Author's response to reviews

Title: Chemotherapy prescribing errors: an observational study on the role of information technology and computerized physician order entry systems

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Author's response to reviews: see over
Dr David Sclar  
Associate Editor  
*BMC Health Services Research*  

8 December 2013  

**RE: MS1815794124110082**  
Title: “Chemotherapy prescribing errors: an observational study on the role of information technology and computerized physician order entry systems”  
Marianna Aita, Ornella Belvedere, Elisa De Carlo, Laura Deroma, Federica De Pauli, Lorena Gurrieri, Angela Denaro, Loris Zanier and Gianpiero Fasola  

Dear Dr Sclar,  

Thank you for your email regarding the potential acceptability of the above manuscript for publication in *BMC Health Services Research*.  

We have revised our manuscript according to the referees’ suggestions and hope that it can now be accepted. Below please find a point-by-point response to the editorial request and the reviewers’ comments.  

All named authors have approved the revised version of the manuscript and have agreed to its submission. Also, on behalf of the authors I confirm that this manuscript has not been submitted, published or is in press in any other scientific journal.  

We thank you and the referees for the helpful comments and suggestions. We are looking forward to hearing from you with a final decision.  

Sincerely,  

Dr Marianna Aita
EDITORIAL REQUEST

1. Kindly provide the name of the Ethics Committee that approved the study and the reference number if applicable.

The study was approved by the Independent Ethics Committee of the Udine University Hospital, Udine Italy. The text has been modified to include the name of the Ethics Committee, as follows (page 8): “The study was approved by the Independent Ethics Committee of the Udine University Hospital, Udine, Italy.”

REFEREE 1:

SUGGESTED DISCRETIONARY REVISIONS

1. Which projects are planned to build upon these findings?

An audit of chemotherapy prescribing errors using the updated version of the CPOE is planned but at present no further publications plans are planned.

2. The overwhelming majority of errors (101 of 181) were noted to be the lack of administration route. If these errors were included in the post-hoc a priori errors, this should be acknowledged clearly in the results or discussion section.

These errors were indeed included in the a priori errors. This is now acknowledged in the Results section (page 10), as follows: “...The analysis by error type revealed a significant proportion of systematic errors which were derived from errors in the predefined chemotherapy protocols in the CPOE system, such as failure to specify route of administration or volume of infusion solution; these errors were often present in prescriptions which otherwise would have been error-free...”

SUGGESTED ESSENTIAL REVISIONS

1. If the secondary endpoints were planned at the time of protocol development prior to collection and analysis of data, this should be noted in the methods as this adds to the validity of the observed findings.

Very good point. The analysis of secondary endpoints was preplanned. We have therefore added the following sentence in the “Error classification and analysis” section of Methods (page 9): “The analysis of all the secondary
endpoints (type of error, degree of preventability, severity and clinical impact) was pre-planned.”

2. **Strongly consider the addition of a table to highlight the observed findings.**
   
   A table summarizing the results has been added (Table 3). Reference to this new table has been added to the text.

3. **Page 12 “….a figure similar to those reported in previous studies”. Please provide references for this statement.**
   
   The following references have been added in support of this statement:

**REFEREE 2:**

**MINOR ESSENTIAL REVISIONS**

1. **Page 1 and 2: Affiliation:** the email addresses of the authors need the same format. I suggest also uniformly describe the departments in English, explicitly for the author: Loris Zanier
   
   As suggested, the authors’ email addresses now have the same format. Zanier’s affiliation has been translated in English.

2. **Page 3: Abstract: Methods:** put the first sentence in an easier way, such as *Up to three electronic prescriptions PER PATIENT RECORD who received....*
   
   As suggested, this sentence has been changed to: *“Up to three electronic prescriptions per patient record were selected from the clinical records of consecutive patients who...”*

3. **Page 3: keywords:** I suggest an additional very important key-word missing: OUTPATIENT
   
   “Outpatient” has been added to the list of key words.

