

prevention of relapse of post-traumatic stress disorder (PTSD) for up to 6 months. I think that this statement needs careful consideration.

First, the authors start by randomising patients into a placebo group and a fluoxetine group; the latter is later subdivided into a fluoxetine/placebo group and a fluoxetine/fluoxetine group. We see the outcome results of both the groups initially treated with fluoxetine, but those of the placebo/placebo group are not included in the paper.

Second, the authors dismiss the issue of discontinuation-emergent adverse effects, referring to a study by Rosenbaum *et al* (1998). That study, also sponsored by Eli Lilly, concluded that fluoxetine had fewer adverse events than other selective serotonin reuptake inhibitors. However, fluoxetine was used up to a maximum dose of 60 mg/day with a mean dose close to 25 mg/day, whereas in the Martenyi *et al* study, the maximum dose was 80 mg/day and the mean close to 50 mg/day – double that in the Rosenbaum *et al* study. This is more significant as the results are not analysed on an intention-to-treat basis. Martenyi *et al* state that there were no significant differences when comparing drop-outs due to adverse events, but if we compare the total number of patients discontinuing the study, the percentages are almost double for those switched to placebo compared with those continued on fluoxetine (33.4% *v.* 17.3%).

Third, the authors mention that the reason behind the failure to show significant differences in the improvement of symptoms between the two treatment groups is the result of inconsistent patient self-rating. Could it not simply be that there are no differences?

The study addresses an important area, but the interpretation of the results should have been more rigorous.

Martenyi, F., Brown, E. B., Zhang, H., et al (2002)
Fluoxetine *v.* placebo in prevention of relapse in post-traumatic stress disorder. *British Journal of Psychiatry*, **181**, 315–320.

Rosenbaum, J. F., Fava, M., Hoog, S. L., et al (1998)
Selective serotonin reuptake inhibitor discontinuation syndrome: a randomised clinical trial. *Biological Psychiatry*, **44**, 77–87.

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Authors' reply: Dr Agell raises concerns regarding the conclusions proposed in our original article (Martenyi *et al*, 2002a) that the results of our study suggest that fluoxetine is effective and well-tolerated in the prevention of PTSD relapse for up to 6 months. Dr Agell's concerns that (a) we do not discuss the results of the placebo/placebo group; (b) we do not adequately address the study results regarding SSRI discontinuation-emergent adverse events; and (c) 'the authors mention that the reason behind the failure to show significant differences in the improvement of symptoms between the two treatment groups is the result of inconsistent patient self-rating'. We will attempt to address each of these concerns.

First, the results presented in our original article pertain to the relapse-prevention phase of a larger study. Results of the acute treatment phase (including the acute results of the placebo/placebo group) may be found in Martenyi *et al* (2002b). The primary objective of the relapse-prevention phase of our study and the focus of our original article was to assess the efficacy and tolerability of fluoxetine in the prevention of PTSD relapse. It then follows that the relevant results should come from acute phase fluoxetine responders who were continued on fluoxetine in the relapse-prevention phase or switched to placebo. The efficacy results from the placebo/placebo group would not address our question regarding the efficacy of fluoxetine in the prevention of PTSD relapse and, therefore, the full relapse-prevention efficacy results from the placebo/placebo group were not provided. We did, however, provide a breakdown of the reasons for discontinuation in the study for all treatment groups (Martenyi *et al*, 2002a, Fig. 1). Of the 31 patients in the placebo/placebo group (note that the sample size is small because the original randomisation was 3:1 fluoxetine : placebo), the discontinuation profile was quite similar to that of the fluoxetine/placebo group. Discontinuation profiles for the fluoxetine/placebo group *v.* the placebo/placebo group, respectively, were: 66.1% *v.* 61.3% completed the protocol; 0% *v.* 0% discontinued because of adverse events; 16.1% *v.* 16.1% discontinued because of clinical relapse; 4.8% *v.* 12.9% were lost to follow-up; 3.2% *v.* 0% discontinued because of patient decision; 9.7% *v.* 6.5% discontinued because of non-compliance; and 0% *v.* 3.2% discontinued because of

lack of efficacy. These discontinuation data suggest that patients with an initial placebo response face a similar risk of recurrence of symptoms to those who had achieved an adequate pharmacological response and were then switched to placebo.

Second, it is true that approximately twice as many patients discontinued from the fluoxetine/placebo group compared with the fluoxetine/fluoxetine group. It is important, however, to note the reasons for discontinuations (Martenyi *et al*, 2002a, Table 2). The protocol specified that patients meeting pre-defined criteria for clinical relapse should be discontinued, which allowed the investigators to provide follow-up care at their discretion. Only one patient in the fluoxetine/fluoxetine group discontinued because of an adverse event compared with none in the fluoxetine/placebo group, and the primary difference between the two treatment groups with regard to reason for patient discontinuation was clinical relapse (5.8% *v.* 16.1% for the fluoxetine/fluoxetine and fluoxetine/placebo groups, respectively). Accounting for all reasons for discontinuation with the exception of clinical relapse, 8 patients (12%) *v.* 11 patients (18%) discontinued early for the fluoxetine/fluoxetine and fluoxetine/placebo groups, respectively (Martenyi *et al*, 2002a, Table 2). It should also be noted that there were no statistically significant differences in the numbers of patients reporting any single adverse event. The adverse events most commonly reported by patients in the fluoxetine/fluoxetine group were insomnia (15%), anxiety (6%) and headache (6%); those most commonly reported by patients in the fluoxetine/placebo group were insomnia (10%), headache (5%) and pain (5%). These data provide further support that the long half-life of fluoxetine and its active metabolite, norfluoxetine, provide benefit with regard to the minimisation of the risk of discontinuation-emergent signs and symptoms.

