

## **Author's response to reviews**

**Title:** Automated dose dispensing service for primary health care patients - A systematic review

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**Author's response to reviews:** see over

Helsinki, November 15, 2012

Dear editor,

Thank you for the comments regarding our manuscript "Automated dose dispensing service for primary health care patients - A systematic review". The comments were valuable and helped us to improve the manuscript notably. Please find enclosed the corrected manuscript. The changes in the manuscript are highlighted (except in Figure 1 and Additional\_file\_1). We provide in this letter the responses to all the comments from the handling editor and from the referee.

**A) Response to handling editor's comments:**

*1) Please address all comments raised by the reviewer. Regarding point 1 - it is not necessary to exclude uncontrolled studies but the results of controlled studies should be reported separately in the result section.*

The controlled studies have been now reported separately, please see the results section (on pages 6-7).

*2) The manuscript should be read by a native English speaker in order to improve the readability.*

A native English speaker has revised the final version of the manuscript.

*3) Throughout the manuscript please refrain from using abbreviations (i.e., AAD, IDU).*

Inappropriate drug use (IDU) has been now spelled out throughout the manuscript (except Table 2). Automated dose dispensing (ADD) is so widely used in our manuscript that we feel it would be difficult to use it every time. We also think that some sentences are more fluent if the abbreviation is used. However, we could spell out also this abbreviation if this is still required.

*4) Abstract: please list all databases or the number of databases searched and other methods used to identify pertinent studies such as reference mining. The search date needs to be included in the abstract. The unit of analysis should be studies, not articles, please revise the working accordingly. Please summarize the effectiveness and safety results of the included controlled studies.*

These changes have been made in the abstract.

5) *Methods: Please add separate sections for the procedure, the data extraction, and quality assessment instead of adding it to the inclusion criteria section. The inclusion and exclusion criteria should be organized by criterion, e.g., setting rather than first listing all inclusion and then all exclusion criteria, the PICOTS framework might be best. The data extraction content and procedure should be described. Methods to minimize reviewer errors and bias and how disagreements were handled should be reported for all stages of the review.*

The methods section has been now rewritten and new subtitles “ data extraction” and “quality assessment” have been added (on pages 4-5). The inclusion and exclusion criteria have been written according to the suggestion (on page 4).

8) *The STROBE checklist is a reporting guideline; it should be specified that you have assessed the quality of the reporting, not the quality of the methodology. This is also an issue in the discussion section.*

The change has been made, please see the abstract, the methods (on page 5) and the discussion sections (on page 9).

9) *Please state what the inclusion criteria were for economic evaluations.*

This issue has been now further clarified in the methods section (please see page 4).

10) *Results: The literature flow should be described in the text.*

The literature flow has been now described in a beginning of the results section (on page 5).

11) *The results of the comparative studies should be presented separately from those of the uncontrolled studies and results should be presented with more scientific detail.*

These suggested changes have been made, please see the results section (on pages 6-7).

12) *It might be worth clarifying that no economic evaluation was identified if that was the case, which is different from included studies not reporting costs.*

This clarification has been made, please see the results section (on page 7).

13) *Discussion: Please discuss experiences with automated dose dispensing services in hospitals.*

A section on automated dose dispensing in hospital settings has been added to the discussion (on pages 8-9). There are quite many changes in the discussion section. The majority of these changes were made in order to improve the readability.

*14) Acknowledgements: Please add more detail to the funding agency (e.g., non-profit) and describe the role of the funder.*

The funding agency has been described more detail (please see page 10).

*15) Tables: The evidence table should be structured according to the key outcomes specified for the review (appropriateness of medication use, medication safety, costs) rather than just summarizing the main results of the study.*

It was not possible to add new columns in Table 2 due to space limitation. The outcomes are now specified more detailed in the main results column, please see Table 2 (on pages 14-16).

