methodological pitfalls that have plagued research in this area.

However, a few concerns about the study persist. Ideally, there is a need for a viable placebo arm to compare the efficacy of both interventions. A comparison of a new agent with a drug previously shown to be active without a placebo comparator is uninterpretable unless one agent is superior to the others. Concluding that a drug is efficacious without a placebo comparator can lead to an incorrect assumption of efficacy if neither the investigational drug nor the active drug was, in that trial, any better than placebo would have been if included. Introducing a drug into therapeutic use on the basis of such a trial would expose patients to a compound with no greater benefit than placebo (Temple & Ellenberg, 2000). A placebo is also important in the assessment of the safety profile, as it provides a base for determining which adverse events are truly related to the investigational drug. For these reasons, placebo-controlled trials are almost universally demanded by regulatory bodies to demonstrate efficacy for any pharmacological intervention.

The authors have not described any investigations carried out to exclude toxic states, epilepsy and other organic conditions. They failed to comment on vital parameters during and after administration of both interventions. They could have assessed the level of satisfaction of the treatment team with the intervention (Petrack *et al*, 1996). They could also have applied any scale for aggression, agitation, alertness and psychopathology (Battaglia *et al*, 1997).

Certain issues merit consideration before accepting the authors' conclusion. The better outcome of the haloperidol–promethazine group compared with the lorazepam group could be because the combination group had more patients with mania than the lorazepam group and the combination group had more moderately ill and less severely ill patients than the lorazepam group. In addition, details of additional medications were not mentioned. It remains possible that some improvement was due to additional medications in both groups.

The authors commented that 23 patients failed to sleep at all during the 4-h follow-up compared with only 8 in the combination group, which is difficult to understand from Table 2. There were some inconsistent findings in the paper: sleep outcome in the combination group at 120 min were 69% and 88% in Table 2 and Table 5, respectively. Similarly, there was a discrepancy in the number of patients in the combination group who were never tranquil (Results and Table 2).

Nevertheless, we feel that the authors have taken a useful step in this relatively neglected area. Further studies are required on the effectiveness of these interventions in the hope that better understanding can lead to better treatment of violent patients.

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Authors' reply We thank Dr Jhirwal *et al* for their interest in our pragmatic trial. In this reply we shall address only those issues that have not already been covered in response to earlier comments.

The first concern regarded the omission of a placebo arm. A placebo group was initially considered but abandoned as clinicians felt this was unethical, difficult to justify and likely to pose practical difficulties in implementation. This was a pragmatic trial and the design was driven by what questions clinicians wanted answered and what interventions they (and the institution's ethics committee) would permit. Moreover, systematic reviews reveal no evidence that placebo interventions in general have clinically important effects, and the role of placebos in clinical trials, apart from helping to minimise bias, is questionable (Hróbjartsson & Gøtzsche, 2004). Our pragmatic trial utilised adequate allocation concealment and masking of primary outcome assessors, two crucial features of trial design that significantly affect the internal validity of a randomised controlled trial (Jüni *et al*, 2001).

Those with toxic states, epilepsy or other organic conditions were invariably excluded from the study as treating clinicians were uncomfortable about their inclusion in a randomised trial with sedative agents. Investigation results are rarely available before the intervention is instituted for violent patients under normal conditions of clinical practice.

All those subjected to tranquillisation received standard levels of care that included monitoring of vital signs and intensive nursing support. Any adverse events with regard to autonomic instability were promptly reported. Only two patients on lorazepam reported any adverse events and this is described in the discussion (paragraph 4, page 65; a printing error in Table 2 ascribes this to the combination group instead of to lorazepam).

Table 2 records that equal numbers in both groups were given additional medication (always a single dose of 100 mg chlorpromazine) and this contradicts the speculation that differences in additional medication could have influenced improvement in favour of any particular group. The proportions that failed to sleep or were never tranquil reported in paragraph 1 on page 65 are correct. Table 2 reports the numbers who were tranquil/asleep and asleep at the times when outcomes were recorded. People who were tranquil or asleep at one assessment did not invariably remain so at other assessments, hence explaining the apparent discrepancy. We acknowledge the error in Table 5 where the proportion asleep at 120 min should be 69% and not 88% for TREC–India.

We hope the interest aroused by this paper will prompt greater use of trials of pragmatic design, free of industry sponsorship and aimed at answering clinical questions of relevance to real world clinical practice.

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