# Correspondence

EDITED BY TOM FAHY



## Suicide and the cost-effectiveness of antidepressants

**Sir:** Hotopf *et al* (1996) reason that while the selective serotonin reuptake inhibitors (SSRIs) are safer in overdose than the older tricyclic antidepressants (TCAs), such an advantage is unlikely to influence overall cost-effectiveness of treatment given that the incidence of suicide is very low. I have recently published figures which contradict this argument.

Currently, the total number of suicides and undetermined deaths in the UK is close to 6000 per annum. It is widely accepted, however, that official statistics for suicide mortality substantially underestimate the true rate (O'Donnell & Farmer, 1995). From my calculations, if one accepts that approximately 70% of suicides are depression-related, then depressive illness is implicated in approximately 4000 deaths per annum (Henry, 1995). I have made the assumption that, of these, 600 or so will be prescribed an antidepressant, since only 15% of depressed patients are ever recognised. Therefore, because the number of antidepressant-related suicides is around 300 deaths per annum, it can be seen that the actual risk of death from overdose in patients prescribed antidepressants may be as much as 10 times greater than crude estimates suggest (Edwards, 1995). Thus, the suicide rate from antidepressant overdose among depressed patients prescribed an antidepressant might possibly be as high as 50%. Furthermore, most deaths from overdose are due to TCAs, with over 80% of these deaths being due to two of those drugs, amitriptyline and dothiepin (Henry *et al*, 1995).

Therefore, although death from antidepressant overdose accounts for a small proportion of all suicides, TCAs are responsible for a high proportion of those suicides which occur in patients prescribed an antidepressant. I am somewhat dismayed that a paper purporting to compare the cost-effectiveness of SSRIs and TCAs should take a superficial view of such a highly complex subject, and in so doing, proffer what can only be regarded as a specious argument.

**Edwards, J. G. (1995)** Suicide and antidepressants. *British Medical Journal*, **310**, 205–206.

**Henry, J. A. (1996)** Suicide risk and antidepressant treatment. *Journal of Psychopharmacology*, **9**, 39–40.

**—, Alexander, C. A. & Sener, E. K. (1995)** Relative mortality from overdose of antidepressants. *British Medical Journal*, **310**, 221–224.

**Hotopf, M., Lewis, G. & Normand, C. (1996)** Are SSRIs a cost-effective alternative to tricyclics? *British Journal of Psychiatry*, **168**, 404–409.

**O'Donnell, I. & Farmer, R. (1995)** The limitations of official suicide statistics. *British Journal of Psychiatry*, **166**, 458–461.

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**Authors' reply:** The tragedy of suicide in patients taking antidepressants makes the tricyclic antidepressants (TCAs) a far less attractive option to prescribers. If Henry's 'back of envelope' calculations are correct, and 50% of completed suicides in those taking antidepressants use antidepressants as their suicide method, one could ask what proportion of people one would need to treat to prevent a single suicide, assuming that giving them a different drug would avert all suicides. For example, assuming the suicide rate per annum is 8 per 100 000, and assuming the relative risk of suicide in *treated* depressed patients is 25, their rate would be 200 per 100 000, of which 100 cases would use antidepressants. To prevent one such death 1000 patients would have to be treated with SSRIs, assuming no substitution. With the current costs of SSRIs still far exceeding those of the tricyclics this is likely to remain a costly approach. For example, if a month's supply of amitriptyline (150 mg) costs £1.53, and one month's supply of fluoxetine is £20.77 (*British National Formulary*, March 1996), the increased cost of a year's treatment of fluoxetine is about £230. The cost for 1000 patients would be £230 000. For sertraline (100 mg) we calculate this cost rises to over £440 000.

