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## Women with gout and COVID-19—an unfortunate combination?



Based on the altruism of over 500 000 participants, the UK Biobank provides one of the largest sources of prospective data, including health data, blood and urine samples, imaging data, and genetic data, and has resulted in over 2500 peer-reviewed publications since 2006.<sup>1</sup> Over 200 publications since 2020 have been related to SARS-CoV-2.

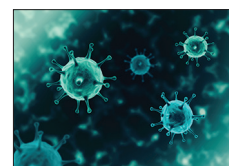
In a Comment in *The Lancet Rheumatology*, Dalbeth and Robinson<sup>2</sup> raised concerns about the recommendations by international rheumatology societies<sup>3–5</sup> regarding COVID-19 and risk factors for adverse clinical outcomes. They highlighted that gout was not mentioned as a potential risk factor for COVID-19-related severe outcomes in guidelines published by the European League Against Rheumatism,<sup>3</sup> American College of Rheumatology,<sup>4</sup> and Asia Pacific League of Associations for Rheumatology.<sup>5</sup> They also pointed out that the combination of gout, renal insufficiency, and cardiovascular comorbidities, which often go hand in hand, could result in patients with gout having the poorest COVID-19 prognosis among all patients with rheumatic disease.<sup>2</sup>

Based on data extracted from the UK Biobank in April, 2021, evidence has emerged that patients with gout are at an increased risk of contracting COVID-19 and of COVID-19-related death. In *The Lancet Rheumatology* Ruth Topless and colleagues<sup>6</sup> present an elegantly conducted analysis of data from the UK Biobank supporting the hypothesis that gout needs attention in patients with COVID-19.<sup>2</sup>

In the population-based analysis, gout was associated with increased risk of COVID-19 diagnosis in unadjusted analysis (odds ratio [OR] 1.49, 95% CI 1.39–1.60), especially in women. In a dataset of patients diagnosed with COVID-19, the risk of COVID-19-related death significantly increased with the diagnosis of gout (2.97, 2.45–3.62). When adjusted for important characteristics (body-mass index [BMI], age, sex, ethnicity, Townsend deprivation index, and smoking status) the risk of COVID-19-related death decreased but remained significant (1.44, 1.16–1.78). The authors also examined the association between gout and COVID-19-related

death in a population-based cohort. Gout was associated with COVID-19-related death, even in the fully adjusted analysis which also included 16 relevant diseases (including hypertension, type 2 diabetes, and chronic kidney disease; OR 1.29, 95% CI 1.06–1.56). In this later analysis, when focusing on sex, women were surprisingly at the highest risk of death (1.98, 1.34–2.94), whereas the adjusted risk for men was not significant (1.16, 0.93–1.45).

This sex difference is striking compared with what previous data have shown, namely that men are at a higher risk of a more severe COVID-19 outcomes compared with women. A 2020 observational study from Lombardy, Italy showed that 79.9% of all consecutive patients admitted to the intensive care unit were men, and the risk of death was higher in men (hazard ratio 1.22, 95% CI 1.08–1.37) than in women (0.73, 0.82–0.92).<sup>7</sup> Another UK Biobank study reported that the relative effect of higher BMI on COVID-19 mortality was stronger in women than in men.<sup>8</sup> In the study by Topless and colleagues,<sup>6</sup> women with gout were older and the prevalence of comorbidities in these women was more pronounced compared with the men with gout in the study (eg, renal insufficiency [25.1% of women vs 13.6% of men], diabetes [26.6% of women vs 17.9% of men], and hypertension [70.8% of women vs 58.1% of men]). This difference was adjusted for in the analysis but remains striking. In a 2021 publication,<sup>9</sup> Topless and colleagues reported results from a smaller sample (2059 patients diagnosed with COVID-19) based on data from the UK Biobank, examining rheumatoid arthritis and gout in relation to COVID-19. That analysis showed no significant increased risk for diagnosis or death in patients with gout.<sup>9</sup> Whether or not the current findings from the UK Biobank are generalisable remains to be determined and will need validation in other studies, ideally including a wider spectrum of ethnicities. How do we apply this new evidence? First, these data add to the existing data on the importance of vaccination of patients with gout. Second, the results might inform health-care providers on the importance of advising patients with gout on the risk related to COVID-19.



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Finally, these data could guide risk assessment and treatment decisions for physicians treating hospitalised patients with COVID-19 with a medical history that includes gout.

COVID-19 study results are affected by multiple factors. Disease outcomes change with different virus variants, treatment strategies, capacities of health-care systems, vaccination enrolment, and behaviour of society according to governmental and media influence. As the omicron variant becomes dominant worldwide and the relative risk of COVID-19-related hospitalisation (and possibly deaths) declines,<sup>10</sup> data interpretation becomes more difficult. Nevertheless, it will remain vital that high-risk patient groups are identified. Even as the pandemic might resolve, new SARS-CoV-2 variants could continue to emerge.

