Reviewer's report

Title: Genetic contribution of catechol-O-methyltransferase variants in treatment outcome of low back pain: a prospective genetic association study

Version: 2 Date: 21 March 2012

Reviewer: Jules Desmeules

Reviewer's report:

Dear authors,

Thank you for your answers on the first series of comments. The modifications you've already made are helping the reader better appreciate the work that was done. However, clarification is still needed on the following issues:

Major compulsory revisions

A. Please define clearly the “clinical outcome” that you are referring to in the abstract. For instance, what is the ODI/VAS “change” (p.10) you are focusing on: Is it for example “the difference between groups (surgery vs. conservative) of the differences overtime after the intervention”? In other words, it is still not clear if you are looking at comparing long term effect of two different types of treatment on LBP in patients according to their COMT phenotypes (or just the “spontaneous” evolution of LBP in patient with different COMT phenotypes that happened to be previously treated? Which variable would you define as primary?

B. Please provide more information on the 19 (mostly female according to the numbers presented in table 1) patients that did not receive the correct randomized treatment.

Minor essential revision

C. Please add to the paragraph on haplotypes' statistical analysis (p.11) that the estimate for the smallest clinically significant difference was calculated for a sample size of 93 subjects

Discretionary revisions

D. Please provide (at least to the reviewer) the results of the additive genetic model on the association between phenotypes and ODI/VAS “change”.

E. Please provide the reference classes for each “single marker” in the association model presented in table 3.

F. Please take into consideration that the minimum clinically significant change was set at 17.4 when discussing the results (discussion section).

G. Please provide the CI for all mean differences (beta) or “changes” (table 3 and 4).

H. Please use the same terminology when describing the changes.
In addition, please give further information on some of the previous comments that (numbers refer to the numbering of the first series of comments).

2. Please provide (at least to the reviewers) the results of the sensitivity analyses done on the ITT (N=93) and PP (N=74).

7. It is rather unlikely that the R software would not be able to compute median values. Please check with your IT or methodology departments.

13. Please provide (at least to the reviewers) the actual results of the analysis of the residuals

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests