Author's response to reviews

Title: Development of a context model to prioritize drug safety alerts in CPOE systems

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Version: 3 Date: 28 March 2011

Author's response to reviews: see over
Dear Sir or Madam,

We thank the editor and the reviewers for taking the time to review our manuscript so thoroughly. We have revised our paper in accordance with this feedback and respectfully submit this revised manuscript for your further consideration. In addition, we include below a point-by-point response to the feedback.

We strongly believe we were able to improve the manuscript by revising the article according to the remarks from the editorial board and the reviewers and again want to thank them for their fruitful comments.

Sincerely,

Daniel Riedmann and Martin Jung, on behalf of all co-authors
Editorial Requests

a) Ethics/Consent

We interviewed five experts in the field of CPOE who were contacted in advance via email whether they are willing to take part. We only called those experts for the telephone interview only if they gave their consent in the first place. No patient data was involved during this research and therefore no approval by safety authorities or an ethical committee had to give their consent in Austria.

b) Authors' Contributions:

We added this section according to your remarks.

Referee 1

Major Compulsory Revisions

C4. Figure 3 is not clear. If you add up all the N= for each tow it does not add up to the N= on the flow chart (e.g. Hand search = 61, Specific PubMed search = 174, Topical PubMed search = 10 totals 245 not 224). This is true for each row/line of the chart. I presume that is because there is overlap, but this fact should be foot noted where relevant.

Thank you for your attentive reading. Due to overlaps between the three search strategies, the sums of papers in each line do not coincide with the number of papers provided after combining the results of the three searches. We added a comment on that fact in the description of the figure.

C5. It is not clear how the main axes of Patient/Case, Alert, and Organizational unit were derived. If this is subjective based on author opinion, it should be stated. If it were derived from interviews, then that should be stated. If there is a reference, it should be cited. In personally reviewing the contexts, I would submit that there should
be another axis for “individual clinician”. Under this, the following contexts would have been placed “professional experience of the user, current task of the user, personal preferences of the user, specialty, and workload”. I would submit that repetition of alerts and override rate of alerts fall under the “alert” axis. This highlights the need for external validation of the model.

Thank you for this comment. In fact, the three categories are just an attempt to structure the found factors. Certainly other ways of organizing them are possible. We added a comment on this in the discussion part of the paper.

C6. The phase 2 inductive category development steps should be outlined in a figure so that the methodology is clear. How were the context factors hierarchically organized? Who participated on the inductive category development and how (simply referencing an abstract of the process is insufficient)? How was MindMeister used and who participated in it?

Thank you for this comment. We added information regarding the roles of the researchers in the process of category development and supplemented some information about the use of mind mapping. Furthermore, the reference ([22]) was adapted to access the full paper.

C12. I don’t believe the entirety of the title is appropriate. The model was created based on a combination of literature research and “expert” interview with internal validation as described by inter-rater reliability testing. Using ‘validation’ in the title might mislead the reader to think that external validation was performed. The title should simply state “Development of a context model for drug safety alerts in CPOE systems”. The authors discuss these same limitations on page 10.
We agree with that and adapted the title according to your suggestions.

**Minor Essential Revisions**

C18. Background, page 1, second sentence. The sentence should be revised. Using “early on” at the conclusion of the sentence is improper grammar. Perhaps an approximate date range could be used, especially since a reference is cited.

The phrase “early on” should have referred to 1991. However we removed this phrase to clarify our message.

C19. Background, page 1, second section “CPOE to prevent medication errors and ADEs”. Both of the first two sentences discuss medication errors and the references all relate, so these should be merged. If the point is to highlight ADE, the thought wording should be changed for the second sentence to reflect only ADE, not both.

Thank you for this attentive comment, we corrected it and merged the two sentences.

C20. Page 2, paragraph 2, sentence 4 beginning with “Alert fatigue …”. I would disagree that it is “best” described as written by the authors. There are other descriptions and this one has not been proven to be the best one.

We agree that the given definition should not claim to be the ‘best’ definition and that other valuable definitions exist. We adapted this sentence in this way but we prefer to stick with the given definition by van der Sijs as we focused on it in this work.

C21. On page 3, the authors cite the use of 5 international experts in the field of CPOE. This sentence to me is an unnecessary rationalization for performing they work they have done. The experts aren’t named, it isn’t clear how the study concept
was presented to them, and their individual opinions of the concept are not presented.

I suggest removing the sentence.

We agree with you and removed the corresponding sentence.


Changed.

C23. Page 5 under “Expert interviews”. Third sentence "indented" should be “intended”. Please clarify what is meant by “saturation”. How many interviews were intended, how many were ultimately done (the total number performed is found in the discussion and description of Table 4, not in the methodology text), and how was the decision made to stop with five?

“Indented” changed to “intended”.

We clarified the term “saturation” and supplemented information regarding the number of interviews and the decision to stop.

C24. Table 4 under the “Alert” axis “Current task of the user” is listed, but it is listed under the “organizational unit” axis on the prior tables. Please revise.

Thank you for your attentiveness and careful reading. We corrected this mistake.

C25. Page 9 discussion paragraph 1. The last sentence beginning with ‘Finally, three out of …” can be consolidated with the preceding sentence.

We consolidated the two sentences.
C26. Page 11, sentence beginning with “A shared international database ..”. I would suggest softening this statement substantially. We are a long ways away from having an international database that could be considered universally acceptable for a variety of fair trade and usability reasons. Reference databases differ substantially from each other in content and differ in how they interface with CPOE systems. Vendor CPOE systems all differ in the user interface, functionality/workflow, and design capabilities.

We softened the statement and indeed, you’re right that we’re a long ways away from having an international database. As mentioned in the paragraph, the integration of pharmaceutical information in SNOMED CT using the Dutch drug database G-standard is a first small step towards an international solution at which we wanted to point in this sentence.

**Discretionary Revisions**

C2. Page 4, Methods, Literature Search. It is unclear how the 10 major ‘magazines’ were chosen, but a significant amount of CPOE-related work has been conducted in other journals as well, particularly in the pharmacy literature. A journal such as the American Journal of Health-Systems Pharmacy should have been had searched as well, although hopefully relevant articles were discovered via the PubMed search.

We agree that including more pharmacy literature in the hand search might have extended this first step. However, the hand search was “just” a first starting point in our literature search and does not claim to be exhaustive. As described in the manuscript, it was performed to extract ideas for contextualized drug safety alerts in CPOE systems. The second step of the literature search (PubMed search) was more comprehensive and did also include the literature mentioned above (e.g American
Journal of Health-System Pharmacy). We adapted the wording in the manuscript to highlight the role of the hand search as a starting point.

C3. A search using “warning” might have yielded a few more articles.
We agree with that. As we also searched the references of the retrieved articles, we think that we covered this search term as well.

C13. Abstract, page I. “Unfortunately, they tend to produce a large number of unspecific alerts, ….”. The term ‘unspecific’ is debatable as many are very specific – certainly they can be highly dependent on the 20 context factors the authors derived from their work.
We agree with your argumentation and changed the term “unspecific” to “irrelevant”.

C14. Background, page 1 first sentence. I’ve seen this quote attributed to St. Augustine and Seneca the Younger. It might be worthwhile referencing the source of the author’s attribution.
Thank you for this hint. To our knowledge, “errare humanum est” is a Latin phrase which is not directly quotable. It is said to be derived either from Cicero (Oratiores Philippicae 12,2) or Seneca the Elder (Epistulae morales VI,57,12). Furthermore, a similar quote can be attributed to Hieronymus and St. Augustine of Hippo (Sermones 164,14). As Seneca the Younger is the son of Seneca the Elder there might as well be a certain overlap in citations. As this quote is a generally accepted and a well-known phrase, we do not see the need to reference any source.
C15. Page 4, Methods, Literature search. The word “journal” is preferred over “magazine”.

We changed the term “magazine” to “journal”.

C16. With respect to the unanswered questions, I would recommend you include pharmacist informatics experts and perhaps other published ordering clinicians with expertise in your panels. Each brings a different perspective but all have substantial contributions to the concepts you are researching.

Thank you for your interesting remark. Indeed, we have included physicians, pharmacists, biomedical informatics experts and specialists from other related fields to the panels of the ongoing studies.

