Author’s response to reviews

Title: Health-related Quality of Life in Patients with Rheumatoid Arthritis

Authors:

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Author’s response to reviews:

James Gwinnutt (Reviewer 1):

1. When was the EQ5D measured - it is clear that the DAS28 is measured longitudinally. Is the outcome of your analyses (i.e. EQ5D) also scored in a similar way, or is the EQ5D score at a single time-point? What about the other predictors (E.g. HAQ) - are these also scored in the same way as the DAS28?

Response: Factors other than DAS28, including HAQ, EQ-5D, and HADS for depression and anxiety assessment were assessed at current visit. We have added these sentences to clarify the HAQ assessment in page 5, line 121-122 “Functional status at current visit was measured using the Thai version of Health assessment questionnaire (HAQ) and add “at current visit” for EQ-5D in the sentence in page 5, line 126 “The Thai version of the EuroQoL five dimensional questionnaire (EQ-5D) at current visit was used for the assessment of HRQoL17”. For depression and anxiety, we had already explained that Depression and anxiety at current visit were assessed by the Thai version of the Hospital Anxiety and Depression Scale (Thai HADs).

2. There is no mention of missing data. It is necessary to report on the amount of missing data and how this was dealt with for the analysis. Perhaps this was a complete case analysis - if so then this should be stated as well as how many patients were dropped and whether these patients differed from the analysis population.

Response: We did not include all patients in our cohorts. As we described in line108-109, page 4 that “All eligible patients from the Rheumatoid Arthritis registries of Siriraj and Phramongkutkla hospitals were consecutively enrolled from September 2016 to March 2018.” All the patients enrolled in this study must have complete data.
3. Would be good to have a "traditional table 1" with descriptives of the whole cohort - this would aid readability and allow the reader to place this cohort of RA patients in context.

Response: - We have added “Table 1 Baseline characteristics of 464 patients with RA” and re-number other tables.

4. I think we need more detail about your modelling decisions (i.e. table 3). Why is gender not included? Why is unemployment/CAD/DM only included in the EQ5D score analysis and not the EQ global health analysis? Vice versa for education and disease duration/dyslipidemia?

Response: - We have added the explanation “Factors that were identified to be different between groups with a p-value of less than 0.2 in univariate analysis were included in a multivariate analysis.” In page 5, line 135-137


Response: - We have deleted this sentence “This has not been previously reported because other studies did not include psychological status in their assessment.” from Page 8, line 200-201

6. There is no mention of treatment - could treatment be playing a key role in determining patients QOL? I think a least some descriptive on the number of patients taking methotrexate / biologics etc. would be useful.

Response: - We did not completely collect the data related to disease modifying anti-rheumatic drugs so we did not include these data into these analysis.

Minor points

7. You say that 49% of patients are unemployed - seems quite high. Does this include retired patients too?

Response: - Yes, this number included retired individuals

8. You note that 8.4% and 9.3% of patients were depressed/anxious. Is this based on the HADS and if so, what scores are you defining as depression / anxiety?
Response: - We have added this sentence “A score of 8 or higher for either type of mood disorder indicated the presence of some degree of anxiety or depression.” at Page 5, line 125-126

9. There are quite a lot of long lists of means in the results text (e.g. lines 168-171) - would these be better in a table? You do have similar results in table 2. Probably only need one or the other? Perhaps just put an effect size from a regression model in the text?

Response: - I have deleted the detailed results of DAS28 and HAQ from line 166-173, page 6 and 7 and add these details in table 3

10. Line 177-178 - you miss that diabetes is also associated with EQ5D

Response: - DM was not significant associated with EQ-5D because its 95 % CI crossed 1 (-0.016 to 0.049) and p = 0.317.

Ian Scott (Reviewer 2):

1. Introduction: I think that the rationale for the study requires further explanation. It is well established that patients with RA have a reduced HRQoL. I am of the understanding that the reason for this study is that HRQoL differs across patient populations, and has not previously been assessed in patients of Thai ethnicity with RA? I think that this needs further expansion e.g. giving information on differences in HRQoL across ethnic groups of patients with RA, and making it clear that HRQoL in patients of Thai ethnicity has not previously been assessed.

