professionals and input from related medical experts in other disciplines (e.g., infectious disease, epidemiology), includes direct participation by patients that reflects their values and preferences, and is typically conducted over an extended time frame (e.g., 1 year or longer). In contrast, the ACR develops "guidance" documents when the components needed to develop a formal guideline are not present, e.g., if the need to provide guidance is more urgent than a longer guideline timeline would allow, there is not enough peer-reviewed evidence available to conduct a formal literature review, or when there is very limited expertise and experience, particularly on the part of patients, to help inform the development of recommendations. In these situations, an expert task force is formed to provide the best guidance possible based on the limited information available. The ACR expects that guidance documents will need to be updated with some frequency as new data become available and greater experience is acquired.

Responding to the need to provide timely guidance to practicing clinicians, the ACR COVID-19 Vaccine Guidance Task Force was created as a branch of the ACR Vaccine Guideline effort, to summarize the available evidence for newly available COVID-19 vaccines and to make timely clinical recommendations to rheumatology providers for their optimal use. It relied on a limited evidence base derived from clinical trials evaluating the COVID-19 vaccines in non-RMD populations and also included indirect evidence regarding the immunogenicity, clinical effectiveness, and safety of other vaccines administered to RMD patients receiving various immunomodulatory therapies. Armed with this information, task force members were asked to extrapolate across diseases and integrate relevant basic science and immunologic principles to inform the use, timing, and prioritization of

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The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention/the Agency for Toxic Substances and Disease Registry.

Supported by the American College of Rheumatology. The effort of some individual authors was supported in part by the NIH (National Institute of Arthritis and Musculoskeletal and Skin Diseases grant P30-AR072583).

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Dr. Curtis has received consulting fees, speaking fees, and/or honoraria from AbbVie, Bristol Myers Squibb, GlaxoSmithKline, Eli Lilly, and Novartis (less than $10,000 each) and from Amgen, Janssen, Pfizer, Myriad, and Sanofi (more than $10,000 each) and research grants from Genentech, Gilead, AbbVie, Bristol Myers Squibb, GlaxoSmithKline, Eli Lilly, Amgen, Janssen, Pfizer, Myriad, and Sanofi. Dr. Johnson has received consulting fees, speaking fees, and/or honoraria from Ikarai and Boehringer Ingelheim (less than $10,000 each) and research grants from Bayer, Boehringer Ingelheim, Corbus, and GlaxoSmithKline. Dr. Baden has received salary support form the *New England Journal of Medicine* (less than $10,000). Dr. Calabrese has received consulting fees, speaking fees, and/or honoriaria from AbbVie and Sanofi Genzyme (less than $10,000 each). Dr. Gravallese has received salary support from the *New England Journal of Medicine* (more than $10,000). Dr. Mikuls has received consulting fees, speaking fees, and/or honoraria from Sanofi, Horizon, Pfizer, and Gilead (less than $10,000 each) and research support from Bristol Myers Squibb and Horizon. No other disclosures relevant to this article were reported.

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Submitted for publication February 16, 2022; accepted in revised form March 2, 2022.

the COVID-19 vaccines available in the US and apply them to the care of RMD patients.

METHODS

Convening the ACR COVID-19 Vaccine Guidance Task Force and defining the scope of the clinical guidance. In October 2020, the ACR began assembling the ACR COVID-19 Vaccination Guidance Task Force. Invitations were made following a general solicitation sent to the broad ACR membership seeking interested volunteers. The task force consisted of 13 members from North America and included 9 rheumatologists, 2 infectious disease specialists, and 2 public health experts. Rheumatology task force members were chosen to represent various areas of specialty expertise within the field and to achieve diversity in geographic region, career stage, practice setting, sex, and race/ethnicity, while also ensuring that the majority of task force members had no conflicts of interest. The task force defined the intended scope of the guidance based on input from individual members, and external input was obtained informally from various stakeholders. The process was informed by the previously published ACR Guidance for the Management of Rheumatic Disease in Adult Patients During the COVID-19 Pandemic (2). The scope of this guidance includes clinically relevant questions that were intended to inform rheumatology patient care related to COVID-19 vaccination and treatment considerations around the time of vaccination. The scoping questions were agreed upon by all panel members at an initial teleconference conducted on December 14, 2020.

Developing the evidence summary. The task force was divided into teams that worked in parallel, each charged with summarizing the published literature and other available evidence spanning 4 topics: 1) the efficacy, immunogenicity, and safety data derived from clinical trials of late-stage (i.e., phase III) COVID-19 vaccines ongoing within the US or COVID-19 vaccines already available under the US Food and Drug Administration (FDA) Emergency Use Authorization (EUA) act; 2) the epidemiology of COVID-19 risk and outcomes in RMD patients; 3) the attenuation of immunogenicity to other vaccines (e.g., influenza, pneumococcal) associated with certain immunomodulatory therapies; and 4) the safety profile (e.g., disease flare, new-onset autoimmune conditions) of non–COVID-19 vaccines in RMD populations. The scoping questions were grouped into these domains and distributed to the teams, which were tasked with gathering and summarizing evidence that addressed the questions within their assigned domains.

The task force agreed that the intended audience for the guidance was rheumatology health care providers managing their individual patients, but they felt that some attention should be directed to a societal perspective, when relevant, around the availability of COVID-19 vaccines and prioritization for individuals with RMDs. The task force took the perspective of developing guidance for a US audience, particularly in view of the fact that the review of COVID-19 vaccine clinical trials was US-focused. Recognizing that RMD patients exhibit high variability with respect to their underlying health conditions, disease severity, treatments, and degree of multimorbidity, these considerations were noted as important facets of individualizing care. Therefore, this guidance was not intended to supersede the judgment of rheumatology care providers nor override the values and perspectives of their patients. Foundational principles, guiding assumptions, and acknowledged limitations were discussed and agreed upon throughout the process (Table 1) and are discussed in this document where most relevant.

