

Thase, M. E. (2003) Evaluating antidepressant therapies: remission as the optimal outcome. *Journal of Clinical Psychiatry*, **64** (suppl. 13), 18–25.

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Authors' reply: We welcome the letters of Dr Kirov *et al* and of Dr Euba who address the important issue of clinical efficacy of electroconvulsive therapy (ECT), which may be greater when bilateral ECT is used instead of unilateral ECT. We have little doubt that this is true, but bilateral ECT is associated with more unwanted effects on cognition than unilateral ECT (National Institute for Clinical Excellence, 2003). This is the main reason why unilateral ECT is still frequently applied, certainly at the beginning of a course of treatment. Some patients experience severe and persistent memory deficits after ECT (see Donahue, 2000). In their systematic review, Rose *et al* (2003) found that about one-third of patients reported significant memory loss after ECT. One can question the validity of this worrisome figure on methodological grounds, as the studies reviewed by Rose *et al* used questionnaires instead of neuropsychological assessments. Nevertheless, cognitive alterations can be very disturbing for the patient, and there remains a need to examine this controversial issue further.

In assessing the somewhat lower clinical response obtained in our study compared with others, it should be borne in mind that all our patients were treatment refractory (i.e. they had unsuccessful treatment response to at least two different types of antidepressants, each given in a sufficient dosage range for at least 4 weeks). Patients with resistance to antidepressant treatment are known to have reduced rates of response (Sackheim *et al*, 2000). For example, less than 30% of those with depression who had failed to respond to one adequate medication trial finally responded to low-dose or moderate-dose right unilateral ECT, in contrast to about 50% who had not received such an adequate antidepressant trial (Sackheim *et al*, 2000). Thus, the therapeutic effect of

ECT in our study was well within the expected range both for the group of patients studied and the type of ECT applied. It should also be noted that participants in the CORE study (Petrides *et al*, 2001) cited by Dr Kirov and colleagues were about 10 years older on average than patients in our study, and that ECT response rates in the CORE study were higher for older patients.

We have stated quite explicitly that our study was not designed to compare the absolute or relative effectiveness of repetitive transcranial magnetic stimulation (rTMS) or ECT. As outlined in our paper, some preliminary randomised trials suggest that rTMS might be as effective even as bilateral ECT in non-psychotic patients but, although the meta-analytic evidence for the clinical efficacy of ECT is strong, the evidence for strong efficacy of rTMS in depression is less conclusive.

Our primary intention was to highlight the continuing need to delineate the cognitive side-effects of ECT in comparison with other treatments. Weighing benefits and side-effects of a specific form of ECT treatment for a specific patient may have to take into account age, prior response to treatments, sensitivity to memory side-effects and other factors. Physicians and patients need better evidence about such side-effects, preferably from randomised controlled trials, but also from audits such as that reported by Kirov *et al*, to make informed decisions on the use of ECT, particularly as other forms of treatment become available.

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Hospital admission rates and diagnosis

We read with interest the article by Thompson *et al* (2004) on changing patterns of hospital admission for adult psychiatric illness. Although they acknowledged the limitations of routinely collected admissions data, the authors reported a lower than anticipated proportion of all admissions in the schizophrenia and related psychoses categories and greater than anticipated proportions for depression and anxiety and substance misuse. A further analysis of admissions for substance misuse suggested that this did not include a large number of patients with dual diagnosis and that psychotic disorder secondary to alcohol or drug misuse accounted for around 10% of admissions for substance misuse.

On a variety of indices, Manchester has the highest level of need for mental health services in England (Glover *et al*, 1999). Using a similar methodology, we have analysed the 2003/4 admissions data for Manchester and found marked differences from the patterns reported by Thompson *et al*: 42% of admissions in Manchester were for schizophrenia and related psychoses (national average 26%), with only 18% for depression or anxiety (national average 29.6%) and 6.5% for substance misuse (national average 19.1%). Further examination of the admissions for substance misuse in Manchester showed that 57% were for psychoses secondary to alcohol or drug misuse.

