Title: Rheumatology in a time of Coronavirus: Lessons from our early experiences.

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Dear Editor,

The *SARS-CoV-2* pandemic arrived unexpectedly, unapologetically and unwelcomed to modern rheumatology practice. It has and continues to challenge us all; patients, rheumatologists and allied health professionals. Recent advances in the understanding of the immuno-pathogenesis of inflammatory rheumatic conditions has led to improved treatment with biologic agents and synthetic disease modifying anti-rheumatic drugs (DMARDs) that target specific components of the immune system. However, in the face of a pandemic such treatments have left our patients feeling vulnerable and rendered the prescriber's mind unsettled. Many patients have enquired whether their immunosuppressive medication should be stopped at this time. Doing so could run the risk of flare and a need for greater immunosuppression as a consequence. Early, retrospective analyses of individuals requiring hospital admission for COVID-19 at the original epicentre in Wuhan, China, did not highlight autoimmune disease or associated immunosuppression as a significant risk factor for requiring intensive care treatment or mortality.[1, 2] However, the absence of evidence is not evidence of absence. Once the virus was declared pandemic by the World Health Organisation, recommendations from national and international public health and collegiate bodies duly followed. Public Health England offered guidance on 'shielding' for those considered extremely vulnerable to COVID-19.[3] Specifically, it was advised that individuals 'on immunosuppression therapies sufficient to significantly increase the risk of infection' should undertake a period of shielding for at least 12 weeks. This point of guidance, although well-intentioned, also made us debate and discuss: What constitutes a significant increase in the risk of infection?

Observational studies suggest that traditional DMARDs do not increase the risk of infection with no significant differences evident between "immunosuppressive" DMARDs such as methotrexate and "non-immunosuppressive" DMARDs such as hydroxychloroquine (HCQ) and sulfasalazine.[4] A meta-analysis of randomised, placebo-controlled trials with various biologic drugs (often in combination with methotrexate or other conventional DMARDs) found an overall relative risk of serious infections of 1.37 (95% CI 1.04-1.82).[5] However, a relatively low absolute risk of 1% was detected estimating that 26/1,000 patients treated with placebo developed a serious infection compared with 35/1,000 patients treated with a biologic. Another timely question is whether different biologic drugs infer different risks of infection? This was recently investigated in a prospective, observational analysis of the British Society of Rheumatology's Biologics Register (BSRBR-RA) which demonstrated similar rates of infection across different biologic drugs with the exception of the interleukin-6 receptor blocker Tocilizumab where rates were higher.[6] It remains unclear whether patients taking any of these agents are at a higher risk of contracting *SARS-CoV-2* or indeed are at a higher risk of mortality from COVID-19 once infected. It had been suggested that HCQ may actually protect against the development of COVID-19 and/or influence its severity. While this question is being evaluated along with Tocilizumab as part of the RECOVERY trial (see https://doi.org/10.1186/ISRCTN50189673), data from observational studies has so far not supported the notion that HCQ is an effective treatment for COVID-19 (Pre-print available from: https://www.medrxiv.org/content/10.1101/2020.04.16.20065920v2). Indeed, observational data have indicated that HCQ may be associated with a significantly increased risk of cardiovascular events compared with sulphasalazine in patients with rheumatoid arthritis (Pre-print available from: https://www.medrxiv.org/content/10.1101/2020.04.08.20054551v1.full.pdf). This emphasizes the importance of only using these treatments for COVID-19 within the context of a randomized controlled trial. While uncertainty is likely to persist for some time, the prompt establishment of data registries such as the EULAR COVID-19 database [7] and the COVID-19 Global Rheumatology Alliance, [8] will provide safety data to support current consensus-based recommendations. For now, biologics and DMARDs should not be stopped as a result of potential COVID-19 risk.

The pandemic has disrupted our daily routine in rheumatology clinics across the U.K. However, patients and healthcare practitioners have demonstrated significant adaptability and

openness to change, with the overall goal of reducing infection risk. Resilience, collaboration and an ability to enact change at pace has challenged routines that have been practised for decades. Relaxation of blood monitoring requirements, switching of appropriate patients from intravenous to subcutaneous drug administration, and a switch from face-to-face, nurse-led group teaching of subcutaneous drug administration to online teaching supported by written information and video demonstrations, have been hugely successful. These strategies will facilitate shielding, reduce costs and manpower burden on primary and secondary care, as well as inform our future guideline recommendations (in the case of DMARD blood monitoring). The necessity for virtual clinic consultations has also been thrust upon us. The way we communicate with patients has evolved in a short space of time. More information is now provided for patients through reliable, trust-led websites and their associated social media outlets. Telephone calls for follow-up rheumatology appointments are the norm. Our experience to date is that the majority of patients are very happy with this method of consultation. It saves patients time and money in travelling to hospital clinic appointments, in addition to having a positive environmental impact. Technology-enabled care such as video-consultation is also on the rise and initiatives such as 'NHS Near Me' are now available in Scotland.[9] While we acknowledge the limitations that virtual consultations confer, [10] and the fact that for many patients clinical or ultrasound examination is necessary, for a sizeable number of carefully-selected patients, video- or telephone-consultations will be a welcome alternative option, with significant benefits.

The COVID-19 crisis has resulted in an unforeseen and seismic change in how rheumatology is currently practised; from trying to minimize infection risk for our patients, balancing this with the risk of under-treatment or disease flare, to the way in which services are delivered. However, despite this disruption, opportunities have serendipitously presented themselves to rapidly implement alternative ways of delivering patient care. The pandemic has forced us to focus our efforts and to lay the groundwork for pursuing novel, more efficient, economical and patient-orientated modes of service delivery. It is important that rheumatologists embrace these opportunities during the current pandemic and into the post-COVID-19 era.

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