Reviewer's report

Title: Cohort studies in chronic diseases using routinely collected databases when a prescription is used as surrogate outcome

Version: 3 Date: 28 November 2010

Reviewer: Arja Helin-Salmivaara

Reviewer's report:

GENERAL
The authors of the report aimed at comparing two different cohort study approaches in analyses that use a prescription as surrogate outcome. The principal idea of the research question is relevant for the actors in the phamacoepidemiology and the clinical scenario is feasible taking into account the clinical conducts at the time of the study. They use a typical database for pharmaepi, based a health care insurance claims. Both the exposure and the outcome are clearly defined. Special thanks to the informative figures. Methods used are appropriate, and the conclusions made are based on the study. The text is well structured and easy to understand. The language is excellent.

MINOR
1. I'm confused to find a kind of a replication of a previous study presented as part of the current one. How does this comply with the journal policy? More specifically: the first part of the results are published previously (reference number 8) but this is not acknowledged clearly enough in the methods (2.1. Cohort study for…), although the reference can be found three times in the results section. As the aim of the study is comparison between different approaches it is obvious that all the options have to be presented clearly for the readers. Would it be possible to describe ‘the cohort study for time to change in the inflammatory status’ in the Discussion? However, if the current structure of the manuscript complies with the journal policy, could the results of the Cox model presented in the table 1 be also referenced by the number 8 as well as the chapter 2.1.?

2. In this study, the assumption of the start of anti-inflammatory effect of statin therapy after the first 90 days is based on one small study in which simvastatin 20 mg and fluvastatin 40 mg were analyzed. However, while defining the statin exposure as 90 days or more, the authors do not consider the statin dosage. During the study years, the most frequently used statin dosages were lower than nowadays, e.g. the strength of the most popular simvastatin preparations was 10 mg. And, if an assumption of one tablet per day -regimen is applied, the 10 mg may not equal to 20 mg causing anti-inflammatory effects. Therefore, the negative results of the anti-inflammatory effect of statin therapy in patients with rheumatoid arthritis may be due to strong assumptions made in the current study. From the clinical point of view, the research questions may still remain
unanswered. Please, consider comments about this issue in the discussion.

3. The heading the report reminds more of a review article than an analytic study. Could it be more specific?

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

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests.