

Analysing the efficacy of clozapine

It is interesting to note that while all the participants in the debate on clozapine *v.* typical neuroleptics referred to Kristian Wahlbeck's meta-analysis (Wahlbeck *et al.*, 2000), none of them referred to her sub-analysis of her own earlier meta-analysis on this topic (Wahlbeck & Adams, 1999). In this subanalysis, all randomised trials comparing clozapine with typical neuroleptic medication for schizophrenia were divided into sponsored (reporting some kind of connection with manufacturers of clozapine) and non-sponsored trials. Odds ratios and 95% confidence intervals were calculated for the primary outcomes of relapse, clinical improvement, and leaving the study early, separately for sponsored and non-sponsored studies. Odds of relapsing were significantly in favour of clozapine in the sponsored trials (OR=0.5, 95% CI 0.3–0.7). Non-sponsored studies reported equivocal findings (OR=0.4, 95% CI 0.1–1.4). Similarly, sponsored studies showed a significant difference in favour of clozapine on the outcome measure of leaving the study early (OR=0.5, 95% CI 0.4–0.7). Non-sponsored studies showed a non-significant difference (OR=0.6, CI 0.3–1.2). Only on the outcome measure of improvement did both sponsored and non-sponsored studies show a significant benefit of clozapine over older antipsychotics. Wahlbeck suggested that those undertaking meta-analysis of drug treatment should investigate for sponsorship bias by using sensitivity analysis.

Outside of psychiatry, similar associations between sponsorship and outcome of trials has been demonstrated in randomised controlled trials (RCTs) published in five general medical journals (Davidson, 1986; Yaphe *et al.*, 2001), RCTs of non-steroidal anti-inflammatory drugs in the treatment of arthritis (Rochon *et al.*, 1994)

and RCTs published in the *BMJ* over 4½ years (Kjaergard & Als-Nielsen, 2002).

Although RCTs and meta-analyses have contributed greatly to increasing our knowledge base about which treatments work and which do not, maybe it is time we began to consider other factors that might explain the observed difference between two treatments in RCTs and meta-analyses, beyond the standard critical appraisal questions. Maybe we need to ask not only how the efficacy of clozapine (or any other drug for that matter) has been analysed but also who has analysed it.

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Case reports still valuable

I read with interest Dr Bourne's claims against the *Journal's* Editor. These claims are only partially right. The reason the *Journal* is considered one of the most prestigious in the field of psychiatry is because

of the editorial policy of encouraging and accepting novel research that strives to the highest scientific and medical levels. Sound research is the basis of all leading medical journals, and this one is no different. This research is the foundation of progress in psychiatry. The fruits of this research are to our benefit as well as that of our patients. Think of the effect of psychotropic drugs in the 1950s and their side-effects and compare them with new, state of the art medication. Psychiatry is a living and developing field which must obtain new and original research at all times in order to be relevant to medicine.

However, the days of case studies are far from over. Every leading medical journal has a section for case studies. The importance of case reports is highlighted by the reporting of a novel mental disorder or medical condition that catches the attention of the medical community, such as concentration camp syndrome (Eitinger, 1961) and severe acute respiratory syndrome (Zambon & Nicholson, 2003) – both good examples of case reports that had an impact on the fields of psychiatry and medicine.

Instead of taking sides in this clash, it would be advisable to introduce a small section for case studies where clinicians could share important insights about patients or unusual cases. This section would also be beneficial to research by stimulating new ideas.

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Eitinger, L. (1961) Pathology of the concentration camp syndrome. *Archives of General Psychiatry*, **5**, 371–379.

Zambon, M. & Nicholson, K. G. (2003) Sudden acute respiratory syndrome. *BMJ*, **326**, 669–670.

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One hundred years ago

Asylum reports

London County Asylum, Bexley Heath (Report for the year ending March 31st,

1904). – The average number of patients resident during the year was 2085, comprising 1012 males and 1073 females. The admissions during the year amounted

to 585 – viz., 282 males and 303 females. Of these, 528 were first admissions. Dr. T. E. K. Stansfield, the medical superintendent, states in his report that “the hopeless