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LETTERS

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COVID-19 vaccine uptake and vaccine hesitancy in rheumatic disease patients receiving immunomodulatory therapies in community practice settings

To the Editor:

Patients with autoimmune and inflammatory rheumatic diseases (AIIRDs) may be more likely to contract SARS–CoV-2 and have greater morbidity and mortality resulting from COVID-19. Recognizing these risks, the American College of Rheumatology (ACR) recently released the second version of its guidance for COVID-19 vaccination in patients with rheumatic and musculoskeletal diseases, recommending vaccination and supplemental (booster) dosing (1). However, patients with AIIRDs may exhibit vaccine hesitancy for a variety of reasons, including fear of side effects (e.g., disease flare, new-onset autoimmune manifestations) (2,3) or uncertainty regarding the benefits of vaccination, given the attenuating effects of immunomodulatory therapy on vaccine response. As part of a research agenda, the ACR Task Force recommended that future studies of COVID-19 vaccination should include approaches to address vaccine hesitancy in high-risk AIIRD patients, with particular attention to vulnerable populations (1).

Given the uncertainties regarding the scale of vaccine hesitancy in rheumatic disease patients, we analyzed data collected for ascertaining SARS–CoV-2 vaccine uptake in a large community practice–based rheumatology research network (Bendcare). The tablet-based, electronic survey was conducted at 101 rheumatology providers' offices from June 2021 to September 2021 and collected information on patients' self-reported vaccination status and, for those not vaccinated, their intent to be vaccinated in the future. The uncompensated survey consisted of ~3 items (depending on responses and branching logic) and was implemented as part of routine care. The survey had a 98% completion rate (the number of patients who finished the survey divided by the number of patients who started the survey) and was linked back to electronic health record data in the network's data repository (Columbus). We used descriptive statistics to evaluate vaccination status by AIIRD condition and multivariable logistic regression to model the association between having an AIIRD condition and vaccine receipt, controlling for age, sex, and race/ethnicity.

In all, 58,529 patients provided complete data, and 20,987 of those patients had an AIIRD and were receiving targeted therapies, including biologics or JAK inhibitors, at the time of data collection. As of September 9, 2021, 77.0% of the patients had been vaccinated (n = 43,675), 16.9% were not vaccinated and did not plan to be, and 6.1% were not vaccinated but still planned to be.

AIIRD patients were significantly less likely to have been vaccinated than patients with osteoarthritis or osteoporosis who had not received treatment with disease-modifying antirheumatic drugs (76.9% versus 87.0%; $P < 0.0001$) (Figure 1). After controlling for age, sex, and race/ethnicity, it was found that individuals with AIIRDs were less likely to be vaccinated (odds ratio [OR] 0.84 [95% confidence interval (95% CI) 0.77–0.92], $P < 0.001$)

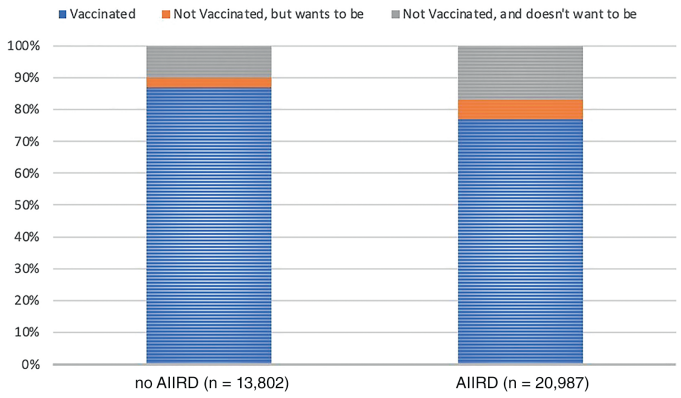

Figure 1. Vaccination status stratified by the presence of an autoimmune and inflammatory rheumatic disease (AIIRD) (patients with rheumatoid arthritis, systemic lupus erythematosus, or spondyloarthritis who were also receiving treatment with a biologic agent or disease-modifying antirheumatic drug [DMARD]) or the absence of an AIIRD (patients with a non-AIIRD condition [e.g., osteoarthritis or osteoporosis] who were also not receiving treatment with a DMARD).

compared to patients without an AIIRD. We also found that older patients and Asian patients were more likely to be vaccinated (OR per 10 years 1.49 [95% CI 1.448–1.530] and 2.42 [95% CI 1.77–3.33], respectively) and Black and Hispanic patients had slightly (but nonsignificantly) lower rates of vaccination (OR 0.92 [95% CI 0.8–1.04] and 0.95 [95% CI 0.85–1.06], respectively).

As anticipated by the ACR Task Force, these findings indicate that vaccine hesitancy remains an important and persistent problem despite the wide availability of the COVID-19 vaccine. Fortunately, increasing data suggest that recommendations from health care professionals may increase patient willingness and intention to receive the vaccine (3). Particularly for at-risk immunocompromised AIIRD patients, health care providers should make specific efforts to both ascertain vaccination status and recommend vaccination and supplemental dosing in the absence of contraindications.

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A clinician's perspective on why the trial did not work: comment on the editorial by Merrill

To the Editor:

Optimization of the signal-to-noise ratio is key to a successful outcome of clinical trials of new treatments for systemic lupus erythematosus (SLE), and this is addressed nicely in the editorial by Dr. Merrill (1). In distinguishing the response to active treatment from the response to placebo, the ratio of signal to noise may be augmented by high disease activity and the use of objective measures of disease activity; for example, a focus on higher swollen joint counts as well as on swollen joints over tender joints may be appropriate as enrollment criteria. However, Merrill's editorial raises several concerns.

First, with the recent availability of several new drugs that are effective against SLE, the rationale for enrolling patients with high disease activity in placebo-controlled trials is problematic. If low disease activity is an exclusion criterion and administration of placebo to patients with high disease activity raises ethical issues, there will be few patients left to enroll. Comparative efficacy studies, which are rare for treatments targeting rheumatic diseases but common for other treatments (2), may need to become the norm. Moreover, head-to-head data are needed by clinicians when considering whether to prescribe a new medication, rather than available alternative drugs, for a particular rheumatic disease. Second, the emphasis on swollen joints ignores patient-centric goals. If a trial demonstrates nothing about whether a patient's tender but not objectively swollen joints will improve, then the incentive for using the trial intervention is diminished in patients for whom joint pain is their primary concern. Third, if available trial data only reflect the 30% of patients with the highest SLE activity, those data will not be applicable to most lupus patients. Fourth, the push to get the perfect subject population makes it increasingly difficult to know if clinical trial data apply to one of my patients. For example, a recent large, multicenter phase IIb trial includes the following inclusion criterion: "Arthritis (at least 3 tender and swollen joints) must involve joints in the hands or wrists for the hSLEDAI scoring" (3). This criterion is not an accurate reflection of hybrid SLE Disease Activity Index (hSLEDAI) scoring; rather, it is a further modification that narrows the hSLEDAI's applicability, and this nuance will not be apparent to most clinicians who use these data.

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