

Correspondence

EDITED BY MATTHEW HOTOPF

Contents ■ Conflict of interest and the *British Journal of Psychiatry* ■ Risk of pregnancy when changing to atypical antipsychotics ■ Hospitalisation in first-episode psychosis ■ Antipsychotics and risk of venous thrombosis ■ Use of antidepressants by nursing mothers ■ Reforming the Mental Health Act – recruitment and retention issues

Conflict of interest and the *British Journal of Psychiatry*

There has been debate in medical journals over the potential for conflicts of interest to bias scientific judgements: “we should pay attention to conflict of interest not only when it is clear that a judgement has been influenced by conflict of interest but simply when it might have been” (Smith, 1994). The *BMJ* requires authors to complete a detailed questionnaire regarding competing interests. Editorial staff may also be vulnerable to conflicts of interest. The editor of the *New England Journal of Medicine* was criticised for links with the pharmaceutical industry (Gottlieb, 2000).

The drug company Wyeth sponsors the educational organisation Neurolink. Although Neurolink has educational components, it may also fulfil a marketing function. Its educational materials appear to give undue prominence to venlafaxine, manufactured by Wyeth. The Editor of the *British Journal of Psychiatry* is a member of the Neurolink Advisory Board as well as a member of the working party which produced the ‘depression guide’ (Neurolink Advisory Board, 2000).

The *British Journal of Psychiatry* has recently included a paper written by two Wyeth employees and a Wyeth consultant (Thase *et al*, 2001). This is a commercially valuable paper in which venlafaxine is described as having benefits compared with other antidepressants. It has already been cited in advertisements for Wyeth’s venlafaxine preparations. I believe that the paper should have contained a declaration of interest by the Editor of the *British Journal of Psychiatry*, making clear his links with Wyeth. Perhaps the editor of a major medical journal should not have such a prominent link with any drug company.

I hope that the *Journal* will strengthen its policy on competing interests, including

a detailed register of interests for editorial staff, referees and authors (including authors of letters) on its website. This should include the magnitude of payments: there is a big difference between a drug company paying someone £10 travel expenses and £10 000 consultancy fees. Significant competing interests should be summarised in the published articles. At the very least, readers would learn a lot about the dependency between medical research and big business.

Declaration of interest

I am paid £2000 per year for editorial work for *Schizophrenia Monitor*, a review journal sponsored by the drug company Novartis.

Gottlieb, S. (2000) Controversy over new Editor at *New England Journal of Medicine*. *BMJ*, **320**, 1358.

Neurolink Advisory Board (2000) *Depression: A Guide to its Recognition and Management in General Practice*. London: Neurolink.

Smith, R. (1994) Conflict of interest and the *BMJ*. *BMJ*, **308**, 4.

Thase, M. E., Entsuah, A. R. & Rudolph, R. L. (2001) Remission rates during treatment with venlafaxine or selective serotonin reuptake inhibitors. *British Journal of Psychiatry*, **178**, 234–241.

I. C. Wright The Old Manor Hospital, Wilton Road, Salisbury SP2 7EP, UK

Author’s reply: Dr Wright correctly notes that the potential impact of ties with the pharmaceutical industry may extend to editorial decisions about whether or not a manuscript is published. This topic was addressed in a recent article in the *Journal of the American Medical Association* (Wilkes *et al*, 2001) and the authors, a group of editors of general medical journals, recommended periodic publication of the editors’ relationships with various companies. Should the Editor of the *British Journal of Psychiatry* choose to accept this suggestion, it would appear to address at least some of Dr Wright’s concerns.

Most of us in academic medicine have some consulting, teaching, or research relationship with the corporations that manufacture medications. I do not know Professor Wilkinson, but I assume that, like me and most others, he works with more than one company.

