Reviewer's report

**Title:** Healthcare utilization and costs in hospitalized patients with schizophrenia or bipolar disorder receiving second-generation antipsychotics: a retrospective cohort study

**Version:** 1  **Date:** 9 October 2011

**Reviewer:** Haya Ascher-Svanum

**Reviewer's report:**

Major Compulsory Revisions

**Title page:** The current title is inaccurate. The manuscript actually reports healthcare utilization and costs in patients with schizophrenia or bipolar disorder following hospital discharge on quetiapine, aripiprazole or ziprasidone: A retrospective cohort study. Please revise.

**Abstract:** The background section needs to also indicate that these are patients assessed following hospital discharge (not “hospitalized” patients) on quetiapine, aripiprazole or ziprasidone.

**Background section:**

This section needs to provide a clear and well supported rational for the study’s focus on only 3 atypicals (quetiapine, aripiprazole or ziprasidone). Why exclude risperidone and olanzapine?

The authors appear to misinterpret (page 3) the results of the CATIE (reference 9), stating that results “support the similar efficacy” of first and second generation antipsychotics. The CATIE study actually concluded differently (page 1209): “The majority of patients in each group discontinued their assigned treatment owing to inefficacy or intolerable side effects or for other reasons. Olanzapine was the most effective in terms of the rates of discontinuation, and the efficacy of the conventional antipsychotic agent perphenazine appeared similar to that of quetiapine, risperidone, and ziprasidone. Olanzapine was associated with greater weight gain and increases in measures of glucose and lipid metabolism.” The CATIE paper also stated (page 1218): “Within this limited range of effectiveness, the olanzapine group had the lowest rate of discontinuation, which might lead one to consider olanzapine the most effective of the medications studied. Its apparent superior efficacy is also indicated by the greater reduction in psychopathology, longer duration of successful treatment, and lower rate of hospitalizations for an exacerbation of schizophrenia. The results for the other second-generation antipsychotic agents and the representative conventional drug, perphenazine, were similar in most respects.”

Please note that 2 recent meta analyses have shown the atypicals are not all alike on efficacy when compared to first generation antipsychotics (Leucht S,
Corves C, Arbter D, et al. Lancet. 2009;373:31-41) and also when compared head to head (Leucht S, Komossa K, Rummel-Kluge C, et al. Am J Psychiatry. 2009;166:152-163). Please revise the background section or delete this segment altogether, considering it is not clear how the statements about CATIE results are related to the current analysis/manuscript.

Please revise the last sentence (bottom of page 3) which states the CATIE results ..."suggest that patients with schizophrenia discontinue therapy at a high rate regardless of the agent received, due to lack of efficacy and/or intolerable side effects." Although CATIE indeed found a high rate of discontinuation for any cause, the time to all-cause medication discontinuation (the study’s primary outcome measure) ranged widely from 9.2 months (olanzapine) to 3.5 months (ziprasidone). Longer time on the medication is a clinically meaningful outcome, as it was repeatedly found – in CATIE and other studies - to be linked to better clinical and functional outcomes (Davis SM, Stroup TS, Koch GG, et al. Stat Biopharm Res. 2011;3(2):253-265; Liu-Seifert H, Osuntokun OO, Feldman PD. Compr Psychiatry. 2011 Feb 8 [Epub ahead of print]; Liu-Seifert H, Adams DH, Kinon BJ. BMC Med. 2005;3:21; Dunayevich E, Ascher-Svanum H, Zhao F. J Clin Psychiatry. 2007;68(8):1163-1171).

Methods. This information needs to be incorporated in the Background, if you opt to keep the CATIE in it.

Study sample: It appears the analysis included patients who “received oral ziprasidone, aripiprazole or quetiapine on their day of hospital discharge or the immediately preceding one.” Please clarify if these patients were only receiving the specified antipsychotic drug - monotherapy. If patients were not on antipsychotic monotherapy, then please report in the Results section - for each medication group and by diagnosis (schizophrenia, bipolar) - the proportion of patients who were also treated with olanzapine or risperidone at the time of discharge or the prior day.

The authors report (page 6) that levels of healthcare utilization and cost during the 6 months pre-admission were examined. Please add this pertinent information to Table 2.

Please clarify if the adherence parameters (MPR, CMGs) were calculated on a uniform follow up period for all patients (e.g., 6 months post discharge).

The authors are using a unique database that links health insurance claims and hospital admission records, but the current report could have been based on any other claims database in the US - due to the focus on resource use and costs in the 6 months post discharge. Please provide unique information, including as the cost of patients’ index hospitalization by diagnosis, the mean hospitalized duration by diagnosis, and the duration of treatment with the studied antipsychotics prior to hospital discharge.

Minor Essential revisions

The authors claim (page 4) that “the relationship between treatment tolerability
and persistency has not been well documented in the literature” citing Cramer et al 2008. However, Cramer et al did not state it. Please provide a supporting reference.

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I am a full time employee of Eli Lilly and company, the manufacturer of olanzapine