Author’s response to reviews

Title: The effect of glucocorticoid therapy on mortality in patients with rheumatoid arthritis and concomitant type II diabetes: a retrospective cohort study.

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Author’s response to reviews:

Dear Dr Studenic,

Thank you to the reviewers for their helpful comments. Please find below our point-by-point response.

Simone Parisi (Reviewer 1):

Dear Author,

this retrospective study is about the effect of glucocorticoid therapy on mortality in patients with rheumatoid arthritis and type II diabetes.

The study is very interesting and well written. The sample is very large and the analyzes performed are correct.

Not having the clinical data available, it would also be advisable to carry out an analysis of the non-measured confounding using, for example, Monte-Carlo Sensitivity Analysis and then evaluate this impact on the conclusions.
Response: Thank you for this comment, we agree that there may be unmeasured confounding with this type of data. Although it would be interesting to investigate possible unmeasured confounding using a method such as the Monte-Carlo Sensitivity Analysis or even the rule out approach (Schneeweiss S, 2006), these would need to be applied to the additive effect of interaction and the methods I have found are applied to a relative risk. However I have added to the discussion that unmeasured confounding is a limitation (Discussion section, page 11, lines 9-11).

Furthermore, it would be interesting to evaluate how many patients have a certain codification for seropositive rheumatoid arthritis (cod. 9707, 12019, 56202, 93715) and to carry out an analysis on this sample in which it is assumed to have some laboratory-clinical data in consideration of their cataloging by confirm the results or highlight differences.

Response: Thank you for this suggestion. This would be interesting to look at, however seropositive rheumatoid arthritis is not well coded within our CPRD dataset. There are 577 patients with seropositive codes in this dataset. These small numbers would make it hard to draw conclusions from any results.

Best Regards

Tânia Santiago (Reviewer 2): This manuscript represents a very important step forward to a better knowledge of the impact of GCs in RA. Its results and conclusions are important for clinical practice.

In the discussion/limitations of the work no information is given regarding GCs doses and route of administration.

Response: Thank you for identifying this oversight; a comment has been added to the limitations that we were unable to explore glucocorticoid dose and intramuscular glucocorticoids (Discussion section, Page 10, lines 24-25 & Page 11, line 1). Additionally, we have indicated in the methods that glucocorticoid exposure refers to oral glucocorticoids (Methods section, page 5, line 10) and added average GC dose during follow-up to table 1, describing this in the results (Results section, page 8, lines 2-4).
In addition, there is no information regarding type of diabetes: insulin or no insulin dependent. Please expand these comments.

Response: A comment has been added to the discussion about type 1 diabetes and how further work would be required to see if the same results would be seen in those with type 1 diabetes (Discussion section, page 11, lines 1-3). Additionally we have added the proportion of people with DM prescribed insulin prior to follow-up to table 1.

In addition to these updates to the manuscript, after reviewing the submission guidelines tables 1 and 2 have been placed at the end of the manuscript rather than being additional files.

Yours Sincerely,

Professor William G Dixon