eventually detecting a spuriously significant treatment difference (type I error). Accordingly, it is good practice to decide in advance precisely what would be sufficiently strong evidence of a treatment effect to merit stopping the trial, taking into account the magnitude of the difference in outcome considered clinically important, the number of interim analyses to be performed, and the level of statistical significance required (Pocock, 1983). Unfortunately, Bisson *et al* do not state whether any stopping rules were explicitly determined before the trial commenced, or whether there was any limit on the number of interim analyses, and it is therefore possible that their study was prematurely stopped at an inappropriate point.

This difficulty would be less important were it not that at the time at which the study was terminated the debriefed group not only had experienced more severe burn traumas than the controls, but in addition almost twice as many debriefed subjects had reported significant previous trauma, both of these factors increasing their risk for the development of more numerous and severe post-traumatic symptoms (McFarlane & Yehuda, 1996). It may be that had the study continued recruiting patients according to its random protocol the background differences between the two groups would have diminished and the outcome findings could have been different.

Bisson, J. I., Jenkins, P. L., Alexander, J., *et al* (1997) Randomised controlled trial of psychological debriefing for victims of acute burn trauma. *British Journal of Psychiatry*, **171**, 78–81.

Hobbs, M., Mayou, R., Harrison, B., *et al* (1996) A randomised controlled trial of psychological debriefing for victims of road traffic accidents. *British Medical Journal*, **313**, 1438–1439.

McFarlane, A. C. & Yehuda, R. (1996) Resilience, vulnerability, and the course of posttraumatic reactions. In *Traumatic Stress* (eds. B. A. van der Kolk, A. C. McFarlane & L. Weisaeth), pp. 155–181. London: Guilford Press.

David Reiss, Morven Leese Department of Forensic Psychiatry, Institute of Psychiatry, De Crespigny Park, London SE5 8AF

Cost-effectiveness of clozapine

Sir: Robert & Kennedy's editorial (1997) on our paper (Aitchison & Kerwin, 1997) cannot pass without comment. This was not a clinical trial of clozapine and should not be judged as such: our study was a cost-effectiveness analysis.

However, we would like to comment on the efficacy figure that they quoted. They quote Baldessarini & Frankenburg (1991) as giving a figure of 13% of patients being better off on clozapine than on typical neuroleptics (from trials, largely double-blind), omitting a comment from the same paper that "it is increasingly apparent that . . . about a third of patients with chronic psychosis improve more in response to clozapine than other drugs". In a more recent review, Umbricht *et al* (1995) concluded that "clozapine is the first antipsychotic agent with proven superiority over conventional antipsychotics in the treatment of severely ill, chronic schizophrenic patients", showing a response rate 26–46% higher than that to chlorpromazine or haloperidol. The Cochrane Collaboration Schizophrenia Group systematic review (Wahlbeck *et al*, 1997) on clozapine currently includes 27 randomised controlled trials, and concludes that clozapine is "convincingly more effective than 'typical' neuroleptic drugs in reducing symptoms of schizophrenia, producing clinically meaningful improvements and postponing relapse".

In the UK those who are eligible for clozapine are refractory to, or intolerant of, standard neuroleptics. The response rate of such patients to standard neuroleptics is therefore very low (the argument is circular). Randomised controlled trials are hardly necessary to conclude that there is a substantial advantage of clozapine over standard neuroleptics in treatment-resistant schizophrenia in terms of efficacy.

Aitchison, K. & Kerwin, R. W. (1997) Cost-effectiveness of clozapine. *British Journal of Psychiatry*, **171**, 125–130.

Baldessarini, R. J. & Frankenburg, F. R. (1991) Clozapine. A novel antipsychotic agent. *New England Journal of Medicine*, **324**, 746–754.

Robert, G. & Kennedy, P. (1997) Establishing cost-effectiveness of atypical neuroleptics. *British Journal of Psychiatry*, **171**, 103–104.

Umbricht, D. S. G., Lieberman, J. A. & Kane, J. M. (1995) The clinical efficacy of clozapine in the treatment of schizophrenia. *Reviews in Contemporary Pharmacotherapy*, **6**, 165–186.

Wahlbeck, K., Cheine, M., Essali, M. A., *et al* (1997) Clozapine for schizophrenia. Clozapine versus 'typical' neuroleptic medication for schizophrenia. In *Schizophrenia Module* (eds C. E. Adams, L. Duggan, M. J. De Jesus, *et al*). The Cochrane Database of Systematic Reviews (available in the Cochrane Library). London: BMJ Publishing.

R. W. Kerwin, K. J. Aitchison Section of Clinical Neuropharmacology, Institute of Psychiatry, London SE5 8AF

Cannabis and schizophrenia

Sir: In their recent editorial Hall & Solowij (1997) were perhaps a little too sanguine about the relationship between cannabis consumption and schizophrenia. At least six studies, several of them prospective, have found a strong relationship between levels of cannabis use before the onset of psychotic symptoms and the subsequent development of schizophrenia and other chronic psychotic illnesses (Boutros & Bowers, 1996). Moreover, those patients with schizophrenia who had used cannabis prior to the onset of their illness are distinct, both demographically and clinically, from those who had not: younger, more often male, with better premorbid functioning, and a different symptom pattern, response to neuroleptics and subsequent disease course (Longhurst *et al*, 1997). Thus, prolonged cannabis use appears to induce chronic psychosis in a group of individuals who are sufficiently different from the general mass of patients with schizophrenia to suggest that, in the absence of such use, they might not be especially vulnerable.

For many years, clinicians have been aware that the use of cannabis may lead to persistent psychosis (Glass & Bowers, 1970). The weight of both decades of clinical experience and the current literature strongly suggests that cannabis use can result in chronic psychoses, including schizophrenia.

Boutros, N. N. & Bowers, M. B. (1996) Chronic substance-induced psychotic disorders: the state of the literature. *Journal of Neuropsychiatry and Clinical Neurosciences*, **8**, 262–269.

Glass, D. S. & Bowers, M. B. (1970) Chronic psychosis associated with long-term psychotomimetic drug use. *Archives of General Psychiatry*, **23**, 997–1003.

Hall, W. & Solowij, N. (1997) Long-term cannabis use and mental health. *British Journal of Psychiatry*, **171**, 107–108.

Longhurst, J. G., Boutros, N. N. & Bowers, M. B. (1997) Cannabis-induced chronic psychosis – an under-acknowledged disorder? *Australian and New Zealand Journal of Psychiatry*, **31**, 305–306.

J. G. Longhurst Department of Psychiatry and Connecticut Mental Health Center, Yale University School of Medicine, New Haven, CT 06519, USA

Author's reply: It is difficult in the space limits of an editorial to do justice to the issues involved in deciding whether cannabis use can produce chronic psychoses such as schizophrenia, when informed opinion differs and the evidence is inconsistent.

https://doi.org/10.1192/bjp.171.6.584b Published online by Cambridge University Press