frequency fell by 88% in Clark *et al*'s study, in the placebo group of Marks *et al* (1993) it fell by 85% (96% if the criterion was spontaneous major panics) despite panics having been more frequent at the start than in the Clark *et al* study.

3. The authors aimed to test how "cognitive therapy compares with alternative, established psychological . . . treatments for panic disorder", but for that comparison used a weak form of exposure therapy – applied relaxation – which only "introduced exposure after 4 sessions". The authors do not note having asked patients to do self-exposure homework for at least an hour a day or to keep self-exposure homework diaries for review at each session. The outcome of exposure therapy depends on how systematically it is given.

The authors report no check of whether cognitive therapy patients had firmer exposure instructions in doing "behavioural experiments" than did the applied relaxation and imipramine groups, which is a possible reason for the differences.

4. "Cognitive measures at end of treatment were significant predictors of outcome at follow-up". The authors' analyses are insufficient to gauge the value of cognitions as predictors. A multiple regression analysis was desirable to control for the effects of pre-treatment severity, treatment condition, and non-cognitive outcome measures, and to test which variables gave the strongest predictions. Clark *et al* did not exclude the possibility that their non-cognitive measures were as predictive as cognitive ones.

"Sustained improvement . . . will depend on cognitive change having occurred during the course of therapy." After rigorous testing the effective ingredients of treatments often turn out to be different from those postulated. The authors have not excluded the role of exposure and/or sense of control regardless of misinterpretations concerning bodily sensations. Basoglu *et al* (1994*b*) found that panic fell dramatically without cognitive therapy, so panic patients can improve without trying to change their interpretations of bodily sensations. Such change may arise because of (i) indirect exposure to such sensations through exposure to external situations or (ii) direct exposure to such sensations (interoceptive exposure) as in Clark *et al*, without a need to do cognitive restructuring.

5. The authors report no test of whether the assessor actually remained blind throughout the study.

6. The cost implications of the lack of balance of therapist time are not addressed. Although imipramine patients had more sessions after six months, their total time with the clinician since the start was $(10.5+1.6+2.8) \times 24 = 358$ min, whereas cognitive therapy patients had $(10.5+2.2+0.4) \times 58 = 760$ min, and applied relaxation patients had $(10.3+2.0+1.5) \times 57 = 787$ min.

7. The authors report 88% of cognitive therapy patients becoming panic-free yet their Table 2 shows a reduction at six months of only 27% in agoraphobic cognitions and 43% in bodily sensations interpretations.

BASOGLU, M., MARKS, I. M., KILIÇ, C., *et al* (1994*a*) Relationship of panic, anticipatory anxiety, agoraphobia and global improvement in panic disorder with agoraphobia treated by alprazolam and exposure. *British Journal of Psychiatry*, **164**, 647–652.

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AUTHOR'S REPLY:

1. Milder panic disorder Marks *et al* claim that the patients in our study "had only 2.7 panics a week, compared to over four a week in larger multinational studies". This is incorrect. It seems that Marks *et al* failed to read our article carefully. The figure of 2.7 refers to a 0–4 point rating scale (see p. 762), not to absolute panic frequency. Absolute panic frequency is a problematic measure as it is never normally distributed and for this reason we made an *a priori* decision not to include it as an outcome measure. In view of Marks *et al*'s comments, we have gone back to the patients' files and can confirm that the absolute panic frequency for patients included in the study is 4.3 per week (range 1 to 40), making it comparable with the other studies cited by Marks. Marks *et al* also claim that our patients were milder because none had "marked agoraphobia". Marked agoraphobia is not a defined term. We used DSM-III-R which has four categories of agoraphobic avoidance (none, mild, moderate, severe). Using these categories 81% of our patients had some degree of agoraphobic avoidance: 48% fell into the mild category and 33% fell into the moderate category. We excluded patients

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with severe agoraphobic avoidance. Some of these patients would have required home-based treatment and for this reason we suspect they would have also been excluded from the multinational studies.

2. Control for non-specific factors Marks *et al* claim that our only control for non-specific factors was a waiting list. Again, they appear not to have read the article. We are not aware of anyone who would consider a waiting list to be a control for non-specific factors. In our study, the group that we used to infer that the effectiveness of cognitive therapy was not entirely due to non-specific factors was a group who were themselves given an active treatment. This stringent test for non-specific factors is explained in considerable detail on p. 767.

Marks *et al* go on to cite their own finding that patients given placebo medication in the London/Toronto study showed a substantial drop in panic frequency. The results obtained with placebo medication in a different study using different selection criteria are not relevant to the issue of the role of non-specific therapy factors in our particular study. In addition, Marks *et al*'s conclusion that their results indicate that "placebo had a major anti-panic effect" is unsound. To determine whether a placebo has an anti-panic effect, it is necessary to compare patients given the placebo with patients who are not given the placebo (e.g. a no-treatment control group). Such a control was not included in the Marks *et al* (1993) study. In a study by Klosko *et al* (1990) which included both placebo and no-treatment groups, no difference was found between the panic-free rates in the two groups. There is currently no reason to suppose that placebo medication has a significant anti-panic effect. In studies which compare active medication with placebo, the only safe inferences one can make concern the question of whether medication had a direct pharmacological effect. Without a no-treatment control group, the response observed in the placebo medication group in a particular study may be entirely due to spontaneous remission. This is particularly likely to be the case when patients are withdrawn from medication immediately prior to the start of the study as in Marks *et al* (1993) as this procedure is likely to produce a transient increase in anxiety and panic which would inflate pre-treatment scores and lead to an over-estimation of pre- to post-treatment change (see p. 762 of our article). Other factors that are likely to produce a high panic-free rate at the end of the placebo medication phase are: failure to exclude patients who record no panic attacks during post-assessment baseline monitoring; selective drop out of cases who do not improve on placebo; and short-lived increases in panic frequency as a result of some agoraphobic patients increasing situational exposure during the baseline period. None of these points apply to our study. We are not able to comment on the extent to which they may or may not have been relevant in the London/Toronto study.

