the long-term efficacy was poor and the CGI severity results were even in favour of placebo at some later weeks.

One other problem not discussed by the authors might be the absence of a correction for centre effects. There were 37 centres in 6 different countries participating in this trial, varying from 1 centre in Finland to 13 centres in France. The question concerning centre effects, which might be anticipated in such a multicentre trial, was not discussed. Apparently nothing about minimum or maximum number of enrolments per centre was written in the protocol. From our own experience we can state that multinational studies in psychiatry in Europe are not easy to organise and conduct. Furthermore, it would be very helpful to know how many international and national training sessions have been organised as well as data concerning the inter-rater variability.

Data from studies without the definition of the major outcome variables *a priori*, should not be accepted as final proof of efficacy. Therefore we tend to see the study of Doogan & Caillard merely as a feasibility and hypothesis-generating study.

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AUTHOR'S REPLY: Our study was reviewed by the Food and Drug Administration, and a number of methodological matters were discussed.

We accept that there was no absolute *a priori* definition of responder mentioned in the protocol. However, all the usual criteria for response were applied in the analysis of this study. Irrespective of which criteria were used, the result always significantly favoured sertraline over placebo. Thus it is not appropriate to suggest that the data analyses were designed arbitrarily.

A key criticism was that the excess rate of discontinuation of placebo patients over sertraline did not allow the use of an observed-cases analysis to adequately assess drug effect. In a maintenance study, patients remaining well will continue in the study. Therefore, comparisons of CGI severity between sertraline and placebo are unlikely to show any significant difference. The most meaningful statistical analysis is the Kaplan-Meyer survival estimate, which is a conventional analysis used in such situations. This analysis, which controls simultaneously for drop-outs, shows superiority of sertraline over placebo at all time points. It is our firm belief that observed-cases analyses are inappropriate at these time points.

One item not discussed in the paper was the analysis of centre effects. This was investigated and no significant treatment by centre interaction was identified. Thus the number of centres was not a significant factor affecting results. Further, we believed it was unnecessary to conduct inter-rater reliability sessions when the key efficacy measure was Clinical Global Impression. Inter-rater reliability is more to be considered when discrete rating scales, such as Hamilton or Montgomery-Åsberg scales, are being used.

This study was an ambitious project to identify if there was any benefit in maintaining patients long term on sertraline treatment. The conclusions of this study remain that sertraline is of benefit in the long term for controlling relapse of depression.

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SIR: I have had the opportunity of independently reviewing the data from the sertraline placebo long-term treatment study and my conclusions have been published (Montgomery *et al*, 1991). The striking finding in the study was that it did not matter which relapse criteria were adopted since there was a significant advantage for sertraline over placebo with the measures that I examined using either the Hamilton Depression scores or the Clinical Global Severity scale.

The criticism that the analysis was made on *post hoc* definitions of relapse is valid as was discussed in our paper. There is debate as to which relapse criteria are most sensitive to long-term treatment effect. The sertraline–placebo database provides one of the few chances of comparing the effect of different relapse criteria.

The efficacy of an antidepressant in long-term treatment is measured by its ability to reduce the number of relapses or recurrences compared with placebo. The long-term treatment studies do appear