Reviewer’s report

Title: Cardiovascular Co-morbidity in Patients with Rheumatoid Arthritis: a narrative review of risk factors, cardiovascular risk assessment and treatment

Version: 0 Date: 30 Oct 2017

Reviewer: Solveig Wållberg Jonsson

Reviewer’s report:

This is a narrative review of risk factors, cardiovascular risk assessment and treatment in RA. Since the literature is by now enormous in this field and continuously growing, a narrative review runs the risk of including some selection bias based on subsets of studies, e.g., availability or author selection. The present review is well written and informative and interesting to read. Generally the references are adequate and actual, however far from comprehensive, and some of them are questionable. Although stated in the end of the Introduction, I think it is important to more clearly emphasize the narrative nature of the review, for example in a section on strengths and limitations. Such a chapter could shortly discuss the narrative review in comparison with systematic reviews and metaanalyses.

Some more specific comments below:

Heading:

State that this is a narrative review in the heading.

I miss a comma between risk factors and cardiovascular risk.

Introduction:

Page 3, line 44; Ref 8 must be wrong

Mortality/morbidity

Be careful to differ statements on mortality overall and CVD mortality. On page 4, I do not think Refs 12 and 13 on line 15, refer to CVD mortality but to overall mortality.

In the chapter on decreasing mortality, a recent publication from Holmqvist M and coworkers may be of interest (ARD 2017, doi: 10.1136/annrheumdis-2017-212131)

The paragraph that starts on page 4, line 51, is somewhat hard to follow, e.g., "50 % increase of CVD death" is followed by "increased risk of CVD by almost 2 folds" (page 5, lines 4-23).
Please clarify the difference between statements regarding cardiovascular morbidity and mortality, respectively.

Traditional Cardiovascular Risk Factors

In this paragraph, it is somewhat hard to know which statements on association between hypertension and inflammation concern general population and RA respectively. For example - line 39 refers to RA as does line 47, but what about lines 42-44 which concern inflammation and hypertension?

Please state also that the initial sentences regarding Insulin resistance/meabolic syndrome refer to the general population.

Smoking

Page 8: Again, I do not think that Refs 12-13 refer to CVD and CVD mortality but to mortality overall. Further, although there are now some support for smoking being a risk factor for CVD in RA, several large studies could not verify this. I think authors should be careful with their conclusions.

RA related factors

Page 11, last lines: In the association between CRP and atherogenesis really determined? The references are rather old and I think this is still rather a hypothesis. I suggest that the authors to be more careful in this statement.

Cardiovascular risk assessment

Maybe Reynold’s risk score” should be mentioned here, since it takes inflammation as measured by CRP into account.

Management

Page 17 line 9. There are several studies showing the predictive effect of IMT so I miss a reference to the statement on limited predictability.

Page 17 line 43. I suggest ”Traditional risk factors and role of RA therapy” in analogy with a.

Page 17 last line and first on page 18: The effects of NSAIDs and glucocorticoids on cardiovascular risk factors are diverse and should be discussed more extensively. The effect of corticosteroids on cardiovascular risk overall may also be beneficial since they lower
inflammation. The overall impact is hard to control for because of "confounding by indication". I miss several references in this area. At least, this issue has to be discussed more extensively by the authors.

Page 19, lines 27-29. As pointed out above, the statement on a decreasing trend of CVD event in RA has weak evidence. I lack references to the statement. Refs 16 and 17 concern trend of overall mortality in patients with RA which should be clarified in the sentence on line 32. Although plausible that this refers to all underlying causes, I suggest a more careful conclusion.

Page 19, last paragraph: I agree with the authors in their recommendations to assess and manage all modifiable cardiovascular risk factors and to control disease activity in patients with RA. However, the emphasis on statin treatment is based on 10-year prediction model from ACC/AHA is valid in USA which has to be stressed. The EULAR recommendations (ref 7) recommend treatment according to SCORE or to prediction models used locally and do not emphasize statin treatment in the last update. This has to be better clarified with due references.

The language is generally good, but there are several misspellings and other typographic errors, e.g.,

Page 3, line 15: "...risk factors and..." what?

Page 7, line 2: "patient’s" ??

Page 7 line 54: " obesity exerts ..."

Page 8 line 3: delete "is" page 10, line 51 "..with s pattern"

Page 11 line 48 ."...in RA patients"

Page 12, line 35 "...diseases have been..."

Page 15, line 20 "...is more?? associated..."

Page 17, lines 12, 15, 23... and on page 18, lines 51-59 there are several small errors. Please look over!

Quality of written English
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:
1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests below.

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal