Author's response to reviews

Title: Assessment of ePrescription quality: an observational study at three mail-order pharmacies

Authors:

Bengt Åstrand (bengt.astrand@hik.se)
Emelie Montelius (emelie.montelius@hik.se)
Göran Petersson (goran.petersson@hik.se)
Anders Ekedahl (anders.ekedahl@apoteket.se)

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Author's response to reviews: see over
To the editor of BMC Medical Informatics and Decision Making

Regarding MS: 1959312778212361 - Assessment of ePrescription quality: an observational study at three mail-order pharmacies

Thank you for all valuable comments. We are looking forward to having our paper published in your journal and have now revised it carefully according to your comments. Our revisions and considerations follow each comment below.

Best regards,
Bengt Åstrand

Comments revision 1

Reviewer: Gillian Bartlett
My comments are discretionary revisions that I believe would strengthen the article and make it more readable.

1. In your writing, you tend to use run-on sentences and awkward grammatical structure. I would suggest having an English proofreader correct some of the wording to improve the clarity and flow.

Author comment: the revised manuscript has now been proofread by PhD Elizabeth Hanson, who is a native British scientist.

2. In the introduction, an interesting description is giving of the history and components of a handwritten prescription but very little detail is given for the e-prescription. What is the new strategy referred to in the introduction? An additional sentence stating what the strategy is would be helpful (i.e. monetary incentive? All prescriptions to be electronic by a certain year?).

Author comment: the historical aspects (section 3) and the strategy (section 4) have been explained in some more detail in the introduction.

3. I think there are more benefits to the e-prescriptions than just getting rid of the paper script and these should be mentioned as there is a large body of literature that refers to this.

Author comment: the sentence has been deleted, as the problems with handwritten prescriptions are mentioned in the 2nd section in Background.

4. What is the national mailbox? Is this a virtual repository for the scripts? This is unclear. Also, what regulations have been applied to the electronic script.
5. The only other modification I would suggest is further justification of why the mail
order pharmacies were chosen and how the results for these pharmacies may
differ from community based pharmacies. This should be address is both the
methods and in the discussion of the results as the findings may be quite
different for community pharmacies where patients are available for discussion of
the script.

Author comment: The initiative to the study came from one of the four MOPs,
experiencing prescription problems and spending time on solving them. This MOP
wanted help with recording and classifying the problem prescriptions and to compare
the results with the other MOPs. Accordingly, all 4 MOPs were invited to participate in
the study, but one of them declined. This is now explained in the first line in Methods
Setting.

The differences and similarities between community pharmacies and MOPs are
mentioned in Methods and also in the Discussion. The present study was the first on
prescription problems, but later studies at community pharmacies have been conducted
with similar methodology. These results will be published separately.

Reviewer: Bryony Dean Franklin
Abstract
6. In the background section (and in the main body of the paper), I did not feel
that the term “ratios” was the correct one to use. “Proportions” or “percentages”
may be easier to interpret for the reader. The results present the error rates in
terms of percentages (rather than ratios) and so this would be the correct term to
use.

Author comment: ratio has been replaced by proportion.

7. In the methods section, it is stated that data on ePrescriptions were compared
with data on all drug prescriptions. However the results section presents the
comparison against paper prescriptions rather than all prescriptions. The two
sections need to match each other.

Author comment: In the Method section we wanted to emphazise that ALL
prescriptions were included. The results, however, were reported in comparison between
the two groups ePrescriptions® and non-ePrescriptions.

* (all ePrescriptions are new prescriptions)

8. Instead of “rate ratio” I wonder if the authors mean “relative risk”? This
comment also applies to the main body of the paper.
Author comment: rate ratio has been changed to relative risk throughout the manuscript.

9. In the results section, the numbers do not add up. It is stated that 312 prescriptions necessitated contact with the prescriber, and then later it states that 89.5% suggested interventions were accepted by the prescriber (which would be 279), then it stated that 192 of 247 were accepted without further modification... I can’t work out where the other 32 have gone? This also applies to the main body of the paper.

Author comment: The sentence ‘Each prescription necessitating a contact with a prescriber contains one or more interventions.’ has been added in Results section 4.

Background
10. I am not clear what is meant by “web” in the phrase “.. transitional stage between paper and web...”. Does this mean electronic prescriptions in general, or is it a specific kind of electronic prescription that is downloaded from the internet? Please clarify.

Author comment: “web” has been deleted.

11. It is stated that ETP was first deployed in 1983 – was this in Sweden, or the first worldwide? The text should state which country this relates to.

Author comment: both in Sweden and worldwide, this is now clarified on page 4-5.

12. The legend for figure 1 is incorrect – instead of inter-country range it should be intra-country range (or just “range”) if all the measurements are from one country.

Author comment: the text reads ‘inter-county’.

13. The aim is “to estimate the quality...”. I don’t feel that this is the correct term. “To assess the quality” would be more correct.

Author comment: The text has been changed accordingly.

Methods
14. It is not clear what is meant by “prospective drug utilization review” in the setting. Is this a medication use review, is this audit, or is it electronic interaction / dose / contraindication checking? Please clarify what is intended.