Table 1. Foundational principles, assumptions, and considerations for the guidance statements*

ACR guidance statements are not intended to supersede the judgment of rheumatology care providers nor override the values and perspectives of their patients. Guidance was, in some cases, based on weak and/or indirect evidence and required substantial extrapolation by an expert task force. All statements, therefore, should be considered conditional or provisional. The ACR is committed to updating this guidance document as new evidence emerges.
The rheumatology community lacks important knowledge on how to best maximize vaccine-related benefits. RMD patients exhibit high variability with respect to their underlying health condition, disease severity, treatments, degree of multimorbidity, and relationship with their specialist provider. These considerations must be considered when individualizing care.
There is limited direct evidence about mRNA COVID-19 vaccine safety and efficacy in RMD patients. There is no reason to expect vaccine harms will trump expected COVID-19 vaccine benefits in RMD patients.
Evidence about the mRNA COVID-19 vaccine suggests that the benefits outweigh the risks in RMD patients.
The risk of deferring vaccination and thus failing to mitigate COVID-19 risk should be weighed against a possible blunted response to the vaccine if given under suboptimal circumstances. As a practical matter, this tension must be resolved in the context of imperfect prediction as to whether those circumstances may be transient as well as a paucity of scientific evidence.
Both individual and societal considerations related to a limited vaccine supply should be considered in issuing vaccine guidance and making policy decisions. Given that context, simplicity should be the touchstone: to avoid confusion, improve implementation, and maintain scientific credibility.
In the future, the ability to give vaccine boosters will no longer be constrained by limited supplies. Any vaccination strategy is a reasonable starting point, and decisions about implementation details reflect tradeoffs in the allocation of scarce vaccine resources.

* ACR = American College of Rheumatology; RMD = rheumatic and musculoskeletal disease.

Development of the evidence review summary document. Given the accelerated time frame for guidance development, a nonsystematic evidence review was completed and included serial PubMed searches supplemented by postings from the Centers for Disease Control and Prevention (CDC); briefings and other documents available from the FDA, such as dossiers

submitted by vaccine manufacturers and transcripts of data presented at the FDA's Vaccines and Related Biological Products Advisory Committee meetings (3,4); and other electronic media sources. References and original articles related to vaccination were culled from the systematic literature reviews developed for ACR guidelines for the management of RA in 2012, 2015, and 2021 (5–7), PsA in 2018 (8), and vaccination guidelines for RMD patients published by European Alliance of Associations for Rheumatology (9–11). Articles were dated 1994 through January 2021 (English language, domestic and international).

The scoping questions and the relevant evidence reviews contributed by team members were collated into a single evidence summary document, which was disseminated by email to the entire task force for review 2 days prior to initial ratings. Following the development of the evidence summary, regular PubMed searches were undertaken, and new evidence was shared with the task force prior to follow-up webinars. As limited direct evidence was anticipated to be immediately available for use of the COVID-19 vaccine in RMD patients, no formal assessment of evidence quality (e.g., using Grading of Recommendations Assessment, Development and Evaluation methodology [12]) was attempted, and all evidence was assumed to be indirect. For this reason, all guidance statements should be considered as provisional, or "conditional," until further evidence becomes available.

Initial ratings. The standard guideline development processes currently used by the ACR (13) were deemed to be too time-intensive to be feasible, given the immediate need for the guidance document. Therefore, following distribution of the evidence review document, the scoping questions were transformed into proposed positive statements for which task force members were asked to rate their initial agreement or disagreement. These statements were grouped into 4 broad categories: 1) general medical considerations that provided foundational information for the guidance document; 2) specific recommendations related to COVID-19 vaccination in RMD patients; 3) treatment-specific considerations regarding the timing of COVID-19 vaccination; and 4) the timing of RMD treatments in relation to vaccine administration.

A modified Delphi approach conducted as part of the RAND/University of California at Los Angeles Appropriateness Method (14) was used for guidance development. This method has been used for some past ACR guidelines and the more recent ACR COVID-19 guidance (15); it has been shown to be reproducible and to have content, construct, and predictive validity. Using this method, an initial round of rating was conducted anonymously by email. Task force members were asked to rate their level of agreement, and all votes were weighted equally. Voting was completed using a numerical rating scale of 1–9 for all items. Ratings of 9 corresponded to "complete agreement," 5 to "uncertain," and 1 to "complete disagreement." Median ratings for each statement falling into intervals of 1–3, 4–6, and 7–9 were interpreted as disagreement, uncertainty, and agreement, respectively. Agreement with each of the proposed guidance statements submitted by individual panel members was tabulated for the entire panel and used to classify consensus. Consensus was deemed "strong" when all 13 panel members' ratings fell within a single tertile (e.g., 7–9, indicative of agreement); all other combinations were considered to reflect "moderate" consensus. A lack of consensus was identified when the median rating fell into the uncertain range (4–6 interval), or more than one-quarter of the ratings fell into the opposite extreme tertile from the median (e.g., ≥4 panelists rated 1–3 [disagree] when the overall median rating was in the 7–9 [agree] range) (14).

Review and iteration for the ratings of the proposed guidance statements by the task force. Results from the first round of rating were reviewed and discussed in a task force webinar on January 15, 2021. Discussion was focused on statements for which there was no consensus. Individuals were given the opportunity to comment on all items presented in the initial rating process. Informed by voting results and the group discussion, the task force members refined the wording of several of the rated statements.

Revised statements were sent back to task force members and agreement was again assessed by email, using the same scoring approach described above. Results from the second round of voting were presented to the task force via webinar on January 22, 2021, and minor text revisions were made iteratively in real time until consensus was achieved. A draft manuscript was developed describing the results of the rating process, and all coauthors were given an opportunity to provide direct edits to the document. The ACR Guidance Subcommittee and ACR Quality of Care Committee were given the document in order to provide feedback. It was subsequently sent to the ACR Board of Directors, which approved these recommendations on February 8, 2021. Public vetting of the guidance document was held via an electronic and widely publicized "town hall" held on February 16, 2021 that was open to ACR members and the public, with questions solicited in advance and during the town hall webinar. Finally, given the multitude of uncertainties and evidence gaps considered by the task force, the panel proposed a research agenda of high-impact topics that would advance the science and inform the optimal use of COVID-19 vaccines in RMD patients treated with immunomodulatory therapies. After publication, an ACR project librarian will refresh the specified literature search on a regular basis and submit new articles to the task force for review, and this document will be updated through a similar process as new evidence emerges.