4. **Page 5:** “In the ASHP 2002 guidelines on preventing chemotherapy medication errors, CPOE...” I would suggest to either use the
expression chemotherapy prescribing errors OR chemotherapy errors

Following the reviewer’s suggestion, “chemotherapy medication errors” has been changed to “chemotherapy prescribing errors”.

5. Page 5: “On the other hand a qualitative study identified 22 situations in which the use of CPOE increased the probability of prescribing errors [6].” Considering the word SITUATIONS: prescribe the situation with e.g. . . . . to better understand the citation, also the citation is too short

The text has been modified taking into account the reviewer’s comment, as follows: “. . . . On the other hand, a qualitative study identified 22 types of medication error risks facilitated by the use of a CPOE system [6]. Examples included patient or medication selection errors due to fragmented CPOE displays preventing a coherent view of patients’ details and medications, pharmacy inventory displays mistaken for dosage guidelines, ignored antibiotic renewal notices placed on paper charts rather than in the CPOE system, medication discontinuation failures, double dosing and incompatible orders facilitated by separation of functions . . . .”

6. Page 7: Only prescriptions for cytotoxic chemotherapy regimens were eligible as these were judged the highest risk. (This sentence is not clear).

Agree that the sentence is not very clear. “. . . as these were judged the highest risk.” has been deleted.

7. Exclusion criteria were (i) prescriptions WRITTEN by not fully qualified oncologists, i.e. supervised oncology trainees; (ii) prescriptions within a clinical trial.

Taking into account the reviewer’s comments, the text has been changed as follows: “prescriptions issued by not fully qualified . . . .” and “prescriptions within a clinical trial.”

8. Page 9: “near misses [16] and preventable adverse drug events (pADEs) [17] (table 1).”

Do not agree on this, i.e. adding the p for preventable: this is not a commonly used abbreviation and might generate confusion.

9. Error analysis: Records containing one or more prescribing errors were 79 out of 334 (PERCENTAGE! is missing)

Percentage has been added (24%)
10. Page 10: "...showed to lack mention of the administration route (n=101),...” This sentence is not clear.

Agree. The sentence "Incomplete prescriptions (n=110) showed to lack mention of the administration route (n=101), the infusion solution volume (n=2) or the number of capsules to be dispensed in case of oral chemotherapy (n=7).” Now reads “Incomplete prescriptions (n=110) failed to specify the administration route (n=101), the infusion solution volume (n=2) or the number of capsules to be dispensed in case of oral chemotherapy (n=7).”

11. Page 10: The analysis by error type immediately revealed the presence of systematic errors resulting from errors in the dictionaries of the predefined chemotherapy protocols in the G2 CPOE system; these errors were often present in prescriptions which otherwise could have been error free. I would suggest simplifying this sentence for easier understanding

The text has been modified as follows: "...The analysis by error type immediately revealed a significant proportion of systematic errors which were derived from errors in the predefined chemotherapy protocols, such as failure to specify route of administration or volume of infusion solution; these systematic errors were often present in prescriptions which would have been otherwise error-free”.

12. The majority of errors were deemed probably (33%) or definitely (65%) preventable. – so 2% were not preventable, is that correct?

Correct.

13. In this perspective 71% and 25% of errors were classified as minor and moderate, respectively, whereas 2% and 1% had at least the potential to produce major or catastrophic injuries respectively. I would suggest to delete the last word.

The last word of this sentence ("respectively") has been deleted.

14. Page 11: Possible explanation for such a difference include the use of different CPOE systems, variability in the definition of prescribing errors and also differences in the study design and ways in which error rates were calculated. I would suggest instead ERROR CALCULATION.

As suggested, “ways in which error rates were calculated.” has been changed to “error calculation”.


15. Page 11: “….there were no major or catastrophic adverse DRUG events”. I would suggest to use simple and throughout the document constant words and definitions

Text amended as suggested. Key word also changed from “adverse event” to “adverse drug event”.

16. Page 12: However, (DELETE word) standardization may be a potential source of systematic error. In our study, (DELETE comma) we have found situations in which the CPOE system not only introduced a priori errors but also facilitated...

Word and comma deleted, as suggested.

