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## Dr. Olfson and Colleagues Reply

TO THE EDITOR: Drs. Rico-Villademoros and Calandre suggest that in our case control study confounding by indication may have attenuated associations of olanzapine with hyperlipidemia and exaggerated associations of risperidone and ziprasidone with hyperlipidemia. While we can not exclude this possibility, the assessment of pretreatment risk of hyperlipidemia among patients who receive these antipsychotic medications remains a challenge in clinical practice. In this context, we believe that by matching comparison subjects to individuals on age, sex, race, psychiatric diagnosis, and time period, we have created comparable groups in terms of underlying pretreatment risk for hyperlipidemia.

The two randomized controlled trials cited by Drs. Rico-Villademoros and Calandre were not adequately powered to detect differences among antipsychotic medications in the development of hyperlipidemia. In the study by Lindenmeyer et al., all of the cholesterol increases remained within the normal clinical range (1). In the CATIE trial, the five study groups (olanzapine, quetiapine, risperidone, perphenazine, and ziprasidone) did not significantly differ from one another in the proportion started on a cholestatin (2).

The study reported by Kingsbury et al. provided preliminary evidence of a reduction in serum cholesterol following switch from olanzapine, risperidone, or a first-generation antipsychotic to ziprasidone (3). However, without an untreated comparison group, it remains unclear the extent to which this decrease was mediated by withdrawal of the previous medication or by initiation of ziprasidone. Comparison of untreated patients and ziprasidone-treated patients is an important feature of our case control study.

We agree that observational research is vulnerable to problems that flow from differences between patient groups in pretreatment risk factors for the disease outcome (e.g., hyperlipidemia) and that randomized controlled trials offer an unrivaled check against such bias. In the absence of adequately powered randomized controlled trials, however, carefully conducted observational research may help physicians in their evaluation of the risks of hyperlipidemia.

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## Effects of Topiramate

TO THE EDITOR: Drew H. Barzman, M.D., and Melissa P. DelBello, M.D., published a case report in the August 2006 edition of *The American Journal of Psychiatry* titled "Topiramate for Co-Occurring Bipolar Disorder and Disruptive Behavior Disorders" (1). This case report suggests that topiramate is "helpful" in the treatment of bipolar disorder and that topiramate monotherapy may be "effective in treating disruptive behavior disorders independent of its therapeutic effect for mania that is possibly related to its efficacy in decreasing impulsivity in binge eating disorder, borderline personality disorder, and pathological gambling in adults" (1, p. 1452). The authors make a broad scientific claim regarding the benefits of topiramate. They suggest a link in efficacy for this anticonvulsant/anti-migraine agent based on observed diagnostic classification, but do not address the possibility that disorders that are related by phenotypic expression may be unrelated genotypically or mechanistically. We are concerned that the authors present information suggesting effectiveness of topiramate without offering balanced commentary regarding the significant side-effects of topiramate, including word-finding difficulty, impaired concentration, depression, confusion, encephalopathy, and memory interference (2, 3). These and other problems with topiramate were recently highlighted elsewhere (4).