appropriately. I suspect that high R^2 values would be obtained if this category were used as the predictor variable, which would lead to rejection of the assumed independence between depression and KSP. Furthermore, the effect of SSRIs on depression would then be a more plausible explanation of the changes in personality traits during antidepressant treatment.

The 'normalising' effect of treatment on KPS requires that regression towards the mean is thoroughly evaluated. The authors dismiss it by pointing out that previous findings are in line with their results. This is an invalid argument. Two methods that can be used to detect this phenomenon come to mind. One consists of evaluating the difference between the two measures of each subject against the arithmetic mean of the measures of each subject, rather than the difference between the two measures against the initial measure as considered by Ekselius & von Knorring. This technique is neither infallible nor a substitute to the second method, that is the use of a control group. Ekselius & von Knorring do not have a control group, which means to me that the study's design is inappropriate for its secondary aim, the measurement of a treatment effect, and its conclusions lack sufficient logical support to be generalised.

Ekselius, L. & von Knorring, L. (1999) Changes in personality traits during treatment with sertraline or citalopram. *British Journal of Psychiatry*, **174**, 444–448.

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Authors' reply: Dr Marchevsky finds it difficult to accept the assumed independence between depression and the majority of the self-rated Karolinska Scales of Personality (KSP). However, the empirical data are in favour of such an assumption. In an earlier study (Perris *et al*, 1979), in-patients suffering from a moderately severe or severe depressive syndrome completed the KSP on two separate occasions. The first investigation was carried out shortly after the patients' admission to hospital when they were depressed, and the second a few months later when they were at home having recovered from the depressive illness. Most of the patients were at that time treated with tricyclic antidepressants or electroconvulsive therapy. The results of that study verified that the inventory measures traits which are fairly independent of the state of the subject. However, significant differences were seen between the two assessments for psychic anxiety, somatic anxiety and social desirability, which is why changes in these scales should be interpreted with caution.

Second, Dr Marchevsky gives an example in which patients with large MADRS changes have small KSP changes while patients with small MADRS changes have large KSP changes. In our opinion, such an example would strongly go against a relationship between the changes in depressive symptomatology and the changes in personality traits.

Finally, Dr Marchevsky raises the question concerning regression towards the mean. He discusses mathematical strategies to handle the problem but concludes that this technique is neither infallible nor a substitute to the second method – the use of a control group. We agree.

He concludes that there is not enough support to generalise the results. We agree, as is clear from the tentative wording of our Clinical Implications (Ekselius & von Knorring, 1999, p. 448).

Thus, we still believe that there is support for our conclusions, although a limitation that we pointed out (Ekselius & von Knorring, 1999, p. 448) must be borne in mind: "Although the personality inventory used has been demonstrated to be fairly independent of the clinical state of the investigated subjects, the improvement in depressive symptomatology may have influenced the results".

Ekselius, L. & von Knorring, L. (1999) Changes in personality traits during treatment with sertraline or citalopram. *British Journal of Psychiatry*, **174**, 444–448.

Perris, C., Eisemann, M., Eriksson, U., *et al* (1979) Variations in self-assessment of personality characteristics in depressed patients, with special reference to aspects of aggression. *Psychiatrica Clinica*, **12**, 209–215.

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More on amiodarone-induced depression

Sir: Ambrose & Salib (1999) assume that the depression induced in their patient by treatment with amiodarone, may not have been due to effects on thyroid functioning. Amiodarone, however, produces a variety of effects on thyroid hormone physiology.

Amiodarone reduces the conversion of thyroxine (T_4) to triiodothyronine (T_3), results in a modest decrease in T_3 serum levels, and a rise in T_4 and reverse T_3 levels. Thyroid-stimulating hormone (TSH) levels rise transiently in the first three months but thereafter return to normal. These effects are similar to the results obtained by Ambrose & Salib of raised T_4 and normal TSH levels after eight months of amiodarone treatment.

The majority of patients treated with amiodarone remain clinically euthyroid, albeit with altered thyroid indices, as in Ambrose & Salib's patient. However, occasional patients may develop overt or subclinical hypothyroidism or hyperthyroidism. In subclinical hypothyroidism clinical symptoms are generally absent, however some studies have reported somatic and psychiatric symptoms such as depressed mood, lethargy, obssessionality and impaired cognitive function. Lithium, another drug which inhibits thyroid hormone release, has been reported to cause thyroid dysfunction even when thyroid function test results remain within normal limits.

It has been suggested that hypothyroidism is a graded phenomenon with varying degrees of clinical severity and biochemical abnormality. It may well be that amiodarone-treated patients, although outside the range for overt hypothyroidism, still have subtle abnormalities in thyroid function. Observations in animal models suggest that amiodarone can antagonise thyroid hormone action at the cellular level by blocking hormone entry and receptor binding. The mildly altered biochemical indices seen in euthyroid patients on amiodarone may represent compensatory effects. Thus, the increased T_4 level may serve to overcome the blockade of T_3 production, thereby maintaining normal T_3 levels, which, in turn, may help to restore TSH levels to normal.

Ambrose & Salib's report is important as it is perhaps only the second report of psychiatric symptoms induced by amiodarone. However, they were quick to dismiss the role which may have been played by thyroid function.

Ambrose, A. & Salib, E. (1999) Amiodarone-induced depression. *British Journal of Psychiatry*, **174**, 366–367.

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