Reviewer's report

**Title:** Utilisation trends of rosiglitazone and pioglitazone in Australia before and after safety warnings

**Version:** 1  
**Date:** 28 January 2014

**Reviewer:** Atonu Rabbani

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Comments on “Utilisation trends of rosiglitazone and pioglitazone in Australia before and after safety warnings”

**Synopsis**

The authors attempt to “identify” the impacts of the various warnings by drag authorities in different countries on use (as measured by drug dispensing) of rosiglitazone and pioglitazone over a period. Glitazones (meant for treating diabetes) have been associated with various adverse clinical reactions and have been under stronger regulation during post marketing periods. The present paper found that initial warnings had strong negative impacts on the prescription of rosiglitazone but not so much on pioglitazone. This implies the role of regulatory authority and information may have on prescription behavior and drug use.

**Major Compulsory Revisions**

1. On page 5, authors mention that in 2008 subsidization for rosiglitazone was withdrawn and this may have an important implication for use of rosiglitazone (or not). It will be very useful if authors discuss the implications of withdrawal of subsidy on drug use in interactions with the warnings.

2. On page 6, Authors may want to elaborate a little more on the datasets. Does the data set cover all Australians? Is the dataset only for the drugs subsidized by the government? How this may bias the results? A little more clarification in the data section will be really helpful for the readers who are less familiar with the institutional arrangements of Australia.

3. Authors discuss the time-series econometrics methods (basically ARIMA and Dickey-Fuller test) on pages 7-8. ARIMA already has an integrating factor and that may take care of the potential non-stationarity. Authors may want to include the results and discuss them later in the discussion section. Now, estimation of an ARIMA model should also include appropriate post-estimation diagnostic tests to properly locate the ARIMA parameters and model that fits the data the best. Authors should carry out the diagnostic tests and report them in the paper.

4. The fall in Rosiglitazone use started in January, 2007. This fall precedes the first FDA warning that came out later. Was there any dissemination of information around this time that led to fall in Rosiglitazone use around this time?
5. Authors mention: “Australian warnings were delayed, less frequently communicated, and unsubstantially accessed compared to the FDA and European warnings” (on page 11). This is an important point. Once the adverse impact of Rosi use and associated FDA warning became public (in the US) it is very likely that Australian prescriber will internalize this information and act on it. Additional warnings may have very limited extra information content. Is there any possibility of showing some evidence on this? Any mention of FDA warning on news or some medical journal(s) would really strengthen this argument and would help to make this case. Authors should look into this.

6. On Table 1 (page 18), authors should mention which ARIMA model was retained to estimate the results presented on the table.

7. Again it seems the reduction in Rosi use started to drop before FDA1 and EMI1 (as suggested by this figure). So the "right" decision to reduce use of Rosi has already started to surface. What can explain this?

Minor Essential Revisions

8. Authors do a good job in describing the background information and issues regarding the use of rosiglitazone and pioglitazone. One important thing is to keep in mind that we are using monthly data to understand the impact of warnings on drug use. Hence, it would have been very useful from the very beginning to be explicit the months when important warnings were announced.

9. Limitations should also reflect the time-series econometrics used in the paper and the extent to which those limitations where addressed in the paper.

Discretionary Revisions

10. On Figure 1 (page 19) Authors should clarify whether all the information will go into the notes for Figure 1? If not, the actual dates (up to month level) should be added to this list.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
'I declare that I have no competing interests'