Interestingly, there may be a differential clinical effect according to the subtype of childhood trauma. In the study by Taylor & Jason,[2] a history of childhood sexual abuse emerged as a significant predictor of post-traumatic stress disorder. Furthermore, significant correlations between scores on a trauma questionnaire and scores for depression, anxiety and post-traumatic stress were observed by Heim *et al*.[3] These correlations remained unchanged when the analysis was restricted to the subscales sexual abuse and emotional neglect.

Recently, our research group examined the impact of childhood trauma in a well-described tertiary sample of patients with CFS. In accordance with the previously mentioned population-based studies, childhood sexual harassment was the best predictor of psychological symptoms in CFS (unpublished data). Taken together, these data emphasise the importance of childhood sexual abuse as a premorbid risk marker for CFS.

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4 Heim C, Nater UM, Maloney E, Boneva R, Jones JF, Reeves WC. Childhood trauma and risk for chronic fatigue syndrome: association with neuroendocrine dysfunction. *Arch Gen Psychiatry* 2009; **66**: 72–80.

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Clozapine *v.* chlorpromazine in treatment-naive first-episode schizophrenia

Girgis *et al*[1] present data on the usefulness of clozapine versus chlorpromazine in patients with first-episode schizophrenia. The authors must be complimented for conducting a follow-up study of the same cohort after 9 years and being able to have such a high retention rate. Further, the study provides information with respect to the naturalistic setting, reflecting the true clinical situation, and the authors have taken care of possible confounders with appropriate statistical analysis proper explanation. However, there are certain issues with the study. First, the title of the article is somewhat misleading because the randomisation phase of the study was only for the initial 2 years and after that the patients received treatment at the discretion of the clinicians. The title would have been appropriate if the authors were describing the outcome in terms of efficacy/effectiveness and side-effect profile by using survival analysis focusing on either of the medications. But actually the authors describe the effect of clozapine and chlorpromazine for the initial 1 year and outcome at the 9-year follow-up. Second, we need to understand that there are controversies in relation to the definition of first-episode psychosis and the definition used by the authors may appear to be very broad.[2] Third, the sample size in each treatment group that remained on the same medication (clozapine (n=21) or chlorpromazine (n=8)) at the 9-year follow-up is too small to generalise. Hence, to conclude that there is no difference between clozapine and chlorpromazine with respect to effectiveness would be wrong. Fourth, the authors also conclude that there is no difference in metabolic and other side-effects between the two groups; besides having incomplete baseline data for weight there is no mention of other metabolic variables such as high-density lipoprotein, triglyceride and blood pressure. Fifth, more than half of the study sample (55% of the chlorpromazine group *v.* 73% of the clozapine group) was not on any anti-psychotic medication at 9-year follow-up, but the authors have not elaborated about their clinical status. Last of all, a quarter of participants (24%) were diagnosed with schizophreniform disorder which might have directly affected the outcome as this group of disorders is considered to have better outcome than schizophrenia.

1 Girgis RR, Phillips MR, Li X, Li K, Jiang H, Wu C, et al. Clozapine *v.* chlorpromazine in treatment-naive, first-episode schizophrenia: 9-year outcomes of a randomised clinical trial. *Br J Psychiatry* 2011; **199**: 281–8.

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Authors' reply: We appreciate Nebhinani & Grover's interest in our study[1] as well as the opportunity to respond to the six comments. First, our study was analysed using the intent-to-treat principle. Implicit in the intent-to-treat principle is that the outcome is not the effect of treatment *per se*, but rather the effect of initial assignment irrespective of treatment(s) received.[2] Second, we agree that there are controversies as to the definition of first-episode psychosis.[3] As reported by Breitborde *et al*, 'duration of psychosis' possesses the most construct validity, followed by other criteria, such as 'duration of antipsychotic medication use' and 'first treatment contact'.[3] We conservatively identified individuals with first-episode schizophrenia using both duration of psychosis and duration of antipsychotic medication use as two of our criteria. Furthermore, we included a maximum age criterion (i.e. 40 years old at the time when symptoms began) and symptom criteria to further narrow and restrict our study participants to those who are most likely to have first-episode psychosis. Third, our conclusions and main outcomes used the intent-to-treat principle and were based on the entire sample, rather than primarily based on the 29 individuals who remained on their originally assigned medication after 9 years. We described characteristics of this smaller group, without an intent to generalise, owing to the obvious lack of representativeness in this subgroup of patients. Furthermore, it is important to note that the generalisability of a clinical finding is determined by the representativeness of the sample observed, rather than the sample size observed.

Fourth, as described in the article, we did not have any missing baseline data for weight for those participants whose weights were included in our metabolic analyses. In addition, we disagree that we indicated that there were no differences in side-effects between the two groups. Rather, we descriptively reported differences in tardive dyskinesia and agranulocytosis between the two treatment groups. Finally, we did not claim that the metabolic findings in this study are generalisable, but we do agree with Nebhinani & Grover that it would have been valuable to report on additional metabolic indices (e.g. lipids and blood pressure). Unfortunately, these data were not available.

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