Author’s reply: Dr Corbyn and Dr Kripalani’s statement that our report ‘brings into question the pharmacological advantage of antidepressant medication over placebo’ is not warranted because our study was designed only to elucidate factors contributing to the placebo response in clinical trials. High placebo response rates in major depressive disorder (MDD) commonly lead to ‘failed’ trials (i.e. no statistical difference between drug and placebo). The fact that the medications showed numerical but not statistically significantly greater efficacy than placebo therefore is not surprising. Corbyn & Kripalani suggest that the lack of statistical difference could represent a type II error. They are correct that we had limited power to detect such a difference, but this is not an error per se because the study was neither designed nor powered to examine the question.

Prior work has suggested that medication might not offer greater benefits than placebo except in moderate to severe depression. Corbyn & Kripalani question whether the symptom severity in our sample was adequate to test our hypotheses. They specifically question our use of the HRSD, which they describe as ‘irretrievably flawed’, and ask whether they ‘can be assured that…’ Not so. We have presented all relevant data and analyses in Table 3. Our analyses examining expectations as predictors of outcome yielded highly significant results. Prior work has suggested that medication might not offer greater benefits than placebo except in moderate to severe depression. Corbyn & Kripalani suggest that the lack of statistical difference could represent a type II error. They are correct that we had limited power to detect such a difference, but this is not an error per se because the study was neither designed nor powered to examine the question.

Our report identified a novel form of expectation that contributed to heterogeneity in response to placebo. Corbyn & Kripalani’s letter highlights the fact that the design of the clinical trial itself may contribute to heterogeneity in outcome. Their analysis underscores the need for future studies to examine the role of expectations in placebo response to confirm our results.