2002). Although parental psychiatric disorder might increase the chance that children become looked after, this is not inevitable and there are many other reasons why children may enter the care system. In fact, only 6% of the children participating in the survey on which our analysis was based were accommodated primarily as a result of any type of parental illness.

As the survey involved no contact with the biological parents of participants and historical information about children who are looked after is notoriously scarce, we had no way of accurately assessing the mental health of the biological parents. Our paper refers to our frustration at the extremely limited amount of information available to the survey and in clinical practice, and we explicitly state that our analysis cannot be seen as covering all potential risk and resilience factors.

Even if we had access to data on the mental health of the biological parents, an excess of children with psychiatric disorder among parents with psychiatric disorder would not necessarily indicate a biological or genetic basis for this finding. The mean age that children participating in this survey entered the care system was between 7 and 8 years, and we know that mental illness can have an impact on parenting practices. Do the children of parents with mental illness have raised rates of psychiatric difficulties as a result of genetic vulnerability and/or exposure to maladaptive parenting, or perhaps both processes occur at the same time and/or moderate each other? The literature suggests that parenting is an important mediating variable, although other genetic and environmental factors also play a part in the familial aggregation of psychopathology (Ramachandani & Stein, 2003). Cross-sectional surveys are not able to disentangle such complex questions, as data about exposures and outcomes are gathered at the same time. Longitudinal designs would be needed to explore Dr Sekar's theory.

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Lithium for prevention of Alzheimer's disease

Nunes *et al* (2007) reported that the prevalence of Alzheimer's disease in a group of elderly patients with bipolar disorder who were on continuous lithium treatment was significantly less than in a similar group without recent lithium therapy. After controlling for age, lithium use remained associated with a smaller risk of Alzheimer's disease (age-adjusted OR=0.079, 95% CI 0.020–0.321). Conversely, Dunn *et al* (2005) showed that patients who received lithium had a significantly higher risk of dementia than those who did not (age-adjusted OR=1.8, 95% CI 1.1–2.8).

Nunes *et al* (2007) found no differences between the lithium and the comparison group in neuropsychological performance after excluding patients with Alzheimer's disease. This is in accordance with our study using Mini-Mental State Examination (MMSE) scores (Terao *et al*, 2006). Our study, however, showed that patients with present and/or past history of lithium treatment had significantly better MMSE scores than patients without any history of lithium treatment (Terao *et al*, 2006). It is important to further investigate lithium in the prevention of Alzheimer's dementia with a large number of patients in prospective studies.

If lithium has a preventive effect for Alzheimer's disease, there may be two possible mechanisms. First, it might indirectly prevent dementia via its prophylactic effects on mood disorders, because the rate of dementia increased 13% with every episode leading to admission for patients with depressive disorder and 6% for patients with bipolar disorder, when adjusted for differences in age and gender (Kessing & Andersen, 2004). Second, lithium might directly prevent dementia via its inhibition of glycogen synthase kinase 3 (GSK-3) alpha (Phiel *et al*, 2003) and GSK-3 beta (Phiel & Klein, 2001). Although Nunes *et al* (2007) found no significant differences in the number of previous depressive and manic episodes between the lithium and comparison groups, at present both possibilities should be borne in mind.

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Authors' reply: Dunn *et al* (2005) identified from the General Practice Research Database in the UK all cases of dementia between 1992 and 2002 (n=9954) and compared the number of prescriptions of lithium for individuals with this diagnosis with a control group without dementia (n=9374). They found that more patients with dementia (n=47, 0.47%) than controls (n=40, 0.43%) were exposed to lithium. We feel that this finding does not allow conclusions to be drawn as to whether lithium protects against or confers a risk for dementia, because it has been shown that patients with dementia have an increased risk of developing mania and depression (Nilsson *et al*, 2002) and are thus more likely to receive treatment, including lithium. Conversely, affective disorders themselves seem to increase the risk for dementia.

