Author's response to reviews

Title: The co-use of conventional drugs and herbs among patients in Norwegian general practice: a cross-sectional study

Authors:

Ane AD Djuv (ane.djuv@gmail.com)
Odd G OGN Nilsen (odd.nilsen@ntnu.no)
Aslak AS Steinsbekk (aslak.steinsbekk@ntnu.no)

Version: 2 Date: 11 July 2013

Author's response to reviews: see over
Dear Editor and referees,

Thank you for considering our article to be published in BMC CAM. The paper entitled “The co-use of conventional drugs and herbs among patients in Norwegian general practice: a cross-sectional study” is revised according to the referees considerations.

A native English speaking colleague has copyedited the paper.

Best regards,

Ane Djuv
On behalf of all authors
Comments by Referee 1: (Professor Hedvig Nordeng)

General comment
1. Is the question posed by the authors well defined? YES
2. Are the methods appropriate and well described? YES
3. Are the data sound? RESPONSE RATE UNCLEAR
4. Does the manuscript adhere to the relevant standards for reporting and data deposition? IMPROVEMENT CAN BE MADE
5. Are the discussion and conclusions well balanced and adequately supported by the data? OK
6. Are limitations of the work clearly stated? OK
7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished? OK
8. Do the title and abstract accurately convey what has been found? ABSTRACT CAN BE IMPROVED.
9. Is the writing acceptable? SOME INCONSISTENCIES

Major Compulsory Revisions:
1. The author’s main aim is to comparing the groups “only herbal-users” vs. “cousers” with regards to demographics. Why? Please describe your hypothesis and the rational for this comparison. It might be even more relevant to focus on the difference in background characteristics between “co-users” versus “only medicine users” in table 6. Answer:
   1. Our main aim was to compare co-user with those who do not, i.e the co-users with all other respondents (= all other patients in general practice) on both demographics and other variables. The rationale for this comparison was to identify a group of patients that GPs should be especially aware of.
   2. We agree that it would narrow down the group the GPs should be especially aware of if we compare co-users with “only medicine users” in table 6.
   3. Due to the comments of the reviewer (see also comment 2) we have added the group terminology used in the text for the four groups: “Co-user”, “only herb user”, “only drug user” “non-user” in the heading of table 1. Furthermore, we have added the results of a new multivariable logistic regression model comparing co-users with only drug users. The results are described in the text (Result section, Multivariable analysis p 14).

2. Table 1 can be presented more clearly with four columns using the terminology used in the text for the four groups: “Co-users”, “only herbal-users”, “only medicine users” “no use”. Consider focusing on the difference in demographics of the four groups “Co-users”, “only herbal-users”, “only medicine users” “no use”. Answer: We have added the words “Co-user”, “Only herbal users”, “Only drug user” and “Non-user” to the columns in table 1 and also used these words throughout the article.

3. Response rate. When calculating the response rate you have to consider how many patients that were approached by the staff and invited to participate in the study versus the number of questionnaires returned. Some surely declined (reasons for not participating??) and some accepted but did not return the questionnaire. If there were 1652 individual visits that week, it seems low that only 402 were approached (1/4) and high that all who were approached initially agreed to participate. Please explain.
Answer: Unfortunately it was not registered systematically how many patients that were approached by the staff that did not agree to participate. The staff said that many had not been offered the questionnaire by the staff in the reception due to lack of time, and about half of the patients declined the questionnaire when asked. This is now stated more clearly in the Method p.8.

4. Did you include information about duration of use, amount and administration form of the different herbals is important when assessing interactions? For example aloe vera is commonly used topically, garlic, ginger and grapefruit as foods and will have low interaction potential used these ways. This should be elaborated on in the discussion. Please state how many interactions actually were clinically important-
Answer: The duration, amount and way of administration were not registered as this study was designed to give a broader overview. We have commented of this in the discussion p.20. The clinical important interactions and way of administration are more elaborated on p.19-20.

5. Results from shops and pharmacies should be presented separately (page 12 & Table 1).
Answer: We have changed this according to the reviewer’s recommendations.

6. Results Table 6. It would be interesting to see these analyses with “medicines only” as a reference group. This would emphasise the factors associated with herbal drug use per se. See comment 1.
Answer: This is done as described in the answer to comment 1.

**Minor Compulsory Revisions:**

Abstract
Include the time period for data collection in the method section.
Answer: the time period for data collection is included.

- Do you mean bilberries or blueberries?
Answer: Bilberries, but blueberries may also be present in products marketed as bilberries. This information has been added as a footnote Table 3.

