Author's reply: Dr McKenna seems to have misread and misunderstood the editorial. I do not argue that ‘atypical antipsychotics’ (whatever they are) can no longer be regarded as having advantages over ‘conventional drugs’ (whatever they are). I argue that the class – the ‘atypical’ antipsychotics – has been fabricated for marketing purposes and has no basis in science or clinical practice. Although some studies do suggest that individual drugs differ in terms of side-effects, potency, efficacy and effectiveness, the differences – with the exception of clozapine for treatment-resistant schizophrenia – are small, and their relative effects are, at least in part, dependent on the potency and dose of the comparator. These differences do not constitute a ‘class effect’.

In the meta-analyses for the schizophrenia NICE guideline, we examined the use of antipsychotics in a number of different clinical contexts (e.g. first episode, acute episode and treatment resistance) and concluded that the differences in efficacy between drugs were unlikely to be clinically important. However, the guideline did acknowledge, as do other meta-analyses, that differences in terms of side-effects allow clinicians and service users to find a drug that suits them. Moreover, all three meta-analyses agree that there are no consistent differences or similarities between ‘typicals’ and ‘atypicals’—this is an important perspective that McKenna seems to have missed.

In undertaking our meta-analyses for the development of a guideline, we were guided by a broad range of clinical review questions. The more specific the question the fewer studies are likely to be able to answer the question. The data underpinning the use of antipsychotics in the treatment of acute schizophrenia included over 72,000 patients, whereas for the first episode this figure dropped below 2000. We could have lumped more data included over 72,000 patients, whereas for the first episode this figure dropped below 2000. We could have lumped more data

would change the central conclusions (that oral antipsychotics are all much the same in terms of efficacy); but it would have significantly diminished the clinical utility of each analysis.

The study by Geddes et al is important not only in highlighting the influence of the comparator dose on efficacy, but also in questioning the integrity and claimed superiority of the class of ‘atypicals’. It is true that Davis et al did not confirm the findings of Geddes et al; nevertheless, I maintain that the findings have clinical face validity. Not irrelevant to this perspective is that Leucht et al, in their paper summarising the debate, said ‘It is a major limitation that only a few studies used mid-potency FGA [first-generation antipsychotic] comparators. We recommend that each new drug is compared with a low-potency, a mid-potency, and a high-potency FGA.’ Explicit in this recommendation is that the potency of the comparator can introduce bias; it would be odd to suggest that the dose of the comparator would not also have an important effect. In any event, McKenna may be in danger of not seeing the wood for the trees: the ‘atypicals’ have surely fallen.

5 Davis JM, Chen N, Glick ID. A meta-analysis of the efficacy of second-generation antipsychotics. Arch Gen Psychiatry 2003; 60: 553–64.