It is neither reasonable nor necessary to assume that any fiscal relationship with a pharmaceutical company should necessitate that the editor exclude himself or herself from the decision-making process. I do not favour the use of a specific level of income to determine whether or not there is a conflict. Frankly, some of the most blatantly biased decisions (about the scientific merit of a manuscript) that I have observed over the past 25 years have involved no money whatsoever. A monetary threshold cannot replace personal integrity or judicious feedback when one’s peers seem to be close to the edge of propriety.

With respect to our paper (Thase *et al*, 2001), we submitted to the *British Journal of Psychiatry* because of the journal’s clear commitment to evidence-based medicine. No aspect of the submission, review, revision, resubmission or acceptance process seemed to be out of the ordinary. The manuscript received very positive ‘blind’ reviews and was praised for being even-handed. The studies incorporated in our pooled analysis were randomised, double-blind trials, the data sets were ‘closed’ (i.e. they had already been subjected to external regulatory review), and the studies were not selected or excluded because of the pattern of findings. In fact, two of the studies in the pooled analysis were ‘rescued’ from the file drawer of unpublishable results. The results were robust: the findings were consistent across multiple outcome definitions and various study characteristics. The findings also were reinforced by a sensitivity analysis, which indicated that the effect was not dependent on the results of any single study.

There are now a number of other studies comparing venlafaxine and selective serotonin reuptake inhibitors (SSRIs), and we tabulated the grouped data of nine such trials in our paper. Additional pooled analyses are underway. Working with an overlapping data set, Freemantle *et al* (2000) observed a similar magnitude of advantage favouring venlafaxine (*v.* SSRIs) using a meta-regression approach to meta-analysis. If venlafaxine is indeed a more effective antidepressant than the SSRI class, there will be ample documentation of this effect.

Although the funding source of a research finding should be considered when reviewing and interpreting the results of a study, hopefully our field has not become so jaded or cynical that all such work is rejected out of hand.

Freemantle, N., Anderson, I. M. & Young, P. (2000) Predictive value of pharmacological activity for the relative efficacy of antidepressant drugs. Meta-regression analysis. *British Journal of Psychiatry*, **177**, 292–302.

Thase, M. E., Entsuah, A. R. & Rudolph, R. L. (2001) Remission rates during treatment with venlafaxine or selective serotonin reuptake inhibitors. *British Journal of Psychiatry*, **178**, 234–241.

Wilkes, M. S., Davidoff, F., DeAngelis, C. D., et al (2001) Sponsorship, authorship, and accountability. *Journal of the American Medical Association*, **286**, 1232–1234.

Declaration of interest

M.E.T. is a paid consultant to Wyeth–Ayerst Laboratories.

M. E. Thase University of Pittsburgh School of Medicine, Western Psychiatric Institute and Clinic, 38 O'Hara Street, Pittsburgh, PA 15213–2593, USA

Response from Neurolink: The members of Neurolink were particularly disturbed by Dr Wright's accusation that the materials produced by Neurolink are unbalanced and favour venlafaxine, manufactured by Wyeth.

Neurolink is a well-established board of 14 mental health experts who pride themselves on their unbiased, professional expertise in anxiety and depression, and their ability, as a multi-disciplinary group of health care professionals, to produce materials of practical value to other health care professionals and patients.

Neurolink is indeed supported by an educational grant from Wyeth Laboratories, and has been since 1995. Board members receive an honorarium for their attendance at Advisory Board meetings and working parties, where production of materials is discussed and agreed in the light of the existing evidence base and consensus of the members of the Board.

We would like to emphasise that the materials produced by Neurolink are balanced items that review all treatment options – including drug and non-drug options – and we would refute all claims that materials give prominence to venlafaxine, or any other drug or treatment, unless there is a body of significant evidence that supports it. In the 6 years that we have been in existence, we have never previously

received comments to suggest that Neurolink materials are not impartial, practical resource items.

