Author's response to reviews

Title: Effect of interventions to reduce potentially inappropriate use of drugs in nursing homes: a systematic review of randomised controlled trials

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Version: 3 Date: 8 February 2011

Author's response to reviews: see over
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Version: 2 Date: 8 February 2011
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Dear Editor,

We appreciate that you have taken our manuscript into consideration. We also appreciate and thank both reviewers for commenting on the manuscript.

We have responded to all of the reviewers’ comments, either by revisions in the manuscript (marked by red type) and/ or with comments in this letter. Furthermore, we have checked the manuscript against the PRISMA guidelines and performed several minor revisions of language and spelling (not marked). We hereby resubmit and we look forward to hearing from you again.

Sincerely,
Louise Forsetlund
Corresponding Author
Reviewer 1

Reviewer's report
Title: Effect of interventions to reduce potentially inappropriate use of medicines in nursing homes: a systematic review of randomised controlled trials
Version: 2 Date: 10 November 2010
Reviewer: Michael Roberts

Reviewer's report:
'Effect of interventions to reduce potentially inappropriate use of medicines in nursing homes: a systematic review of randomised controlled trials'

Overall Comments
The review is well structured and includes detailed description of each study included. Overall, review emphasises more on quality of evidence included rather than on collaborative findings/results generated from review.

Some of the key references are missing which are mentioned in detail below.

Author needs to address issues like exclusion criteria needs to be clear and explicit, population demographics should be included in review, important interventions like changes in regulatory policies on the inappropriate prescribing, multi-disciplinary teamwork and multi-facet interventions should be included in review.

Discretionary Revisions (which are recommendations for improvement but which the author can choose to ignore)

1. Background: Lacks in explaining the significance of appropriate medicine use. A brief description of what inappropriate medicine use is, how it is assessed and what can be consequences of it, will give readers overall view of problems associated with inappropriate medicine use.

Comments from authors:
As a response to these comments we have now added the following text in the Background chapter:
“*Inappropriate use or prescribing of drugs comprises over-use as well as underuse of drugs, prescribing of multiple drugs with known interactions, for the wrong indication or in wrong doses or for too long duration. Appropriateness of prescribing can be assessed by validated tools for reviewing drug utilization*. ” (more detailed description of the tools that were actually used in the articles we identified are described in the Outcomes chapter.) And further below in the Background chapter: “For these reasons, many residents use several drugs
simultaneously, with increased risk of interactions between drugs, adverse effects and medication errors, with the possibility of increased morbidity and mortality.”

2. Results, Outcomes, Last line: “In the remaining 13 studies use or prescription of selected drugs were measured on a general basis” is not clear. What is meant by general basis should be explained in the review. For instance does this mean reduction in overall number of medicines prescribed or reduction in prescription of targeted class of medications?

Comments from authors: We have changed the sentence to make this clearer: “Reduction in overall number of drugs prescribed were measured in two studies (Cavallieri 199311, Zermansky 200628) while the remaining 11 studies measured reduction in prescription of targeted classes of drugs.”

3. A table or figure summarising which of the interventions were effective in reducing inappropriate prescribing and which were unsuccessful will provide a clear picture of the outcomes of the systematic review.

Comments from authors: We have evaluated this, but find that the complexity and low quality of the findings makes this difficult, and it may be misleading to the reader. We have therefore chosen not to include this.

4. There is no mention of follow up of the studies. It would be informative to include if any of the studies were followed up to find long term benefits of interventions.

Comments from authors: Follow-up for each study is reported in the GRADE tables. We have added a summary statement in the text with reference to further information, in the Outcome chapter:

“The follow-up period in all studies ranged from 1 month to 12 months (details are given in GRADE tables).”

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

1. Results, Medication review, Drug use 1st line: Number of drugs prescribed instead of number of drug prescriptions because it is confusing.

Comments from authors: Corrected.

2. Methods, Literature search: Abbreviated terms are not elaborated like DARE, HTA.

Comments from authors: Corrected.
**Major Compulsory Revisions** (which the author must respond to before a decision on publication can be reached)

1. Title: ‘Effect of interventions to reduce potentially inappropriate use of medicines in nursing homes: a systematic review of randomised controlled trials’

   In review the term drug is used instead of medicine which makes it inconsistent with the title. Also, not sure whether in British Journals word drug is used or medicine/medication is used instead of that.

   **Comments from authors:** “Medicine” in the title and throughout the paper has been changed to “drugs” for consistency. “Drugs” appear to be an accepted term in British English (cf. Oxford English Dictionary).

2. Methods, Inclusion and exclusion criteria: Exclusion criteria are not clear. In additional file 2, reason for exclusion of review is elderly population is general but in text there is no mention that studies which included only elderly population are not included. Does this mean that author has excluded studies which specifically included elderly population? But if nursing home studies are considered, a large proportion of population will be elderly.

   **Comments from authors:** To make this clearer we have changed the title of this section to “Inclusion criteria” and put in the words “for elderly people” before the following text ‘in nursing homes settings’. As stated among our inclusion criteria, our review only included studies of elderly in the nursing home setting. In Additional Table A2 (previously additional file 2), “Population: Elderly in general” referred to studies where the setting was not stated and/or where subgroup analyses of nursing home residents was not performed. In an effort to make this clearer, we have changed the phrase to "Population: Elderly in general; no subgroup analyses of nursing home residents". Exclusion criteria as previously stated are now moved and stated in a separate section.

3. Results: Description of demographics of population e.g. age, if added to review will strengthen the results. Age of participants from various studies is not mentioned in the review except for one study in Table 1, last row for Testad 2010 study. Age is important determinant in effectiveness of interventions to improve inappropriate prescribing as intervention to optimise prescribing in younger patients might not be applicable to frail elderly because of several comorbidites and polypharmacy. Similarly, if studies include patients with specific disease condition and polypharmacy, the results of interventions will differ. Hence, patient demographics and characteristics are important factor in determining the success of any intervention.

