this approach will be inaccurate. Ideally, a prospective study is needed with the enrolment of SLE patients at the time of aPL detection and close observation over a long follow up time.

2) The lack of standardisation of both lupus anticoagulant and anti-cardiolipin tests continues to be a major problem in interpreting clinical data published on antiphospholipid antibodies.² However, better interlaboratory agreement was achieved when IgG and IgM aCLs were recorded in a semi-quantitative fashion (that is, negative, or low, medium, high positive).³ Ghirardello *et al* do not specifically comment on such standardisation for their own laboratory.

3) The ELISA assay for aCL is clearly a more sensitive assay for detecting aPLs than the Russell viper venom time.⁴ Interestingly, in this study LA positivity was only found in those patients who were aCL positive. Furthermore, a significant association between high titres of IgG aCL and arterial thrombosis suggests that the aCL titre may be more important than the presence of aCL in SLE patients. Previous reports have suggested that aCL, rather than LA, is a better predictor of fetal death in SLE pregnancy,⁵ and that high titre aCL carries a worse prognosis.⁶ In this regard, Ghirardello *et al* have not studied aPL complications at different titres of aCL. Furthermore, patients in 'risk pregnancies' were treated with aspirin which could influence the frequency of complications observed.

In summary, larger prospective studies of SLE patients with aPL, better standardisation of aPL assays, and analysis of differing titres of aCL in respect of aPL complications are needed.

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AUTHORS' REPLY Dr Hopkinson *et al* suggest caution in interpreting the conclusion of our study regarding the specificity of antiphospholipid antibodies (aPL) for aPL complications in systemic lupus erythematosus (SLE). However, it seems they did not take into account the second part of our conclusion; that is, "the measurement of IgG anticardiolipin antibody (aCL) level seems to be a valuable requirement before attributing clinical value to aCL positivity". We believe therefore that our conclusion summarised our results regarding LA and both aCL positivity and level.

Dr Hopkinson also comments adversely about some of the methodological approaches we used.

1) Our study was a cross-sectional rather than a retrospective study. In fact, individuals were concurrently classified as 'SLE with aPL complications' or 'SLE without aPL complications' and as 'aPL positive' or 'aPL negative' at a single point in time.¹ Nevertheless, we decided to include some anamnestic manifestations which occurred after SLE diagnosis to define individuals as 'SLE with aPL complications' and to be able to evaluate possible relationships between aPL and some low prevalence aPL complications. Such a study design, that has been widely used to investigate the clinical significance of aPL,²⁻⁴ has both well known advantages and disadvantages. As Dr Hopkinson and colleagues pointed out that the time that elapsed between the occurrence of anamnestic manifestations and the aPL determination may be a bias in our study. However, the relevance of this bias depends on some variables, particularly on the total amount of anamnestic data recorded and the length of time elapsed from their occurrence and the aPL determination.

Although the prospective study may be considered 'ideal' for this purpose, some ethical considerations should be taken into account by authors who are interested in research as well as in patient care. In performing such studies antithrombotic and anticoagulant treatment should also be avoided in patients considered at risk of thromboembolic complications on the basis of previous studies, including cross-sectional ones (for example, patients with LA and/or high IgG aCL level). This methodological requirement seems to be particularly unethical in setting up studies on SLE pregnancy outcome, since aspirin is now largely and effectively administered to pregnant women who are at risk for preeclampsia,⁵ a complication frequently observed in pregnant patients with SLE.

2) We currently record aCL positivity in a semi-quantitative manner, according to the KAPS group international guide-lines on aCL test standardisation.⁶ Otherwise, in our study we expressed aCL results by calculating a cut-off point and testing its specificity for aPL complications in SLE by ROC curve analysis.⁷ We considered as optimum cut-off aCL mean levels +4 standard deviations (SD) of 100 healthy subjects and found that, by increasing the number of SD (for example,

to 6 SD), the specificity improved although to a lesser extent than the sensitivity loss.

3) We agree with Dr Hopkinson regarding higher sensitivity of ELISA assay in respect to the Russell viper venom time for aPL detection, as well as a better value of high IgG aCL titre rather than the only aCL presence in SLE, as it stated in our paper. Conversely, we agree with other reports^{2,8,9} that LA rather than aCL positivity is a predictor of aPL complications in SLE, since we assessed specificity using an original approach, that is, the evaluation of aPL profile only in aPL positive patients with and without aPL-related manifestations; patients with complications of aPL syndrome definitely due to factors different from aPL were thus excluded.

Finally, Dr Hopkinson's reference 5 seems inappropriate in this context since Lockshin's patients "do not represent a random cross-section of pregnant patients with SLE" as they were specifically referred to him because of prior fetal death.¹⁰

In conclusion, a cross-sectional study seems to be a suitable design to reach a goal like ours. A large prospective study, but with some ethical reservations, could provide more striking results.

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