RESULTS

Of the guidance statements considered across the 2 rounds of ratings, the majority were rated with a median score of 7, 8, or

Table 2. General considerations related to COVID-19 vaccination in patients with RMD*

Statement domain	Guidance statement	Level of task force consensus
Clinical practice	The rheumatology health care provider is responsible for engaging the RMD patient in a discussion to assess COVID-19 vaccination status.	Strong
Clinical practice	The rheumatology health care provider is responsible for engaging the RMD patient in a shared decision-making process to discuss receiving the COVID-19 vaccine.	Moderate
Epidemiology	AIIRD patients are at higher risk for incident viral infections compared to the general population.	Moderate
Epidemiology	After considering the influence of age and sex, AIIRD patients are at higher risk for COVID-19 hospitalization compared to the general population.	Moderate
Epidemiology	Acknowledging heterogeneity due to disease- and treatment-related factors, AIIRD patients have worse outcomes associated with COVID-19 compared to the general population of similar age and sex.	Moderate
Epidemiology	Across AIIRD conditions, and within any specific disease, there is substantial variability in disease- and treatment-related risk factors for COVID-19 that may put some patients at higher risk than others.†	Moderate
Public health	Based on increased risk for COVID-19, AIIRD patients should be prioritized for vaccination before the nonprioritized general population of similar age and sex.	Moderate
Vaccine safety	Beyond known allergies to vaccine components, there are no known additional contraindications to COVID-19 vaccination for AIIRD patients.	Moderate
Vaccine effectiveness	The expected response to COVID-19 vaccination for many AIIRD patients receiving systemic immunomodulatory therapies is blunted in its magnitude and duration compared to the general population.	Moderate
Disease-related	As a general principle, vaccination should optimally occur in the setting of well-controlled AIIRD.	Moderate
Disease-related	A potential risk exists for AIIRD flare or disease worsening following COVID-19 vaccination.	Moderate
Vaccine safety	The benefit of COVID-19 vaccination for RMD patients outweighs the potential risk for new-onset autoimmunity.	Moderate

* RMD = rheumatic and musculoskeletal disease.
† For examples of these autoimmune and inflammatory rheumatic disease (AIIRD) conditions, see Supplementary Table 1, on the *Arthritis & Rheumatology* website at http://onlinelibrary.wiley.com/doi/10.1002/art.42109.

9 (i.e., agreement), and 3 of them were not agreed upon. Among the statements achieving agreement, consensus was strong for 9 and moderate for the remainder. One guidance statement related to COVID-19 vaccination in children was rated with a median value of 5 (uncertain) by the task force, in part reflecting the desire to obtain more feedback from pediatric rheumatology providers. Additional input was therefore sought from the ACR Pediatric Rheumatology Clinical Guidance Task Force. This task force has acknowledged ongoing clinical trials of COVID-19 vaccines in children and evolving FDA EUAs for the COVID-19 vaccine in children younger than age 16 years, although it recognized that ≥1 COVID-19 vaccine clinical trial has enrolled patients as young as age 5 years (ClinicalTrials.gov identifiers: NCT04649151 and NCT04368728) (16–19). On this basis, our task force and the Pediatric Task Force have consistently recommended to await appropriate evidence from clinical trials regarding the safety and effectiveness of COVID-19 vaccination in children and align our guidance with FDA EUAs. The second statement for which the task force was unable to reach consensus relates to vaccination in the context of ongoing treatment with high-dose glucocorticoids, discussed in detail below.

General considerations related to vaccination against COVID-19 in patients with RMDs. Twelve guidance statements related to general considerations of COVID-19 vaccination in RMD patients achieved consensus (Table 2). Statements were descriptively categorized into ≥1 domain to facilitate ease of reference. The panel concurred that rheumatology health care providers were responsible for engaging RMD patients in discussions to assess whether they had been vaccinated against COVID-19 and to document related details (e.g., which vaccine had been administered, timing of vaccination, whether the series had been completed). For those not vaccinated, and similar to other vaccination guidelines for immunocompromised patients such as those from the Infectious Diseases Society of America (20,21), it was thought that the rheumatology provider should share responsibility with the patients' primary care provider (when available) to ensure appropriate vaccinations are administered. Rheumatology providers should also engage patients in a shared decision-making process to discuss the following: their attitudes, intent, and concerns related to vaccination; local incidence of COVID-19; individual circumstances (e.g., disease activity, medications, comorbidities) that may affect risk; ability to adhere to nonpharmacologic public health interventions; and vaccine efficacy and potential safety concerns (e.g., local or systemic reactogenicity, potential for disease worsening or flare).

The epidemiology of viral infection risk in RMD patients, and specifically, the risk for infection due to SARS–CoV-2, was then discussed. For this topic, the task force elected to narrow the scope of the patient population under consideration and define a presumably higher-risk subgroup of patients with RMDs. Some RMD conditions would include those managed by rheumatology

providers but not generally associated with high levels of systemic inflammation (e.g., osteoarthritis, fibromyalgia, osteoporosis) and for which conventional, biologic, or targeted synthetic disease-modifying antirheumatic drugs (DMARDs) or other therapies with immunosuppressive effects are typically not indicated. The patient population was thus restricted to those with AIIRDs (see Supplementary Table 1 for definitions, available on the *Arthritis & Rheumatology* website at http://onlinelibrary.wiley.com/doi/10.1002/art.42109). Among these individuals, the risk for incident viral infections (e.g., herpes zoster) was rated as being higher than in the general population (22–24). There was also agreement that AIIRD patients are likely to be at increased risk for hospitalized SARS–CoV-2 infection (25–29) and that age, race/ethnicity (especially for underrepresented minorities), and sex were important risk factors that needed to be considered (30–33) in evaluating risk at the individual patient level.

Multimorbidity was felt to likewise play an important role in the risk for developing COVID-19. While some population-based epidemiologic studies of COVID-19 incidence and outcomes in AIIRD patients have controlled for general multimorbidity or specific comorbidities (25,26,34), the panel recognized that some comorbidities that increase infection risk were shared risk factors for development of AIIRDs (e.g., smoking and related pulmonary conditions associated with incident RA). These may represent direct manifestations such as interstitial lung disease associated with some AIIRDs, or they could be downstream sequelae causally related to the underlying inflammatory processes of AIIRDs or their treatment (e.g., premature and advanced atherosclerotic vascular disease in systemic lupus erythematosus (SLE) patients; obesity, diabetes, and features of the metabolic syndrome in PsA patients or those receiving long-term glucocorticoids). For that reason, adjustment for these comorbidities might be inappropriate and would underestimate the risk of COVID-19 infection in patients with AIIRDs. Therefore, age- and sex-adjusted risk estimates were preferred by some task force members when comparing risk and outcomes of COVID-19 in AIIRD patients to the general population.

The few large population-based studies of COVID-19 incidence and outcomes in AIIRD patients had minimal demographic diversity, and therefore race/ethnicity could not be easily evaluated as an independent risk factor. Finally, the panel acknowledged challenges in being able to disentangle the independent role of the disease activity and severity of various AIIRDs from the medications used to treat them (e.g., higher-dose glucocorticoids [35]), so-called confounding by severity, as risk factors for worse COVID-19 outcomes.

