Reviewer’s report

Title: REAL WORLD LONG-TERM IMPACT OF INTENSIVE TREATMENT ON DISEASE ACTIVITY, DISABILITY AND HEALTH-RELATED QUALITY OF LIFE IN RHEUMATOID ARTHRITIS

Version: 0 Date: 01 Sep 2018

Reviewer: Swan Yeap

Reviewer's report:

The authors have performed an observational study based on electronic medical records of a cohort of RA patients. As with all observational studies, there are methodological problems which the authors have discussed in the Discussion. However, just discussing it cannot overcome some of the limitations of the data. I have the following concerns and comments.

1. One of the major problems is that patients are being compared at different time points in their disease course. So, to give an overall average DAS28 for patients that may be 15 years into their disease together with someone who is only 1 year into their disease may not be representative of true disease activity in the group. Could there be an analysis to take into account of duration of disease prior to the start of the study?

2. Another major concern is that the number of patients seen at least once a year for 3 years is less than 50% of the total - only 753 out of 1693. Why were the others not seen so regularly? What was the average time between assessments/clinic visits? The authors state that the patients had "intensive management", which is not the case if they are seen less than once a year.

3. Following on from comment 2, it is not clear exactly what "intensive management" meant.

   a. From the graphs, the mean DAS28 in 2015 was still above 3.2, so the average was still moderate disease activity. This is similar in those followed for more than 3 years, they also ended up with an average DAS28 of >3.2. Was there an explicit treatment target? If so, how many patients reached the target?

   b. Although there was an increase in the number of patients in remission (Results page 7), was this persistent remission, or remission at any one time point? I would suggest that it would be difficult to have a definite figure if over 50% of the patients were not followed-up consistently.
4. Table One should compare the overall group, those followed-up annually for at least 3 years, and those who did not have regular follow-up, as we would want to check that those not regularly followed up did not have characteristics that were different from those who were regularly followed up.

5. The authors need to clarify how they arrived at the mean values in all the figures - DAS28, ESR, TJC, SJC, remission, active disease etc. In the figures, there is only 1 time point per year, so were all the values just averaged? How were the repeated values from individual patients analysed? Was there a statistical correction for the analysis of repeated values from single individuals?

6. The information on medication usage should be included. For example, how many patients were on biologics in 2005, compared to 2015, for the whole cohort. Is the improvement in the disease activity/remission due to increased use of biologics? There should be some adjustment for drug use in the analysis.

7. A comment: It would seem intuitive that those in remission would be on less medication compared to those with active disease, as drugs will be tapered once patients are in remission. It would be interesting to see if those who went into remission were on biologics prior to achieving remission, and what proportion of those achieving remission had had biologics. Is this information available?

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

No

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Unable to assess

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

No

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

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