N. Zohoury replies

To the Editor:

I was pleased to read the letter by Zhang, *et al*[1] regarding our November 2017 published work, "Closing the Serological Gap in Antiphospholipid Syndrome: The Value of 'Non-criteria' Antiphospholipid Antibodies."[2] There are several valuable points that Zhang, *et al* bring up in their letter that I would like an opportunity to highlight and expand upon.

First, their results show significant clinical value for the IgG and IgM antiphosphatidylserine/prothrombin complex (aPS/PT) test for both diagnosing antiphospholipid syndrome (APS) and helping in risk stratification (thrombotic vs non-thrombotic). Their results showed the combination of IgG or IgM aPS/PT with lupus anticoagulant (LAC) gave a higher positive likelihood ratio compared to IgG or IgM anticardiolipin antibodies with LAC (84.84 vs 75.49) and significantly higher than IgG or IgM anti-β_2-glycoprotein I and LAC (84.84 vs 24.72). There have been a number of studies that show the utility of aPS/PT in place of or in addition to LAC[3,4,5] and others that show its utility as a diagnostic marker that aids in risk stratification[6,7,8,9,10].

Second, and possibly more significantly, I highlight their choice to categorize 12.8% of their APS population (31 out of 241) as seronegative APS. Their study is part of a growing body of evidence that continues to suggest that a significant subset of patients with APS are missed by currently accepted serological markers[11,12]. These patients show clinical manifestations suggestive of APS but repeatedly test negative for the "criterion" markers. This subset of patients was the main focal point of our study[2], leading to our conclusion, similar to that of Zhang, *et al*[13]: there should be a reevaluation of the current APS criteria so that patients with true APS are not missed, helping prevent severe outcomes.

I thank the team of Zhang, *et al* for both their attention to our work and their continued efforts on this important topic. The group's result moves this field forward and contributes to improving the diagnostic approach to APS[13]. Their results broadly corroborate our publication, strengthening the evidence for the need to update the APS classification criteria. We agree that the addition of specific new markers such as aPS/PT should be considered based on the strong individual, as well as combined, performance of aPS/PT. Further, we reemphasize our suggestion that future updates to the APS classification criteria should also consider implementation of algorithms and/or scoring methods that could better evaluate patients based on an expanded antibody profile and clinical presentation.

NAVID ZOHOURY, BS, Inova Diagnostics Inc., 9900 Old Grove Road, San Diego, California 92131, USA. Address correspondence to N. Zohoury. E-mail: nzohoury@inovadx.com. Inova Diagnostics Inc. is the supplier of the kits used in the publication by Zhang, *et al*[13]. Although N. Zohoury did not personally participate in this study or have any relationship with the authors, another Inova employee was a participant in the source paper by Zhang, *et al,* referenced here[13] and a co-author of *The Journal's* publication "Closing the Serological Gap in Antiphospholipid Syndrome: The Value of 'Non-criteria' Antiphospholipid Antibodies."[2]

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