Dr Chande is sweeping in suggesting that if the logic of my argument is accepted, every medical and psychiatric diagnosis is suspect. Some diagnoses, like schizophrenia, have increasing amounts of corroborative physical and prognostic evidence, and we should also look at the striking success of appropriate treatments in conditions like depressive disorders and anxiety states. Comparable results do not appear to be obtainable with the diagnosis of multiple personality disorder as a result of treatments directed to that diagnosis. There are other diagnoses which I agree could be suspect, including hysterical symptoms mimicking organic disease in patients who have seen cases of physical disorder. (Charcot's cases of hysteria and the history of shell-shock in the First World War provide excellent examples). However, I doubt if many who use the diagnoses of schizophrenia, endogenous depression and obsessional neurosis, among others, will see much resemblance between these conditions and those where suggestion has been so prominent.

I wish to reiterate that many of the patients who are now diagnosed as having multiple personality disorder appear to have substantial problems in their early lives and current adjustment, and in their personalities. In-depth psychotherapy may well help them, but the benefits of producing and reuniting disparate personalities have not been demonstrated.

Dr Fahy surmises that I felt this article would be more acceptable to British than to North American psychiatrists. She is right, but no doubt she is aware of the high standing of the *British Journal of Psychiatry* which is widely read in North America.

I would like to take the opportunity to correct a misprint which escaped me in the proof, and to clarify a point. The misprint is the word 'liable' in the first column on page 327 which should read "labile". The clarification has to do with the *Three Faces of Eve*. I wrote that there was an important difference between the psychiatrist's account and the patient's account in the presentation of her maiden name, saying that the point was not evident in the psychiatrist's account. That is correct, but the fact that the patient reverted to her maiden name was not concealed by Thigpen & Cleckley (1957). However, they only report it a page later in parentheses and do not discuss the choice of name there, so that the importance of this item is lost in their text.

I did not always disbelieve in MPD. I thought it might occur as a rare event. The astonishing growth of improbable cases prompted me to look more closely at the phenomenon, and it was only then that I came to the conclusion that there was no veridical evidence which would be adequate to support the diagnosis, and the mere spread of enthusiasm for it had itself served to make it impossible to prove that it existed. Such a diagnosis deserves to be characterised by the term doxogenic disease which has been used until not long ago (Dorland, 1957) to characterise illnesses due to the patients' own mental conceptions (from doxe, meaning opinion and genon, to produce). In this case the opinions are largely received as a result of external influences which are medical, journalistic, literary, broadcast and theatrical.

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Sertraline in the prevention of depression

SIR: Data on the efficacy and safety of antidepressants in prevention of relapse are relatively scarce. As the European Guidelines Commission of the European Communities, 1989 recommend investigation of continuation therapy with antidepressant agents, the initiative of Pfizer Central Research to conduct a relapse trial with sertraline is greatly appreciated (Doogan & Caillard, *Journal*, February 1992, **160**, 217–222). However, the analysis of their study results is not in harmony with the analysis of the reviewer of the Food and Drugs Administration (FDA), Dr Hillary Lee (Lee, 1990*a*,*b*). Major problems of this study identified by Lee were the absence of *a priori* decisions in the protocol related to efficacy parameters: an objective definition of satisfactory response was not provided and relapse was not defined beforehand (Lee, 1990*a*). Data sets for analysis were prepared arbitrarily by the sponsor. In a separate analysis done by the FDA, it was stated that the *P*-values for the comparison of sertraline versus placebo based on the clinical global impression (CGI) severity are far from showing the long-term efficacy of sertraline. Out of eleven four-weekly analyses of CGI severity scores, only the *P*-value at week four was highly significant. Therefore, it was concluded that the statistical support for

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