G. Jackson Neurolink, Middlesex House, 34 Cleveland Street, London W1P 5FB, UK

T. Brown St John's Hospital, Livingston, UK

J. Butler Bedfordshire and Luton Community NHS Trust, Bedfordshire, UK

P. Cowen Warneford Hospital, Oxford, UK

C. Freeman Royal Edinburgh Hospital, Edinburgh, UK

H. Freeman Green College, Oxford, UK

L. Gask University of Manchester, Manchester, UK

G. Kassianos Bracknell PCG, Birch Hill Medical Centre, Bracknell, UK

A. Kirby Health Media Ltd, Cardiff, UK

S. Koppel Glan Rhyd Hospital, Bridgend, UK

D. Nutt University of Bristol, Bristol, UK

P. Shaw Maidenhead PCG, William Symons Medical Centre, Maidenhead, UK

C. Vardy Gateshead PCG, Gateshead, UK

Editor's response The *Journal* is committed to openness and I was pleased several years ago to introduce a requirement for authors to make a declaration of their interests with regard to publication of their papers. Last year this requirement was extended to include editorials and items of correspondence (Wilkinson, 2001).

As an elected Honorary Officer (not a paid employee) of the Royal College of Psychiatrists I am required regularly to complete a Declaration of Competing Interests form. My form states that I have an annual renewal of a consultancy with Neurolink, sponsored by Wyeth (£2000 per annum). These forms are available to members of the College, and to non-members of the College at the discretion of the President, Registrar and the College Secretary.

The issues raised by Dr Wright were discussed by the Editorial Board in June 2001. To quote from the minutes of that meeting:

"It was not felt that the Editor had acted at all improperly. . . . It was agreed that a general policy of openness was desirable, but it was generally felt that a detailed on-line register of interests for all staff, referees and authors such as that suggested by Dr Wright was impractical. . . . The 'Recommendations for publication' form sent to all assessors would [be amended to] give the assessor the opportunity to declare an interest in the publication of the paper."

Following that decision, since October 2001, referees have been required to state explicitly if they have an interest in the

publication of any paper they are asked to assess. If that is the case, they are required to return the manuscript without assessment.

It has always been the case that when I have an interest in a paper's publication by virtue of being a co-author, another nominated member of the Editorial Board acts as Editor for that paper. That person's identity is not divulged to me, and I am kept blind to the peer-review process as it applies to that manuscript. Since receipt of Dr Wright's letter (in April 2001, subsequent to the acceptance of another paper reporting work funded by Wyeth; Allgulander *et al*, 2001), the same procedure has been extended to any submission connected with Wyeth. Finally, in keeping with these developments, I am beginning the evaluation of open peer review as a policy from this month (i.e. all assessors will be required to identify themselves to authors).

I am doing what I can to address these important issues, and I am grateful to Dr Wright for this opportunity to clarify our procedures to our readers.

Allgulander, C., Hackett, D. & Salinas, E. (2001)

Venlafaxine extended release (ER) in the treatment of generalised anxiety disorder. Twenty-four-week placebo-controlled dose-ranging study. *British Journal of Psychiatry*, **179**, 15–22.

Wilkinson, G. (2001) Declaration of interest. Editor's response (letter). *British Journal of Psychiatry*, **179**, 175.

Greg Wilkinson Editor, *British Journal of Psychiatry*, 17 Belgrave Square, London SW1X 8PG, UK

Risk of pregnancy when changing to atypical antipsychotics

We have become aware of a number of pregnancies which have occurred in women with chronic psychotic illnesses whose medication has been changed from traditional oral or depot antipsychotics to atypical drugs. This can be explained by the loss of the contraceptive side-effects produced by drug-induced hyperprolactinaemia in these women. Most atypical antipsychotic drugs (e.g. olanzapine, quetiapine, clozapine) have a negligible effect on prolactin levels, whereas older drugs such as chlorpromazine and haloperidol, as well as sulpiride, amisulpride and risperidone, can cause significant hyperprolactinaemia in some women. Although these should not be considered as contraceptives, there is undeniably a contraceptive effect.