Author's response to reviews

Title: Delirium Risk Screening and Prophylaxis Program in hip fracture patients is a helpful tool in identifying high-risk patients, but does not reduce the incidence of delirium

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Author's response to reviews: see over
June 17, 2011

Dear editor and reviewers of *BMC Geriatrics*,

Thank you very much for your very useful and constructive consideration of our paper “Delirium Risk Screening and Prophylaxis Program in hip fracture patients is a helpful tool in identifying high-risk patients, but does not reduce the incidence of delirium”.

We appreciate your comments highly.

In this cover letter we answered point by point your remarks.

Furthermore, we would like to change the title to “Delirium Risk Screening and *Haloperidol* Prophylaxis Program in hip fracture patients is a helpful tool in identifying high-risk patients, but does not reduce the incidence of delirium”, as of the suggestion of dr. Michaud.

We trust that our answers and improvements will be to your approval and will lead to publication in your journal.

Yours sincerely,

On behave of all authors,

Anne JH Vochteloo
Orthopaedic surgeon

Comments and answers point by point:

Editorial Requirements:

*Requesting Consent Statement:*

As you may be aware, it is a requirement to have written informed consent from all patients for publication and we will not proceed with your manuscript until you have confirmed this. The manuscript should therefore include a statement to this effect in the Acknowledgements section, as follows: "Written consent for publication was obtained from the patient or their relative."

We added "Written consent for publication was obtained from the patient or their relative. This was documented on the standard questionnaire all patients or their relative fill out on the Emergency Department." to the Acknowledgements section.

*Requesting proof of ethics committee approval:*

Experimental research that is reported in the manuscript must have been performed with the approval of an appropriate ethics committee. Research carried out on humans must be in compliance with the Helsinki Declaration ([http://www.wma.net/e/policy/b3.htm](http://www.wma.net/e/policy/b3.htm)), and any experimental research on animals
must follow internationally recognized guidelines. A statement to this effect must appear in the Methods section of the manuscript, including the name of the body which gave approval, with a reference number where appropriate.

As our study is a survey of our general practice and an evaluation of the delirium protocol. We consider it to be a “Post Marketing Surveillance”. As such, approval of a medical ethical committee is not necessary. We added “As this study is an evaluation of our delirium protocol, it is considered to be a “Post Marketing Surveillance”. Therefore, approval of a medical ethical committee was not necessary” to the Methods Section.

“Please list the source(s) of funding for the study, for each author, and for the manuscript preparation in the acknowledgements section. Authors must describe the role of the funding body, if any, in study design; in the collection, analysis, and interpretation of data; in the writing of the manuscript; and in the decision to submit the manuscript for publication.”

None of the authors were funded, nor was the manuscript preparation. We added “None of them received any fundings regarding this study or the preparation of the manuscript” to the “competing interests” section

Tables as additional files: We notice that you have included tables as additional files. If you want the tables to be visible within the final published manuscript please include them in the manuscript in a tables section following the references. Alternatively, please cite the files as Additional file 1 etc., and include an additional files section in the manuscript.

We added figures 1 and 2 and tables 1 and 2 to the main document, after the references part.
Reviewer's report  
Reviewer: Laurent Michaud

Dear dr Michaud,

Thank you very much for your time and careful consideration of our study. You brought up very useful comments and limitations.

Questions
1. Is the question posed by the authors well defined? Partly, see major revision 1
2. Are the methods appropriate and well described? Partly, see major revisions
3. Are the data sound? Yes mostly
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? Partly, see discretionary revisions
6. Are limitations of the work clearly stated? Partly, see major revision 3
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? Partly, title should mention that prophylaxis is by mean of haloperidol and abstract should be revised considering the revisions below We changed the title

Major Compulsory Revisions
1. We do not understand the rational of the statistical design of the study. This investigation has the objective to determine if haloperidol prophylaxis could be effective in reducing delirium incidence for a specific high-risk group and the major (negative) result use the comparison between the incidences in the whole prospective group (i.e. high risk AND low risk patients) and the whole control (historical) groups. In our comprehension, the right comparison should be between the high risk group in the prospective group (2008-2009) and the high-risk group in the historic cohorts (2005-2006-2007). Even if we consider that it is likely that the control historic groups are comparable with the studied group, this should be established.

