

## Challenging judgement of a low-positive ACPA test in the context of individuals at risk of RA

We thank Bossuyt<sup>1</sup> for his letter and the comments related to our previous published study.<sup>2</sup> We agree that the calculated test likelihood ratios for low-positive anticitrullinated protein antibody (ACPA) reflect the relative uncommonness of low-titre ACPA in prevalent rheumatoid arthritis (RA) (despite a significant association between). However, in contrast, a low-ACPA titre result in the context of testing for future incident RA might represent an intermediate stage in disease development in individuals on their way to develop RA. We have preliminary unpublished data showing a significant association between low-ACPA titre and future incident RA in our cohort. Judgement of the ACPA test results is therefore more challenging in such context and probably additional information (such as presence or absence of the human leukocyte antigen (HLA)-shared epitope risk gene alleles) will improve the discrimination of individuals who will not and those who will continue to develop high ACPA titres and eventually RA. More studies addressing the additional benefit of a higher relative weight for high titre as compared with low-ACPA titre in the context of clinical manifest RA and future RA are needed.

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