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REPLY

The controversy of using PGA to define remission in RA

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We thank Ferreira and colleagues for their correspondence (The controversy of using PGA to define remission in RA. *Nat. Rev. Rheumatol* https://doi.org/nrrheum.2018.35 (2018))[1] regarding our commentary (van Tuyl, L. H. D. & Boers, M. Remission — keeping the patient experience front and centre. *Nat. Rev. Rheumatol.* **13**, 573–574 (2017))[2,3]. Ferreira and colleagues once again advocate removal of patient global assessment (PGA) from the remission criteria by creating two separate targets: a measure of inflammatory activity (physician's perspective) responsive to immunosuppressive therapy, and a measure of disease impact (patient's perspective). For the former, they proposed the 3v-remission (which is the current remission criteria minus the PGA requirement).

Ferreira and colleagues argue that PGA "has no more than a weak correlation with disease activity", without citing evidence. We have evidence to the contrary (as discussed here and in our original commentary[2]), but first note that they seem to mix the concepts of 'inflammatory activity' and 'disease activity'. The former has to our knowledge not been properly defined. Do the authors refer to joint inflammatory activity, systemic inflammatory activity or both? If the former, an argument can be made to look only at the joints, but perhaps clinical assessments are then not sufficient; if the latter, the inclusion of acute phase reactants is reasonable. However, neither fully encompasses the construct of disease activity, which is broader than inflammatory activity, as defined in the core set of outcome measures developed by the Outcome Measures in Rheumatology Clinical Trials (OMERACT) group and other groups in the early 1990s[4–6].

PGA, as well as physician global assessment (PhGA), Health Assessment Questionnaire (HAQ) and pain, were key components of these core outcome sets, and PGA was also a key component of the disease activity score (DAS)[7]. Inclusion of PGA was key as this added essential information for distinguishing active from inactive disease (DAS) and for distinguishing placebo from active treatment and for prognostication[8]. PGA and PhGA were closely correlated in those exercises, but both were retained in the core set to achieve consensus between European and American constituencies.

In other words, to measure disease activity as a target for therapy, joint counts and acute phase reactants fall short. This caveat remained true in the development of the remission criteria: the 3v-remission was the starting point, but candidate criteria performed better when either PGA (that is, the current remission criteria) or pain was added[9].

We acknowledge again that domains other than disease activity have an impact on PGA and other patient-reported outcomes such as pain and fatigue, and that this effect can influence the classification of patients as being in remission. However, the remission criteria are designed for research and for optimum specificity, and not for use in treat-to-target schemes. To reiterate: "We are convinced that most rheumatologists in practice do not need new instruments to decide which patients are most likely to have residual disease and are in need of switching their treatment as opposed to patients with comorbidities that confound the interpretation of their RA symptoms."[2]

Finally, the authors promote the Rheumatoid Arthritis Impact of Disease (RAID) score as a tool to measure impact. Although an important addition to the instrument armamentarium and useful in the clinic, the RAID score contains core set measures usually already measured separately, several of which (pain, function and fatigue) also measure disease activity. This inclusion blurs the distinction the authors are trying to make, and potentially creates double counting when patients are assessed[10].

We conclude that current instruments are inadequate to fully distinguish inflammation from disease impact.

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Author contributions
Both authors researched data for the article, wrote the article, made substantial contributions to discussion of its content and reviewed and/or edited the manuscript before submission.

Competing interests
The authors declare no competing interests.