In a series of studies based on data from the Danish psychiatric case register, Kessing *et al* found that 14% of elderly patients with bipolar disorder and 16% with

unipolar disorder developed dementia (MMSE < 24) compared with 3.4% of age-matched controls (Kessing, 1998; Kessing *et al*, 1999). Even within a younger sample of psychiatric patients (approximate mean age 50 years), Kessing *et al* (1999) reported that people with bipolar disorder had the highest risk of receiving a diagnosis of dementia, followed by those with unipolar affective disorder, schizophrenia and neuroses. Thus, if affective disorders do increase both the risk of dementia and the likelihood of receiving lithium treatment, then owing to the sampling method used by Dunn *et al* one could expect to find more lithium treatment among elderly people with dementia. Dunn *et al* discussed this alternative explanation of their findings as a 'reverse causation' possibility.

Dr Terao mentions the possible effects of lithium on GSK-3 beta. We recently investigated the effects of lithium on the transcriptional regulation of GSK-3 beta and found a significant reduction of its expression in primary cultures of rat hippocampal neurons as well as a reduction in regional intracerebral expression in lithium-treated adult rats and in leukocytes of elderly patients undergoing chronic lithium therapy for bipolar disorder (details available from the authors). These observations suggest a mechanism for GSK-3 beta inhibition by lithium, which may influence the formation of both amyloid plaques and neurofibrillary tangles, the two neuropathological hallmarks of Alzheimer's disease.

We think that it is important to investigate further the potential protective effect of lithium in Alzheimer's disease, as this could represent a low-cost universally available strategy to reduce the prevalence.

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Mortality and electroconvulsive therapy

Munk-Olsen *et al* (2007) reported that the mortality rate from natural causes was lower for patients undergoing electroconvulsive therapy (ECT) than for other psychiatric in-patients. The lower relative risk was particularly significant for mortality linked to respiratory disease (RR=0.67, 95% CI 0.55–0.95) and a trend was founded for cardiovascular disease (RR=0.85, 95% CI 0.70–1.03). The authors concluded that this decreased risk of mortality from natural causes is unlikely to be the result of a selection bias. They based this statement on: (a) the absence of absolute contraindications to ECT in the international guidelines; and (b) the concordant findings of previous studies.

At variance with this statement, clinical practice suggests that psychiatrists are generally reluctant to consider ECT in patients with medical illness, and are more likely to ask for the opinion of a colleague in such a case (e.g. anaesthetist, cardiologist) (Benbow & Shah, 2002). Thus, patients with severe medical illness could be less likely to be treated by ECT. Furthermore, identification of cardiovascular diseases or pulmonary disorders, as well as physical examination and standard laboratory tests are part of a systematic screening procedure before ECT. This practice improves the diagnosis and the treatment of medical comorbidities. Indeed, the absence of such preliminary medical examination led to a high level of cardiac complications after ECT in the past (Gerring & Shields, 1982).

Accordingly current guidelines emphasise the importance of identifying and carefully managing patients with risk factors before, during and after ECT, as well as assessing the risks associated with anaesthesia (National Institute for Clinical Excellence, 2003). Patients receiving ECT are therefore not representative of all psychiatric in-patients. The careful assessment and treatment of their physical comorbidities contrasts with the increased rate of untreated physical illness in psychiatric patients, mostly because of inadequate somatic care in psychiatric units (Rasanen *et al*, 2006). Therefore, the observed diminution of mortality from natural causes in patients with ECT is more likely to be related to appropriate medical assessment and treatment than to a direct effect of ECT on physical health.

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In an era that has seen ECT being opposed for political not clinical reasons, it was heartening to see an article on ECT addressing the very important issue of mortality. The study of Munk-Olsen *et al* (2007) is based on the Danish registry system which is acclaimed for its reliability, but certain issues need further clarification. It would have been relevant to know the total number of patients who received ECT and the total number of ECT treatments received by patients over the study period. Furthermore, the results could be better understood if information regarding physical comorbidity and the age of patients at the time of ECT had been provided. These variables can have a strong influence on mortality rates. In addition, as the study included only in-patients it is likely that the sample included patients who were severely ill. Also, the results show that inclusion of 'days since last ECT treatment' in the analysis causes the relative risk of mortality from natural causes of patients 'discharged within the past 8–30 days' to rise.

The relative risk of mortality from natural causes is also highest within 7 days of last ECT (RR=2.11), which is similar to the trend seen in deaths due to unnatural causes, especially suicide. Both these figures go against the conclusion of the authors that the mortality from natural causes is lower with ECT. It must also be noted that the relative risk of dying by suicide after