Reviewer's report

**Title:** Potential drug-drug and drug-disease interactions in prescriptions of ambulatory patients in Family Medicine Clinics in Mexico

**Version:** 1  **Date:** 21 June 2007

**Reviewer:** Yen-Fu Chen

**Reviewer's report:**

General

Overall this is an interesting paper with clear objectives. Although similar work has been done elsewhere, there appears to be lack of such information from Mexico as the authors have stated.

The study was based on data collected for another study (EEA), and thus the subjects were selected older adults who were prescribed non-opioid analgesics (as oppose to a representative sample of ambulatory patients seen in family medicine clinics). This is clearly described in the abstract but should probably also be reflected in the title.

The provision of more details for the EEA study and some other important aspects of the study methods (see below) may be required to allow readers to replicate the work and/or correctly interpret the study findings.

The results are generally well presented. It may be desirable to report the numerical results of bivariate analyses irrespective of their statistical significance, and to provide the full list of factors explored in logistic regression.

Discussions are relevant to the study findings, although care needs to be taken when quoting the results of previous studies and comparing study findings (see below). The conclusion appears to be supported by the study findings.

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**Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)**

**Introduction section**

1. The statement (referring to the study by Zhan et al, Reference 3) that ‘2.58% of 50 ambulatory patients examined showed one or more of them (potential drug-disease interaction)’ is erroneous and should be corrected.

The study by Zhan and colleagues included 70,203 outpatient visits by patients aged 65 and older, and found that 2.58% of the visits with at least one prescription had one or more of the 50 inappropriate drug-disease combinations that they screened.
Methods section

2. The study background (e.g. the methods for the EEA study), setting and the selection/inclusion of study subjects should be described in more detail.

For example, did the 127 family doctors represent all family doctors in the two clinics, or were they a selected/volunteered subset of all doctors in the two clinics? Are IMSS Family Medicine Clinics typically of this size? The clinics seem to be very large according to the number of doctors. How were the four patients for each doctor selected (e.g. consecutive, convenient, volunteered, or according to other criteria)? Four patients per doctor for 127 doctors would add up to 508 patients, not 624 patients?

The authors may also wish to describe what information was collected from patient interviews and whether this was used to verify/supplement the data from electronic case notes. Inclusion of information from patient interviews in addition to electronic case notes could well be one of the strengths of the study.

3. The prescriptions that were included in the analysis need to be clarified.

Was there a pre-defined rule with regard to what prescriptions were included in the analysis? For example, were medications prescribed for occasional use (‘as needed’) included? Were topical preparations included? Were the 7-day non-opioid analgesics described in the method section included? Were medications prescribed by the doctors during the consultation in which the data were collected included in the analysis?

4. The potential interactions that were screened in the study should be described in more detail.

The authors stated that ‘potential interactions were identified by literature review’. It is not clear how the final list of potential interactions that were subsequently used to screen the prescription data was compiled. Was it purely based on the Swedish Classification System and the paper by Zhan and colleagues, or was it based on other references or drug interaction databases? It would be helpful to make available the list of potential drug-drug and drug-disease interactions that were actually screened. Clarification is also needed with regard to how the clinical relevance/significance for a specific drug-drug or drug-disease interaction was assigned if this was not published in the literature.

5. The full list of variables/risk factors that were explored in bivariate analysis and logistic regression should be described (i.e. not just those with significant results).

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

6. A few texts / drug terms appear to be written in Spanish:
- Methods section, last paragraph: ‘C y D’
- Page 10, last paragraph: ‘taking 5 or more medicines’
- Table 3: ‘Pentoxifylline + hypoglycemiante’ (better know as ‘hypoglycemic agents’ in English?)
- Table 3: ‘INEs’ in patients with previous peptic ulcer

7. Table 4 the 95% confidence interval for the adjusted odds ratio for cardiovascular disease has redundant text ‘gg’ attached.

8. Reference 11 (Becker et al) has just been published and should be updated (Pharmacoepridemiology & Drug Safety 2007;16:641-651)

Discretionary Revisions (which the author can choose to ignore)

Title
9. The title could be modified to reflect more accurately the population being studied.

Results section

10. Second paragraph – the second sentence describes the findings regarding type D interactions. The subsequent (third) sentence then states ‘The most frequent drug combination with this class interactions were combinations of NSAIDs with antihypertensive drugs, and with low doses of acetylsalicylic acid (ASA)’ – which is about type C interactions. Is there a general statement about type C interaction missing between sentence two and three?

11. Could the numerical results of bivariate analysis be presented?

12. Table 4 shows the results of logistic regression for drug-drug interactions. Was logistic regression performed to examine factors associated with drug-disease interactions?

Discussion section

13. Comparisons between study results need to take into account differences in how the samples were selected. The higher prevalence of potential drug-drug and drug-disease interactions found in this study compared to previous studies is likely attributable to the characteristics of the study sample (selected older adults with very high prevalence – nearly 90% - of NSAID usage) among other reasons.

14. Page 10 first paragraph: the accuracy of the statement ‘Other authors have reported that both types C and D show similar hospitalization frequencies’ needs to be checked. The cited reference by Merlo and colleagues was a database study of ‘potentially harmful’ drug combinations – as far as I am aware no outcome regarding hospitalization was assessed in the study.
15. The (substantial) differences between the prevalence/incidence of ‘potential interactions’ (as measured in this study) and the actual incidence of adverse events resulting from these hazardous drug-drug or drug-disease combinations reported in published literature (such as those reported by Becker et al, reference 11) may need to be highlighted and be taken into account when interpreting the study findings.

**What next?**: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

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

**Declaration of competing interests**:  
I declare that I have no financial competing interest. I had conducted research of drug interactions in primary care settings in the UK and have active research interest in this field.