Thank you for your question on this subject; this is a very important issue. We would have compared the delirium incidence in high-risk groups if we could have indentified the high-risk patients in the historical cohort. However, the RD-score was implemented fully in 2008 on our department. Before this implementation, patients were not labeled structurally as high- or low-risk. However, we strongly believe that the cohorts 2005-2007 en 2008-2009 are similar and therefore can be compared.

To demonstrate this, we added “The mean age of the prospective cohort 2008-2009 (83.7 years) was not significantly different from the historical cohort 2005-2007 (82.9 years) (P=0.082) The percentage of male patients was 26.2% in the prospective cohort and 24.3% in the historical cohort were the same as well (P=0.515).” to the Results part (paragraph on historical comparison)
We acknowledge that this is the second-best comparison, however it is the best we are able to perform. To emphasize this, we added to the Discussion paragraph on the limitations of the study “Another limitation is the comparison of the delirium incidence in the whole cohort with the historical cohort. Ideally, we would have compared only the high-risk groups of both cohorts. However, we could not identify high-risk patients in the historical group as the RD-score was implemented fully in 2008. We did demonstrate that both cohorts were comparable regarding mean age and number of male patients, being the main risk factors in the multivariable analysis of the prospective cohort, besides a high RD-score. Therewith one could have observed a decline in delirium incidence due to prophylaxis with haloperidol.”

2. Ways of diagnosing delirium both in the experimental and control groups should be better explicated in the method. We understand that the diagnosis was made as part of a routine evaluation by the staff of the hospital (and not in a proactive way by specific and educated investigators and by means of specific tools (for example CAM)). As noted in the article, delirium is usually massively underdiagnosed. Consequently, it is likely that the study measures indeed the incidence but also the identification (recognition) of delirium by the staff. This implies a possible major bias: that the identification of the delirium enhances with time, education of the staff and attention given on this pathology by the research.

To make it more clear, we added to the Methods part “Patients were observed for these criteria by both doctors and nursing staff during their daily rounds and assessments. When signs of delirium were notified, they were recorded in the medical and nursing records.”

We agree with you on the point of lacking a score device like a CAM and believe we made this clear by describing the limitations of the study in the discussion. We do not believe that in our hospital “the identification of delirium enhanced with time, education and attention” was a major bias, as observing older patients for a delirium is a standard part of nursing and medical work and has been an important issue in our hospital since 2004. There has been training for doctors and nurse as a standard part of education since 2004.

3. In the results, we understand that the 23 patients with a low risk for delirium were wrongly prescribed haloperidol prophylaxis and that this group had a significantly higher incidence of delirium. That should be addressed in the discussion because it is in contradiction with the study hypothesis.

We added; “Twenty-three low-risk patients were prescribed haloperidol prophylaxis, against the protocol. This group had a higher percentage of delirium than the rest of the low-risk group, which was not hypothesized. The doctor that prescribed haloperidol against protocol might be triggered by patient factors that are not taken into consideration by the score but that do predispose to a delirium as they have a higher delirium incidence. However, it is only a small group.” to the Discussion.

- Minor Essential Revisions

1. In the paragraph Method/patients, the sentence “Minimum follow-up was 1
year” should be developed: does it mean that some patients were followed for more than 12 months?

This sentence was formulated not clear enough. We changed it to “Duration of follow-up was 1 year”

2. In the last paragraph of Methods, it is stated that the model was developed in 2004 and we could understand that haloperidol prophylaxis was introduced at the same time. We suppose that it is not the case (this would suppress the difference between investigation and control group!) but it should be better formulated.

Your assumption is right, we therefore added “The RD-score and the delirium protocol were implemented fully on the departments of Orthopaedics and trauma surgery in 2008, as a part of the integrated hip fracture care pathway” to this paragraph.

3. Page 6: a . is missing after ref 11-17

This has been changed.

4. Page 9: is it the right website?
No, this is a mistake. Thank you very much for noticing this. We deleted the website and changed the text to “A receiver-operating characteristic (ROC) curve (figure 1), made of the continuous outcome of the RD-score showed an area under curve of 0.722 (CI 0.674 - 0.767, p<0.0001)”

5. Table 1 could be easier to consult if only the percentages were given.

This has been changed.

