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**Antidepressants Added Nothing to Mood Stabilizers Alone: Reply to Terao**

**To the Editor:** Dr Terao's letter commenting on our study<sup>1</sup> makes an excellent observation. Indeed, we wanted to see if antidepressants were effective when combined with mood stabilizers, versus mood stabilizers alone. If we had not allowed patients to enter the study unless they already were taking mood stabilizers, as is commonly the case, then the study would have been biased against mood stabilizers. In that case, since all patients had to be depressed, they would have failed their mood stabilizers already, and the resulting study would have been a study of bipolar depression that was treatment-resistant to mood stabilizers. Most clinicians do not practice this way and instead either use antidepressants alone or give antidepressants plus mood stabilizers together. The study design was left flexible so as to be generalizable to this treatment setting. The "placebo" group reflects "mood stabilizer plus placebo," and thus the study results answer the practical question whether antidepressants should be given with mood stabilizers in clinical practice, or whether mood stabilizers alone are just as effective. The answer was that mood stabilizers alone were just as effective, and adding antidepressants provided no further benefit. Whether that benefit from mood stabilizers is a pharmacologic effect, or a natural history effect, or another placebo-based effect is irrelevant. The randomized trial provides causal evidence that adding antidepressants to mood stabilizers, contrary to long-standing and difficult-to-change popular belief, does not provide further meaningful clinical benefit.

**REFERENCE**

1. Ghaemi SN, Whitham EA, Vohringer PA, et al. Citalopram for Acute and Preventive Efficacy in Bipolar Depression (CAPE-BD): a randomized, double-blind, placebo-controlled trial. *J Clin Psychiatry*. 2021;82(1):19m13136.

**S. Nassir Ghaemi, MD, MPH<sup>a,\*</sup>**

<sup>a</sup>Department of Psychiatry, Tufts University School of Medicine, and Department of Psychiatry, Harvard Medical School, Boston, Massachusetts

\*Corresponding author: S. Nassir Ghaemi, MD, MPH, Department of Psychiatry, Tufts Medical Center, 800 Washington St, Boston, MA 02111 (Nassir.Ghaemi@tufts.edu).

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