Despite these important methodologic caveats and acknowledged limitations in the evidence base, AIIRD patients were rated as having worse outcomes (e.g., need for intensive care unit [ICU] treatment, mechanical ventilation, persistent infection, death) following COVID-19 compared to patients of similar age and sex without such conditions (25–29,36). In terms of the policy implications of this reasoning, the task force agreed that in general, AIIRD patients should be prioritized to be allocated to receive vaccination before the nonprioritized general population of similar age and sex (37). The panel recognized important heterogeneity across AIIRD conditions, such that (for example) an RA patient with quiescent disease treated only with hydroxychloroquine likely has a lower risk for COVID-19 and adverse outcomes compared to a patient with very active vasculitis treated with intravenous (IV) cyclophosphamide or rituximab (RTX) and high-dose glucocorticoids (33), although the protection conferred by COVID-19 vaccination may also differ greatly.

Turning attention to vaccination of individual patients, the task force felt that there were no additional known contraindications to receipt of the COVID-19 vaccine other than known allergies to vaccine components as stipulated by guidance from the CDC (38). Extrapolating evidence derived from studies of other vaccines, the expected response to vaccination in many AIIRD patients receiving certain systemic immunomodulatory therapies was deemed likely to be blunted, albeit with uncertain diminution in either the magnitude or duration of response compared to the general population (38,39). The task force acknowledged a paucity of direct evidence supporting this assertion and placed great importance on prioritizing this topic as part of a future research agenda. The timing of vaccination was considered more ideal in the setting of well-controlled disease, yet the task force noted that patients and their providers should not be dissuaded from vaccination under less-than-ideal conditions, with additional timing considerations as discussed below.

Based on data derived from the published literature, a potential risk for a flare of the patient's underlying AIIRD following vaccination was acknowledged. For example, based on randomized controlled trial data (40), the frequency of flare was higher in RA patients randomized to have methotrexate (MTX) withheld at the time of influenza vaccination compared to those randomized to continue (10.6% versus 5.1%, respectively), with flare defined as an increase in the Disease Activity Score in 28 joints (DAS28) of >1.2, or >0.6 if the baseline DAS28 was ≥3.2 (41). A subsequent pooled analysis that included that trial and another showed that while the mean change in DAS28 did not differ between groups, the adjusted flare rate in the 2-week withhold group (MTX withhold) was 2.90-fold higher (95% confidence interval 0.96–4.56, $P = 0.063$) compared to the group that continued MTX (MTX continue), with a difference in proportions experiencing flare of 10.8% (MTX withhold group) versus 5.8% (MTX continue group) (40,42–44). This risk of flare or disease worsening was catalogued as an important topic slated for the future research agenda. Finally, although some new-onset AIIRDs (e.g., RA, vasculitis) or flares of preexisting AIIRDs have been reported after COVID-19 in published case reports (45,46), the expected benefit of vaccination for AIIRD patients was thought to outweigh any theoretical risk for the development of new-onset autoimmune conditions or

Table 3. Recommendations for primary and supplemental dosing of the COVID-19 vaccine in RMD patients*

Statement domain	Guidance statement	Level of task force consensus
Clinical practice	RMD patients should receive COVID-19 vaccination, consistent with the age restriction of the EUA and/or FDA approval.†	Strong
Clinical practice	RMD patients without an AIIRD who are receiving immunomodulatory therapy should be vaccinated in a similar manner as described in this guidance as AIIRD patients receiving those same treatments.	Moderate
Vaccine effectiveness/ safety	**For AIIRD patients who are not yet vaccinated, either of the mRNA vaccines is recommended over the Johnson & Johnson vaccine. There is no recommendation for one mRNA vaccine over another.**	**Moderate**
Vaccine effectiveness	For a multidose vaccine, AIIRD patients should receive the second dose of the same vaccine, even if there are nonserious adverse events associated with receipt of the first dose, consistent with timing described in CDC guidelines (32).	Strong
Clinical practice	**For patients who previously completed the 2-dose mRNA series, an additional COVID-19 vaccine dose is recommended ≥28 days after the completion of the vaccine series for AIIRD patients receiving any immunosuppressive or immunomodulatory therapy other than hydroxychloroquine monotherapy.**	**Moderate**
Clinical practice	**For patients who previously completed the mRNA COVID-19 vaccine series or 1-dose J&J COVID-19 vaccine, and who are receiving a booster dose, an mRNA vaccine supplemental dose of either type (Pfizer or Moderna) is preferred.**	**Moderate**
Clinical practice	Health care providers should not routinely order any laboratory testing (e.g., antibody tests for IgM and/or IgG to spike or nucleocapsid proteins) to assess immunity to COVID-19 postvaccination, nor to assess the need for vaccination in an as-yet-unvaccinated person.‡	Strong
Public health	Following COVID-19 vaccination, RMD patients should continue to follow all public health guidelines regarding physical distancing and other preventive measures.§	Strong
Clinical practice	**AIIRD patients at high risk for poor outcomes related to COVID-19 should receive monoclonal antibody therapy, either as prevention (i.e., post-exposure prophylaxis for asymptomatic, recently exposed patients) or as treatment for newly symptomatic patients, if licensed or approved under FDA EUA.**	**Moderate**
Clinical practice/public health	Household members and other frequent close contacts of AIIRD patients should undergo COVID-19 vaccination when available to them to facilitate a "cocooning effect" that may help protect the AIIRD patient. No priority for early vaccination is recommended for household members.	Moderate
Vaccine effectiveness/ disease-related	While vaccination would ideally occur in the setting of well-controlled AIIRD, except for AIIRD patients with life-threatening disease (e.g., in the ICU for any reason), COVID-19 vaccination should occur as soon as possible for those for whom it is being recommended, irrespective of disease activity and severity.	Strong
Vaccine effectiveness/ disease-related	In AIIRD patients with life-threatening disease (e.g., in the ICU for any reason), COVID-19 vaccination should be deferred until their disease is better controlled.	Moderate
Vaccine effectiveness/ disease-related	AIIRD patients with active but non–life-threatening disease should receive COVID-19 vaccination.	Strong
Vaccine effectiveness/ disease-related	AIIRD patients with stable or low disease activity AIIRDs should receive COVID-19 vaccination.	Strong
Vaccine effectiveness/ disease-related	AIIRD patients not receiving immunomodulatory treatments should receive the first dose of the COVID-19 vaccine prior to initiation of immunomodulatory therapy when feasible.	Moderate

