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Dr. Conway et al reply

We thank Sauret et al[1] for their interest in our systematic literature review that explored potential diagnostic confusion between giant cell arteritis (GCA) and the coronavirus disease 2019 (COVID-19). This was a particularly important consideration during the early months of the COVID-19 pandemic, when community testing for SARS-CoV-2 was limited and diagnostic tests for GCA were restricted or unavailable due to redeployment of staff.[2]

The case reported by Sauret et al[1] should be interpreted with caution. GCA is a multifactorial autoimmune disease; infections and vaccines are possible triggers, but a direct causal relationship has never been demonstrated. *HLA-DRB1**04 allele carriage is common in Northern European populations; as well as being one of the genetic factors associated with GCA[3] and rheumatoid arthritis, *HLA-DRB1**04 carriage has also been linked with immunosenescence and "inflamm-aging."[4,5]

Notwithstanding the temporal association described by Sauret et al,[1] causal links cannot be established from isolated cases. Assuming a conservative incidence of 7 cases per 100,000 people and a population of 26 million people over the age of 50 years in a Northern European country, one would expect approximately 1820 cases per year of GCA. Assuming a random incidence within the year and and absence of causal association with COVID-19 vaccination, over 100 cases would be expected within 2 weeks of COVID-19 vaccination (Table 1). Large, population-based studies, ideally with the dates of both GCA symptom onset and GCA diagnosis, might help to determine whether the incidence of diagnosed GCA is genuinely increased during periods of mass COVID-19 vaccination, or whether patients are simply more likely to present promptly to medical care if they develop symptoms after a new vaccine (detection bias).

People—both patients and physicians—may be inclined to make sense of illnesses by making links to other elements of the medical history. In a community-based UK study of 654 patients with polymyalgia rheumatica,[6] many respondents related their condition to a prior event, including personal stress, injury, infection, statins, various treatments or surgeries, insect bites, weather conditions, unaccustomed exercise, and (occasionally) influenza vaccination. However, well-designed epidemiological studies are necessary to determine whether such relationships truly exist in the population. Given the limitations associated with uncontrolled observational case reports, and the inevitability that, by chance alone, some patients will be diagnosed with new diseases after a vaccine, we must be cautious in the reporting and interpretation of cases such as this.[1] Caution is especially relevant at times like these when we see variations in population vaccine uptake. Stories have power, and we must be careful to use that power wisely.

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Table 1. Estimates of the number of new cases per year of various rheumatic diseases that might be expected, by chance, to present within 2 weeks of receiving a COVID-19 vaccine.

Rheumatic Disease	Annual Incidence per Population Denominator	New Cases/Year in France[a]	New Cases/Year in France Occurring by Chance Within 2 Weeks of COVID-19 Vaccine[b]
Giant cell arteritis	7–10 per 100,000[c,d]	1820–2600	140–200
Polymyalgia rheumatica	94.9–96.8 per 100,000[e,f]	31,317–31,944	2409–2457
Rheumatoid arthritis	8.8 per 100,000[g]	5896	454
Systemic lupus erythematosus	3.32 per 100,000[h]	2224	171
ANCA-associated vasculitis	23.1 per 1,000,000[i]	1548	119

[a] Assumes the following population in France: 67 million (total); 26 million (aged > 50 yrs); 33 million (aged > 40 yrs); and 51 million (aged > 20 yrs). [b] Assumes a 2-dose annual vaccine and 100% vaccination rate. [c] Aged > 50 yrs. [d] Mahr et al[7] (2020). [e] Aged ≥ 40 yrs. [f] Partington et al[8] (2018). [g] Guillemin et al[9] (1994). [h] Arnaud et al[10] (2014). [i] Pearce et al[11] (2016). ANCA: antineutrophil cytoplasmic antibody; COVID-19: coronavirus disease 2019.

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The authors declare no conflicts of interest relevant to this article.

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