



**UNIVERSITY OF LEEDS**

This is a repository copy of *Treating rheumatoid arthritis to an imaging target produces better outcomes, or does it?*.

White Rose Research Online URL for this paper:  
<https://eprints.whiterose.ac.uk/163822/>

Version: Accepted Version

---

**Article:**

Mankia, K, Gul, H and Emery, P [orcid.org/0000-0002-7429-8482](https://orcid.org/0000-0002-7429-8482) (2021) Treating rheumatoid arthritis to an imaging target produces better outcomes, or does it? *Rheumatology*, 60 (1). pp. 3-4. ISSN 1462-0324

<https://doi.org/10.1093/rheumatology/keaa659>

---

© The Author(s) 2020. Published by Oxford University Press on behalf of the British Society for Rheumatology. This is an author produced version of an article published in *Rheumatology*. Uploaded in accordance with the publisher's self-archiving policy.

**Reuse**

Items deposited in White Rose Research Online are protected by copyright, with all rights reserved unless indicated otherwise. They may be downloaded and/or printed for private study, or other acts as permitted by national copyright laws. The publisher or other rights holders may allow further reproduction and re-use of the full text version. This is indicated by the licence information on the White Rose Research Online record for the item.

**Takedown**

If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing [eprints@whiterose.ac.uk](mailto:eprints@whiterose.ac.uk) including the URL of the record and the reason for the withdrawal request.



[eprints@whiterose.ac.uk](mailto:eprints@whiterose.ac.uk)  
<https://eprints.whiterose.ac.uk/>

Rheumatology Editorial

## **Treating rheumatoid arthritis to an imaging target produces better outcomes, or does it?**

Kulveer Mankia, Hanna Gul, Paul Emery

Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds NIHR Biomedical Research Centre, Leeds, UK

### **Address for correspondence**

*Prof Paul Emery*

*Leeds Institute of Rheumatic and Musculoskeletal Medicine, Chapel Allerton Hospital, Chapeltown Road, Leeds LS7 4SA, UK*

[p.emery@leeds.ac.uk](mailto:p.emery@leeds.ac.uk)

### **Disclosures**

*KM has provided expert advice to Lilly, Abbvie, UCB*

*HG none*

*PE has provided expert advice to Pfizer, Abbvie, Amgen, MSD, Roche, Sanofi, BMS, Novartis, Lilly, Gilead, Samsung, Celltrion*

### **Funding**

*There are no funders to report.*

For the management of rheumatoid arthritis (RA) the agreed target is remission. But there are various definitions of remission with most experts considering disease activity score (DAS28) based remission too lax, for example allowing swollen joints and the subjective patient global assessment (PGA) score in the definition (1). Indeed, it is clear that a proportion of patients fulfilling DAS remission criteria deteriorate clinically and can progress radiographically (2) .

Attempts to improve this include using more stringent definitions (e.g. ACR Boolean Remission Criteria, Simple Disease Activity Index (SDAI), Clinical Disease Activity Index (CDAI)) and also increasing objectivity by using highly-sensitive imaging such as ultrasound (US), since a major reason for radiographic progression is likely to be subclinical synovitis(2). Baseline US assessment in patients in remission has been shown to predict flare in patients both on stable therapy and those tapering treatment, thus the use of targeted ultrasound approaches have been proposed (3-5).

Attempts to prove the success of this approach have produced variable results but many suffered with methodological issues (6). In the current issue Moller-Bisgaard et al describe use of MRI inflammation (osteitis) as an additional aid to clinical features for escalation of therapy in a blinded randomised-controlled trial (RCT).

The authors showed in the multivariate analyses of the RCT, allocation to the MRI treat-to-target group independently predicted achievement of stringent remission targets, including CDAI remission (OR 2.94 (1.25-7.52)), SDAI remission (OR 2.50 (1.01-6.66)), and ACR/EULAR Boolean remission (OR 5.47 (2.33-14.13)). Low tender joint count, low patient VAS pain and VAS global at baseline also independently predicted more stringent remission. Furthermore, when baseline data from all patients was combined, the significance of MRI-detected inflammation on outcomes was further highlighted. MRI osteitis predicted progression of erosions and joint space narrowing whilst MRI tenosynovitis also independently predicted erosion progression.

