chance expectancy (Stallone *et al*, 1975). Contact with trial lithium patients, therefore, can lead to unblinding.

As the Cochrane Collaboration proceeds in its systematic review of clinical trials it has sought to determine whether controlled trials are properly randomised. In the Cochrane Pregnancy and Childbirth Database evidence of complete randomisation is associated with less treatment effect (Schulz *et al*, 1995). However, it may be necessary to conclude that a truly double-blind trial of lithium cannot be performed (Double, 1995).

CALIL, H. M., ZWICKER, A. P. & KLEPACZ, S. (1990) The effects of lithium carbonate on healthy volunteers: Mood stabilization? *Biological Psychiatry*, **27**, 711–722.

DOUBLE, D. B. (1995) Unblinding in trials of the withdrawal of anticholinergic agents in patients maintained on neuroleptics. *Journal of Nervous and Mental Disease*, **183**, 599–602.

MONCRIEFF, J. (1995) Lithium revisited. A re-examination of the placebo-controlled trials of lithium prophylaxis in manic-depressive disorder. *British Journal of Psychiatry*, **167**, 569–573.

SCHULZ, K. F., CHALMERS, I., HAYES, R. J., *et al* (1995) Dimensions of methodological quality associated with estimates of treatment effects in controlled trials. *Journal of the American Medical Association*, **273**, 408–412.

STALLONE, F., MENDLEWICZ, J. & FIEVE, R. R. (1975) Double-blind procedure: an assessment in a study of lithium prophylaxis. *Psychological Medicine*, **5**, 78–82.

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SIR: The editorial by Moncrieff (1995) contained a number of errors in reference to our paper (Coppen *et al*, 1971) on a prospective trial of lithium in the prophylaxis of unipolar and bipolar patients.

The report was concerned with 68 patients who completed the trial. The patients' plasma lithium was regularly monitored and it was found that six patients were poor compliers with inadequate or absent lithium levels. The results were still highly significant after adding these poor compliers. Thirteen patients dropped out of the trial during the initial 16 weeks of the trial, two were on lithium and 11 on placebo. A global rating of response was made independently by a social worker and the psychiatrist in charge of the patients. The two ratings were highly concordant. Eighty-six per cent of lithium patients were rated as showing little or no morbidity compared to only 8% of the placebo group. Similar results were found for unipolar and bipolar patients analysed separately. Other indices of response included time spent in hospital or with an out-patient episode and other treatment required. They all indicated a highly significant difference between the lithium and placebo patients. A particularly striking difference was found in the use of electroconvulsive therapy; no patient on lithium required this therapy as compared to 43% of the placebo group.

Following our trial we set up a mood disorder clinic in our unit and follow-up studies after many years have shown a very low morbidity in these patients. (Coppen & Abou-Saleh, 1988) and as Professor Goodwin pointed out a very low suicide rate.

The most comprehensive meta-analysis of lithium treatment is by Davis *et al* (1993) using only double blind, random assignment, placebo controlled studies. In eight studies of maintenance treatment by lithium in unipolar depression they found an improvement in response rate (compared to placebo) of 34% ($P<3 \times 10^{-9}$); in bipolar illness (10 studies) they found a difference of 55% in response rate ($P<10^{-29}$). They comment that this is roughly the order of magnitude of improvement shown with streptomycin treatment in comparison to bed rest alone for patients with tuberculosis.

The poor results of management of mood disorder may be attributed to the medical profession who, by and large, have failed to adequately treat the common, serious and potentially lethal conditions of depressive and mood disorders.

COPPEN, A., NOGUERA, R., BAILEY J., *et al* (1971) Prophylactic lithium in affective disorders. *Lancet, ii*, 275–279.

—— & ABOU-SALEH, M.T. (1988) Lithium therapy: from clinical trials to practical management. *Acta Psychiatrica Scandinavica*, **78**, 756–762.

DAVIS, J. M., WONG, Z., & JANICAK, P.G. (1993) A quantitative analysis of clinical drug trials for the treatment of affective disorders. *Psychopharmacology Bulletin*, **29**, 175–181.

MONCRIEFF, J. (1995) Lithium revisited. *British Journal of Psychiatry*, **167**, 569–573.

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SIR: It seems possible to me that the results of the early trials of lithium were influenced by the highly emotional climate in which they took place. In the 1960s and '70s, the so-called Cinderella of psychopharmacology was a pioneering drug, a cause célèbre. Handicapped by its toxicity problems and lack of interest from drug companies, it took on something of the mantle of the depressives it treated, and champions emerged to rescue its reputation and fight for its recognition.

In the Baastrup *et al* study of 1970, for example, patients who sensed from the side-effects that they