patients with cancers before the skin cancer were retained in the analysis or not (Frisch *et al*, unpublished data). This argues against Sasieni and Bataille's proposal.

By no means do we consider our observations to be evidence of a causal role for ultraviolet light in the pathogenesis of non-Hodgkin's lymphoma. Sasieni and Bataille and Robert Newton suggest that immunosuppression rather than ultraviolet light explains our findings. We do not disagree with this. As we suggested in our paper, one of the possible mechanisms that link skin cancers and non-Hodgkin's lymphoma is the local and systemic immunological dysregulation caused by ultraviolet light.^{3,4} The considerable indirect support for such an association⁵ needs further consideration.

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Meta-analysis of antidepressant prescribing

Drop out rates were presented in a misleading manner

EDITOR,—The meta-analysis by I M Anderson and B M Tomenson is an interesting development in the literature addressing the effectiveness and cost effectiveness of prescribing of antidepressants.¹ The authors estimate that the risk of patients stopping treatment is 10% lower with selective serotonin reuptake inhibitors than tricyclic antidepressants. They note, however, that this corresponds to an absolute reduction in the total drop out rate of only 2.5% (their table IV) and is of borderline significance. Also, as they suggest, biases such as “patient selection, previous treatment, methodology, and study setting” may exist and make this result unreliable.

Unfortunately, although this is an apparently carefully constructed and methodologically sound paper, the results are presented misleadingly in the abstract, which states that “the total discontinuation rate was 10% lower with selective serotonin reuptake inhibitors than with tricyclic antidepressants... and the drop out rate due to side effects was 25% lower.” As this statement refers to the relative risk of dropping out rather than overall drop out rate, it is clearly ambiguous and open to misinterpretation.

The authors state that the newer second generation antidepressants in the tricyclic group included in our previous analysis² are not commonly used in primary care in Britain. The table shows that the newer tricyclic and related drugs had a volume

Market share of antidepressants by cost and volume in primary care in England, April 1993 to March 1994. Figures are percentages

	Cost*	Volume†
Newer tricyclics	13.2	13.3
Selective serotonin reuptake inhibitors	62.6	23.2
Older tricyclics	23.5	63.2

*Derived from reimbursement data from Prescription Pricing Authority.
†Estimated in person years of treatment.³

share of 13% compared with 23% for the selective serotonin reuptake inhibitors in the year from April 1993. However, 63% of the cost of prescribing of antidepressants in primary care in the NHS was spent on selective serotonin reuptake inhibitors. Clearly the newer tricyclic and related antidepressants, as a group, are neither “of minor importance clinically in terms of numbers of prescriptions” nor “nearly as expensive as the selective serotonin reuptake inhibitors.”

A fundamental tenet of cost effectiveness analysis is that all relevant comparisons are identified. Any discussion of the relative cost effectiveness of selective serotonin reuptake inhibitors and older tricyclic antidepressants is a partial one since, as the authors state, second generation antidepressants (“newer tricyclics”) share with the selective serotonin reuptake inhibitors the property of lower toxicity in overdose,³ but they achieve this at a substantially lower cost and may merit more frequent use in future. The authors attempt to apply the drop out rates they report to Jönsson and Bebbington's cost effectiveness analysis.⁴ This model, however, has flaws due to miscalculation and heroic assumptions based on the opinion of an expert panel and cannot safely contribute to this debate.⁵

The authors correctly outline the limitations of the studies included in their analysis and point to the need for further research. Perhaps the greatest limitation is the use of rates of stopping treatment as a proxy for tolerance of treatment and as an even poorer proxy for the success of treatment. Large comparative, pragmatically designed, randomised controlled trials that use reliable measures of outcome and include analyses of cost effectiveness as well as effectiveness are required to inform prescribing of antidepressants in practice.

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Important differences exist between second generation antidepressants

EDITOR,—I M Anderson and B M Tomenson discuss the relative tolerability of second generation antidepressants and state: “However, they are of minor importance clinically in terms of numbers of prescriptions and, with regard to cost effectiveness analyses, many (for example, lofepramine and trazodone) are nearly as expensive as the serotonin reuptake inhibitors.”¹ An article in a recent *PACT Report* dealt with the use of antidepressants.² During analysis of prescribing data for this article it was found that the use of lofepramine in particular was not minimal. The use each quarter from 1992 to mid-1994 was consistently about 8 million defined daily doses written on 200 000 prescriptions. The usage of trazodone was much lower, 0.6 million defined daily doses per quarter written on 40 000 prescriptions. For comparison, the use of fluoxetine during the same period rose from 4.8 million defined daily doses to 11.6 million defined daily doses written on 140 000 prescriptions rising to 330 000 prescriptions.

While the cost (based on defined daily doses and drug tariff prices) of treatment with trazodone is similar to that of treatment with selective serotonin reuptake inhibitors, that for lofepramine is much lower.

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Acceptability of side effects as reason for stopping may bias results

EDITOR,—I M Anderson and B M Tomenson raise the issue of compliance with selective serotonin reuptake inhibitors and tricyclic antidepressants and the importance of side effects in determining this.¹ The occurrence of side effects is only one of many factors affecting compliance, as the authors' analysis shows. Even with a difference in drop out rate of 25% between the classes of drug due to side effects, there was only a very small difference in the overall drop out rates. Other researchers have examined this area, with mixed results.^{2,3}

Many patients may give side effects as their main reason for stopping antidepressants when this is not the only factor. It is a reason that carries legitimacy with the medical profession and, patients know, will not offend the sensibilities of their doctor. Lack of faith in the benefit of treatment is a potent factor in stopping treatment that patients cannot easily disclose to their doctor. A survey commissioned for the “defeat depression campaign” in 1992 found that only 48% of respondents believed that tablets helped depression (compared with 85% who thought that counselling did) and 78% believed that antidepressants were addictive.⁴

Patients also, however, have faith in their doctors, and perhaps more time spent explaining the rationale, possible side effects, and delayed effectiveness of antidepressant drugs would have more impact on improving compliance than changing one set of side effects for another.

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Postgraduate deans will deal with accusations of fraud

EDITOR,—In drawing the lessons from the Pearce affair, Stephen Lock questions whether postgraduate deans are aware of the report of the Royal College of Physicians, *Fraud and Misconduct in Medical Research*—let alone the role, in the NHS,