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: 06 Sep 2018

Reviewer: Sarah Skeoch

Reviewer's report:

This is an interesting and valuable study, particularly as it is based on real world clinical data and includes a large number of patients. It adds to the literature on temporal trends in RA. The figures included in the manuscript are particularly helpful in understanding the trends.

However I have some concerns that I think need to be address in order for the manuscript to be suitable for publication.

My main concern is that, based on the information included in the current manuscript, I think the conclusion in the abstract and some statements in discussion are too strong regarding the effect of intensive management on temporal trends in disease.

"Intensive management reduces disease activity and disability levels in routine practice. " (abstract)

This is an observational study and cause and effect cannot be assumed. Particularly given that it is not clear at what time point and to what extent intensive management was instituted within the cohort (see below). The data do show an upward trend for use of combination therapy and biologics over time and a reduction in disease activity but I don't think one can conclusively be attributed to the other. I think that the statement would need to be altered.

Other major comments include:

Methods section:

1) Details on treatment strategy

The authors report that an intensive management approach was instituted during the follow up period and that UK guidance was followed. I suspect that details of this are available within the references but the link provided for the best practice award doesn't seem to work. It would be helpful to have the following information clarified in the methods and/or supplementary data if it is available:
* What the departmental policy on intensive disease management was

* When was the policy (or policies) instituted

* Is there any evidence to demonstrate how well the policy was adhered to within routine practice in the department?

2) Inclusion/exclusion criteria

The authors report physician diagnosed RA patients within the clinic were included but were there any additional inclusion/exclusion criteria? E.g. did patients only need to contribute one visit or have a minimum amount of data recorded to be included?

3) Missing data

There are often significant issues with missing data in routinely collected clinical datasets. The authors have included % missing data on baseline demographics but no detail on amount of missing data for disease measurements (DAS28, HAQ, EQ5D) at baseline or over time. What proportion of data was missing (suggest include in results section) and how was missing data handled?

Results section

1) Incident vs prevalent cases

It would be helpful to understand more about the case-mix. Did the proportion of incidence/prevalent cases vary significantly over time? If so did variation influence the changes in DAS28? If this is not possible to examine, would suggest commenting further in the discussion section. If it is possible, would be really interesting to analyse trends in the 2 groups separately, to expand on milder disease phenotype/early referral versus better treatment debate (if the authors have the opportunity to do so).

2) Numbers at each time point

It would help the reader to know number of patients contributing to the annual time points, even if only 2005, 2010, 2015 in the main manuscript and other years in supplemental data.
3) Follow up

Although a separate analysis of patients with 3 or more years of follow up has been included, there is no mention of follow up time (either mean years follow up or number of visits per patient) for the whole population or the 3 year subgroup. I think it would be important to add this information in, particularly when interpreting those in remission always/sometimes/never in the 3-year group.

4) "Changes in Treatment and Remission Status" section states differences in medications between the remission groups but no values or significance levels detailed in the text.

Discussion

1) There was no significant improvement observed between 2010 and 2015. Given that the NICE guidelines were published around 2009, is this an unexpected finding? It may be that the intensive management was introduced much earlier in the department, leading to a stabilisation but would be interested to hear the author's thoughts on this in the discussion.

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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Acceptable

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