* Boldface text indicates updates that were added to the version 4 summary document at the end of 2021. RMD = rheumatic and musculoskeletal disease; EUA = Emergency Use Authorization; FDA = US Food and Drug Administration; AAIRD = autoimmune and inflammatory rheumatic disease; CDC = Centers for Disease Control and Prevention; ICU = intensive care unit.
† Age ≥5 years as of October 29, 2021.
‡ Given uncertainties in the interpretation of laboratory testing following vaccination as it would impact clinical decision-making, the panel reaffirmed this statement in Version 4 of this guidance document.
§ The task force discussed the possibility of recommending additional and more sustained public health measures for patients with AIIRD. After deliberation, they did not elect to exceed current public health authority guidance given uncertainties about the clinical effectiveness of vaccination in such patients. The appropriateness for continued preventive measures (e.g., masking, physical distancing) should be discussed with patients as their rheumatology providers deem appropriate.

other potentially immune-mediated manifestations or abnormalities (e.g., Bell's palsy, Guillain-Barré syndrome, anti-RNA antibodies in SLE patients, immune thrombocytopenic purpura) following vaccination.

Indications for vaccination and timing considerations. As summarized in Table 3, and consistent with guidance from the CDC for the general US population, the panel recommended that RMD and AIIRD patients be offered and receive vaccination against SARS–CoV-2. Discussion was held regarding the age cutoff for vaccination, and the panel agreed that guidance should be made consistent with the EUA of available vaccines (i.e., age ≥5 years as of October 29, 2021), with the potential for that cutoff to change in the future based on future revisions to EUAs for existing vaccines, forthcoming EUAs for new vaccines, or age restrictions applicable to FDA licensure.

Recommendations on which patients should be vaccinated were extended to patients with RMDs who did not have conditions typically considered to be AIIRDs but for which immunomodulatory or DMARD therapies might be used off-label. For example, patients with erosive osteoarthritis might receive MTX, or gout patients treated with pegloticase might be concomitantly treated with MTX to reduce pegloticase immunogenicity. These circumstances, in which MTX or another immunomodulatory therapy is being used for a non-AIIRD condition, would be treated synonymously with the guidance for MTX offered in this document. However, within the category of patients with AIIRDs and/or those receiving immunomodulatory therapies, substantial heterogeneity of disease- and treatment-related risk factors was noted. Some AIIRD patients were expected to be at higher risk for infection and morbidity than others, and thus the impetus for COVID-19 vaccination might be stronger for some individual patients or patient groups (e.g., patients with SLE receiving cytotoxic therapy and higher-dose glucocorticoids, or patients receiving RTX therapy), although the vaccine might be less effective in these same individuals.

Extensive discussion was held regarding whether consideration for a particular vaccine or vaccine platform (e.g., messenger RNA [mRNA] versus adenoviral vector) might be preferred in general, or for select patients, based on potential differences in effectiveness or safety. Based on the task force members' ratings and the vaccine options in the US, the expert panel reached consensus on the guidance that RMD patients undergoing vaccination are recommended to receive whichever SARS–CoV-2 mRNA vaccine is available to them. Either of the mRNA vaccines is recommended over the single-dose Johnson & Johnson vaccine. The task force noted that none of the other SARS–CoV-2 vaccine candidates in development would be classified as a canonical live virus vaccine, including the adenoviral vector–based vaccines which are replication deficient (47). Thus, the usual prohibitions against the use of live virus vaccines in immunosuppressed patients do not apply.

Following receipt of the first dose in a vaccine series, patients were recommended to receive the second dose of the same type of vaccine, assuming no contraindication to the second dose per CDC guidance (e.g., a severe allergic reaction, or an immediate allergic reaction of any severity to the vaccine or any of its components, including polyethylene glycol) (37,48). Persons who develop SARS–CoV-2 infection between the first and second dose of a 2-dose vaccine series should delay the second dose until they have recovered from the acute illness (if symptomatic) and discontinued isolation, and then they should receive the second dose without delay (37,48). Consistent with CDC guidance (48), SARS–CoV-2–infected patients who received monoclonal antibodies (e.g., bamlanivimab, casirivimab, imdevimab) or convalescent plasma as part of treatment for COVID-19 are no longer recommended to defer vaccination following receipt of antibody products (anti–SARS–CoV-2 monoclonal antibodies or convalescent plasma). Also consistent with CDC guidance (48), providers may co-administer other vaccines at the same time as COVID-19 vaccines, and without regard to the timing of other vaccines.

For patients who previously completed the 2-dose mRNA series or received the 1-dose Johnson & Johnson COVID-19 vaccine, a supplemental/booster COVID-19 vaccine dose is recommended ≥28 days after the completion of the vaccine series. This guidance applies to AIIRD patients receiving any immunosuppressive or immunomodulatory therapy other than hydroxychloroquine monotherapy. In making this statement, the task force recognized the high potential for confusion related to nomenclature between an additional primary dose and a booster dose. A "third dose" is the term typically used to refer to an additional primary dose of a vaccine given to patients who previously completed the primary vaccine series (i.e., the 2-dose mRNA vaccine series) and who may have mounted a suboptimal response due to immunosuppressive medications or an immunocompromised medical condition (48–53). In contrast, a "booster dose" refers to an additional dose given to patients who are expected to have mounted an adequate response but in whom the response may have waned over time (e.g., ≥6 months) (48,53–59). For patients who already received a third dose, the booster may be a "fourth dose" (48). The timing of an additional primary/third dose might occur as early as 28 days after completion of the primary vaccine series, whereas a booster dose likely would be given ≥6 months later (48).

While these are distinct scenarios, the task force sought to simplify the nomenclature in relation to its guidance statements and therefore adopted a composite term "supplemental/booster dose" throughout the remainder of this document. The task force reviewed the evidence for homologous versus heterologous (i.e., "mix and match" supplemental/booster dosing) (60–67). After consideration, and similar to the preference for an mRNA vaccine for primary vaccination, patients who previously completed the mRNA COVID-19 vaccine series or 1-dose Johnson & Johnson COVID-19 vaccine are recommended to receive an mRNA vaccine supplemental/booster dose, either Pfizer or Moderna (68–70).

Thus far, there is no proven laboratory-based immune correlate of protection against SARS–CoV-2 following natural infection or vaccination. Moreover, some commercially available SARS–CoV-2 serologic assays do not detect antibody responses to spike protein generated by the currently available mRNA vaccines, but rather measure antibodies to nucleocapsid protein. Therefore, the task force recommended that health care providers not do any of the following: routinely order laboratory testing to assess the need for vaccination in an unvaccinated person, screen for asymptomatic SARS–CoV-2 shedding, or assess SARS–CoV-2 immunity following vaccination. The task force expressed strong interest in modifying this guidance once additional data evolve regarding the potential utility of laboratory-based testing that might be helpful in select patients.