In the sentence starting with” two of three herbal users”, please use exact percent.
Answer: We changed to drug users to fit the changes made in table 1 (see comment 1). We have also not added the exact percent as this is given in the table.

“Close to 40% of patients on anticoagulants co-used herbs” (please specify the most commonly herbs from table 4.)
Answer: The most common herbs are now included in the text.

Co-users had significantly (p<0.05) increased odds ///. Compared to what?
Answer: We have added “Compared to all other patients, co-users…”

Background
When introducing an herb for the first time it is preferable to include the Latin name.
Answer: This information has been added
Aims Please consider to reformulate the aim of the study into primary and secondary aims.
Answer: We have changed this according to the reviewer’s recommendations.

Materials and methods
State the time period for data collection.
Answer: This information has been added

Results
On page 11. “nearly two out of three used conventional drugs regularly”. Give numbers please.
Answer: We have included the percentage in the text,

Be consistent when using the Latin and/or herb names in the same paragraph– see inconsistency page 12.
Answer: We have gone through the article and corrected this.

Tables
- The lay out of the tables can be ameliorated. Include (n) in the table and remove (%) if it is presented it in the head row (table 1 and 3).
Answer: We have changed this according to the reviewer’s recommendations

Table 2.
- Please order the herbals according to the most frequently used herbal.
Answer: This will be inconsistent with Table 4, thus making it more difficult to locate the same herb. We have therefore kept the alphabetical order.

Table 4.
Consider highlighting the clinically most important potential interaction in bold characters.
Answer: We have highlighting the clinically most important potential interaction.

Discretionary Revisions
Keywords
- Consider whether drug-toxicity and self-disclosure are appropriate key words.
Answer: We have deleted drug-toxicity and self-disclosure as key words and added “safety” and “disclosure”.

Background
On page 1. Marked->market?
Answer: We have changed to market.

“Co-use of herbs and drugs might alter the drug’s bioavailability and metabolism or the herb might have an additive effect to the drug, hence causing unexpected adverse effects of the drug”. Strictly speaking, an additive effect is not the only possible effect (agonistic effects). Consider using "pharmacodynamic" interaction.
Answer: We have changed this to "pharmacodynamic interaction”.

Methods
Consistent wording: Use general practioners instead of physicians throughout
“Defeat an illness”? Could treat or cure be a more appropriate word?
Answer: We have changed to treat.

Table 2.
Was Aloe Vera topical? Please include this information in the table.
Answer: We have added information as a footnote in Table 2: “May include either topical or oral Aloe vera use”.

Table 4.
Use herbal names instead of product names (i.e. Medox, Natto K2).
Answer: We have changed to herbal names

References
Please add the date of access. (i.e nr. 36).
Answer: We have added the date of access to the web references

Comments by Referee 2 (Dr Titilayo O Fakeye)
I have observed the following, and I believe that the authors need to clarify or make modifications
1. Starting sentences in figures (Abstract)
Answer: We have changed this according to the reviewer’s recommendations.

a. Was any ethical approval taken before the start of the study?
Answer: As stated the study was approved by an ethical committee (part of the public national ethical review system), and they agreed to regard a returned questionnaire as an ethical approval. This is a common procedure when no personal ID is collected from the participants. The participants were informed about the study in the beginning of the questionnaire.

b. What was there to show that the patients who participated did not do so out of obligations to their GPs
Answer: The GPs had no role in the recruitment and were asked not to talk to the patients about the study. Although there was no control of this, we think it is very unlikely that the participants did so to “please” their GP.

c. I also believe the patients should have been informed about the objectives of the study before giving their consent as opposed to what was done.
Answer: The patients were informed in the form of a poster in the waiting room and orally by the staff in addition to an information letter on the first page of the questionnaire. This is information is included in the Methods section (p.8)

3. More information is needed on how respondents were educated on the general classes of drugs (Table 3) the patients were supposedly on. Having a good education does not assume that the respondent knows that the class of drug he is on is a vasodilator, for example.
Answer: We have added” The drug categories covered most of the common regular prescribed drugs based on data from the Norwegian Institute of Public Health and were exemplified with common Norwegian sales name to make them recognizable for the patients”. Methods section (p.8)
4. Under Results, what does “Off sick” mean?
Answer: We have added “Sick leave”

5. Table 4 is not very clear. There are some words that are missing. The authors may decide to use a smaller font size.
Answer: We have changed the font size.

The discussion is well written and the results were discussed in the light of similar or related studies.

Authors additional changes:
An error was discovered at p.14 and was directed to “The herbs most frequently used of those experiencing adverse effects were garlic (n=5), bilberry (n=4), green tea (n=4) and ginger (n=3). “