Our own earlier analyses of admissions in the north west of England (Harrison *et al*, 1995) also found marked variation according to diagnostic group and suggested that health districts with higher levels of deprivation admitted a higher proportion of patients with psychotic diagnoses and fewer patients with anxiety and depression. Similarly, the King's Fund report into London's mental health (King's Fund, 1997) argued that a high proportion of admissions for schizophrenia reflected increased need for services. This could explain some of the regional variation in admissions according to diagnostic group reported by Thompson *et al* and our own recent findings. Admissions for substance misuse may also be influenced by deprivation and availability of in-patient beds, with some areas only admitting patients with secondary psychoses rather than drug or alcohol dependence.

The continued variation in the use of in-patient facilities across England requires further attention, particularly as it suggests that current means of resource allocation do not adequately address the marked impact of deprivation on need for mental health services.

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Obesity and schizophrenia

After reading less than half of 'Metabolic syndrome and schizophrenia' (Thakore, 2005) I checked the Declaration of interest and found the expected link to the pharmaceutical industry. On rereading the whole paper carefully I could not pinpoint a single statement that seemed wrong. However, the uneasy general impression remained that the author attempted to suggest that the metabolic syndrome was rather a result of schizophrenia itself and/or the associated stress than the antipsychotic drugs. Therefore, I would like to draw attention to the high probability that patients with schizophrenia were rarely overweight before the advent of neuroleptics. First, Kretschmer (1961) found that 50.3% of 5233 people with schizophrenia had a leptosome (or *asthenisch*) body build, for which he measured an average waist/hip ratio of 0.67 (74.1/84.7 cm) in men and 0.82 (67.7/82.2 cm) in women. Only 13.7% of 5233 people with schizophrenia were *pyknisch*, characterised by a strong development of circumference of the holes for the intestines (*starke Umfangsentwicklung der Eingeweidehöhlen*) and an average waist/hip ratio of 0.97 (88.8/92.0 cm) in men and 0.84 (78.7/94.2 cm) in women. The rest of the

schizophrenia sample was classified as athletic, dysphasic or *uncharakteristisch* (not typical of any of the aforementioned). Among the 1361 people with manic-depressive illness, 64.6% were *pyknisch* and only 19.2% leptosome. The leptosome body build, which does not seem to indicate a risk of developing the metabolic syndrome, was thought of as typical for schizophrenia.

Second, I asked a student to classify the patients with schizophrenia on old photographs in Bleuler's textbook (1969) as probably underweight, normal weight or overweight, without letting her know the reason. She quite rightly protested that she could not carry out the task with any certainty. However, as she appears rather underweight herself and as most people tend to use themselves as a yardstick, it is unlikely that she underestimated the number of overweight patients with schizophrenia. She classified 25% (5 out of 20) as overweight, 60% (12 out of 20) as normal weight and 15% (3 out of 20) as underweight. Thus, in spite of Thakore's paper, I still think that neuroleptic drugs contribute considerably to the development of obesity and its consequences.

Declaration of interest

None.

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Author's reply: In response to Professor Thiels letter, intra-abdominal fat (IAF) is critical in determining the overall risk of physical morbidity and one does not need to be overweight, or indeed obese in the conventional sense, to have an excess of IAF (Thakore, 2005). For example, patients with melancholic depression, who by definition have usually lost weight, have twice as much visceral fat as matched controls, and have higher mortality rates than the general population (Thakore *et al*, 1997). Hence, the patients with schizophrenia described by Kretschmer may have been

underweight or of normal weight but still have carried excessive amounts of IAF, which would have increased their risk of developing a host of physical problems.

The waist/hip ratio is an indirect anthropometric measure of IAF whose value is greatly influenced by exactly where the tape measure is placed. Using a direct measure of IAF, computed tomographic scanning, we have shown in two separate studies that first-episode drug naïve non-obese patients with schizophrenia have over three times as much IAF as matched controls (Thakore *et al*, 2002; Ryan *et al*, 2004). The amounts of IAF in both of these samples were far in excess of what one would see in simple obesity, but were similar to what one might observe in patients with Cushing's syndrome. There is little doubt that most of the widely used neuroleptics (old and new) cause weight gain. Yet, using computed tomographic scanning, an acknowledged gold standard, we have shown that there is no significant increase in IAF with two commonly used atypical antipsychotics (Ryan *et al*, 2004). Therefore, we should be asking questions such as what has a greater physical impact on patients with schizophrenia – the illness, with all of its associated stress and poor lifestyle choices, or the medications used to control symptomatology?

Declaration of interest

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