Correspondence

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Cognitive–behavioural therapy for bipolar disorder

Dr Lam (2006) comments on our study (Scott *et al*, 2006*a*), the largest randomised controlled trial (RCT) of psychological treatment for bipolar disorder conducted so far. We respond as follows.

(a) Dr Lam seems to misinterpret the nature and purpose of pragmatic trials. It is not a matter, as he suggests, simply of appropriate outcome measures, which should be a feature of all trials. Pragmatic trials are intended to test therapies in the practical circumstances of everyday clinical settings, using large multicentre samples (Hotopf *et al*, 1999). Most previous trials of therapies for bipolar disorders were single-centre efficacy studies designed to try out new interventions in specialist services or where the originator worked.

(b) Dr Lam comments on the number of cognitive–behavioural therapy (CBT) sessions received. We believe that 20 sessions with 2 boosters is as many as is practical in most National Health Service (NHS) settings. That patients attended about 14 of the sessions offered is frustrating but reflects clinical reality and is remarkably similar to the attendance achieved in Dr Lam's own study (Lam *et al*, 2003: average 13.9 sessions, s.d.=5.5).

(c) Our analysis strategy was determined before inspection of the data under the scrutiny of a trial steering committee appointed by the Medical Research Council. Dr Lam confounds several issues and recommends an actuarial analysis that is fundamentally incorrect in the context of an RCT (ICH Harmonised Tripartite Guideline, 1999). In an intention-to-treat analysis, the date of randomisation determines the start of the clock and everyone who is randomised is analysed; it is wrong to delay the inclusion of any participant in the analysis until they are asymptomatic. We also reported in the text on the issue he raised, namely that there was no difference in time to next bipolar episode or mean severity of symptoms in the sample who were in acute bipolar episode at baseline, not in acute bipolar episode at baseline or the whole sample.

(d) Dr Lam suggests it was inappropriate to include in our study individuals who were in a current episode or not on mood stabilisers. However, given that RCTs of therapy for mental disorders are usually undertaken with participants who are currently symptomatic, we believe it is important and informative to explore the potential effects of therapies commenced in the acute phase of bipolar disorder. Furthermore, in Judd *et al*'s (2002) 12-year follow-up it was shown that individuals with bipolar disorder spend 50% of their time with syndromal or sub-syndromal symptoms of mood disorder, predominantly depression. Not receiving or not adhering to recognised mood stabilisers is a similar well-documented issue in 20–50% of individuals with bipolar disorders (Scott & Colom, 2005). Our sample thus reflects the realities of clinical practice.

(e) It is standard practice in RCTs to control for design variables and also to pursue additional analyses that control for potential confounders (Schulz & Grimes, 2005). None of our analyses failed to converge, a common consequence of multi-collinearity.

(f) Dr Lam points out that a median split of a continuous variable can lose information. In fact, this was the reason why we looked for a trend across four groups as shown in Fig. 4 (p. 318).

Previous studies of psychological therapies have mostly involved more selected populations at relatively lower risk of relapse. In those circumstances CBT appears beneficial. Our study used a mixed patient sample; many were high-risk or currently symptomatic. We designed the trial in this way to address an issue not explored so far in any other psychological therapy study, namely whether the treatment would be effective in all patients who might be considered for it. Patients were only excluded if participation was unfeasible or unethical.

Our findings indicate that 22 sessions of CBT may not be effective for most people seen in NHS general adult psychiatry settings. In our lower-risk subgroup, similar in characteristics to Dr Lam's sample (Lam *et al*, 2003), CBT may be very helpful. The clinical implications are that for a stable, lower-risk population, early in their history of bipolar recurrences, CBT should be considered as an adjunctive treatment option to further enhance their outcome. For high-risk, complex cases, other forms of therapy should be considered, such as those targeted at medication adherence or relapse prevention, before considering CBT. These recommendations are consistent with the results from published meta-analyses and other findings on psychological therapies in bipolar disorders (Scott & Colom, 2005; Scott *et al*, 2006*b*).