Further studies are needed to investigate to what degree a diagnosis of gout is a risk factor for COVID-19, and whether treatment modifies the risk of a severe disease course. However, in the interim, the results of this study could be considered when risk stratifying patients with gout in view of vaccination recommendations and early treatment interventions.

We declare no competing interests.

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- 1 Sudlow C, Gallacher J, Allen N, et al. UK biobank: an open access resource for identifying the causes of a wide range of complex diseases of middle and old age. *PLoS Med* 2015; **12**: e1001779.
- 2 Dalbeth N, Robinson PC. Patients with gout: an under-recognised group at high risk of COVID-19. *Lancet Rheumatol* 2021; **3**: e317–18.
- 3 Landewé RB, Machado PM, Kroon F, et al. EULAR provisional recommendations for the management of rheumatic and musculoskeletal diseases in the context of SARS-CoV-2. *Ann Rheum Dis* 2020; **79**: 851–58.
- 4 Mikuls TR, Johnson SR, Fraenkel L, et al. American College of Rheumatology guidance for the management of rheumatic disease in adult patients during the COVID-19 pandemic: version 3. *Arthritis Rheumatol* 2021; **73**: e1–12.
- 5 Tam LS, Tanaka Y, Handa R, et al. Care for patients with rheumatic diseases during COVID-19 pandemic: a position statement from APLAR. *Int J Rheum Dis* 2020; **23**: 717–22.
- 6 Topless RK, Gaffo A, Stamp LK, Robinson PC, Dalbeth N, Merriman TR. Gout and the risk of COVID-19 diagnosis and death in the UK Biobank: a population-based study. *Lancet Rheumatol* 2022; published online Jan 28. [https://doi.org/10.1016/S2665-9913\(21\)00401-X](https://doi.org/10.1016/S2665-9913(21)00401-X).
- 7 Grasselli G, Greco M, Zanella A, et al. Risk factors associated with mortality among patients with COVID-19 in intensive care units in Lombardy, Italy. *JAMA Intern Med* 2020; **180**: 1345–55.
- 8 Peters SAE, MacMahon S, Woodward M. Obesity as a risk factor for COVID-19 mortality in women and men in the UK biobank: comparisons with influenza/pneumonia and coronary heart disease. *Diabetes Obes Metab* 2021; **23**: 258–62.
- 9 Topless RK, Phipps-Green A, Leask M, et al. Gout, rheumatoid arthritis, and the risk of death related to coronavirus disease 2019: an analysis of the UK Biobank. *ACR Open Rheumatol* 2021; **3**: 333–40.
- 10 UK Health Security Agency. SARS-CoV-2 variants of concern and variants under investigation in England. Technical briefing: update on hospitalisation and vaccine effectiveness for Omicron VOC-21NOV-01 (B.1.1.529). Dec 31, 2021. [https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment\\_data/file/1045619/Technical-Briefing-31-Dec-2021-Omicron\\_severity\\_update.pdf](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1045619/Technical-Briefing-31-Dec-2021-Omicron_severity_update.pdf) (accessed Jan 11, 2022).



## Who will respond to type I interferon receptor blockade in SLE?

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In systemic lupus erythematosus (SLE), results obtained using scientific instruments often need to be translated into concepts that are directly applicable to clinical care. In *The Lancet Rheumatology*, post-hoc analyses by Eric Morand and colleagues<sup>1</sup> help to translate data from the TULIP-1 and TULIP-2 trials of the interferon receptor inhibitor anifrolumab into clinical practice. By providing information on individual disease manifestations, the data help to define which patients with SLE are most likely to benefit from the drug.

The best available classification criteria and clinical outcome measures still cannot be directly used for clinical practice, most likely because of the complexity of SLE. SLE classification criteria,<sup>2</sup> for example, have high specificity with a limited number of well defined items but fail to identify SLE in some individuals with the

disease. Even less suitable for routine clinical practice are the composite endpoints that are currently used in clinical trials in SLE—the SLE Responder Index (SRI)<sup>3</sup> and British Isles Lupus Assessment Group (BILAG)-based Combined Lupus Assessment (BICLA).<sup>4</sup>

The SRI was originally chosen as the primary endpoint for the two phase 3 TULIP trials of anifrolumab. TULIP-1 failed to meet this endpoint, but the trial would have been successful if BICLA had been chosen as the primary outcome measure.<sup>5</sup> BICLA was thus set as the new primary endpoint for TULIP-2, in coordination with the US Food and Drug Administration (FDA) and before the data were analysed. When analysed, TULIP-2 was successful based on both BICLA and SRI.<sup>6</sup> As a result, anifrolumab was approved by the FDA and is expected to be approved by the European Medicine Agency.