

## Response to: 'Can solid-phase assays replace immunofluorescence for ANA screening?' by Bizzaro

We would like to thank Dr Bizzaro for his commentary<sup>1</sup> on our article<sup>2</sup> on the variability of testing for antinuclear antibodies (ANA) by indirect immunofluorescence (IIF). Along with other letters that have been published in response to our article,<sup>3-9</sup> Dr Bizzaro's letter highlights the concerns about the IIF, its status as the 'gold standard' and the availability of other technologies (eg, solid phase assays) that alone or together can provide testing with comparable or better sensitivity and specificity than the IIF. As Dr Bizzaro indicates, the utilisation of these technologies may have advantages in terms of overall costs of patient care.

We agree with Dr Bizzaro that the role of different assay approaches must be evaluated and interpreted in the context of the clinical setting and that the issues for screening may differ for classes of diseases (eg, connective tissue disease and autoimmune liver disease) as well as individual diseases (eg, systemic lupus erythematosus and Sjogren's syndrome). As we have discussed, for systemic lupus erythematosus, the stakes for testing are high since ANA positivity is used as a criterion for disease classification, entry into clinical trials and prescription of medications for products approved for active, autoantibody positive disease.

At this point, we think that it is time for professional organisations and regulatory agencies to recognise the strong evidence for assay variability and start the process of evaluating different assays and platforms for specific purposes and provide guidance for better standardisation. An important first step may be to reopen the question of whether there is in fact a 'gold standard' for ANA testing in general and then determine the best test(s) for specific applications. We are glad that our article has sparked so many letters and believe that the data and ideas presented indicate clearly that re-evaluation of ANA is essential in view of new technologies and new uses for this venerable and widely performed test.

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