Author's response to reviews

Title: Development and evaluation of a computerised clinical decision support system for switching drugs at the interface between primary and tertiary care.

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Author's response to reviews: see over
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Revision of MS: 1916443512776070
Development and evaluation of a computerised clinical decision support system for switching drugs at the interface between primary and tertiary care

Dear Dr. Aldcroft:

Many thanks for giving us an opportunity to submit a revised version of the above mentioned manuscript. We are grateful for the Reviewers’ thoughtful comments which helped us to improve this manuscript in critical areas. Hence, please find attached a document stating how we dealt with each comment and the revised manuscript which we would like to submit as an original article to the Journal.

We hope that with these changes this paper is now acceptable for publication.

Sincerely yours

(Walter Haefeli
(Prof. Walter E. Haefeli,
Professor of Medicine
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MS: 19164435112776070 - Response to reviewer reports:

Reviewer 1 (J. Coleman; 1626483881830477_comment.pdf):

1) Abstract – this is where I believe there is an error. In the results section it should read “… of 202 documented consultations (1,333 drugs)…” not 202 medications.

   The Reviewer is right and we are sorry for this mistake. We have thus changed the wording accordingly.

2) The sentence relating to the results of the first evaluation was a little confusing to me and I had to re-read it to understand what it meant. Assuming that I have assimilated the figures correctly, I would suggest that the authors change this to the same format used to describe the equivalent results from the second evaluation (which flows easier with the narrative). Thus instead of “The review of these differences by an expert revealed that in 42.0% of them both suggestions were appropriate and equivalent, in 27.1% the CDSS results and in 30.9% the initial switch by the pharmacist was considered superior” to “The review of these by an expert revealed that in 42.0% of these cases suggestions of pharmacists and CDSS were equivalent, in 27.1% the CDSS suggestion and in 30.9% the pharmacists’ suggestion was considered superior”.

   We agree and changed the sentence accordingly (page 9).

3) Discussion – “switching may cause considerably differing exposures to the active compound” may be better than using the phrase “differing exposures with active compound”.

   We agree and changed the sentence accordingly (page 11).

4) Discussion – when discussing contacting the pharmaceutical manufacturer when information is not available – I would leave out the word “helpful” – as this makes the example seem slightly pejorative (as though only unhelpful information was available).

   In response to this comment we have modified the respective sentence (page 13) which now reads: “Furthermore the human specialist is able to consult information sources beyond the CDSS database (e.g. by contacting the pharmaceutical manufacturer when additional drug information is needed and not available electronically).
Discretionary Revisions

5) The last point is that the system in Germany makes such a CDSS switching development essential, but this is in part driven by the fact that healthcare professionals cannot use patient’s own drugs during hospitalised care. The authors therefore hint at the wider applicability of such a system, but I think this could be brought out a little more clearly in the discussion. In the UK there is still a lot of requirements for formulary substitutions where for example patients are admitted as emergencies and do not have their own drugs or where there is insufficient quantity of medicine to support the whole of an inpatient stay. A brief sentence or two may just clarify applicability in different models of medicines provision between different countries.

This is a very valid and valuable point and we are happy to include this suggestion and add a brief sentence to the Discussion (bottom of page 12).

Reviewer 2  (K.E .Hersberger; 1877052208315369_comment.pdf ):

Major Compulsory Revision

A. According to the methods section, evaluation of the CDSS was performed by one clinical pharmacist. According to the results an “expert” evaluated differences between manual and automatic switching. (same person?) Later in the discussion, “experts” evaluated drug switches and an interdisciplinary team is mentioned. This process needs clarification, and if only one clinical pharmacist (=expert) performed the evaluation, this should be discussed as a limitation of the results.

In this project an interdisciplinary team developed the system and its algorithms (page 5, 12). An expert clinical pharmacist evaluated its performance on the basis of independently and prospectively documented switch procedures in our hospital. The latter was done by a team of clinical pharmacists.