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Trial of risperidone in India – concerns

The study by Khanna *et al* (2005) on the effectiveness of risperidone in acute mania raises many questions.

Why was the study done? The authors do not indicate that existing treatments have limitations that led them to test risperidone as an alternative.

Why was a placebo used when an effective treatment exists? This is particularly worrisome because, as the authors state, acute mania can be life-threatening and carries an increased risk of suicide.

Patients undergoing psychiatric treatment are a vulnerable group. How did patients give informed consent during an episode of acute mania?

Where were the trial sites? Who were the participants and what quality of care did they receive? What were the adverse events? How were seven participants from the placebo group lost to follow-up?

Regarding the 'wash-out' period before the trial, is it medically and morally justified to withhold treatment from patients during an episode of illness in intensive care?

Four authors state that they are drug company employees. Do the other authors have any competing interest to declare?

In what sense was the trial conducted according to the Declaration of Helsinki? Why do the authors mention the Declaration as revised in 1989, rather than a more recent revision?

We suggest that this trial could not have been conducted in a high-income country but may have been conducted in India because regulatory requirements could be fulfilled there. The use of a placebo when an effective treatment exists – and other elements of the study as mentioned above – goes against the Helsinki guidelines and those of the Indian Council of Medical Research (2000). Finally, publication of such studies in a leading journal such as the *British Journal of Psychiatry* gives credibility to unethical medical research and practice and is a matter of serious concern.

Declaration of interest

The authors are editors of the *Indian Journal of Medical Ethics* and have previously written or spoken against certain drug company practices, including sponsored research.

Indian Council of Medical Research (2000) *Ethical Guidelines for Biomedical Research on Human Subjects*. http://icmr.nic.in/ethical.pdf

Khanna, S., Vieta, E., Lyons, B., *et al* (2005) Risperidone in the treatment of acute mania: double-blind, placebo-controlled study. *British Journal of Psychiatry*, **187**, 229–234.

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Although it is encouraging to see the *Journal* take an active role in redressing 'editorial racism' as discussed in a previous editorial (Tyrer, 2005), there is a need to ensure that promotion of positive discrimination does not exacerbate the problem.

We feel that a recently published randomised double-blind placebo-controlled trial of risperidone performed in India illustrates the dangers inherent in such a policy (Khanna *et al*, 2005). The report had a number of serious shortcomings, which included omission of crucial details of the process of randomisation, interrater reliability and the measures taken to ensure masking. However, the most worrying aspect of the trial was the use of a placebo in the control group and the apparent absence of any ethical approval to proceed with this study. What was the justification for denying severely unwell and vulnerable patients access to appropriate treatment? Why was there no discussion about the ethical dilemmas associated with this study?

We support the *Journal* policy of combating editorial racism by promoting positive discrimination in the instructions to referees. However, the *Journal* must not relinquish its responsibilities as the official journal of the Royal College of Psychiatrists by failing to act as final arbiter for the quality (including the ethics) of the *Journal*'s content.

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With a sample size of 290 patients the report by Khanna *et al* (2005) buttresses the data about efficacy of atypical antipsychotics in the treatment of acute mania, but the article also raised the following concerns.

One of the sites had to be withdrawn from the study after enrolling three participants because of concerns about data quality. However, the data from these individuals were still included in the safety analyses. We are of the opinion that if there were concerns about the data from one particular site, then that site should have been excluded from any further analyses.

We also have concerns about the legitimacy and validity of the informed consent obtained from 145 patients with acute mania and a mean Young Mania Rating Scale score of 37.5 to be enrolled in the placebo arm of a clinical trial. Article 4 of the World Medical Association Declaration of Helsinki (World Medical Association, 1989) states that biomedical research involving human participants cannot legitimately be carried out unless the

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