Dr Gao and Colleagues Reply

To the Editor: We thank Dr Citrome for his comments on our article[1] and for proposing the use of likelihood to be helped or harmed (LHH) for clinical decision-making.

We agree that the atypical antipsychotic family of medications will continue to play a growing role in the treatment of major depressive disorder (MDD) given the high population prevalence of MDD and because only one-third of patients reach remission with initial antidepressant treatment and only two-thirds of patients achieve remission after sequential treatments, including switching and augmenting with different pharmacologic agents.[2] The US Food and Drug Administration has approved 3 atypical antipsychotics—aripiprazole, olanzapine, and quetiapine—for the treatment of patients with MDD who failed an initial treatment with an antidepressant. These approvals have provided those who prescribe treatments and their patients with much needed options to relieve the suffering associated with depression. However, some side effects including "tolerable" side effects such as somnolence/sedation, akathisia, and weight gain cannot be ignored.

We also agree that LHH, a ratio of the number needed to treat to harm (NNTH) to the number needed to treat to benefit (NNTB), can be used to help clinicians quantify the benefit versus risk.[3] We also propose that future treatment guidelines incorporate such metrics when devising algorithms and recommendations for the management of MDD. When combining the NNTH for discontinuation due to adverse events in our study[1] and the NNTB for response and remission in Dr Citrome's study,[4] the LHH of these 3 antipsychotics in MDD was close to 1. However, if measured with regards to reported somnolence associated with olanzapine and quetiapine and akathisia associated with aripiprazole, the LHH of these 3 antipsychotics was only about one-third to one-half.

More importantly, the impact of these acute side effects on the long-term treatment outcome remains unclear. In our previous studies, we found that patients with different psychiatric disorders have differential vulnerabilities for developing extrapyramidal side effects, somnolence/sedation, and weight gain with the treatment of antipsychotics.[5,6] Patients with MDD were more likely to discontinue study participation due to adverse events than those with schizophrenia or bipolar mania.[5] Therefore, the use of atypical antipsychotics in MDD should be carefully justified.

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Keming Gao, MD, PhD
keming.gao@uhhospitals.org
David E. Kemp, MD, MS
Joseph R. Calabrese, MD

Author affiliations: Department of Psychiatry, Mood and Anxiety Clinic in the Mood Disorders Program, University Hospitals Case Medical Center, Case Western Reserve University School of Medicine, Cleveland, Ohio.

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