AUTHOR'S REPLY: We thank Freemantle and his colleagues for their interest in our article on cost-effectiveness. They raise several points that we will try to answer in order.

Many patients suffer badly from depression and the available treatments are far from perfect. There is a great need for therapeutic progress and it is understandable that when new treatments become available, doctors will try them. Since the alternative therapies are very old, new drugs are likely to appear expensive by comparison. However, we must not look at drug costs alone, and several cost-of-illness studies have been published for depression showing that drugs are a small part of all costs, particularly when indirect costs are included (Stoudemire *et al*, 1986; Kind & Sørensen, 1993). We must also consider the reduction in quality and quantity of life that is a consequence of depression. However, studies answering questions about cost-effectiveness must be based on clinical data.

Our study was aimed at demonstrating the methods and evidence needed for undertaking cost-effectiveness studies in depression. We were well aware of the problems and limitations of our data, and our conclusions, as indicated in the last three paragraphs of the discussion, were much more tentative than Freemantle and his colleagues aver. However, we trust the readers, particularly the medical readers, of this journal, with a judgement of the limitations of the clinical evidence. Clearly, if Freemantle *et al* feel that they should be reminded of the need to be critical of what they read, we can have no objections. However, it is improper of them to accuse the authors of economic evaluations published in referred journals of bias because their studies have been used in promotion, given that marketing is an inescapable consequence of market forces. Or are there different criteria for medical and economic evaluations?

The issue of dropout rates is obviously crucial to our model. Our study is a comparison between paroxetine and imipramine based on a meta-analysis published in the *BJP*. This was the clinical foundation of the paper and the source of dropout rates used in the model, as we documented clearly. While the meta-analysis carried out by the York group found relatively little difference in drop-out rate between SSRIs and older antidepressants, the differences were minimised by their choice of comparison, as pointed out in subsequent correspondence to the *British Medical Journal* by Jönsson (1994). Recently, Montgomery *et al* (1994) have provided a meta-analysis of more specific comparisons between SSRIs and tricyclics suggesting an overall difference in dropout rate somewhere between 4 and 8%. In our paper, the sensitivity analysis relating to dropout rate suggested that a difference as little as 4% would still give the SSRI the advantage in terms of cost per successfully treated patient.

Freemantle *et al* point out that treatment switching in response to dropout will tend to reduce the impact of cost differences. This is true, but the assumption of treatment switching is reasonably in line with clinical practice: if a tricyclic proves unacceptable because of side-effects, most doctors would probably switch to a different group rather than try another tricyclic, and the same is true if the initial drug is an SSRI. Our model was based partly on estimates provided by our expert panel: they suggested that dropouts attending out-patients would do so five times. The '%' in item 10 of Table 2 is a misprint: the value '5' refers to the number of out-patient visits. However, if only 20% of dropouts are referred, the calculation for the contribution of out-patient costs to the average cost of treatment failure falls from £180 to £36. The cost of treatment failure then becomes £344. Even if none are referred the cost of treatment failure remains at £308. In the paper we did conduct a sensitivity analysis to explore variation in treatment failure cost (although this seems to have been disregarded by Freemantle *et al*). At a treatment failure cost of £300, the cost per treated patient for paroxetine and imipramine is £340 and £314 respectively.

We agree entirely with Freemantle *et al* that findings of a study like ours must be treated with reservation, and we felt that our conclusions in the paper were appropriately cautious. There have actually been no empirical studies even of the *effectiveness* of antidepressant drugs in ordinary clinical practice – indeed, it is possible that they are used so badly that they are not effective at all (Brugha *et al*, 1992). Because of the cost of treating depression, the Department of Health has a responsibility to fund proper clinical and economic studies of ordinary usage of antidepressants. In the meantime we are left with simulation models of the type used by ourselves (and indeed by Freemantle *et al* (1994)). Despite the criticisms that can be directed at both papers, we think our conclusion remains valid: that an expensive pill can be more cost effective than an apparently cheaper alternative when all relevant costs and contingencies have been taken into account.

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Tourette's syndrome and psychiatric disorders

SIR: Pauls *et al* (*BJP*, February 1994, **164,** 215–221) claim to provide evidence against our proposal (Comings & Comings, 1987; Comings, 1995*a,b*) that depression and anxiety disorders are genetically related to the *TS (Gts)* gene(s). In reality their report provides strong evidence in favour of such a relationship.

Pauls *et al* have consistently maintained that the wide range of psychiatric disorders comorbid to Tourette's syndrome (TS) are all due to proband ascertainment bias, and would not be increased in frequency in the relatives of TS probands. Now they find that in fact the frequency of generalised anxiety disorder, major depressive disorder, panic disorder, simple and social phobia are significantly increased in frequency in 338 relatives of TS probands compared with 113 relatives of controls (Table 2). To extricate themselves from this turn of events, they now retreat to the extraordinary position of claiming that these disorders are unrelated to the *Gts* genes because their frequency is not significantly higher in first degree relatives *without* TS, chronic tics (CT) or obsessive–compulsive disorder (OCD) compared with relatives of controls. However, their own studies state that TS is inherited as an autosomal dominant trait with 100% penetrance in males, and when OCD is included, 71% penetrance in females (Pauls & Leckman, 1986). Thus, only 15% of relatives of TS probands without TS, CT or OCD should be carrying the *Gts* genes. As such, one would not be able to identify any of the pliotrophic effects of the *Gts* genes in a group of subjects where so few carry the genes. This would be analagous to attempting to claim that the Huntington's disease gene does not cause dementia because none of the relatives *without* HD show dementia.

They next claim that the increased frequency of these behaviours in the relatives that they observed was not due to the *Gts* gene(s), but was instead due to the presence of OCD. Again they seem to have forgotten their own paper (Pauls & Leckman, 1986) showing that the *Gts* gene(s) can cause OCD with or without tics. Thus, they would accept that *Gts* genes cause OCD, and that OCD produces depression and anxiety disorders, but deny the whole equation that *Gts* genes can cause depression and anxiety disorders. The demonstration by Pauls *et al*, of the increased frequency of associated behaviours in relatives with OCD but no tics, totally supports our suggestion that some individuals in the general population without tics may have these conditions because they carry *Gts* genes.

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ECT seizure duration and efficacy

SIR: The study by Fear *et al* (*BJP*, October 1994, **165,** 506–509), their prior correspondence (*BJP*, March 1993, **162,** 421–423), and two previous studies (Mitchell *et al*, 1991; Malsch *et al*, 1992) resurrect the issue of whether ECT seizure duration *per se* is related to the antidepressive efficacy of ECT. For example, Malsch *et al* (1992) state that "one of the unsolved questions of [ECT] is the effect of seizure duration on the efficacy of treatment".

The notion that ECT seizure duration might be related to its antidepressive efficacy has been advanced by the works of Maletzky (1978) and Kramer (1983). However, neither investigation demonstrated a significant positive correlation

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