Reviewer’s report

Title: The comparative effectiveness of statin therapy in selected chronic diseases compared with the remaining population

Version: 1 Date: 11 February 2012

Reviewer: Gabriel Chodick

Reviewer’s report:

In an extensive and ambitious study, the authors analyzed a population-based longitudinal datasets to determine the efficacy and effectiveness of statins therapy among individuals with major chronic co-morbidities. The results are interesting and, according to the authors, suggest that statins are less effective in patients with co-morbid conditions both as primary or secondary prevention of CV events. There are, however, several methodological questions that need to be addressed:

Major Compulsory Revisions

1. The study population consisted of Tayside residents who were registered with a GP between 1993 and 2007, allowing for up to 15 years of retrospective follow-up. It is therefore unclear why the mean follow-up was about 2.5 to 4.5 years.

2. Table 1 provides information on simvastatin daily dose. Why only simvastatin and not other types of statins? The method of calculating mean daily dose is missing (is it based prescriptions or dispensed medications?).

3. In this aspect, previous studies have shown that chronically ill patients have a higher compliance with statins. This may have affected the study results.

4. Many of the chronically ill patients have several diseases. How was this taken into account?

5. TC decrement after therapy initiation is relatively rapid (several weeks) and so is the elevation with therapy discontinuation. Was the TC reduction calculated between baseline and next measurement or end of follow-up? In non-persistent patients, therapy discontinuation date is crucial for this analysis.

Minor Essential Revisions

1. In Table 3, what were the variables adjusted for?

2. A reference to figure 2 should be given in text.

3. Index date of chronic disease was defined as the first date of diagnosis. How do the authors distinguish between incident cases and prevalent cases (who were first diagnosed before 1993)?

4. Since observational studies such as this one are limited in establishing causality, please avoid statements such as “Use of statins significantly improved survival” (Discussion, 1st paragraph).
Discretionary Revisions

1.95% confidence interval could be informative in Figures 1 and 2.

2. The authors raise several speculations to explain the lower baseline TC in chronically ill patients. Could it also be due to greater tendency of physicians to begin statins therapy earlier in patients with several risk factor of CV events?

3. In Results, the authors may reduce the data given in text to improve reading fluency.

4. Consider adding a survival (or cumulative incidence) plot for major outcomes (e.g. all-cause mortality).

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

'I declare that I have no competing interests'