**Discretionary Revisions**

1. In the discussion, emphasis could be more on the necessity of non-pharmacological interventions for delirious patients and/or high-risk patients.

We added this remark to the Discussion:
“We believe that more emphasis should be given on non-pharmalogical interventions to prevent a delirium. These interventions include providing orientation with calendars, clocks and photographs and maintain day-night rhythm. However, they take valuable manpower from the nursing staff. To make this more cost-effective, When these interventions can be targeted to the high-risk group (as identified with the RD-score) it would be preferable.”

2. Conclusion could also mention that maybe haloperidol prophylaxis is simply not effective in reducing delirium incidence.

We changed to conclusions sentence to “Using the Risk Model for Delirium and prophylactic treatment with haloperidol did not reduce delirium incidence in hip fracture patients.”
**Statistical review**

Yes, but I do not feel adequately qualified to assess the statistics. Particularly, one question would be to know if it is relevant to include age and dementia in the confounding variables as they are part of the RD.

This is relevant in our opinion. Age and dementia are known risk factors for delirium. Age does not determine patients to be in the high or low risk group on itself, as it gives a maximum of 2 points. In both risk-groups, the age varies and can therefore be a confounder, despite that it is already in the score. Dementia accounts for 5 points and determines patients straight to the high-risk group. However, not all patients are suffering from dementia within the high-risk group. Therefore it can act as a confounding variable.

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**Reviewer’s report**

**Reviewer: Sébastien Ouimet**

Dear dr Ouimet,

Thank you very much as well for your time and careful consideration of our study. Your sharp reading has improved the paper and your final suggestion is very worthwhile.

**Minor Essential Revisions**

1. p. 9, paragraph 2: "cut- of-point" should be spelled “cut-off point”.

Thank you for your sharp reading. This has been changed.

**Discretionary Revisions**

1. p.4 paragraph 2: I am unsure if the word "debatable" is appropriate in this case. I believe a shortening of a delirium event and its severity have major impacts on patient care, costs involved with complications, and patient outcomes. I would phrase it like this: "Although prophylaxis with haloperidol has not lowered delirium incidence, duration of episodes and severity might be reduced".

Thank you for the suggestion. We changed it to “However, prophylaxis with haloperidol did not lower delirium incidence, it did reduce duration of episodes and the severity in a recent randomized controlled trial”

2. p.8 paragraph 1: The second sentence should be revised. I think you meant that the patient-to-nurse ratio was too high to make an assessment?
We changed it to “Due to the inability of patients to participate or a patient-to-nurse ratio that was too high at some moments, the RD-score was incomplete or not performed in 67 patients.”

3. p.12, paragraph 2, 1st sentence: I think the term "psychopathologic drugs" could be defined or examples given.

You are right. We changed the term “psychopathologic drugs” to “psychotropic drugs” and we added “(for example benzodiazepines)”

4. General: I cannot help thinking that unlike the general hospitalized geriatric population, post-op patients (especially for major orthopedic surgery) would fall into an ICU Delirium profile. As reported in the literature, ICU delirium is not age-specific, and can effectively be screened by the Delirium Rating Scale and other tools that can predict severity and outcomes of a delirium event. I would suggest consulting Dr. Yoanna Skrobik's work on ICU delirium for future trials and perhaps looking at patients with this particular set of risk factors and screening tools would show results that are more in line with what was expected by haloperidol prophylaxis.

Thank you very much for this advice.
The intermediate category as described in ‘Subsyndromal delirium in the ICU: evidence for a disease spectrum’ in Intensive Care Medicine 2007 is very interesting. Especially with regards to prophylactic haloperidol treatment. We could hypothesis that people at high risk for delirium as identified by the RD-score suffer less from a subsyndromal delirium.

For further papers we introduced a DOS scale in all hip fracture patients, as we mentioned in our discussion. Our intention for introducing this scale is both for earlier diagnosing delirium and registration dept and duration of a delirium. We did however not think of registration of subsyndromal delirium. But this is a useful suggestion and we will as certainly take it into account. Furthermore, we will have a close look on the ICDSC that you described in your papers with dr. Skrobik, this could be a very useful score for us as well.