AIIRD patients at high risk for poor outcomes related to COVID-19 were recommended to receive monoclonal antibody therapy with casirivimab and imdevimab (Regeneron) if available, either as prevention (i.e., post-exposure prophylaxis for asymptomatic, recently exposed patients) or as treatment for newly symptomatic patients. Household members and other frequent close contacts of AIIRD patients were recommended to undergo COVID-19 vaccination when available, in order to facilitate a "cocooning effect" that may help protect at-risk AIIRD patients. However, the priority for vaccination for these close contacts should not be elevated for this reason.

A series of statements were rated by the panel with respect to the general timing of COVID-19 vaccination in relation to AIIRD disease activity, again acknowledging a dearth of direct evidence. Except for those with severe and life-threatening illness (e.g., a hospitalized patient receiving treatment in the ICU for any condition), vaccination was recommended irrespective of disease activity and severity. Even for ICU-treated patients for whom vaccination was recommended to be deferred for a short time, the task force felt that when the patient was well enough to be discharged from the hospital, vaccination would likely be appropriate. Acknowledging a balance between vaccinating and obtaining a blunted but still modest response, and the duty to allocate vaccine resources toward the settings in which they are likely to have the greatest benefit, the panel identified this scenario as an important evidence gap. For AIIRD patients in other settings, including those with either active but non–life-threatening disease, and certainly for patients with stable and/or low disease activity, vaccination was recommended. Finally, patients naive to or not currently receiving immunomodulatory therapies were recommended to receive their first dose of vaccine without delay. Additional considerations for medication timing are subsequently discussed.

Treatment-specific timing of primary vaccination. There was recognition that the ability to carefully time COVID-19 vaccination is sometimes limited in a real-world setting, and the overarching view was that COVID-19 vaccination should be given rather than not given if timing in relation to immunomodulatory drugs is not under the provider's or patient's control.

Strong consensus was achieved regarding the statement to not delay COVID-19 vaccination for patients receiving hydroxychloroquine, sulfasalazine, leflunomide, apremilast, or IV immunoglobulin (10,71). A similar recommendation with moderate consensus was achieved for most of the remaining immunomodulatory therapies considered (72–83).

One exception was RTX (10,11,84–88), for which the panel recommended to schedule vaccination such that the vaccine series would be initiated ~4 weeks prior to the next scheduled RTX dose. For example, a patient receiving RTX as a 2-dose cycle (spaced 2 weeks apart), with cycles repeating every 6 months, would be recommended to initiate vaccination ~5 months after the start of the prior RTX cycle. RTX dosing could then be resumed 2–4 weeks after the second COVID-19 vaccination, as discussed in the next section. Those receiving RTX cycles at 4-month intervals would initiate vaccination 3 months after the prior RTX cycle. In order to follow this recommendation, the task force invoked the assumption that a patient's COVID-19 risk was low or able to be mitigated by preventive health measures. The rationale for this recommendation comes from a study demonstrating minimal response to influenza vaccination in 11 patients vaccinated 4–8 weeks after RTX treatment, with modestly restored responses in patients vaccinated 6–10 months after their last RTX dose (89), as well as data demonstrating that B cell–depleting therapy greatly attenuates the response to COVID-19 vaccination (90).

As the second statement for which consensus was not achieved, the panel was uncertain about whether to delay vaccination if an AIIRD patient was receiving glucocorticoids at a prednisone-equivalent dose of ≥20 mg per day. Controversy stemmed as to whether vaccine response might be blunted in this circumstance, which may relate to the glucocorticoids themselves or to the presumably high disease activity and severity (91,92). Other factors discussed included the disease being treated and the medical management considerations if the patient were to manifest systemic reactogenicity (e.g., persistent high fever). Concern regarding an attenuated response to the vaccine in this circumstance would be partially mitigated if there was a possibility to later order serologies or other laboratory tests, and clinicians were able to assess vaccine-induced immunity and administer a booster or revaccinate if needed. However, such laboratory-based correlates of protection are not currently available.

Use and timing of immunomodulatory therapies in relation to COVID-19 vaccination administration. The task force continued to update its literature review through October 2021, including published information regarding the immunogenicity and safety of primary vaccination in RMD patients (68,69,93) and the literature on supplemental/booster vaccine dosing in non-RMD patients (94,95). Considering the goal to align guidance for recommendations related to primary vaccination, additional primary vaccination, and booster dosing to facilitate ease of implementation, the task force harmonized their recommendations for the use and timing of immunomodulatory therapies related to all vaccine administrations. Updated recommendations are shown in Table 4.

Based on some evidence that immunosuppressive therapies may attenuate vaccine response (68,96–98), for abatacept, belimumab, and most conventional (e.g., mycophenolate mofetil, MTX, azathioprine) and targeted (e.g., JAK inhibitor) immunomodulatory therapies, the task force recommended to withhold these for 1–2 weeks after each COVID-19 vaccine dose, assuming disease activity allows. For biologics that inhibit certain cytokines (e.g., tumor necrosis factor, interleukin-6 receptor [IL-6R],

Table 4. Guidance related to the use and timing of immunomodulatory therapies in relation to COVID-19 vaccination administration in RMD patients*

Medication(s)	Timing considerations for immunomodulatory therapy and vaccination	Level of task force consensus
Abatacept (IV)	**Time vaccination to occur 1 week prior to the next dose of abatacept (IV).**	**Moderate**
Abatacept (SC)	**Withhold for 1–2 weeks (as disease activity allows) after each COVID-19 vaccine dose.**	**Moderate**
Acetaminophen, NSAIDs	Assuming that disease is stable, withhold for 24 hours prior to vaccination. No restrictions on use postvaccination if symptoms develop.	Moderate
Belimumab (SC)	**Withhold for 1–2 weeks (as disease activity allows) after each COVID-19 vaccine dose.**	**Moderate**
TNFi, IL-6R, IL-1Ra, IL-17, IL-12/23, IL-23, and other cytokine inhibitors†	**The task force failed to reach consensus on whether or not to temporarily interrupt these following each COVID-19 vaccine dose, including both primary vaccination and supplemental/ booster dosing.**	**Moderate**
Cyclophosphamide (IV)	**Time cyclophosphamide administration so that it will occur ~1 week after each vaccine dose, when feasible.**	**Moderate**
Hydroxychloroquine	**No modifications to either immunomodulatory therapy or vaccination timing.**	**Strong**
Rituximab or other anti-CD20 B cell–depleting agents	**Discuss the optimal timing of dosing and vaccination with rheumatology provider before proceeding.‡**	**Moderate**
All other conventional and targeted immunomodulatory or immunosuppressive medications (e.g., JAK inhibitors, MMF) except for those listed above§	**Withhold for 1–2 weeks (as disease activity allows) after each COVID-19 vaccine dose.**	**Moderate**