As stringent remission is probably the optimal goal of treatment, this carefully preformed study appears to have produced a clear-cut answer. So, it would be a surprise to most readers to find that that the same authors with the same data set could conclude in an earlier publication in JAMA "These findings do not support the use of an MRI-guided strategy for treating patients with RA"(7). How this unusual situation has arisen bears some analysis and raises some important issues for publication.

This conclusion was reached on the basis of failure to achieve their pre-defined primary end-points, which were DAS28 CRP remission and halting radiographic erosive progression. There are well recognised problems with use of DAS28 and radiographic erosions as primary end-points with issues with the former mentioned above, and the latter insensitive to change over a limited period of long standing disease in clinical remission (8).

Although it is technically correct to say this RCT failed to meet the primary end-points, it is incorrect to dismiss the intervention, which successfully reached several very desirable and perhaps more clinically relevant outcomes. The fact that the two papers, based on the same RCT dataset, present different narratives, highlights the duty of authors to keep clinical implications at the forefront of their considerations.. This is particularly pertinent in the

current situation, when differing pre-defined primary outcomes in the two papers have led to different results, which may directly impact clinical decision making.

We are pleased the authors have had the opportunity in this Rheumatology article to present a more balanced review of the data than would be derived from a quick review of the JAMA paper. There are occasions when strict adherence to methodological principles are not optimal. It is the duty of clinicians to remind others of the primary objective of clinical research.

## References:

1. Smolen JS, Breedveld FC, Burmester GR, Bykerk V, Dougados M, Emery P, et al. Treating rheumatoid arthritis to target: 2014 update of the recommendations of an international task force. *Annals of the rheumatic diseases*. 2016;75(1):3-15.
2. Brown AK, Quinn MA, Karim Z, Conaghan PG, Peterfy CG, Hensor E, et al. Presence of significant synovitis in rheumatoid arthritis patients with disease-modifying antirheumatic drug-induced clinical remission: evidence from an imaging study may explain structural progression. *Arthritis and rheumatism*. 2006;54(12):3761-73.
3. Wakefield RJ, D'Agostino MA, Naredo E, Buch MH, Iagnocco A, Terslev L, et al. After treat-to-target: can a targeted ultrasound initiative improve RA outcomes? *Annals of the rheumatic diseases*. 2012;71(6):799-803.
4. Alivernini S, Peluso G, Fedele AL, Toluoso B, Gremese E, Ferraccioli G. Tapering and discontinuation of TNF-alpha blockers without disease relapse using ultrasonography as a tool to identify patients with rheumatoid arthritis in clinical and histological remission. *Arthritis research & therapy*. 2016;18:39.
5. D'Agostino MA, Terslev L, Wakefield R, Ostergaard M, Balint P, Naredo E, et al. Novel algorithms for the pragmatic use of ultrasound in the management of patients with rheumatoid arthritis: from diagnosis to remission. *Annals of the rheumatic diseases*. 2016;75(11):1902-8.
6. D'Agostino MA, Boers M, Wakefield RJ, Emery P, Conaghan PG. Is it time to revisit the role of ultrasound in rheumatoid arthritis management? *Annals of the rheumatic diseases*. 2017;76(1):7-8.
7. Moller-Bisgaard S, Horslev-Petersen K, Ejbjerg B, Hetland ML, Ornbjerg LM, Glinatsi D, et al. Effect of Magnetic Resonance Imaging vs Conventional Treat-to-Target Strategies on Disease Activity Remission and Radiographic Progression in Rheumatoid Arthritis: The IMAGINE-RA Randomized Clinical Trial. *JAMA*. 2019;321(5):461-72.
8. Haavardsholm EA, Lie E, Lillegraven S. Should modern imaging be part of remission criteria in rheumatoid arthritis? *Best practice & research Clinical rheumatology*. 2012;26(6):767-85.