To clarify this point we have made the following changes:

• We have added the developing interdisciplinary team to the Methods section (page 5).
• In a few sections we have added the term “team of clinical pharmacists” (page 8, 10) to refer to the group generating the routine data as opposed to the clinical pharmacist evaluating switch quality. Moreover, whenever we refer to this group plural is now used (page 12).
• The clinical pharmacist (expert) evaluating switch quality was a senior clinical pharmacist. This is now clarified and the term “human expert” has been replaced if it referred to the group of clinical pharmacists (page 9, 13).
• As suggested by this Reviewer we have also added the information of only one person (albeit a rather experienced expert) evaluating switch performance as a limitation to the respective section (page 15).
B. The authors correctly distinguish in their algorithm between pharmaceutical equivalents, pharmaceutical alternatives and therapeutic equivalents. The performance of the system improved from version 0.9 to 1.0 ending up with evaluation of 100% correct switches. However, this improvement caused an increase (6.5 to 8.4%) of “no CDSS-switch”. I assume that mostly therapeutic equivalents were concerned. Overall, therapeutic equivalents only represented 8.3 vs. 7% of all switches. And, switching to therapeutic equivalents poses much more challenge for an automatic system and perhaps needs a manual check by an expert. I would suggest some comments on the switching performance of therapeutic equivalents in the discussion and I would consider a watchful follow-up during implementation.

The Reviewer is right that switching to therapeutic equivalents is indeed the most challenging task in this context and, indeed, was the main reason for errors in version 0.9 of the tool. Therefore 4 ATC classes were removed mainly for two reasons: First, switching has its limitations if patient characteristics or co-morbidities have to be considered, which are often not yet (and some of them likely never) electronically available on admission of a patient. This was the reason why we removed ATC codes A10A and V03AE from the list (version 0.9). Second, another important aspect of our tool is that it currently does not support switching to brands with differing release characteristics (e.g. instant release <-> controlled release) and that it does not modify dosing intervals although simplification of regimens (by prolongation of intervals) is in fact often possible (Ref #22 of manuscript). For this reason we removed ATC code C02CA from the initial list (version 0.9).

These aspects are mentioned in the manuscript on page 9 where the differences between version 0.9 and the final version 1.0 are detailed. In addition and in response to this comment we have added a sentence to the Discussion stressing these relationships (page 12):

“These weaknesses mainly albeit not exclusively concerned the switch to therapeutic equivalents, which in some cases required additional patient information or a switch to formulations with differing release characteristics.”

Minor Essential Revisions
A. The authors report main results in the abstracts section, which are difficult to retrieve in the full paper; e.g. the total of 21 different drug classes covered by the tool and the 202 “documented” medications. In addition, the term “therapeutic” substitution is confusing because pharmaceutical equivalents and alternatives were switched as well. This section should be rephrased in order to present the most important findings.

We appreciate this comment and, in response to it, made the following changes:

- Abstract: 21 drug classes: The drug classes covered by the tool are mentioned in the main text (Methods, page 5, last paragraph) and also compiled in Table I. We therefore believe that no further reference is necessary.
- Abstract: documented medications: We agree and have rephrased this sentence (please also refer to our response to comment #1 of Reviewer 1).
Abstract: “therapeutic substitution”: The Reviewer is right that the tool suggested all, pharmaceutical equivalents and alternatives AND therapeutic substitutions. Obviously, the latter is most complex and one of the strengths of the developed CDSS. To clarify this valuable point we changed the sentence in the Abstract to: “After iterative optimisation of the logical framework the tool was able to switch drugs to pharmaceutical equivalents and alternatives; in addition, it contained 21 different drug classes for therapeutic substitution. In this final version it switched 91.6% of 202 documented medication consultations (containing 1,333 drugs) automatically, leaving 8.4% for manual processing by clinical professionals.”

B. Legend for figure 4: comparing with suggestions of the clinical pharmacists (plural?)

Plural is correct because it refers to the team of clinical pharmacists of the hospital pharmacy who previously performed the switch consultations used for evaluation. Hence, the plural form is correct and was kept (please also refer to our response to the first comment of this Reviewer).

C. Table 2: Data are presented as %, but total n is missing

We agree and added this information to the Table.