Response to: Correspondence on ‘2023 ACR/EULAR antiphospholipid syndrome classification criteria’ by Tang et al

We appreciate the comments by Tang et al in response to the publication of the 2023 American College of Rheumatology/European Alliance of Associations for Rheumatology (ACR/EULAR) antiphospholipid syndrome (APS) classification criteria.1-3 We were interested to read about their study describing the performance of the classification criteria in 963 potential APS patients of Asian descent in China. Compared with their ‘gold standard’ involving clinical assessment of each potential APS case by two experienced rheumatologists, the authors report a specificity of 98% (95% confidence interval (CI) 97% to 99%) and sensitivity of 82% (95% CI 78% to 85%), comparable to the findings from our final validation cohort (specificity 99% (95% CI 98% to 100%), sensitivity 84% (95% CI 77% to 91%)). Similar to our findings, the authors report a lowered specificity of 90% (95% CI 87% to 92%) when using the revised Sapporo APS classification criteria. Although we have some questions regarding the gold standard used in this study—including whether cases were classified, rather than diagnosed, as APS for the purpose of defining a sufficiently homogeneous cohort for entry into clinical studies and trials, whether the existing revised Sapporo classification criteria were used (thus potentially leading to some circularity in reasoning and higher performance of the Sapporo criteria), and whether adjudication and joint consensus was achieved between case reviewers—we believe that this work is important. As major goals for future research in APS are to understand the role of demographic factors such as race, ethnicity and region, and to ensure generalisability of the 2023 ACR/EULAR APS classification criteria across race/ethnicities, this study provides an important contribution to the external validation of the new criteria in diverse cohorts.

We also value the authors’ additional input and provide responses to specific points: (a) microvascular domain and its ‘remarkable effectiveness and precision’—we agree that the incorporation of microvascular domain criteria for APS classification may reclassify patients as APS using the 2023 ACR/EULAR APS classification criteria who previously did not meet revised Sapporo APS classification criteria,4 and has led to a substantial increase in specificity; (b) thrombocytopenia raising concerns about ‘APS overdiagnosis’—classification criteria should not be used for diagnosis,5 which requires detailed assessment of multiple clinical factors; furthermore, items that are ‘equally or more likely’ to be secondary to another aetiology such as systemic lupus erythematosus should not be scored; (c) redefined pregnancy morbidity resulting in some patients not fulfilling the new criteria and ‘concerns about managing obstetric patients’—first, certain pregnancy morbidity items were considered insufficient for APS classification in the absence of other aPL-related clinical findings during multiple phases of criteria development, and second, classification criteria should not be used to guide treatment decisions, but should help guide clinical trials and studies in relevant aPL-positive subgroups; and (d) isolated IgM positivity as not being sufficient for APS classification—the steering committee agreed that additional studies are needed on isolated moderate and high level anticardiolipin antibody and/or anti-β2-glycoprotein antibody—IgM positive patients who fulfil the clinical section of the new classification criteria, which is included as a high priority research agenda item in our manuscript,4 5 and may potentially guide future updates to the criteria (please also refer to our response6 to comments by Damoiseaux and van Beers3).

In conclusion, we applaud the authors for their timely and important external validation of the new 2023 ACR/EULAR APS classification criteria and welcome the opportunity to highlight important points related to the real-world application of the criteria.

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REFERENCES
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