Author's response to reviews

Title: Gender differences in presentation and diagnosis of chest pain in primary care

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Version: 2 Date: 7 October 2009

Author's response to reviews: see over
Dear BioMed Central Editorial Team,

Thank you for considering the attached manuscript for publication. Please find below the answers to the editors’ requests and the reviewers comments in bold letters. According changes in the manuscript text have been highlighted in yellow colour.

Please do not hesitate to contact me should further changes be required.

With kind regards
Stefan Bösner

Dear Dr Bösner,

Your manuscript has now been peer reviewed and the comments are accessible in PDF format from the links below. Do let us know if you have any problems opening the files.

Editorial request:
- Please clarify whether informed consent was required and obtained. Informed consent must also be documented. Manuscripts may be rejected if the editorial office considers that the research has not been carried out within an ethical framework, e.g. if the severity of the experimental procedure is not justified by the value of the knowledge gained.

Informed consent was gained and also documented for all patients participating in the study; I have added a sentence in the methods section.

Please also ensure that your revised manuscript conforms to the journal style (http://www.biomedcentral.com/info/ifora/medicine_journals). It is important that your files are correctly formatted.

I have formatted the manuscript accordingly.

Reviewer’s report (Reviewer 1)
Title: Gender differences in presentation, course and diagnosis of chest pain in primary care
Version: 1 Date: 15 August 2009
Reviewer: Frank Buntinx
Reviewer's report:
Comments to Bösner et al: Gender differences in presentation, course, and diagnosis of chest pain in primary care.
1. Is the question posed by the authors well defined?
Yes
2. Are the methods appropriate and well described?
It is not totally clear from the methods which results are use to base the final conclusions upon. From the results, I suppose it is the significant variables after multivariate analysis. However, the authors also present LRs, which could suggest that these are the main results. Please clarify. (minor)

Final conclusions are based on a combination of the above mentioned two points. Table 5 (clinical recommendation) lists all significant variables taken from table 4; however LRs were calculated based on univariate data derived from 4x4 tables. I have added a sentence in the methods section. (N.B.: new methods are currently being developed to also calculate multivariate LRs; we hope that we can use these for future publications).

Second last line: I suppose this is the p-value for removal of variables from the initial model. Correct? (minor)

We have corrected the methods section accordingly.

3. Are the data sound?
Yes
4. Does the manuscript adhere to the relevant standards for reporting and data deposition?
Yes
5. Are the discussion and conclusions well balanced and adequately supported by the data?
Yes. A quick reader may suppose to find diagnostic information, quod non. However, the authors clearly indicate what can be expected or not.
6. Are limitations of the work clearly stated?
Yes
7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished?
Yes
8. Do the title and abstract accurately convey what has been found?
Yes
9. Is the writing acceptable?
Yes
Additional comments:
The part on follow-up (results on page 8) is interesting, but not really necessary for this paper. I would suggest the authors to drop it from this manuscript and to further analyze this in more detail for a next paper. (discretionary)

Thank you for this suggestion. As reviewer two had also additional suggestions to further analyse the follow up data, we think that a more detailed analysis would present too much additional material for this manuscript. We have therefore dropped this section and made according changes in the title, abstract and manuscript text.
Reviewer's report (Reviewer 2)

Title: Gender differences in presentation, course and diagnosis of chest pain in primary care
Version: 1 Date: 3 September 2009
Reviewer: Marie Pirotta
Reviewer’s report:
Thank-you for the opportunity to review this interesting research paper. The research question is well defined and will be of interest to general practitioners. The method is rigorous and well thought through.
First of all thank you for your thoughtful and valid comments that will help to improve this manuscript.

My main suggestion to improve the paper is that in each of the main diagnostic groups, apart from CHD which is well characterised, the results should be presented by final diagnosis rather than as a heterogenous group. The grouped results are not very helpful to clinicians.
I am sorry but I did not completely understand this suggestion. Do you mean that we should calculate tables similar to table 3 for each other diagnostic category (e.g. for psychogenic problems, chest wall syndrome etc.)? We would like to stress again that the main emphasis of our analysis are gender differences in regard to CHD. While table 2 still presents as a kind of introduction also other underlying diseases for chest pain, the rest of the manuscript concentrates on CHD as we also outline in the introduction. I would rather like to chance the title to make this more evident that to add several other bulky tables (listing gender differences for all clinical characteristics for other diseases as well) that would make the manuscript rather unreadable. But perhaps I misunderstood the above suggestion. In this case please clarify.

Discretionary Revisions (which are recommendations for improvement but which the author can choose to ignore)
Some specific questions and suggestions that may improve the paper:
Methods
1. Please define “delayed-type reference standard” when this term first appears. Explanation marked in yellow on page 5 (bottom).

2. Please explain how the 209 GPs to be approached for the study were chosen. We used an existing network of research practices and known interested colleagues. Changes were made accordingly in the manuscript text.

