Reviewer’s report

Title: Use of antidepressants and benzodiazepine-related hypnotics before and after initiation of TNF-α inhibitors or non-biological systemic treatment in patients with rheumatoid arthritis, psoriatic arthritis or ankylosing spondylitis

Version: 0 Date: 22 Jul 2019

Reviewer: Katie Druce

Reviewer's report:

General comments:
By the end of the introduction I am not sure that I understand why you think that changes in the use of antidepressants and benzodiazepine related hypnotics would be important? I also am not clear why you have selected these drugs as you do not mention them until the aims… are these just the most commonly used ones?

I don't really understand what this manuscript has added to our knowledge as, in my opinion there is just so much missing information.

Specific comments:

Abstract:
Page 2 line 8 - I think the word "qualified" should be changed to "eligible". At this point I'm also wondering about the sentence in general, what is the evidence that mental health is worse among those eligible for TNFi? (You may cover this more in the intro).

Page 2 line 18 - The "National Patient Register" needs a location - I assume it is from Sweden, as all the co-authors are, but you need to be more clear.

Page 2 line 34-35 - inconsistent use of "-" and "to" in brackets.

Page 2 line 45-49 - I don't think this conclusion is very meaningful or impactful.

Introduction:
Page 3 line 10: Are the "10%-23%" data in brackets confidence intervals? Please make it clear what they are. In addition, if they are CIs, is this really higher that the ">20%" in anti-TNF eligible patients? Why be so vague about the prevalence in this population if they are of importance?

Page 3 line 14: again here (and throughout) please change "qualified" to "eligible".

Page 3 line 18 to 19: the use of "both" in "increased both work disability (12) and mortality (13)" is a bit clunky and not really needed.

Page 3 line 23-26: could you please separate out the references for RA and AS risk and the link between PsA QoL and anxiety. These are two different points so the original sources may be of interest to different people.

Page 3 line 25-29: I am not sure what the relevance of the sleeping problems is, given that this appears to be about mental health complaints? If sleep problems are relevant please make more mention of this.

Page 3 line 37-48: I am confused by these points. First you appear to say that cytokine promoting treatments are associated with increased depression. But then you refer to something being "even more promising", and appears that you are taking about the impact of interventions. These two points are not the same, so the results cannot be "even more promising".
Page 3 line 53-61: I am not sure you discuss this enough. Are these increased rates during the course of biological therapy treatment, or prior to commencing it? Does this support your evidence that anti-TNFi would be useful or not?

Methods:
Page 5 line 45: why were data only used until December 2013? The dates mentioned here are from approximately 6 years ago, which feels like a lot of data to not include.
Page 6 line 15: the use of "and/or" suggests you could have multiple diagnoses. If this is correct how did this impact on the analysis?
Page 6 line 15-24: what if people weren't on mono-therapy, how do they get included? You later mention (Page 6 line 52) that inclusion of NBD to TNFi regimen is not a reason to censor, but it is not clear if it is a reason for initial exclusion. Would inclusion of NBD not likely effect subsequent treatment choices?
Page 7 line 21-23: This sentence is not very clear. Please revise.
Page 7 line 38-45: I am not sure you need to re-iterate the intervals. I think it is sufficient to say this only once.
Page 7 line 53-55: I am not sure what this sentence is here for - it feels more like a justification for the study?
Page 8 line 5-10: Would this not make them existing participants, not controls?
Page 9 line 2-19: why are there no actual values of data included here? It is not sufficient to just say things are "higher" or people are "younger". Same applies in lines 21-29.
Page 9 line 42-44: I'm not sure what "however with statistically significant PRR only for the 6 to 12 months period in the NBS-population." Given the way it is written it is not clear what the comparison was.
Page 9 line 46: This is the first use of "ADs"
Page 9 line 48-50: The sentence "even if the smooth increase is interrupted during the actual reference period in NBS controls." Does not read well. It does not sound very factual and is a bit "flowery".
Page 9 lines 31-60: Why are no actual values reported to emphasise (for example) the start and end of the trend?

Discussion:
Page 11 line 51-55: Can you provide refs for this?
Page 12 line 5-9: statistically significant between the treatment groups, or the time-points? As mentioned above it is not always clear what your comparison is.
Page 12 lines 46-50: Can you provide refs for this? This feels crucial to the premise of this paper.
Page 12 lines 56-60: Can you provide refs for this?
Page 13 line 24: Is this really a crossover-study? You aren't predicting anything but are looking at prevalence rates? I am not convinced this is an appropriate description.
Page 13 line 27-31: I really don't understand what you mean by this sentence.
Page 13 line 50-62: I am unclear what this paper has added to our knowledge, given this quite fundamental limitation.

Conclusions:
Page 14 like 2-10: I think this conclusion is not at all supported by the data provided. You have no idea whether there was a decrease in depression, anxiety and sleeping problems. As you do not show information about this there is no reason to investigate mechanisms underlying it. I also think this does not support the final conclusion about treatment priorities.
ALSO, why sleeping problems is here when it is not a focus of the paper is confusing.
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.

Yes

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

No

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I am able to assess the statistics

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