

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.

Davidson, R. A. (1986) Source of funding and outcome of clinical trials. *Journal of General Internal Medicine*, **1**, 155–158.

Kjaergard, L. L. & Als-Nielsen, B. (2002) Association between competing interests and authors' conclusions: epidemiological study of randomised clinical trials published in the *BMJ*. *BMJ*, **325**, 249–253.

Rochon, P. A., Gurwitz, J. H., Simms, R., et al (1994) A study of manufacturer-supported trials of nonsteroidal anti-inflammatory drugs in the treatment of arthritis. *Archives of Internal Medicine*, **154**, 157–163.

Wahlbeck, K. & Adams, C. (1999) Beyond conflict of interest. Sponsored drug trials show more favourable outcomes (letter). *BMJ*, **318**, 465.

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Yaphe, J., Richard, E., Knishkowsky, B., et al (2001) The association between funding by commercial interests and study outcome in randomized controlled drug trials. *Family Practice*, **18**, 565–568.

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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.

Bourne, H. (2004) A new name for the *Journal*? (letter) *British Journal of Psychiatry*, **184**, 455.

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

character as to the possibility of recovery of the bulk of the admissions during the year is clearly demonstrated.... The axiom the sooner the disease can be brought under treatment the greater hope there is of recovery applies more to mental alienation perhaps than to any other form of disease." Only 30 per cent. of cases came under treatment within three months of the beginning of the attack, owing to which, adds Dr. Stansfield, "not only is the possibility of recovery greatly diminished but when recovery does take place the permanent injury present in every case is proportionately greater. The importance of *habit* in relation to mental diseases is but little appreciated and yet to my mind it is one of the most powerful factors in the development of chronic insanity and it remains after the first causes have passed away, as is well illustrated by the bulk of cases in every asylum. All this points to the urgent necessity of patients being bought [*sic*] under proper observation and treatment at the earliest period of their alienation before

insane habits of thought and action become fixed." Melancholia was present in 23 per cent., paranoia and delusional insanity in 14 per cent., primary dementia in 13.5 per cent., and general paralysis in 6 per cent. of the admissions. Among the causes of insanity were arteriosclerosis, senile decay, alcoholic intemperance, insane parentage, and syphilis, in descending order of frequency. "The important part played by heredity in the causation of mental disease was demonstrated by the fact that insane heredity was made out in 132 cases or 22.5 per cent." The number of cases discharged as recovered during the year amounted to 162 – viz., 56 males and 106 females, or 7.7 per cent. of the average number resident. The deaths during the year amounted to 167, or 8 per cent. as calculated on the same basis. Of the deaths seven were due to renal disease, nine to colitis, 13 to cerebral softening, 18 to cardiac disease, 19 to pulmonary and other forms of tuberculosis, 46 to general paralysis of the insane, and the rest to other

causes. The Commissioners in Lunacy state in their report that the general scheme and management of the asylum deserved favourable commendation, that the patients appeared to be well dressed and well cared for, that the day-rooms and dormitories were bright throughout, and that the medical case books were kept in a highly satisfactory manner. They recommend that in case of fire the high level water-tank should be used. The committee of management states in its report that plans have been prepared and adopted for the erection of a hospital villa to accommodate 50 male patients and the necessary staff. The internal decoration of the asylum is now complete.

REFERENCE

Lancet, 14 January 1905. 112.

Researched by Henry Rollin, Emeritus Consultant Psychiatrist, Horton Hospital, Epsom, Surrey

Corrigenda

Cannabis as a psychotropic medication (letter). *BJP*, 185, 78. The correspondent's name should read: S. K. Chaturvedi.

Pituitary volume in psychosis. *BJP*, 185, 5–10. The pituitary gland was indicated incorrectly in Fig. 1 (left, p. 6). The correct figure is reproduced below.