3. Why was the age of 35 years chosen as the cut-off for eligibility? CHD was the main outcome parameter of the study. Including younger patients would have meant a much higher necessary sample size in order to power the study accordingly.

4. What training did the research associate of the Department who sat on the reference panel have to assess diagnoses of chest pain? This was also a trained GP; I have added this in the text.

Results
1. How many practices were involved in the data collection?

58 practices (included in the manuscript)

2. How was the total number of patients attending during the data collection period estimated?

Total patient attendance was measured for one week in each practice and then extrapolated for the corresponding recruitment period.

3. Is it possible to compare both the GP and patient characteristics to those of the whole country or region?

We compared GP characteristics to central data of the state of Hesse. The data show that our sample is representative. I have added a sentence in the results section. No comparison was done for patient characteristics.

4. Was there any data collected on patients NOT approached or missed in data collection?

No, we do not have data on this population.

5. When providing results it would be helpful through to include percent of total patients with either chest pain in general or of those with CHD. Sometimes it was hard to discern which group was being reported.

This is a helpful observation. I have changed the table headings accordingly to make it more clear which study population was analysed (either all patients with chest pain or only the subgroup of patients with the diagnosis CHD).

6. When reporting risks and comorbidities, there is no mention of age – was this adjusted for?

The text section in the results part is a mere descriptive analysis. However, in regards to the diagnostic value of risk factors (see table 4) we used logistic regression to adjust risk factors and comorbidities for age.

7. In Table 3 there is a symbol after “Continuous pain” that is not explained.

This is an editing mistake; I removed the symbol.

Discussion

1. Did you explore or consider whether other issues may have an impact on the length of time that passed before people presented with their chest pain? Do women wait longer before presenting?

This is an interesting assumption that we also discussed within our team, however, we do not have valid data to answer this question.

2. It would be interesting to explore why so many women had chest pain persisting at 6 months – as I mentioned earlier – it would be very interesting for you to present these data by diagnostic group. Are women under-diagnosed or under-treated?

See my comment to reviewer 1. We would like to follow his suggestion and drop the follow up data, in order to analyse these further for a separate publication. Your above suggestions are very helpful and we will take them into account, when we do further data analysis.
Minor Essential Revisions
1. The Flow Chart is very useful.
   a. Could you also insert percentages of the total agreeing to participate at each stage
   b. Include the 6 week data
   c. Include the 60 lost to follow up and 11 deaths on the chart.

   I have inserted suggestions a and c in the flowchart; suggestion b I omitted as we also dropped the follow up information from the manuscript.

2. Is there any demographic data available for the 34 cases where information was lacking or incomplete? Is there any reason to suspect that any systematic bias may have occurred in this regard?
   There was no difference in mean age between the above cohort and the total study population (58yrs. Vs. 59yrs.). However there were more women with incomplete information (64% vs. 56%).
   I have added a remark in the limitations section.

3. Could you include in the results the total (%) by gender where no diagnosis was able to be made by the reference panel?
   I have included this information in the results part.

4. It would be particularly useful to report the course of chest pain by diagnostic category rather than as a total.
   As already stated we dropped the follow up data to be presented separately.

5. Results of the random audits are not reported.
   We conducted 68 random audits. Of the 68 recruitment days analysed, 54 GPs did include all patients, 8 GPs forgot to include 1 patient, 3 GPs forgot to include 2 patients and 2 GPs forgot to include 3 patients. For all the missed patients the case report form could still be completed.
   (I included the above sentence in the results section)

6. In Table 2 hypertension is listed as a cause of chest pain, which does not make sense to me.
   I understand your point; I think GPs and the reference committee meant patients with chest pain due to transient angina pectoris because of high blood pressure. As this is rather vague I deleted the column and added the numbers to the others section.

7. The statement: “…our findings do not support a different clinical presentation of CHD in women” belies a belief that men represent the norm or standard. Perhaps you could express that there was no difference between the two groups.
   Sorry for that; I did not intend to express it this way. I have changed the sentence accordingly.

8. There seems to be an important word omitted in the sentence “…only chest wall tenderness in palpation largely ruled out acute MI…”
   Thank you for spotting this crucial mistake; I have added the word “out”.

9. In the final paragraph you mention Bayesian approach. To make the results
relevant to family doctors, it would be useful to explain what this approach is and how it is used.

I have added an explanation in the discussion part of the manuscript.

Major Compulsory Revisions (which the author must respond to before a decision on publication can be reached)

1. Statistics – were the data adjusted for clustering and for baseline findings? Thank you for this valid suggestion. Our data were not adjusted for clustering and baseline findings. We are aware of this procedure which to our knowledge is the appropriate method for cluster randomized trials[1] (which we also conducted in our department). In this case one would indeed use multilevel analysis.

However, our sample is homogenous and also represents the wider majority of GPs in the state of Hesse (as outlined above). All doctors were trained by the same study team. We wrote the statistical analysis plan with the input of two highly experienced statisticians; none of them mentioned the necessity to analyse our data according to clusters.

Reference List