Reviewer's report

**Title:** Non-adherence to drug therapy and drug acquisition costs in a national population - an individual-based register study

**Version:** 1  **Date:** 14 July 2011

**Reviewer:** Michael A Fischer

**Reviewer's report:**

**Major Compulsory Revisions**

General comment: My main concern with this paper is with the overall concept. As noted in the specific comments below, the basic assertion of this paper is that medications purchased but never taken represent a source of potentially needless spending. This assertion is hard to argue with. However, the percentage of medications never taken is basically assumed by the authors, which makes the results of the paper seem arbitrary. At a minimum, the authors should provide much more robust justification for why they assume the rates of secondary adherence that they use in this analysis, as well as a stronger argument for why this analysis represents a contribution beyond the intuitive concept summarized above.

Abstract: A terminology issue, here and throughout: “drug acquisition cost related to non-adherence” does not precisely capture the phenomenon the authors describe. Nor does the term “redundant” that they use later. A more precise definition would be helpful.

Page 4, bottom: The terms primary and secondary adherence are not always defined this way. In other papers, authors use primary adherence to refer to the filling of a prescription after it is first written and secondary adherence to refer to continued filling of medications after that. The authors should clarify if they are proposing new definitions of these terms or if these definitions have been used previously in the literature.

Page 9: The specification of the model seems to me to be an overcomplication of a relatively simple concept. The concept shown in the equation can be stated as “the percentage of dispensed medications that are not taken by patients represents wasteful medical spending.” One may choose a different term than “wasteful,” but the concept is the same and is almost a tautology. This is the central issue with this paper - does it really show us anything beyond a multiplication exercise?

Page 10: Given the critique above, the sections on page 10 are the crux of the entire paper. The authors need to provide a more robust justification, with citations from the literature, to support the three adherence rates that they choose to apply to different types of therapy. Otherwise the entire set of calculations seems unduly arbitrary.
Page 14, second-last paragraph: I am not certain in this case how varying the primary non-adherence rate (based on the definitions of primary and secondary used by the authors) should change the estimates at all, since the calculations are based entirely on secondary adherence.

Page 17, top: The final sections of this first paragraph are very problematic. The assumptions that the authors make about medication-taking behavior drive the entire study. If these are all rough assumptions, the reader is left much less certain about the importance of this analysis.

Page 20, limitations: The authors must discuss at length here the fact that this analysis is driven entirely by some strong assumptions (outlined in the comments above) and that several of those assumptions do not have clear support in the literature.

Minor Essential Revisions

Page 17, last line: “denominators” should be “determinants” or a similar word

Discretionary Revisions

Page 6, first paragraph: This paragraph can be cut.

Page 18, second-last paragraph: The point made about the relationship between secondary and primary adherence is reasonable, but unless that relationship is included in the models used in this paper, it is not clear what this point contributes.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

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

Declaration of competing interests:

I declare that I have no competing interests