

- 7 Geddes J, Harrison P, Freemantle N. New generation versus conventional antipsychotics. *Lancet* 2003; **362**: 404; author reply 404–5.

Peter McKenna, FIDMAG Germanes Hospitalàries Research Foundation, and CIBERSAM, Barcelona, Spain. Email: mckennapeter1@gmail.com

doi: 10.1192/bjp.200.3.256

Author's reply: Dr McKenna seems to have misread and misunderstood the editorial.¹ 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 potency² and dose³ of the comparator. These differences do not constitute a 'class effect'.

In the meta-analyses for the schizophrenia NICE guideline,⁴ 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,^{3,5,6} 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 together: it is very unlikely that increasing the numbers of studies and participants with different presentations in the meta-analyses

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*³ 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*⁵ did not confirm the findings of Geddes *et al*;³ nevertheless, I maintain that the findings have clinical face validity. Not irrelevant to this perspective is that Leucht *et al*,² 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.

- 1 Kendall T. The rise and fall of the atypical antipsychotics. *Br J Psychiatry* 2011; **199**: 266–8.
- 2 Leucht S, Wahlbeck K, Hamann J, Kissling W. New generation antipsychotics versus low-potency conventional antipsychotics: a systematic review and meta-analysis. *Lancet* 2003; **361**: 1581–9.
- 3 Geddes J, Freemantle N, Harrison P, Bebbington P. Atypical antipsychotics in the treatment of schizophrenia: systematic overview and meta-regression analysis. *BMJ* 2000; **321**: 1371–6.
- 4 National Institute for Health and Clinical Excellence. *Schizophrenia: Core Interventions in the Treatment and Management of Schizophrenia in Adults in Primary and Secondary Care (Update)*. NICE, 2009.
- 5 Davis JM, Chen N, Glick ID. A meta-analysis of the efficacy of second-generation antipsychotics. *Arch Gen Psychiatry* 2003; **60**: 553–64.
- 6 Leucht S, Corves C, Arbter D, Engel RR, Li C, Davis JM. Second-generation versus first-generation antipsychotic drugs for schizophrenia: a meta-analysis. *Lancet* 2009; **373**: 31–41.

Tim Kendall, Director, National Collaborating Centre for Mental Health; Director, Royal College of Psychiatrists' College Research Unit; Medical Director and Consultant Psychiatrist, Sheffield Health and Social Care NHS Foundation Trust, UK. Email: tim.kendall@shsc.nhs.uk

doi: 10.1192/bjp.200.3.257