Reviewer’s report

Title: The rising tide of polypharmacy and drug-drug interactions: population database analysis 1995-2010

Version: 1
Date: 5 February 2015

Reviewer: Anthony Avery

Reviewer’s report:

1. Is the question posed by the authors new and well defined?
Others have looked at the issue of changing prevalence in polypharmacy, but this paper will be a valuable addition to the literature because of the size of the study, the duration of the study and the detailed analysis.

2. Are the methods appropriate and well described, and are sufficient details provided to replicate the work?
Overall I thought the methods were well described. There are a couple of things that it would be worth the authors addressing:

   i) I think it would be helpful to be a little bit more explicit (Either in the Objectives or in the Methods) That One of the Key Objectives Is a Comparison of Data between 1995 and 2010, and That Alongside This the Authors Conducted an Analysis of Changes in Prescribing over the 15 Year Period.

   II) I Think Will Be Helpful to Give More of an Explanation of How the authors defined potential drug interactions. They mention referring to the British National Formulary, but a little more detail would be helpful, e.g. are we talking about just 'black dot' interactions here?

3. Are the data sound and well controlled?
As far as I can tell the data are sound.

4. Do the figures appear to be genuine, i.e. without evidence of manipulation?
As far as I can tell the figures appear to be genuine (and look like what I would expect from previous studies).

5. Does the manuscript adhere to the relevant standards for reporting and data deposition?
Yes.

6. Are the discussion and conclusions well balanced and adequately supported by the data?
Yes, although I felt that the conclusion in the abstract went a little beyond the
data presented in the paper. One important issue here is the importance of potential drug-drug interactions. The prevalence of this is high (particularly in 2010) and as a clinician one might expect to see more harm to patients as a result of this high prevalence. Are the authors able to comment on how important potential drug-drug interactions are in terms of patient morbidity?

7. Do the title and abstract accurately convey what has been found?
Yes.

8. Is the writing acceptable?

Overall it is a well written paper, but could do with a final bit of 'polishing'. I know that sounds a bit non-specific, but I think the authors will know what I mean.

I don’t have any suggested major compulsory revisions.

The comments have made above probably fall into the category of minor essential revisions (although the bit about polishing up the article is discretionary).

I found one typo on the second line of the section titled 'statistical methods' in the methods section. I think it should be 'experienced' rather than 'experience'.

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I have no competing interests.