Reviewer's report

Title: Clinical and economic ramifications of switching antipsychotics in the treatment of schizophrenia

Version: 2 Date: 19 December 2008

Reviewer: Barry D Lebowitz

Reviewer's report:

I. Major Compulsory Revisions

A. The authors need to report the number of patients that were randomized to the medication they were taking at trial initiation and then need to differentiate the experience of those randomized to the same drug vs those randomized to a different drug. Essock et al. 2006 show a substantial difference between these populations in CATIE.

B. Similarly, the authors need to report on dosing, so as to be able to consider the hypotheses that those switched had been inadequately dosed in the initial randomization.

C. In CATIE, approximately 2/3 of the switching was for lack of efficacy and there were differences in the primary outcome based on reasons for the switch (Lieberman 2005). The authors should present similar data.

D. The interpretation strongly emphasizes the supposed negative effects of switching, eg "desirable to avoid switching. (p 10)". This conclusion is based upon the notion that switching is a proxy for treatment failure. But it may also be a proxy for clinical severity and complexity leading to the totally unremarkable conclusion that "brittle" patients cost more. This conclusion needs to be considered in the overall interpretation of the data.

E. The outcomes represent a selective sampling of patient outcomes of interest: suicide, incarceration, significant exacerbation of symptoms or of functional deficits necessitating change in residence (eg move to long term care facility, board and care facility etc). This selection may be biasing results and needs to be addressed.

II. Minor Essential Revisions

A. No IRB approval is noted

B. Trial registration is strictly on industry databases. ClinicalTrials.gov?

Level of interest: An article of importance in its field

Quality of written English: Acceptable
**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I have no competing financial interests related to this manuscript. I was a principal in the CATIE trials (schizophrenia and Alzheimer's disease) and have co-authored a number of papers, posters, and conference presentations. I do not believe that this involvement distorted my review.