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Correspondence

Contents: 'Number needed to treat'/SSRIs versus tricyclics/Pathogenesis of white matter lesions in Alzheimer's disease and depression/Drug induced psychosis/Ultra-rapid mood cycling/No right to a Mental Health Review Tribunal.

'Number needed to treat'

SIR: We agree with the conclusions of Hotopf *et al* (1996) in their review of the cost effectiveness of SSRIs – that there is, as yet, insufficient evidence to justify their first line prescription on either clinical or economic grounds. Systematic review and meta-analysis of total dropout rates in the limited and small scale studies comparing SSRIs with tricyclic antidepressants suggests either no difference or one that is small, statistically significant, but clinically unimportant. If there is a true difference, the largest reported absolute difference in total dropouts of 2.6% (Anderson & Tomerson, 1995), presented with its risk ratio of 0.90, is difficult to translate into clinical practice. In common with many research findings, the reader is left wondering about the clinical meaning of a statistically significant result.

One increasingly popular way of translating research evidence into terms that can be readily appreciated by clinicians is through the presentation of the 'Number Needed to Treat'. This value is readily calculated as the reciprocal of the absolute difference in risk of an adverse outcome (such as discontinuation of treatment) between two interventions (Cook & Sackett, 1995). In this case an absolute difference in risk of discontinuation of 2.6% would translate into a NNT of 38 (1/0.026). The meaning to the individual clinician of this finding and its statistic is as follows: 'I would need to treat at least 38 patients with more expensive SSRIs instead of tricyclics in order to prevent one patient discontinuing the anti-depressant medication which I prescribe'.

This statistic presents an intuitive and relevant addition to the routinely presented measures of effect, such as absolute risk reduction, and odds and rate ratios. It is increasingly being used to present research evidence in clinically relevant terms, particularly within systematic reviews (Sackett, 1996). We would recommend that, where applicable, authors calculate and include this statistic in their presentation of research evidence within the Journal.

ANDERSON, I. M. & TOMERSON, B. M. (1995) Treatment discontinuation with selective serotonin reuptake inhibitors compared with tricyclic antidepressants: a meta-analysis. *British Medical Journal*, **301**, 1433–1438.

COOK, R. J. & SACKETT, D. L. (1995) The number needed to treat: a clinically useful measure of treatment effect, *British Medical Journal*, **310**, 452–454.

HOTOPF, S., LEWIS, G. & NORMAN, C. (1996) Are SSRIs a cost effective alternative to tricyclics? *British Journal of Psychiatry*, **168**, 404–409.

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SSRIs versus tricyclics

SIR: We are not convinced that the economic considerations for using tricyclic antidepressants (TCAs) as opposed to SSRIs proposed by Hotopf *et al* (1996) would satisfy either the coroner or the relatives of a patient who dies following a TCA overdose. In addition, the authors have not taken into consideration the cost of intensive care treatment following TCA overdoses. They do point out that the SSRIs have a better safety record. However, there has been insufficient evidence to show that the SSRIs are either as effective or have a lower overall dropout rate than the TCAs. Balancing these complex issues is difficult. We believe that an emphatic statement recommending the TCAs above the SSRIs as the first line antidepressant drug is not justified at this stage. It may be prudent to admit that we do not yet have an ideal antidepressant and that suicide prevention is still an enigma.

HOTOPF, M., LEWIS, G. & NORMAND, C. (1996) Are SSRIs a cost effective alternative to tricyclics? *British Journal of Psychiatry*, **168**, 404–409.

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Pathogenesis of white matter lesions in Alzheimer's disease and depression

SIR: O'Brien *et al* (1996) highlight the associations between deep white matter lesions (DWML) and depression and between periventricular lucencies (PVL) and Alzheimer's disease. Although the contribution of vascular risk factors to these associations was closely examined, the influence of cerebrovascular disease in the pathogenesis of both white matter lesions remains unclear. Firstly, it is striking that vascular risk factors were significantly more common in depressed subjects than in those with Alzheimer's disease. However, notwithstanding the fact that the association between DWML and depression still existed after controlling for these risk factors, it is possible that other vascular risk factors may not have been taken into account. Those subjects with depression who had a past history of transient ischaemic attacks do not appear to have been excluded from the sample; it is possible that such episodes may have contributed to the development of DWML. The role of 'silent' infarcts may also be important, given their association with radiological changes and disruption of frontal connections (Meyer *et al*, 1995). A role for DWML as a risk factor for depression is put forward; again, a vascular contribution may be important in view of 'pre-stroke depression' found to be a possible risk factor for completed stroke (Colantonio *et al*, 1992).

The authors found no evidence of an association between PVL (which they suggest may involve other pathophysiological mechanisms) and vascular risk factors. Using both linear and volumetric measures, Schmidt (1992) found PVL to be significantly more common in vascular dementia than probable Alzheimer's disease. Furthermore, such lesions have also been shown to predict later development of clinically apparent cerebrovascular disease (Lopez *et al*, 1992). Thus, the role of cerebrovascular disease in the development of PVL remains open to speculation.

Before a more definitive statement about the role of vascular risk factors in the pathogenesis of white matter lesions can be made, prospective clinicopathological studies (including the use of *in vivo* neuroimaging) are needed to allow a better understanding of the relative contributions of vascular and non-vascular factors to such lesions in depression and Alzheimer's disease.

COLANTONIO, A., KASI, S. V. & OSTFELD, A. M. (1992) Depressive symptoms and other psychosocial factors as predictors of stroke in the elderly. *American Journal of Epidemiology*, **136**, 884–894.

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MEYER, J. S., MARAMATSU, K., MORTEL, K. F., *et al* (1995) Prospective CT confirms differences between vascular and Alzheimer dementia. *Stroke*, **26**, 735–742.

O'BRIEN, J. T., DESMOND, P., AMES, D., *et al* (1996) A magnetic resonance imaging study of white matter lesions in depression and Alzheimer's disease. *British Journal of Psychiatry*, **168**, 477–485.

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Drug induced psychosis

SIR: We agree with the main conclusion of Poole & Brabbins (1996) that the use of the term "drug induced psychosis" may cause misunderstanding and should be discontinued. We would nevertheless like to draw the readers' attention to what seems to be a misunderstanding of our research on cannabis and schizophrenia (Andréasson *et al*, 1987, 1989; Allebeck *et al*, 1993).

The aim of our studies was not to elucidate the concept of "drug induced psychosis", but to assess the role of cannabis as one of several risk factors for schizophrenia. Poole & Brabbins are incorrect in saying that we did not take account of confounding factors that might be related to the exposure (cannabis use) as well as the outcome (schizophrenia). A number of potential confounders were analysed first by stratified analysis and then in a logistic model. The relative risk of schizophrenia among cannabis users decreased in these analyses, indicating that some of the association could be explained by these factors. Even in the logistic model, simultaneously controlling for a number of background factors, the relative risk for schizophrenia was significantly increased among high consumers of cannabis as compared to non-users. Additional analyses (Andréasson *et al*, 1989) showed that cannabis use indeed preceded the onset of schizophrenic symptoms and that other indicators of mental disturbances, which could act as precursors of both