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Are treat-to-target and dose tapering strategies for rheumatoid arthritis possible during the COVID-19 pandemic?

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The global pandemic of COVID-19 has dramatically altered the delivery of rheumatology outpatient services because of the redeployment of staff and efforts to minimise infection risk to patients and clinicians in line with physical distancing guidance. Departments have converted most face-to-face appointments to telephone clinics or, less frequently, to video clinics. The National Institute for Health and Care Excellence (NICE) COVID-19 rapid guidelines for rheumatology suggest that face-to-face consultations are only required for patients who have a disease flare. Implicit is the presumption that those with so-called stable disease will be managed remotely. Departments are now planning the restoration of services as we move towards a recovery phase in the UK. The advantages of telemedicine remain because physical distancing is mandated as part of the effort to reduce the likelihood of a second wave of infections, and hospital outpatient settings have limited physical space. It is therefore pertinent to reflect on the meaning of stable disease, as applied to rheumatoid arthritis, and whether remote clinics are compatible with the therapeutic framework of treat-to-target.

Treat-to-target has been a cornerstone in the management of rheumatoid arthritis over the past decade and has the ultimate aim of achieving disease remission.¹ This strategy was first tested through randomised clinical trials, and was then assessed in clinical practice, initially in patients with early rheumatoid arthritis and subsequently in those with established disease.^{2,3} Studies report that

treat-to-target strategies can attain higher remission rates compared with other, less structured therapeutic approaches.^{2,3} Up to 50% of patients can achieve remission, depending on its definition, through the application of treat-to-target, the optimal use of conventional, targeted synthetic, and biological disease-modifying antirheumatic drugs (DMARDs), and the implementation of well defined metrics of remission. So, where does the concept of stable disease fit within treat-to-target? Stable disease could encompass patients with low or moderate disease activity whose disease trajectories have not worsened (ie, patients not having a disease flare). Both disease states are associated with worse outcomes compared with remission, leading to pain, stiffness, and disability.⁴

Treat-to-target requires frequent monitoring with clinical examinations and blood tests, followed by appropriate modifications to treatment, particularly in the early phase of disease. A comprehensive assessment of the number of tender and swollen joints, a key component of the metrics used to measure disease activity and distinguish between remission and low or moderate disease activity, can only be adequately done through a face-to-face encounter. A face-to-face visit would include a physical examination, blood tests, and the recording of patient-reported outcomes. Although adding joint ultrasound examinations to treat-to-target methods does not appear to confer additional benefits compared with conventional treat-to-target strategies in a clinical trial setting,⁵ the inclusion of ultrasound imaging in the

face-to-face visit could help to achieve disease remission in real-world practice. Recognising that treat-to-target had not been uniformly adopted as standard practice in the era before COVID-19, despite increasing evidence of benefit, is important.³ Further barriers to delivering treat-to-target, such as the reduced availability of face-to-face visits, and consequent challenges in precisely defining disease activity, are likely to lead to fewer patients with rheumatoid arthritis reaching remission.

The concept of dose tapering (also described as dose reduction, dose adjustment, or dose optimisation) as a therapeutic strategy has partly evolved because of the increasing number of patients who are in clinical remission. Tapering is included within the 2018 NICE guidelines on the management of rheumatoid arthritis and within the recommendations published by the European League Against Rheumatism⁶ for those patients who are in sustained remission. The incentives of dose tapering over not changing dose, which could include fewer adverse effects, a reduced risk of infection, less need to self-inject for biologics, and lower medication costs, are more relevant than ever. Concern over becoming ill with COVID-19 during the pandemic might have led to some patients, independently of their physician, stopping or tapering DMARDs to reduce the risk of infection. Of note, research is ongoing regarding the safety of DMARDs with respect to COVID-19, but early observational data are reassuring.⁷ Similar to treat-to-target strategies, dose tapering requires that patients be monitored diligently and frequently with physical examinations because disease worsening often occurs, an issue that has decreased the uptake of tapering methods.⁸ Because many patients have disease flares following tapering, and data suggest that not all patients will regain remission after returning to their original dose, further research is urgently required to identify biomarkers that can predict sustained remission upon tapering.⁹ This translational research will need access to patient samples to understand the mechanism of action of therapies and how remission can be sustained.

Translational and clinical research in the field of rheumatology has produced several, novel biological therapies, has helped to improve remission rates through the application of treat-to-target methods, and is needed to guide tapering strategies. Current and future research should not be compromised by the widespread adoption of remote consultations. The COVID-19 pandemic offers the opportunity to test the usefulness of patient-reported

outcomes and web-based monitoring applications to aid in the remote management of patients with rheumatoid arthritis. However, the application of validated patient-reported outcomes related to disease activity, such as the Routine Assessment of Patient Index Data 3 (known as RAPID3), without clinical examination is unsatisfactory.¹⁰ Overtreatment, which can be just as damaging as undertreatment, has led investigators to ask whether the patient global assessment should be removed from definitions of remission.¹¹ Although patient-reported outcomes should be integrated into rheumatology practice to improve patient care, more research regarding their usefulness is required, and even their most ardent supporters do not argue that these measures can replace clinical examination.¹² Compounding the sole reliance on patient-reported outcomes, the use of remote technologies and the assessment of disease based only on medical history might disadvantage some patients because of economic or social factors. It is our view that creating multidisciplinary, one-stop shop face-to-face clinics might, in the long term, reduce visits to hospitals where patients receive necessary input from clinicians, nurses, physiotherapists, hand therapists, and podiatrists, and attend for blood tests, imaging scans, and research purposes.

Treat-to-target and safe tapering strategies should continue to be essential in the management of rheumatoid arthritis, regardless of new approaches that streamline the patient experience and reduce the number of hospital visits. Every effort should be made to mitigate the perceived and actual risk of patients attending hospitals during the pandemic. Patients with rheumatoid arthritis on minimal or no DMARDs and in sustained remission might be candidates for remote consultation. However, certain terms, such as stable or well controlled, should not be used in the lexicon of rheumatology practice without reference to the maintenance of remission, nor should patients with stable moderate or low disease activity be forgotten if the landscape of rheumatology care shifts to an increasingly virtual form. Amid the flurry of creating the new normal, patients with rheumatoid arthritis should not have to turn to increasing their dose of non-steroidal anti-inflammatory drugs as joints slowly erode, reminiscent of the dark days of rheumatology in the 20th century when stable disease was an acceptable target.

We declare no competing interests.

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For more on the 2018 NICE guidelines see <https://www.nice.org.uk/guidance/ng100/chapter/Recommendations#monitoring>

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