

Correspondence

Edited by Kiriakos Xenitidis and
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Antidepressants in rapid-cycling bipolar disorder

Amsterdam and colleagues¹ frankly acknowledge the multiple methodological deficiencies of their paper. However, this does not prevent them from drawing unfounded conclusions. In his editorial, Thase² makes the same error in accepting conclusions that are clearly not warranted by the data presented. What is most striking about Amsterdam *et al's* paper is that the results of lithium, fluoxetine and placebo are equally poor. The study is invalidated by the small sample size, the use of an 'enriched' sample and an inadequate analysis of the emergence of hypomania.

In the fluoxetine group, only 11 out of 28 participants completed the study (36%). Only 4 patients with rapid-cycling bipolar disorder completed this arm (33%). If we calculate this on the basis of the 42 patients in the rapid-cycling group who entered the first phase of the study, this amounts to a 10% completion rate! In the lithium arm, only 5 out of 26 participants completed the study (20%).

It is not possible to justify the conclusion that antidepressant monotherapy has a place in the treatment of rapid-cycling bipolar disorder based on these small numbers. In fact, it is potentially dangerous to do so. There is evidence that antidepressants, by accelerating the course of bipolar disorder and precipitating mixed states, can lead to protracted morbidity and increased risk of suicide.³

- 1 Amsterdam JD, Luo L, Shults J. Efficacy and mood conversion rate during long-term fluoxetine v. lithium monotherapy in rapid- and non-rapid-cycling bipolar II disorder. *Br J Psychiatry* 2013; **202**: 301–6.
- 2 Thase ME. Antidepressants and rapid-cycling bipolar II disorder: dogma, definitions and deconstructing discrepant data. *Br J Psychiatry* 2013; **202**: 251–2.
- 3 Eppel AB. Antidepressants in the treatment of bipolar disorder: decoding contradictory evidence and opinion. *Harv Rev Psychiatry* 2008; **16**: 205–9.

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Authors' reply: We appreciate Dr Eppel's thoughtful comments. Our study was an exploratory analysis of fluoxetine monotherapy in patients with rapid-cycling bipolar II disorder v. patients with non-rapid-cycling bipolar II disorder. It was a secondary analysis

from our National Institute of Mental Health-funded, prospective placebo-controlled study designed to compare the safety and efficacy of long-term fluoxetine v. lithium monotherapy in preventing relapse and recurrence of bipolar II major depressive episode.¹

We respectfully disagree with Dr Eppel's assertion that we drew unfounded conclusions from our results. We acknowledged the limited sample size, the exploratory nature of the analyses, and the fact that our findings are not definitive. We also acknowledged that larger sample sizes would be needed to detect small differences in mood conversion rates between groups.

Dr Eppel described a low completion rate for the study. In this regard, we previously explained to Dr Eppel the design of our peer-reviewed study and the fact that the response rate was based on patients who entered the entire trial.² We also explained that (in the primary analysis) if we conservatively assumed that all patients who were 'lost to follow-up' had relapsed, then the percentage of patients who remained well would be computed as the percentage of patients who completed the study, or 39.3% ($n=11/28$) for fluoxetine, 19.2% ($n=5/26$) for lithium, and 25.9% ($n=7/27$) for placebo.²

We also disagree with Dr Eppel's claim that 'It is not possible to justify the conclusion that antidepressant monotherapy has a place in the treatment of rapid-cycling bipolar disorder based on these small numbers'. We submit that we did not draw this conclusion. Rather, we clearly reported that 'Although not definitive, these findings suggest that maintenance lithium or fluoxetine monotherapy are similar to placebo in preventing depressive relapse and treatment-emergent conversion episodes during long-term relapse-prevention therapy of rapid- and non-rapid-cycling disorder.'

Dr Eppel cites one review article, based largely on uncontrolled studies in the literature, to support his assertion that there is evidence that antidepressants can lead to an increased risk of morbidity and mortality. In contrast, we presented prospective controlled data showing no significant increase in cycling frequency, mood conversion rates or worse efficacy during antidepressant monotherapy. Nevertheless, we clearly noted the caveat that the current study results are not definitive owing to the small sample size and exploratory nature of the analysis.

- 1 Amsterdam JD, Shults J. Efficacy and safety of long-term fluoxetine versus lithium monotherapy of bipolar type II disorder: randomized, double-blind, placebo-substitution trial. *Am J Psychiatry* 2010; **167**: 792–800.

- 2 Shults J, Amsterdam JD. Response to Eppel Letter. *Am J Psychiatry* 2010; **167**: 1408–9.

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Correction

Improving quality of life for people with dementia in care homes: making psychosocial interventions work. *BJP*, **201**, 344–351. Funding (p.349) should read: National Institute for Health Research (NIHR) Mental Health Biomedical Research Centre and Dementia Unit at South London and Maudsley NHS Foundation Trust and

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