17. Page 13: CURRENTLY, we are also working on an updated version of the CPOE system, in which all information functions are separated in two domains: the first is a context area, with clinical data on patients’ history, past and current treatments, laboratory/radiological exams; in the second section, alerts will play a key role in the management of compelling information, as the system will detect the lack of crucial data and hold up the access to critical functions until the appropriate field is filled in.

As suggested, “currently” has been inserted at the beginning of this sentence.

18. “Second, it has been suggested that comparing the frequency of medication errors among..” – what is first and what is second (of the first?)

Agree: it is confusing. There was a “first” a few paragraphs above. Both “first” and “second” have been deleted.

19. There is an urgent need for a better definition of the detail with which events should be classified,... Correctives strategies; and for an error classification which could transform safety information collected from different systems into a shared learning model [37]. (This sentence is not clear).

Agree. As suggested, this paragraph has been re-written, as follows: “...There is a need for a more detailed and standardized definition and classification of prescribing errors, to collect useful and usable information which may ultimately be applied to improve patient care, guide health policy planning and perform good quality research [37].”
20. Table 1: I would suggest to make 2 tables, to give them a clear structure and to explain the source of the classification with the title of the 5 themes.

Table 1 has been split in two tables, as suggested. We have added reference to these tables in the text, as appropriate.

21. GENERAL: the actual clinical impact is not clear. It is only mentioned in the results section very shortly and with no reference, but not described in the discussion. This needs to be ameliorated and underlined with more details.

To address this important comment, the following paragraph has been added to the discussion:

"The errors identified in this study had no or little impact on patients. Briefly, the majority of errors (68%) were near misses. These errors were intercepted by a pharmacist, chemotherapy nurse or clinician, and corrected before any harm was caused to the patient. Specifically, most of these errors were systematic prescribing errors due to errors in the predefined chemotherapy protocols (the a priori errors); examples of these errors are failure to specify the administration route, solution volume or infusion time in the prescription. In these cases, the errors were detected and the prescriptions amended before chemotherapy was administered. The remaining errors were not detected and resulted in ADE. These events, all potentially preventable, did not result in significant harm to the patient. Examples are errors of chemotherapy dose due to failure in recalculating the chemotherapy dose based on up-to-date body weight or taking into account changes in organ function or previous toxicity, omission of adequate allergy prophylaxis following a reaction as per local guidelines, omission to prescribe prophylactic G-CSF in a patient at high risk of neutropenic fever. None of these patients experienced significant toxicity as a result of the error but we acknowledge that these errors had the potential for major or catastrophic consequences in a few cases. Of note, most of these errors are prevented in the updated version of the CPOE system with the presence of mandatory fields for up-to-date weight, critical blood results and alerts in case of not adequate parameters/values."

DISCRETIONARY REVISIONS

1. Page 10: With regards to the actual clinical consequences of the identified errors, 68% were classified as intercepted near misses. This expression was found in one article (Rothschild et al., Medication safety in a psychiatric hospital, 2006) whereas in another article (Kessels-Habraken et al., Defining near misses 2010) it was not found. Definitions are very broadly used, as you also stated in
your article. For the reviewer “Near misses” is already conclusive for itself, so I would suggest to delete the word “intercepted”.

Agree. The word intercepted has been deleted from text and Table 1 (now Table 2).

2. List of abbreviations: ADE: Adverse Drug Event – I would suggest to use singular in all abbrev.

   Text changed as suggested, using singular for all abbreviations.

3. Conclusion: The conclusion is short and concise, maybe a sentence like “Additional evaluation…. is needed and should be the focus of future studies...” could be added.

   As suggested, we added a final sentence to the conclusions (page 14): “..Additional evaluation of CPOE systems for chemotherapy prescribing is needed and should be the focus of large prospective and ideally multicenter studies. The development of standard definitions for error type and the use of robust study designs are vital.”

ADDITIONAL CHANGES

1. The references have been reformatted according to the journal’s Instructions for Authors.

2. The authors order has been reviewed to better acknowledge individual contribution to the study and to the manuscript preparation/revision.