   **Comments from authors:** Age is now included in tables.

3. Results, Categorisation: First two categories enlisting educational interventions
are not clearly differentiated. Study by Avorn 1992 is categorised under education outreach initiative included educational meeting intervention, then why is it separated from educational meeting interventions category. A clear description of different types of interventions will be easy for readers to understand.

Comments from authors: Studies were classified according to what we defined as the main intervention component. This implies some subjective judgment and we acknowledge that others may disagree, as previously noted in the discussion chapter ‘Possible weaknesses’. A more detailed description of the interventions included under each category is given in the presentation tables and may be checked there. We have now changed the sentence introducing the categories: “We classified the interventions into seven categories on the basis of their main component.”. Also, we have moved and expanded the section were we emphasized that there could be other ways to categorise the interventions to the general Discussion chapter: “It is important to be aware of the fact that the boundaries between the categories we classified the studies by are not clear cut. For example, both Roberts 200124 and Crotty 2004a13 could have been classified as medication reviews rather than as composite educational intervention and educational outreach initiatives, respectively. Also, several of the interventions could have been classified as multifaceted but we wanted to emphasize what we thought was the main content. Likewise, interventions such as pharmacists working in a multidisciplinary team could have been classified as multidisciplinary, but we wanted to emphasize the pharmacists’ role.

4. Discussions, Last paragraph, 1st line: ‘preselected primary outcomes were prescription and use of drugs’. This is not consistent with primary outcomes mentioned in inclusion criteria which are inappropriateness of drugs and specific drug categories. ‘Use of drug’ needs to be elaborated as this term can be misleading as it includes many other aspects how drug is used.

Comments from authors: To avoid misunderstandings we have elaborated on the inclusion criteria and changed the wording from ”inappropriateness of drugs” to ”Studies were only included if the primary outcome, drug use, was assessed by explicit or implicit criteria or where specific drugs were targeted for reduction as defined by authors.“

5. Table 1, Roberts 2001: It has been mentioned that extent of implementation of this study is not reported. It should be noted that this study led to nation-wide implementation of mandatory twelve monthly medication reviews for all residents in nursing homes by pharmacist. (Reference: Roughead EE, Semple SJ and Gilbert AL. Quality Use of Medicines in Aged-Care Facilities in Australia. Drugs Aging 2003; 20 (9): 643-653)

Comments from authors: We consider this to be about two separate issues: Degree of implementation of the intervention in or during the study and implementation in practice by
others afterwards. We think that the reviewer here refers to the second issue, while we by the statement in the tables refer to whether the authors reported implementation of interventions within the study (e.g., how many actually received the intervention).

6. This review has not considered interventions like effect of changes in regulatory policies on the inappropriate prescribing, multi-disciplinary teamwork and multi-facet interventions. It should be clarified, either studies conducted using these interventions does not meet inclusion criteria or the outcomes of these interventions is not effective in reducing inappropriate prescribing.

Comments from authors: As stated in the inclusion criteria we considered all interventions in nursing homes that aimed to reduce potential inappropriate drug use and which were tested in randomised controlled trials. These were the only prior criteria for an intervention to be included. We had no prior requirements on content or that they should be effective. As in all systematic reviews, from this follows that if an intervention type is missing, it either did not meet inclusion criteria or it was not identified (which we do not think is the case here). In addition to studies of regulatory policies, there are most likely many other types of interventions that have not been identified due to failing to meet one or more of the inclusion criteria. To name a few, potentially relevant interventions could be implementation of guidelines, audit and feedback, and use of reminders or physical exercise. In the light of this we hope it is appreciated that we feel it would be improper to highlight only some of these interventions.

7. Some of the key references are missing. In case, they do not meet the selection criteria, these should be listed in excluded studies table. Below are some of the examples:
Comments from authors: None of the above studies appear to meet the eligibility criteria as judged by their titles and abstracts. Except for Briesacher 2005 and Kaur 2009, there is no mention of residents in nursing homes or related terms in the abstracts. Briesacher 2005 is not a randomised controlled trial and correctly fell out of the reference pool when it was combined in the search with the filter for randomised controlled trials, whereas Kaur 2009 was identified in the search and therefore is listed as excluded in Additional Table A2. Consequently, except for Kaur 2009, we do not consider it appropriate to list these studies as excluded. According to the Cochrane Handbook for Systematic Reviews of interventions only “studies that may appear to meet the eligibility criteria, but which were excluded, should be listed and the reason for exclusion should be given” (p.71).
Reviewer 2

Reviewer's report
Title: Effect of interventions to reduce potentially inappropriate use of medicines in nursing homes: a systematic review of randomised controlled trials
Version: 2 Date: 2 January 2011
Reviewer: Ian Cameron

Reviewer's report:
This is an interesting and important systematic review. The methods used are appropriate. As the review is an update of an existing systematic review, that presumably has been peer reviewed, there are very few changes to be made.

Comments from authors
The original publication was reviewed independently by two peer reviewers internal at our institution and two external reviewers.

Major compulsory changes
The reviewer was not able to find an abstract. This needs to be provided and reviewed.

Comments from authors
Abstract was uploaded, but there might have been an error. We will make sure the abstract is correctly uploaded for this version.

Minor discretionary changes
In some places the formatting is incorrect, for example page 38 and the flow diagram.

Comments from authors
Formatting has been corrected in several places and Figure 1 (flow chart) and additional files are now provided as separate PDFs.

There are a few spelling errors that will be corrected by the copy editor.

Comments from authors
We have (hopefully) identified and corrected these errors.