#### **B) Response to Dr. Wallerstedt concerns:**

*1) The design of this systematic review and the choice of articles to be included need revision. The aim of the study was to review the influence of ADD on the appropriateness of medication use, medication safety, and costs in the primary health care. To achieve this aim, ADD users need to be compared with non-users, that is, a control group is required. Hence, I suggest all non-controlled studies to be omitted from the review, since they do not add any information as regards the aim of the manuscript. Indeed, the review would benefit from using the PICO approach, that is, to clearly define Patient (e.g. patients in primary care), Intervention (ADD), Comparison (not ADD/usual care), and Outcome (medication use, medication safety, and costs). Only studies that meet these criteria should be included in the review. Thus, the study by Kwint et al does not meet the inclusion criteria; the intervention investigated in that article was not ADD, but pharmacist-lead medication reviews. Consequently, I also suggest the discussion on medication reviews in the discussion to be omitted.*

Thank you for these comments. We have used PICO in the study selection process. It is now stated more clearly in the methods section (please see Inclusion and exclusion criteria, on page 4). We agree with the comment on the inappropriate inclusion of the study performed by Kwint et al, and this study is now omitted from the review. Handling editor suggested that the results of uncontrolled studies could be reported separately in the results section, and we have done accordingly. These uncontrolled studies do give some useful information on appropriateness of medication and safety when using ADD. However, the conclusions of our study are not based on these studies. We can also consider the removal of the uncontrolled studies from the review if this is still required.

The results of the controlled Swedish studies indicate that ADD patients have higher risk to use certain potentially inappropriate drugs (Johnell et al and Sjöberg et al). Thus, we feel that some kind of interventions to assure appropriate medication use are needed, and therefore, we would like to keep medication reviews as a part of the discussion section.

*2) The conclusions need to reflect the findings more properly. Johnell et al. (reference 18) and Sjöberg et al.(reference 17), the only publications which concern medication use (prescribed drugs) within an ADD system, indicate safety concerns as regards ADD (see point 3 below), and this needs to be made clear. The main conclusion of the review could be something in line with: "ADD may involve drug safety concerns, since inappropriate drug use is more common among ADD users. However, no studies on patient outcomes and costs have been performed." The present conclusion of the manuscript "The ADD service may improve medication safety in primary health care..." is inadequate, although I agree with the latter part of the sentence; that more evidence is needed. This also applies to the first paragraph in the discussion section and the last sentence of "Conclusions".*

Thank you for this comment. The conclusion section has been revised (please see pages 9-10). The changes have been made also in the first paragraph of the discussion section (on pages 7-8) and in the abstract.

*3) The following needs to be clarified: In the nation-wide study from Sweden (Johnell et al. reference 18), data were only obtained from SPDR and in an attempt to adjust for confounding factors, the results on quality indicators for drug use were adjusted for number of drugs used. The following regional study by Sjöberg et al. (reference 17) was performed to better control for confounding factors, than had been done in the previous one (the authors of the first article were also involved in the second one). The article by Sjöberg et al. thus contains fewer individuals, but these are more alike when it comes to burden of disease, and SPDR-data were linked to other registers in order to control for relevant confounding factors such as burden of disease and residence.*

This issue has been further clarified in the results section (please see page 6).

*4) The quality assessment could be further described. What were the criteria for a "good" and an "acceptable" study? (results, first paragraph)*

The criteria have been now further described in the methods section (please see page 5).

5) *In the abstract, the results of the quality assessment of the included articles could be reported, as well as the design (for example that no randomized controlled studies on outcomes of ADD have been performed).*

These additions have been now made in the abstract.

6) *In Table 2, an extension of the text in the fourth column of Sjöberg et al. (reference 17) is needed: "Data was collected from the SPDR in 2007, linked with register data on patient diagnoses and residence." Furthermore, in Sjöberg et al. (reference 16), a multi-level analysis is performed, with drugs at the first level and individuals at the second one. This need to be clarified in the column "Population and data collection". The third column (levels of ADD) needs further clarification. It seems strange that the levels of ADD differ between the publications from Sweden, since all patients in Sweden use the same system.*

"Population and data collection"-column concerning studies performed by Sjöberg et al. has been further clarified in Table 2 (please see pages 14-16). Levels of ADD are determined according to article's text (title of the column is now clarified in Table 2). Thus, the levels of ADD differ between the publications from Sweden.

Thank you again for these valuable comments. We hope that the revised version of our manuscript will be acceptable for publishing in Systematic Reviews. We would be happy to clarify any aspect of our response and I look forward to hearing from you.

Sincerely yours,

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