Third, statistically significant differences were detected between treatment groups for the *a priori* defined primary analysis (time to relapse, $P=0.027$; Martenyi *et al*, 2002a, Fig. 2). In addition, using repeated-measures analysis of variance (Martenyi *et al*, 2002a, Fig. 3), we can see that those patients in the fluoxetine/fluoxetine group continued to improve over time, with a statistically significant difference between groups occurring from week 28 to the study end-point (week 36), based on our primary efficacy measure, and

other significant differences were detected between groups in several other illness severity measures (Martenyi *et al*, 2002a, Table 3). Other patient-rated secondary measures were used in this study and, as reported, failed to show a significant difference between groups (Martenyi *et al*, 2002a, Table 3).

We believe that the results of this study are robust and support our conclusions, and we maintain our opinion that the study results suggest that 'fluoxetine is effective and well-tolerated in the prevention of PTSD relapse for up to 6 months'.

Declaration of interest

This work was sponsored by Eli Lilly and Company. E.B.B., A.P. and C.M.M. are employees of Eli Lilly and Company.

Martenyi, F., Brown, E. B., Zhang, H., et al (2002a) Fluoxetine v. placebo in prevention of relapse in post-traumatic stress disorder. *British Journal of Psychiatry*, **181**, 315–320.

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The Edinburgh Postnatal Depression Scale

The Edinburgh Postnatal Depression Scale (EPDS; Cox *et al*, 1987) is one of the most widely used self-report instruments to screen for depression in the post-partum and antenatal periods. As with all instruments, it is important for validity that the wording of a measure remains faithful to that described in the original validation study. While checking our EPDS against the original, we noticed a difference in the wording of one of the items. We believe that the EPDS used elsewhere may also

contain the same anomaly. Item 4 on the EPDS provided in the paper by Cox *et al* (1987) is phrased: 'I have been anxious or worried for no good reason'. However, the version reproduced in Cox & Holden's book (1994), which is also likely to be the source from which many centres copy their EPDS, is different: 'I have *felt* worried *and* anxious for no *very* good reason' (differences from the journal version italicised for clarity). In addition, the order of anxious and worried has been reversed. Personal communication with Professor Cox has confirmed that the wording in the journal paper is correct. That these mistakes have occurred in a book about the 'use and misuse' of the scale is somewhat ironic. Indeed, this makes us a little anxious and worried!

What effect might these differences have on the self-reports of women or men? It is hard to know – hopefully, none. It would not, however, be surprising if these alterations lead to differential responding and scores.

Over the many years of our involvement in this field, we have also noted usage where the EPDS preamble was omitted or altered, provenance (e.g. authors and date) was not acknowledged, and incorrect cut-off scores were inadvertently applied. We should all, therefore, be more rigorous in our use of this scale.

Cox, J. L., Holden, J. M. & Sagovsky, R. (1987) Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. *British Journal of Psychiatry*, **150**, 782–786.

— & — (eds) (1994) *Perinatal Psychiatry: Use and Misuse of the Edinburgh Postnatal Depression Scale*. London: Gaskell.

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Authors' reply: We are indebted to our distinguished colleagues in Australia for pointing out this ambiguity. We will be indicating in our definitive EPDS book, soon to be published by Gaskell (Cox & Holden, 2003), that the scale from the first validation study as published in 1987 contains the correct and original wording.

The differences between 'being' and 'feeling', 'anxious or worried' and 'worried and anxious' are not only semantic. Perhaps committed EPDS advocates, like your correspondents, will test their hypothesis that these word changes may affect the total EPDS score. We doubt it, but a local grant-giving body might support an ambitious master's student.

The EPDS is not, of course, a precise measuring-rod of feelings, but its total score has been shown to provide a remarkably accurate indication of the likelihood of clinical depression in many cultures and countries.

Our new book, *Perinatal Mental Health: A Guide to the Edinburgh Postnatal Depression Scale (EPDS)*, is our definitive and final attempt to ensure that the EPDS is used as frequently as appropriate; and misused – never!

Declaration of interest

J.C. and J.H. developed the EPDS and are authors of Cox & Holden (2003), sales of which may generate personal royalty payments.

Cox, J. & Holden, J. (2003) *Perinatal Mental Health: A Guide to the Edinburgh Postnatal Depression Scale (EPDS)*. London: Gaskell.

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One hundred years ago

Royal Asylum of Montrose (Annual Report for 1900)

Suicidal tendencies were marked in a large proportion of the patients admitted, and the inquiries of Sir John Sibbald now

published for the first time show that Forfarshire and the neighbouring county of Kincardine have a larger proportion of suicides compared with the population than the rest of Scotland. The same authority states that 'the counties of the east coast

of Scotland all show higher suicidal rates than the western counties. It is curious that the city of Dundee shows a lower rate than the rest of Forfarshire. It is so far in favour of the view of those who say that Celticism and Catholicism prevent suicide, for