Author comment: it is an automated review of the prescription for drug interactions/contraindication etc, the text has been clarified accordingly.

15. It would be helpful to explain what is meant by prescriptions for non-pharmaceuticals (I assume this means prescriptions for compression stockings, dressings etc, but it would be helpful to clarify this for non-pharmacist readers).
16. In the section on work organisation, it is stated that some prescription problems may have been resolved by the pharmacists themselves by consulting the patient etc. Did this take place before or after consulting with the prescriber? And were these queries included in the study?

Author comment: It took place after trying to consult the prescriber. For some problems, the pharmacists were not able to get in contact with the prescriber. Some of the problems were finally solved in contact with the patient.

17. In the data collection section, what is meant by the “protocol” that the prescriptions were attached to?

Author comment: An Additional file 1 has now been added and is referred to in the section Type of study. It is an English translation of the Swedish protocol. Reference 26 has been added as a source for the additional file.

18. In the section on statistics, need to state explicitly what the two groups were between which the comparisons were made.

Author comment: see comment 7.

19. Did the prescribers know that the study was taking place? This needs to be stated.

Author comment: No. This has now been added in the section Work organization.

20. Was ethics approval required / obtained? This needs to be stated explicitly.

Results

Author comment: Not required. This has now been added in the section Type of study.

21. In the second line, “contained” is not the correct word – “comprised” may be better.

Author comment. The sentence has been changed to comprised.

22. Need to state how many refills were electronic and how many were paper. Why was the comparison between electronic and paper prescriptions only made for new prescriptions, and not for refills?

Author comment: The study was not designed to assess refill prescriptions, as the available statistics on ‘all dispensed prescriptions’ did not distinguish between ePrescriptions and paper prescriptions.

23. It is stated that the RR for “Dosage and directions for use” compared to other causes of intervention was 7.6. However the data presented in table 2 suggest that this RR relates to the comparison between ePrescriptions and non-ePrescriptions (rather than between different types of intervention). This
needs to be made clear.

**Author comment: see comment 7.**

24. It is stated that the mean duration of contact was lower for ePrescriptions – was this difference statistically significant?

**Author comment: The difference was not statistically significant. The mean values have been changed to the median values, as the distributions were rather skew. The outliers are now included.**

25. Why were the 9 outliers excluded from this analysis? this needs to be justified.

**Author comment: see comment 24.**

26. Table 1- are the figures for all prescriptions cited before or after the adjustment for 15/20?

**Author comment: As commented below the table 1, the monthly statistics are adjusted.**

27. Table 2 – caption – instead of “divided by” I think this should read “presented according to”

**Author comment: This has been changed accordingly.**

Discussion

28. It is stated that new ePrescriptions were associated with more clarification contacts than non-electronic prescriptions. I believe this should be NEW non-electronic prescriptions, based on the analysis presented in the results section?

**Author comment: This has been changed accordingly.**

29. Need to comment on WHY there is a higher rate of clarification contacts needed with ePrescriptions than for non-ePrescriptions, in particular those involving “dose and directions for use”.

**Author comment: In the first section in Discussion the following sentence has been added “This may be due to the widespread use of abbreviations, like 1t3d (one tablet three times daily), which not have been standardized among different EMRs. The abbreviations may be translated by the EMRs in a fashion not anticipated by the prescribers before transferring the prescription to the pharmacy. “

30. Last paragraph of page 13 – “prescribe” should be “prescriber”

**Author comment: prescribe has been changed to prescriber.**

Conclusion

31. The conclusion implies that there was an increase in clarifications needed for all ePrescriptions, whereas the results section only presents data for NEW
ePrescriptions. The two sections need to match.

Author comment: NEW has been added in Conclusion and Abstract. To be clear, we have added the sentence “At time of study, ePrescriptions with refills were handled and recorded as ePrescriptions only at the first dispensing occasion.” to the Definition of ePrescriptions section on page 8.

Discretionary Revisions

Abstract
32. In the results section it would be helpful to present error rates for both ePrescriptions and paper prescriptions as this is the aim of the study.

Author comment: error rates have been added.

Background
33. It may be helpful to refer to computer-generated paper prescriptions as these have many of the advantages of ePrescriptions in terms of less ease of falsification and greater clarity of interpretation.

Author comment: due to the high penetration rate of EMRs in Sweden, a majority of paper prescriptions were computer-generated, handwritten prescriptions constitutes just a minor proportion.

34. The statement “there are a number of advantages to ePrescriptions; for one thing, they eliminate the need for paper prescriptions” is a tautology. It would be more helpful to give specific advantages.

Author comment: the sentence has been deleted, see comment 3.

Results
35. The data presented on clarification rates for new versus refill prescriptions is not listed as an objective of the study, and these data therefore seem rather incongruous.

Author comment: This has been deleted in the Abstract Results. We still believe it may be of value to mention this in the Results, to better understand the communication between the prescribers and the pharmacists.

36. It would be helpful to give examples of the types of problem that accounted for the increase in clarifications due to “dosage and directions for use” for the electronic prescriptions. I was left wondering what types of problem these were!

