Response to: 'Increasing the threshold for patient global assessment in defining remission may have a different impact in patients with early and established rheumatoid arthritis' by Bugatti et al

We thank Bugatti *et al* for their interest in our paper and for sharing their results on applying a 2 cm cut-off for the patient global assessment (PGA) criterion of the Boolean remission criteria for rheumatoid arthritis (RA) within the setting of a real-world database,[1] which confirm the data presented in our recent report based on a clinical trial population.[2] An appropriate definition for remission is of utmost relevance to prevent structural progression or functional deterioration, regardless of the treatment regimen used; in fact, such a definition is clearly needed in clinical practice, where today a significant proportion of patients is able to attain very good control of disease activity.[3–6] The currently used provisional ACR/EULAR remission should be revisited to no longer be provisional.[7] Ideally, the definition of remission should be applicable to all people with RA independent of disease duration.

Since more patients fulfil the index-based remission definition (15% in early RA, and 6.8% in established RA at 6 months) compared with Boolean remission (12.4% and 5.9%, respectively), in our original study we investigated at which cutpoints of the PGA in Boolean criteria there was best agreement with index-based remission definition (simplified disease activity index (SDAI) ≤3.3). While Bugatti *et al* have shown many similarities in the performance of our proposed 2 cm PGA cut-off using real-world data to those we reported using trial data,[2] they did not analyse their data in a way that permits them to assess agreement of different Boolean definitions with the SDAI definition of remission, and were therefore not enabled to draw respective conclusions. In terms of analysing agreement, Bugatti *et al* needed to look at one group that met original Boolean definitions and another that met the expanded definition (this latter group also includes those who meet the original Boolean definition). Bugatti *et al* rather, as noted in a footnote to their table 1, examined the stratum that had higher PGA assessments separately. Given the close association of PGA with pain and function,[8] it is expected that those with higher PGA's would have more pain and have worse health assessment questionnaire (HAQ) scores.

We have been conservative in the interpretation of comparative analyses in non-overlapping remission groups (using the different PGA cut-points) since sample size was rather small. The exact number of people in Boolean 2.0 remission is unfortunately not depicted in Bugatti *et al* nor is the rate of people in Boolean remission. Taking into account that the transition of the PGA cut-off to 2 cm led to an increase of a bit more than 4% of remitters makes it possible to convey that only few patients could be accounted to the discrete group of Boolean 2.0 remitters, which may affect performance of kappa statistics applied to this stratum.

We did not recommend a Boolean definition using solely this stratum but rather an expanded Boolean definition that included those who met the original definition and liberalised this definition to include those with slightly higher PGAs. Bugatti *et al* should have performed agreement analyses using this expanded definition, a definition that includes those who met the original Boolean definition, as it would apply in the clinical setting.

Overall, these published findings should make us more confident that in trials as well as clinical practice a PGA cut-off of 2 out of 10 can be used in evaluation of Boolean remission.

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► https://doi.org/10.1136/annrheumdis-2020-217488

Ann Rheum Dis 2020;**0**:1. doi:10.1136/annrheumdis-2020-217705

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