* This guidance applies to both primary vaccination and supplemental/booster dosing. Boldface text indicates updates that were added to the version 4 summary document at the end of 2021. For details on the history of updates to these guidance statements, see Supplementary Table 6, on the *Arthritis & Rheumatology* website at http://onlinelibrary.wiley.com/doi/10.1002/art.42109. RMD = rheumatic and musculoskeletal disease; IV = intravenous; SC = subcutaneous; NSAIDs = nonsteroidal antiinflammatory drugs; TNFi = tumor necrosis factor inhibitor.
† Examples of cytokine inhibitors include the following: for interleukin-6 receptor (IL-6R), sarilumab and tocilizumab; for IL-1 receptor antagonist (IL-1Ra), anakinra and canakinumab; for IL-17, ixekizumab and secukinumab; for IL-12/IL-23, ustekinumab; for IL-23, guselkumab and rizankizumab.
‡ Some practitioners measure CD19 B cells as a tool with which to time the booster and subsequent rituximab dosing. For those who elect to dose without such information, or for whom such measurement is not available or feasible, a supplemental vaccine dose 2–4 weeks should be provided before next anticipated rituximab dose (e.g., at month 5.0 or 5.5 in patients being administered rituximab every 6 months).
§ Includes apremilast, azathioprine, calcineurin inhibitors, cyclophosphamide (oral), IV immunoglobulin, leflunomide, methotrexate, JAK inhibitors (tofacitinib, upadacitinib, baricitinib), mycophenolate mofetil (MMF), and sulfasalazine.

IL-1R, IL-17, IL-12/23, IL-23), the task force failed to reach consensus on whether or not to temporarily interrupt these following each COVID-19 vaccine dose. Some panel members felt that withholding treatment for 1–2 weeks was unnecessary, had minimal effect on vaccine response (68,99), and could put the patient at greater increased risk for disease to worsen. In contrast, other task force members felt that even limited evidence suggesting the possibility that these therapies could attenuate vaccine response should result in a recommendation of a temporary interruption of therapy (100,101). For that reason, no consensus was reached, and decision-making was deferred to the discretion of individual providers and patients.

Hydroxychloroquine was a notable exception, as the task force recommended that this therapy not be interrupted. Given the complexities of RTX dosing for RA, vasculitis, and other potential off-label uses (e.g., SLE), as well as the substantial literature suggesting that vaccine response is attenuated by B cell–depleting therapies (68,96,102,103), the task force recommended that patients discuss the optimal timing of RTX and other B cell–depleting therapies and vaccination timing with their rheumatology provider before proceeding. While some clinicians measure CD19 B cells and use the information to time the vaccine booster and subsequent RTX dosing, this option may not be available in community practice settings. For those who elect to dose B cell–depleting therapies without such information, or for whom such measurement is not available or feasible, additional doses of the vaccine were recommended 2–4 weeks before the next anticipated dose (e.g., at month 5.0 or 5.5 for patients on an recurring 6-month RTX dosing schedule).

Finally, based on the literature suggesting that acetaminophen and/or nonsteroidal antiinflammatory drugs may somewhat impair vaccine response (104), the task force recommended withholding these for 24 hours prior to vaccination, assuming that disease is stable. There was no prohibition against their use in patients who experience local or systematic symptoms postvaccination (48).

Table 5. Research agenda for future COVID-19 vaccine studies in RMD patients proposed by the task force*

Conduct clinical efficacy and laboratory-based immunogenicity studies in RMD patients following vaccination, especially for AIIRD patients receiving certain immunomodulatory therapies (e.g., methotrexate, abatacept, JAK inhibitors, rituximab, mycophenolate, GCs).
Optimize response to primary vaccination and supplemental/booster dose by considering timing related to intentional short-term cessation of certain immunomodulatory therapies (e.g., methotrexate, subcutaneous abatacept, JAK inhibitors, mycophenolate mofetil) to optimize vaccine response.
Evaluate risk of disease flare, disease worsening, and systemic reactogenicity following COVID-19 vaccination in RMD patients, by disease and in relation to background immunomodulatory therapies.
Directly compare vaccines and vaccine platforms for the above efficacy, immunogenicity, and safety outcomes: notable given the potential for some COVID-19 vaccines to achieve the minimum threshold for the FDA's EUA yet have seemingly lower vaccine efficacy based on large clinical trials in non-RMD patients.
Long-term follow-up for durability and magnitude of vaccine protection in relation to various immunomodulatory medications, and as new SARS–CoV-2 strains emerge.
Assess benefits and timing of additional COVID-19 vaccine administration (i.e., booster doses).
Generate real-world evidence (e.g., large pragmatic trial or observational studies) embedded in routine clinical practice to study the above topics, especially to promote large-scale safety surveillance.
Establish a biorepository with associated clinical data infrastructure to facilitate future COVID-19 (and possibly other) vaccine-related research in RMD patients, considering the future potential to identify laboratory-based correlates of protection relevant for individual patients.
Identify laboratory-based serologic testing to identify patients with a suboptimal response to COVID-19 vaccination who might be candidates for a booster dose or need to repeat the vaccination series.
Evaluate the impact of coadministration of the COVID-19 vaccine given concurrently with other, non–live-virus vaccines (e.g., shingles, influenza, pneumococcal) on vaccine immunogenicity and tolerability.
Optimize approaches to address vaccine hesitancy for high-risk RMD patients who are reticent or unwilling to undergo vaccination, with particular attention to vulnerable populations (e.g., underrepresented racial/ethnic groups).
Identify COVID-19 vaccine–induced immune parameters (immunogen-specific neutralizing antibody levels, total immunogen-specific antibody levels or isotypes, T cell immunity, innate immunity) or host determinants that are predictive of successful host response to vaccine, as reflected by protection from infection or mitigation of morbidity during subsequent infection.
Conduct large epidemiology studies of COVID-19 outcomes (e.g., using large administrative databases of health plans, electronic health record data [e.g., the ACR RISE registry], or other data sources or methods) and examine the role of AIIRD disease features, treatments, and vaccination. While risk factors for incident disease may be shaped by confounding and unmeasured variability in exposure, examining outcomes conditioning on incident COVID-19 diagnosis may be more fruitful.