These calculations are crude, and our main point in the original paper was that the impact of SSRIs in preventing rare events is very difficult to assess. Clearly the cost per life saved will depend on the increased risk of suicide. We would not argue that those assessed to be at risk should not be prescribed SSRIs. The question is whether SSRIs should be given as first-line treatment to everyone who presents with depression. Thus the argument is more to do with costs and benefits at a population level. If policy decides that TCAs should not be prescribed because of serious risk to public health in terms of suicide, one must ask how much the alternatives cost. If, as Freemantle *et al*'s (1994) model suggests, the cost per life years saved from suicide of widespread use of SSRIs is £50 000 this is an unprecedently costly *preventive* intervention. In reality, patients who are prescribed SSRIs appear to commit suicide more often than those prescribed TCAs (Jick *et al*, 1995). Assuming this is due to selection bias (i.e. doctors who recognise patients as suicidal give them an SSRI) this implies two things are happening: first, doctors already prescribe SSRIs to those with increased suicidal risk; and second, patients substitute tablets for alternative methods.

The arguments are not simple, but suicide is fortunately a rare event and one which we would argue is unlikely to make big impacts in the cost-effectiveness of the treatments, despite the obvious emotive argument.

**Freemantle, N., House, A., Song, F., et al (1994)** Prescribing selective serotonin reputake inhibitors as a strategy for prevention of suicide. *British Medical Journal*, **309**, 249–253.

**Jick, S. S., Dean, A. D. & Jick, H. (1995)** Antidepressants and suicide. *British Medical Journal*, **310**, 215–218.

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## Inappropriate antidiuretic hormone secretion and SSRIs

**Sir:** Voegeli & Baumann (1996) observed hyponatraemia in an elderly depressive patient treated with the SSRI citalopram.



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The patient had previously developed several periods of hyponatraemia while taking diuretics. We have recently submitted a paper reporting a case of hyponatraemia due to the syndrome of inappropriate antidiuretic hormone secretion (SIADH) following commencement of therapy with citalopram in an elderly patient. Her only other medications were aspirin, folic acid, multivitamins and senna, none of which is known to be associated with hyponatraemia and SIADH.

A wide variety of psychotropic drugs have been implicated in causing SIADH, described in a large number of case reports (Spigset & Hedenmalm, 1995) but systematic epidemiological and clinical studies are lacking. While some authors suggest hyponatraemia due to SIADH is an idiosyncratic effect of any antidepressant drug (Committee on Safety of Medicines, 1994), others postulate it is most likely a class effect of the SSRIs (Ball & Herzberg, 1984), although a cross-over effect with TCAs has been reported (Bouman *et al*, 1997, in press). None the less, the exact mechanism remains to be clarified.

Surprisingly, Voegeli & Baumann (1996) state that age does not represent a risk factor for developing SSRI-induced hyponatraemia due to SIADH. We would disagree with this statement. Although the exact nature of age-related changes in sensitivity to ADH remains an area of controversy, elderly people are particularly prone to developing hyponatraemia due to SIADH (Ball & Herzberg, 1994; Committee on Safety of Medicines, 1994; Spigset & Hedenmalm 1995; Bouman *et al*, 1997, in press). In the large majority of published case reports (>90%) the age of the patient is over 65 years, particularly among those treated with SSRIs.

**Ball, C. J. & Herzberg, J. (1994)** Hyponatraemia and selective serotonin inhibitors. *International Journal of Geriatric Psychiatry*, **9**, 819–822.

**Bouman, W. P., Johnson, H., Trescoll-Serrano, C., *et al* (1997)** Recurrent hyponatraemia associated with sertraline and lofepramine. *American Journal of Psychiatry*, in press.

**Committee on Safety of Medicines (1994)** Antidepressant-induced hyponatraemia. *Current Problems in Pharmacovigilance*, **20**, 5–6.

**Spigset, O. & Hedenmalm, K. (1995)** Hyponatraemia and the syndrome of inappropriate antidiuretic hormone secretion (SIADH) induced by psychotropic drugs. *Drug Safety*, **12**, 209–225.

**Voegeli, J. & Baumann, P. (1996)** Inappropriate secretion of antidiuretic hormone and SSRIs (letter). *British Journal of Psychiatry*, **169**, 524–525.