Response: - We have added this sentence “Currently, there is no data related to HRQoL in Thai population with RA” in line 103-4, page 4

2. The grammar in the introduction lines 94-98 does not make sense to me, and requires rewriting.

Response: - Prior to submission, this manuscript was reviewed and edited by Mr. Mark Silverman who works with our university for editing English manuscript. I have discussed this issue with him and he suggested delete “Since” from this sentence “HRQoL measures reflect a subjective evaluation of the following key dimensions: the physical dimension (pain and deterioration of physical functioning), the psychological dimension (anxiety and depression), the intellectual or cognitive dimension (attention and memory), and the social dimension (self-esteem and interpersonal relationships)” in line 94, Page 4
3. Methods: I am unclear precisely how the cumulative DAS28 score was calculated. Could the explanation of this please be altered to make it more accessible?

Response: - We described the method used to calculate cumulative DAS28 in line 122-4, page 5. “Cumulative disease activity were calculated using the time-adjusted mean DAS28, which is the area under a curve (AUC) of DAS28 plotted against time, divided by the total length of time from first to last measurement”. This method has been used to calculate cumulative disease activity in many studies in rheumatic and autoimmune diseases areas in the situation, where the frequency of follow up time is not similar across cohort.

4. Methods: were patients consented to take part in this study?

Response: - Yes, they did. We described this in line 116-7, page 5

5. Methods: What is the time point of the cross-sectional EQ-5D and HAQ scores included in the analysis? Why only undertake a cross-sectional analysis, if longitudinal data are available for these outcomes?

Response: - EQ-5D and HAQ were collected at current visit as described and response to reviewer 1 (above).

6. Discussion: I think that the opening statement needs to contain the caveat that these findings were from a cross-sectional assessment of HRQoL. Presumably HRQoL can vary over time, and patients will have different EQ-5D scores on different days therefore the mean EQ-5D score in this population of Thai patients could vary if measured on a different day. Were the analyses in the studies of other ethnic groups also cross-sectional?

Response: - We have added this sentence “These findings were from a cross-sectional assessment of HRQoL. HRQoL can vary over time” in line 190-1, page 7

- Yes, most study were cross-sectional study.

7. Discussion: the authors write that "Furthermore, we showed that depression and anxiety are additional factors related to quality of life. This has not been previously reported because other studies did not include psychological status in their assessment”. Are the authors certain that depression and anxiety have not previously been reported to have an inverse association with HRQoL?

Response: - The same as response to reviewer 1 (above Query 5)
8. Discussion: the authors write that "Therefore EQ-5D should be one of the patient-reported outcome measures routinely used in clinical trial and daily practice due to its comprehensiveness, relevance, and feasibility". Whilst I agree that it is important to measure PROMs in routine care, I'm not sure that the authors can conclude that it is the EQ-5D that should be used based on the data reported in their study?

Response: - As I mentioned that the EQ-5D is validated questionnaire that is comprehensiveness, relevance, and feasibility

9. Results: Table 2- why dichotomise the continuous variables e.g. age, and disease duration? Why report variance for all the variables?

Response: - Just to make them easy to intuitively understand, eg. Age > 60 years refers to geriatric population, disease duration > 10 years refers to long standing RA

- In Table 2, which is now table 4 in revision version, we keep beta and SE to demonstrate the direction of association between dependent and independent variables, but we agree that R2 is not necessary in univariate analysis so we deleted all R2 in this table.

10. Results: Table 3- Is it necessary to report both the SE and the 95% CI of the beta? Also why report both the T-statistic and the P-value? The constant isn't usually reported. Why are non-significant variables from univariate analyses included in the multivariate model (e.g. the univariate P-value for age is 0.184)?

Response: - We have added the explanation “Factors that were identified to be different between groups with a p-value of less than 0.2 in univariate analysis were included in a multivariate analysis.” In page 5, line 135-137

11. Results: Figure 1- how were these HAQ cut-offs decided on?