* RMD = rheumatic and musculoskeletal disease; AIIRD = autoimmune and inflammatory rheumatic disease; GCs = glucocorticoids; FDA = US Food and Drug Administration; EUA = Emergency Use Authorization; ACR = American College of Rheumatology; RISE = Rheumatology Informatics System for Effectiveness.

As an outgrowth of the evidence report, the task force assembled a research agenda where evidence was lacking (Table 5). Given that there was little direct evidence in any RMD population, the topics were broad and spanned domains related to clinical effectiveness, safety, flare, reactogenicity, study design, immunogenicity, and laboratory-based correlates of protection. With the relatively small size of the task force, no attempt was made to prioritize these topics given the expectation that they would evolve over time and as new science in non-RMD populations was forthcoming.

DISCUSSION

This ACR guidance encompasses the optimal use of COVID-19 vaccines, including supplemental/booster dosing, for patients with rheumatic and musculoskeletal diseases. It is intended to aid in the care of individual patients but not to supplant personalized care or constrain shared decision-making with patients. The mRNA vaccine platform is novel, and considerations for vaccines developed on this platform may differ from those relevant to other vaccines. The guidance regarding the use and timing of immunomodulatory medications was often based on extrapolation of the available evidence of their immunologic effects as they relate to other vaccines and vaccine platforms. As such, all of these recommendations are considered conditional. Finally, the task force advised health care providers to avoid being overly dogmatic in following these recommendations. The attempt to optimize vaccine response in relation to the use and timing of immunosuppressive medications should not compromise a willing patient's ability to undergo vaccination in a timely manner and risk a missed vaccination opportunity.

As an overarching principle, the sparsity of information regarding COVID-19 vaccination in RMD patients yielded a need for extrapolation based on the literature published for other vaccines. The evidence base was, therefore, of low or very low quality and suffered from indirectness (12) in almost all respects. The guidance provided herein represents a balance between evidence regarding efficacy, effectiveness, safety, feasibility (e.g., withholding a therapy with a long half-life or extended recirculation like leflunomide may be unrealistic), expected vaccine availability, and tradeoffs in resource utilization. For example, vigorous debate was held about whether it was preferable to vaccinate a high-risk patient in a suboptimal circumstance (e.g., active disease, receiving high-dose glucocorticoids, receiving cytotoxic therapy), under the assumption that the vaccine would confer at least some protection to a patient at high risk for a poor outcome if they contract COVID-19. Or rather, might it be preferable to wait until a more optimal circumstance presented itself? However, given the uncertainty in most medical settings to predict the future course of a patient's AIIRD or the need for additional immunomodulatory treatments, a more salutary setting to optimize vaccine response might never

materialize. Thus, the task force typically favored proceeding more immediately with vaccination.

If a laboratory-based correlate of protection existed that could serve as a proxy for immunity, and if a booster dose could be administered or the vaccine series repeated at a later time, there would be greater certainty to recommend vaccinating all patients immediately, regardless of setting or underlying treatment. These societal considerations regarding vaccine allocation in light of constrained vaccine supply and regional resource limitations to revaccinate posed important tradeoffs for the panel. Given tradeoffs like these, the extant uncertainties posed by the scoping questions informed by imperfect evidence, and the highly dynamic environment of vaccination implementation, the task force recommended as it did.

The strengths of this effort are notable given the urgent need presented by the availability of new COVID-19 vaccines and critical questions about how to best use those vaccines for RMD patients. The task force generated an evidence summary over a very compressed time frame and leveraged a well-established consensus methodology process used previously by the ACR. Of high importance, the task force's composition included experts in rheumatology, infectious disease, and public health, representing a plurality of different stakeholder perspectives.

Regarding important limitations, our ability to generalize from the literature for other vaccines and vaccine platforms in RMD patients to the novel COVID-19 vaccines now available in the US is limited. Vaccination against SARS–CoV-2 raises different issues than those for other vaccine-preventable illnesses, given the potential for ongoing public health measures to partially mitigate exposure. This guidance therefore must be interpreted by clinicians and patients in light of underlying principles rather than considering them either prescriptive or proscriptive. For example, an AIIRD patient with minimal public contact who is able to strongly adhere to all preventive health measures might choose to withhold RMD treatments or briefly defer vaccination in accordance with this guidance, whereas this same decision may not be possible for a patient employed in a high-risk setting (e.g., front-line health care, or long-term care facility). From a vaccine policy and recommendation context, the task force prioritized simplicity, noting that this guidance would be expected to apply to the care of most RMD patients in most settings.

Finally, the procedures used to develop this guidance did not follow the rigorous methodology routinely used by the ACR when formal clinical practice guidelines are created, although they were adherent to the ACR standardized operating procedures for guidance documents (13). This was an expected limitation given the accelerated time frame desired by the ACR to issue practical and timely recommendations both to its membership and to the rheumatology community. Once the urgency of the pandemic has passed, the work of this task force will eventually be folded back under the aegis of the broader ACR vaccine guideline development group, charged with covering this and all other vaccines in the context of RMDs, and the more typical guideline development process favored by the ACR will be applied. Additional and important input from other stakeholders, including patients and patient advocates, will also be sought, as the ACR has done for past clinical practice guidelines (6).

As new safety and efficacy evidence becomes available for COVID-19 vaccines in patients with RMDs and AIIRDs, the ACR's guidance document will continue to be updated and expanded, consistent with the notion of a "living document." The need for future updates will be routinely assessed by the ACR, this task force, and the larger ACR guideline development group. The ACR is committed to maintaining this process throughout the pandemic to facilitate evidence-based practice and promote optimal outcomes for all patients with RMDs and AIIRDs with respect to mitigating COVID-19 risk.

ACKNOWLEDGMENT

The task force would like to thank Regina Parker (ACR) for her role in coordinating the activities of the Task Force.

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Curtis had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design. Curtis, Johnson, Anthony, Arasaratnam, Baden, Bass, Calabrese, Gravallese, Harpaz, Kroger, Sadun, Turner, Williams, Mikuls.

Acquisition of data. Curtis, Johnson, Anthony, Arasaratnam, Baden, Bass, Calabrese, Gravallese, Harpaz, Kroger, Sadun, Turner, Williams, Mikuls.

Analysis and interpretation of data. Curtis, Johnson, Anthony, Arasaratnam, Baden, Bass, Calabrese, Gravallese, Harpaz, Kroger, Sadun, Turner, Williams, Mikuls.

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