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## Outcome of panic disorder

**Sir:** The conclusion of O'Rourke *et al* (1996) in their follow-up study that panic disorder "is a stable clinical entity" is at variance with almost all other comparative studies, which show a wide variation in clinical diagnostic outcome ranging from complete recovery to alcohol dependence, major depression, social phobia, obsessive–compulsive disorder and agoraphobia. The authors defend their single assessment at five years only by the somewhat curious argument that their method avoids the "distorting research effects intrinsic to the prospective method". It is surely relevant that the authors found that an unspecified number of patients "experienced temporary episodes of depression and alcohol misuse" during the follow-up period but this does not enter into the analysis at five years. The choice of the ninth edition of the Present State Examination as a diagnostic bastion for evaluating panic disorder is also odd as this instrument has only one question concerned with panic in its 140 items and does not derive a CATEGO diagnosis of panic disorder. The sample of patients chosen in the study was also not typical of panic disorder as it was a particularly chronic group that had been ill for a mean of five years. As all patients were known to have panic disorder at the time of follow-up there could also have been some tendency for the original symptom pattern to be identified and replicated, particularly if Dr O'Rourke (the assessor) expected this at the outset of the study.

In our own work, diagnostic assessments by structured interview at onset and after 10, 16, 32, 52 and 104 weeks showed that of 66 patients with panic disorder at outset, 60 (91%) had at least one diagnostic change over the next two years, 13 (20%) to a depressive disorder only, 23 (35%) to another anxiety disorder only, and 14 (21%) to both. We should therefore like to suggest that the findings of O'Rourke *et al* make a useful contribution to the debate over the validity of individual diagnoses within the neurotic spectrum but should not be taken as typical of panic disorder as it exists in clinical practice. It would be interesting to know whether the same diagnostic stability in the Galway sample continues to be maintained over the longer time scale as, if the same findings are found with formal diagnostic schedules, the existence of special features such as the higher prevalence of anancastic personality features in Ireland (Kelleher, 1972; Scott *et al*, 1982) might contribute to such unusual stability.

**Kelleher, M. J. (1972)** Cross-national (Anglo-Irish) differences in obsessional symptoms and traits of personality. *Psychological Medicine*, **2**, 33–41.

**O'Rourke, D., Fahy, T. J., Brophy, J., *et al* (1996)** The Galway study of panic disorder. III: Outcome at 5 to 6 years. *British Journal of Psychiatry*, **168**, 462–469.

**Scott, A., Kelleher, M. J., Smith, A., *et al* (1982)** Regional differences in obsessionality and obsessional neurosis. *Psychological Medicine*, **12**, 131–134.

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**Authors' reply:** Tyrer *et al* wrongly assert that we concluded that panic disorder is a stable clinical entity. We said that the mirror image of Present State Examination (PSE) test–retest after six years, although not conclusive, was difficult to reconcile with the notion that panic disorder is but one facet only of a general neurotic syndrome. That PSE does not define panic disorder with precision is very much to the point: PSE CATEGO-derived diagnoses are thereby less likely to be influenced by diagnostic bias. Their suggestion that our single rater cooked the PSE data is difficult to absolutely refute: if so, then the data were cooked to a turn – to a correlation of 0.92 to be exact, a culinary achievement all the more remarkable since baseline PSE data were not available until after follow-up was complete.

Our sample of panic-disordered patients was not a "particularly chronic group": most reviewers, including Argyle & Roth (1990), estimate mean chronicity at index as five to 10 years (five years in our sample). Tyrer *et al* ignore this notorious chronocity of panic disorder before treatment in their insistence on diagnostic musical chairs over time *after* treatment. They suggest that the reason why some results do not tally with theirs is that the former are biased by hospital practice. This time, however, the objection has no validity; our patients were treatment-naive, unpaid and were referred by general practitioners, as we have pointed out (Fahy *et al*, 1992; O'Rourke *et al*, 1996). If our patients were in any way special, it was in the notable absence of severe

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