3. Exposure compared with cognitive therapy All three treatments in our study (cognitive therapy, applied relaxation, and imipramine) included systematic self-exposure homework assignments and the treatment sessions did not differ in the amount of time devoted to this procedure (p. 762). We therefore concluded that the superior results obtained with cognitive therapy were unlikely to be entirely due to exposure homework instructions. This does not mean that some other more intensive and comprehensive form of exposure could not produce as good results as those obtained with cognitive therapy. We cited a recent study by Margraf *et al* (1993) which found that a combination of intensive interoceptive and situational exposure was as effective as cognitive therapy. They compared pure cognitive intervention, pure exposure (interoceptive and situational), their combination, and no treatment. Only 5% of the no-treatment group became panic-free compared to over 75% in each of the three treatment groups. The apparent success of an exposure programme with a major interoceptive component is entirely consistent with the cognitive theory of panic (Clark, 1986). What is less clear is how the more traditional situational exposure programme used by Marks *et al* (1993) compares with cognitive therapy. The London/Toronto study found that this type of exposure was no more effective in reducing panic than relaxation whereas our study clearly showed that cognitive therapy was more effective than relaxation in reducing panic.

Marks *et al* correctly assert that we did not keep a record of patients' self-exposure to feared situations. Such data would be of interest but would also be difficult to interpret. If one group engages in more self-exposure than another it could either be because that group has improved more and the increased self-exposure is a consequence of that group's reduced fear and greater ability to return to everyday life, or because that group intentionally did more exposure assignments as a way of overcoming their fears.

4. Predicting outcome at follow-up We reported a series of analyses which suggested that patients who had a residual tendency to misinterpret bodily

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sensations at the end of treatment were more likely to relapse. In particular there was a significant correlation between BSIQ-Panic at 6 months and the panic/anxiety composite (an overall measure of severity) at 15 months and this remained significant when panic-anxiety composite scores at 6 months were partialled out (p. 767). This clearly indicates that a cognitive measure taken at the end of treatment is a significant predictor of subsequent symptomatology even when current symptomatology is controlled for. Marks *et al* argue that multiple regression analysis would have been a preferable technique. We disagree. With our sample size ($n=60$) multiple regression would have little advantage as statisticians (Stevens, 1992) usually require a minimum of 15 subjects per independent variable entered into the regression equation. Marks *et al* also argue that we have not ruled out the possibility that some other non-cognitive variable might also predict outcome at follow-up. This is correct but it was not our aim. We assume the variable that Marks *et al* might be particularly interested in is residual avoidance. To address this question, we have reanalysed the data set. The correlation between agoraphobic avoidance at 6 months and the panic/anxiety composite at 15 months, with agoraphobic avoidance at 6 months partialled out, is non-significant ($r_{(57)}=0.07$, $P>0.5$).

5. Assessor blindness We made strenuous efforts to ensure that our assessors were blind to treatment allocation throughout the study. However, we did not assess blindness. This is also true of previous studies by Marks' group. When our study was already underway, Margraf *et al* (1991) reported that physicians who were supposedly blind in a similar study were better than chance at guessing allocation to drug v. placebo. This suggests that future studies should include a test for assessor blindness.

6. Cost implications We did not discuss the cost implications of our results. These are difficult to quantify because they depend on who delivers the pharmacological treatment (psychiatrists or general practitioners) and whether long-term outcome (more patients relapsed after imipramine) is factored into the calculation. Our study was unusual in having one-year follow-up data on almost all (87%) of the sample. The London/Toronto study was less successful in obtaining follow-up data as 51% (78/154) of the sample had been lost by week 43. The other study cited by Marks *et al* was no more successful. Such high drop-out rates make long-term outcome data difficult to interpret because attrition is unlikely to be random – patients who have responded well are particularly likely to be selectively retained.

7. Calculations and comparison errors Marks *et al* have incorrectly calculated several per cent change scores. For example, they state that we "report 88% of cognitive therapy patients becoming panic-free yet their Table 2 shows a reduction at six months of only 27% in agoraphobic cognitions and 43% in bodily sensations interpretations". The correct calculations are 57% reduction in agoraphobic cognitions and 89% reduction in bodily sensations interpretations. Marks *et al* seem to have assumed the minimum values on each scale are 0 despite Table 2 clearly stating they are 15 and 7, respectively. Marks *et al*'s comparisons of per cent reduction in panic frequency between the Oxford and London/Toronto studies are also misleading. First, the scales used in the two studies are different (0–4 point rating v. absolute panic frequency) and hence cannot be compared. Second, the comparisons are for completers only and the two studies show dramatic differences in drop-out rates. In the Oxford study, the drop-out rate for cognitive therapy is only 5%, even at one-year follow-up. In the London/Toronto study, the drop-out rates for exposure are 18% (14/78) at 8 weeks, 33% (26/78) at 18 weeks and 49% (38/78) at 43 weeks.

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