C17. I would suggest you pursue external validation and determine if there are more than 20 context factors in your future work.

That is right and we agree with that. In fact, as indicated under “unanswered questions” in the discussion section and in the conclusion, we plan to pursue external validation of the model within the ongoing studies.

Referee 2:
Major compulsory revisions

i) Page 1 – the authors make mention of “medication errors” and ADEs. However, the words are interspersed and the difference is not clearly defined. The authors provide a definition of an ADE and explain that ADEs associated with a medication error are considered to be preventable. The last paragraph of the page says that CPOE systems can reduce medication errors as well as ADEs. This leaves the reader somewhat
confused. Are the two concepts the same thing? Is one a subset of the other? This appears to be an important distinction that needs to be clarified early.

That is indeed true, those two terms overlap. We added the definition of medication errors and supplemented some information regarding their relation.

ii) Page 3 in paragraph 3 the paper mentions “partly context-sensitive CDS systems”. This description invites confusion and seems like an ill-chosen choice of words. What is a “partly context-sensitive” system? Is there a scale or classification of context sensitivity? Does this suggest that we can have fully context-sensitive system? Given that the paper is aiming to identify factors that can be used to prioritise and present alerts on context, I would like the authors to be a little more precise in their terminology.

We removed the term “partly context-sensitive”. The expression of ‘partly context-sensitive’ CDS systems is derived from the fact that CDS systems comprise different levels of decision-support and therefore also different levels of contextualization of such. With “partly context-sensitive” systems we wanted to generally express that the developed systems are just contextualized to certain factors, without providing a scale or classification. A fully context-sensitive system would be perfectly adapted to every clinical situation and present a doctor with only relevant alerts and is therefore utopia.

iii) The model is interesting and potentially very valuable. The individual factors that make up the model are also well described. Clearly the authors have achieved the main part of their aim. Despite this I found the Discussion section of the paper somewhat lacking. I believe this is because the concept of a “context model” invites the expectation that we can expect more than just a listing of factors but their
synthesis into something (a model) that can help explain, understand and guide future work. The authors actually do provide such a synthesis as evidenced by Table 3. The Discussion could be strengthened by discussing the “model” a little more, drawing attention to its distinguishing features and addressing the model in relation to how other research has approached the subject of models, context and safety. This would position this interesting and important piece of work alongside some similar developments currently being undertaken in the area of patient safety by the World Health Organization’s World Alliance for Patient Safety.

Thank you very much for your valuable remark. We agree that that one might expect a more comprehensive form of a model. However, this is the first step of eliciting single context factors and structuring them in a simple representative form (model). For this moment, we left the term “context model” in the paper. If the editors feel that this may be seen as misleading, we are happy to change it to another suggested term. As you suggested, we strengthened our discussion by adding more information about its relation to other research. We would have liked to position this paper alongside ongoing research by the WHO Alliance for Patient Safety. Unfortunately we have no access to their current developments.

**Minor essential revisions**

a) Page 1 we are told that “Medication errors have been identified to be a common type of medical errors early on.” The problem with expression here is that “medication errors” is plural and “a common type” is singular. However, I am not sure what “early on” means. Is early on sometime in the early twentieth century or are we referring to the time of Seneca the Elder?
According to Byers [1], there are several types of medical errors, medication errors, as a general expression, are one such type. The phrase “early on” should have referred to 1991. However we removed this phrase to clarify our message.

b) Page 2 – the first paragraph says that drug-drug interactions checking suffers from low specificity. I believe the authors need to explain this concept and how it relates to the point that CDS-triggered warnings are frequently overridden. Otherwise it reads like a non-sequitur.

We rephrased this paragraph according to your request to make this statement clearer.

c) Page 10, paragraph 2 – The statement that van der Sijs “also warned for turning off alerts” is not clear. Do the authors mean “also warned about turning off alerts”? Yes thank you, indeed we meant “also warned about turning off alerts”. We corrected it.

**Discretionary revisions**

1. Page 4, paragraph 4: Can the authors tell us if the “ten major magazines in the field of health informatics” are peer-reviewed?

We added an extra column to the table in Supplement 1 regarding information about peer-reviewing state of the journals.