The authors ask whether the hypothesis of undertreatment has been tested by comparing the data of patients who received a modern antidepressant with those who were treated with a classic antidepressant (36 *v.* 82% sub-optimal dose). The design of the study with outcome measures only at discharge did not permit such an analysis because all patients who had more than one treatment usually received both a modern and a classic antidepressant, but analysis of subgroups in the sample may give an answer in the future.

Undertreatment, however, is not only low-dose treatment but also the tendency not to set a next step in the treatment strategy when incomplete recovery occurs.

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BSE and human prion disease

Sir: In his review of our current understanding of the possible relationship between bovine spongiform encephalopathy (BSE) and human prion diseases Harrison (1997) appears reasonably certain that "all potentially infectious material has been banned from the food chain" as a result of the 1989 Specified Offals Ban. I fear that his confidence on this point may be misplaced.

The Specified Offals Ban excludes organs which contain significant amounts of central nervous system tissue ante mortem, principally brain and spinal cord. However, the slaughter process itself, consisting as it does of significant brain trauma from a 'bolt', may result in embolisation of central nervous system tissue to other parts of the body around the time of death. This was graphically demonstrated by Garland *et al* (1996*a*), who found macroscopic quantities of brain tissue (confirmed histologically) in "the main pulmonary artery of 2.5–5% of cattle after slaughter" – the largest embolus found was 14 cm in length! Such brain embolisation is a long-recognised complication of both open- and closed-head trauma in humans (McMillan, 1956).

Despite a claim by the Ministry of Agriculture, Fisheries and Food (MAFF) that "there is . . . no evidence that human lungs present a source of human exposure to bovine brain tissue in the UK" (Taylor, 1996), bovine lungs are legally permitted in certain meat products "sold for consumption without further cooking", such as salami and patés (MAFF, 1984). In addition, the British Veterinary Association, in a fax cited by Garland (1996*b*), confirmed that "it is perfectly legal for bovine lungs to enter the human food chain", and that "lungs can legally be sold in their fresh state".

Given Garland *et al*'s findings, our still-limited understanding of the risk to humans of the ingestion of prion-containing bovine tissue and the possible prevalence of currently incubating 'new-variant' Creutzfeldt–Jacob disease (Cousens *et al*, 1997), we should ensure that *no* part of any BSE-infected animal enters the human food chain, rather than merely excluding central nervous system tissue, as at present.

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McMillan, J. B. (1956) Embolism of cerebral tissue in lungs following severe head injury. *American Journal of Pathology*, **32**, 405–415.

Taylor, K. C. (1996) Brain emboli in the lungs of cattle. *Lancet*, **348**, 749.

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Risk assessment and clinical risk management

Sir: Reed (1997) states that risk factors for future violence are summative, and that the co-existence of mental illness, psychopathic disorder and substance misuse may present a very significantly increased risk. This is not necessarily so. A study of patients discharged from a special hospital (Jones *et al*, 1994) found that, specifically in the case of patients classified as psychopathically disordered, co-morbidity in the form of mental illness or substance misuse significantly reduced the risk of further convictions for serious criminal offences after discharge.

We hypothesised that the existence of a psychotic illness, or substance misuse, could provide a focus for treatment, and a specific risk factor which could be reduced by treatment. In contrast, 'pure' psychopaths, for whom no definitive treatment may be available, and in whom improvement may be harder to quantify, are likely to represent a higher future risk to others.

Historical data, by its very nature, remain unchanged by the therapeutic process. Risk, in contrast, is dynamic, and accurate risk assessment must be able to modify actuarial consideration in the light of treatment response. Risk assessment is a complex procedure, relying crucially upon a detailed clinical understanding of an individual patient. General principles must always be considered only as a starting point for assessment, and factors which in general increase risk may, if amenable to therapeutic interventions, paradoxically serve to reduce that risk, if their impact on future behaviour can be altered.

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Serotonin: 5-HT_{2A} receptor occupancy *in vivo* and response to the new antipsychotics olanzapine and sertindole

Sir: Up to a third of patients do not respond to typical antipsychotics which potently block-dopamine type 2 (D_2) receptors. This treatment is often associated with distressing extrapyramidal side-effects. The novel atypical antipsychotic drugs clozapine, risperidone, sertindole and olanzapine appear relatively free from extrapyramidal side-effects. It has been suggested that this is secondary to 5-HT_{2A} antagonism. *In vitro* and indirect evidence suggests that the ratio of 5-HT_{2A} to D_2 blockade may be crucial to the clinical profile of atypical antipsychotics (Kapur & Remington, 1996).

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