Author comment: see comment 29.

37. It would be helpful to explain what is meant by interventions that were accepted “after a modification”

Author comment: the modification could be any kind of change of the suggestions made by the pharmacist. The sentence has been slightly changed to “… after a modification by the prescriber during the contact.”
38. Was there a difference in the percentage of prescriptions requiring clarification contacts between the three pharmacies?

Author comment: Yes; 1.2, 1.5, and 2.0% for the three sites, respectively.

39. It would be helpful to give examples of contacts that fell into the “other” category, as this forms a significant proportion of the overall clarification contacts.

Author comment: “Other” represented a wide array of reasons to contact the prescriber, however, no single cause was frequent; questions on license preparations, half tablets prescribed when not possible, duplicate prescriptions, formal requirements not fulfilled, unauthorized prescriber, not in stock but urgent according to the customer, etc.

Reviewer: Brian Quilliam
Discretionary Revisions:

40. Consider rounding the estimates to one decimal place.

Author comment: This is now changed throughout the manuscript.

41. Consider deleting Figure 1 altogether and expanding the message derived from the figure in the text. As is, the figure adds little to the manuscript.

Author comment: We would prefer to keep the figure 1 as the fast quantity growth may be one reason to the detected quality deficiencies.

Minor Essential Revisions:

42. The term “clarification contact” utilized throughout is awkward. Please expand/revise this term to make the outcome of interest more readily apparent to the reader.

Author comment: We have considered other terms but do think that this is the most appropriate. Clarification contacts has also been used by others, see reference 22.

43. In the results section of the abstract, please remove the word “increased” from the statement “The increased rate ratio (RR) for clarification contacts for new ePrescriptions…” as this is unnecessary and potentially leading the reader.

Author comment: Increase has been deleted.

44. Should Figure 1 remain, the statement “The development of ePrescriptions in Sweden…” may be better worded as “Trends in the use of ePrescriptions in Sweden…”.

Author comment: Legend for Fig 1 has been changed to Trends in transferred ePrescriptions in Sweden…
45. In the methods section, it is not entirely clear why the 4th MOP was excluded and how this site differed from the other 3 included sites. This is an essential revision and the reason for exclusion of this site based on sound methodology should be apparent to the reader.

**Author comment:** see comment 5.

46. In the methods “setting” section, please confirm that the number of non-pharmacy outlets and the other community pharmacies were both ~900 (or is this a typo?).

**Author comment:** Both are approximately 900.

47. On page 6, you state the MOPs differ from other pharmacies as they do not have “face to face” contact with patients. On page 8, you mention “consulting with the patient…” as an option. I am assuming that this is via phone, however, directly stating the modes of communication possible would be helpful to the reader.

**Author comment:** by phone has been added.

48. In table 2, the * indicating statistical significance is not necessary given the confidence intervals are presented.

**Author comment:** The * are now deleted.

49. Table 1 is confusing as presented. It would be helpful to the reader if the prescriptions were presented following their natural order, that is 1. Total prescriptions 2. Total E-prescriptions 3. Total Non-E-prescriptions and then subcategories under each of these for new and refills. Also, percentages throughout would be helpful.

**Author comment:** Table 1 has been rearranged.

50. Table 3 would benefit from the inclusion of percentages.

**Author comment:** Percentages have been added to table 3.

**Major Compulsory Revisions**

51. The nature of the funding by Apoteket AB must be more fully disclosed. Was the grant an unrestricted educational grant? As much detail as possible regarding the nature of the relationship between the authors and the funding source is essential to the readership. Further, it is unclear of the relationship between Apoteket AB and the 3 included MOPs. If there is a relationship, this must also be disclosed. Lastly, the source of “data” on file from Apoteket AB is not fully highlighted. As presented, the source of this data is unclear and since it is not published, as much information as possible regarding the source, type, and any other information regarding these estimates is essential for transparency.
Author comment: Two of the authors were, at time of study employed by the Apoteket AB, which is fully owned by the government and runs all Swedish pharmacies, MOPs included. The eHealth institute is partly funded by the Apoteket AB. Apoteket AB is also obliged by the Swedish government to provide sales statistics for the Swedish pharmacy market. This has now been declared in the Conflict of interest section.

52. As written, the discussion section is suboptimal and only a brief summary of this study’s findings in isolation. To my knowledge, several other studies have looked at the unintended effects of the e-prescribing in other countries. The discussion section must be expanded detailing what other studies have found on this topic (as well as related topics) and how this is in support/contrast to the findings of this study. This section should be the bulk of the discussion and will assist the reader in assessing how this study adds to what we already know about this area and what gaps still exist in this knowledge.

Author comment: To the best of our knowledge, there are very few, if any, published papers on unintended effects of ePrescriptions (=electronically transferred) for outpatients. However, there are some papers on computer-aided prescribing. There are many papers on problems/errors with paper prescriptions and also on the expected benefits of ePrescriptions. Also there are studies on problems/errors with CPOE systems within hospitals. To our knowledge this is one of the first studies on unintended effects related to ePrescriptions for outpatients.