Author's response to reviews

Title: Influence of arthritis and non-arthritis related factors on areal bone mineral density (BMDa) in women with longstanding inflammatory polyarthritis: a primary care based inception cohort

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Author's response to reviews: see over
Dear Dr Norton,

Re: Influence of arthritis and non-arthritis related factors on BMD\textsubscript{a} in women with longstanding inflammatory polyarthritis: a primary care based inception cohort
Pye SR et al.

Thank you for your email dated 24\textsuperscript{th} February regarding this paper and enclosing the reviewers and editorial team comments which we found constructive and helpful.

We have now addressed each of the comments in turn (see below). The only point we have not addressed is the discretionary revision point 1 from reviewer 3. We have made modifications to the text and enclose a revised manuscript with the changes highlighted so that they can be easily identified.

We hope that the paper will now be suitable for publication and look forward to hearing from you in due course.

Yours sincerely,

Stephen Pye
Reponses to reviewers

Reviewer 1

1. Pages 4-5: The bone health survey is described as being “derived from a previously validated questionnaire on osteoporosis lifestyle risk factors.” How was the original instrument modified and was reliability or validity testing performed on the revised version? A description of the modifications and a statement of whether or not it was validated would be sufficient. If it was validated then it would be interesting to see this data.

Questions concerning physical activity, smoking, alcohol consumption and gynaecological history were taken from the questionnaire used in the European Vertebral Osteoporosis Study. Minor changes were made to the questions concerning smoking and HRT use. The revised questionnaire was not formally validated. A statement to this effect has been added to the methods section (page 5, lines 19-20).

2. Page 6: The results suggest that 51% of participants had ever smoked. Do you know how many of these participants were current smokers or smoked during the 10 year period? This data could be helpful in interpreting the results. If this data is not available it would be beneficial to mention this limitation in the discussion.

We did not ask about current smoking or smoking during the 10 year period in the revised questionnaire. This has been added as a limitation to the discussion (page 10, lines 1-3).

3. Page 6: The results suggest that 60% reported taking oral contraceptive pills. Do you know how many of these participants were currently taking oral contraceptive pills or had taken them during the 10 year period? This data could be helpful in interpreting the results. If this data is not available it would be helpful to mention this limitation in the discussion.

We did not have data on current OCP use or OCP use during the 10 year period. This limitation has been added in the discussion (page 10, lines 1-3).

4. Page 6: Mean CRP levels are reported as “units”. Were the measuring units mg/L?

We thank the reviewer for bringing this to our attention. CRP is indeed in mg/L. This has been corrected in the text (page 7, line 6) and in table 2.

5. Page 6-7: Were the 36 participants who underwent hand radiographs statistically similar to the rest of the study cohort (e.g., age, weight, age of
menarche, CRP)? Coincidentally, it would be helpful if this sentence clarified which radiographs were performed.

The 36 subjects who underwent hand radiographs were slightly older, had more joint involvement, higher CRP levels and HAQ score at 10 years compared to those who had not had radiographs. This has been incorporated into the discussion (page 9, lines 20-25 and page 10, line 1). We clarified also the fact that hand radiographs were taken in the results section (page 7, line 9).

6. Page 7: The results are reported for “age at natural menopause”. How many participants in the study had natural menopause?

38 subjects had reached natural menopause. This has been added to the results section (page 6, lines 18-19).

7. Page 7: It is stated that “Those with a CRP greater than 10 at baseline had higher BMDa at both the spine and femoral neck at baseline and also follow up…” My interpretation of this paper was that BMDa was only measured at the 10-year follow-up but this sentence seems to suggest otherwise. Clarification of this issue in the manuscript would be helpful.

We thank the reviewer for bringing this to our attention. BMDa was indeed only measured at the 10 year follow-up, we were referring to the CRP measurements at baseline and follow-up. This has been clarified (page 8 lines 6-8).

8. Page 8: How many participants in this cohort satisfied the ACR tree criteria for RA at baseline and 10 years?

71 (66%) satisfied the ACR tree criteria for RA at baseline, and 86 (80%) at 10 years. This has been added to the results section (page 7, lines 6-7).

9. Page 9: The authors accurately state that there is some concern about a selection bias in this subcohort but the data they reference is not shown. The addition of some of this data would help with the data interpretation.

We looked at swollen joint count, HAQ and CRP in those who had BMDa measured and those who did not - the results suggest no difference providing some reassurance against significant bias. This information is now included in the text (page 9 line 17-19).

10. Page 9: The authors state that the “inter- and intra-observer variation in assessment of joint counts was good”. Briefly including this data in the methodology would be beneficial.
Annual assessments were performed to ensure standardisation of assessment. Typically four patients (with active joints) were invited to take part in the assessment process and each nurse assessed each patient together with an independent observer. Results were compared, discrepancies discussed and repeat examinations performed as necessary to ensure agreement. We include additional text in the discussion highlighting the steps taken to ensure standardisation (page 10, lines 6-12).

Minor Essential Revisions
1. It would be helpful if the authors defined each abbreviation when it first appears (e.g., IP [inflammatory polyarthritis]).

All abbreviations have now been defined at first use (see also Reviewer 3, minor essential revisions, point 1).

Reviewer 2:

Additionally, the most significant finding of the association with joint erosion is I assume based on the smaller cohort of those receiving hand radiographs (n=36). Although a description of the criteria or how the radiographs are assessed and by whom is not outlined in the methods section.

Associate Editor comment: Can this description be added?

A description of the radiographic assessment has now been included (page 4, lines 19-25 and page 5, line 1).

Reviewer 3:

Minor Essential Revisions:

1. Several abbreviations are not defined anywhere in the text. These include: NOAR (should be added to page 4, line 13, where Norfolk Arthritis Register is first used), CRP and ARA (not defined anywhere), IP (abbreviation shows up in discussion only, so I would advise just using “inflammatory polyarthritis” rather than “IP”), and ESR (not defined anywhere). Defining all of the abbreviations at first use will enhance readability.

All abbreviations have now been defined at first use (see also Reviewer 1, minor essential revisions, point 1): NOAR (page 4, line 14), CRP (page 4 line 17), ARA has been changed to ACR (page 7 lines 6-7) and ESR (page 10 line 16). The abbreviation “IP” has been replaced in the discussion (page 9 lines 11-12)
2. The discussion states that no influence of corticosteroid use, those this might reflect the relatively low dose used in this group. The typical range of doses needs to be stated, or this point needs to be removed. However, since their finding of no influence is in contrast to some other studies, it would be strengthen their conclusions and might even drive the prescribing of lower steroid doses in the future if the range of dose that did NOT effect BMD was stated in either the results or the discussion.

Given the setting (primary care) it would be expected that patients would require lower doses of steroid – this was the rationale behind our use of the phrase in the paper. There is, however, limited information in the cohort about current and cumulative steroid dose during the follow up period. We have now omitted the phrase about low dose steroids and added additional text highlighting the limitation of our data in relation to dose. (page 10, lines 22-25).

**Major Compulsory Revisions**

1. The authors state that “Those with CRP greater than 10 at baseline had higher BMD” at both sites examined. Yet, table 2 does not show this finding. Perhaps this was an oversight. The discussion related to CRP is also confusing. They state a positive relationship between CRP and bone mass, yet Table 2 does not indicate that statistical power of $p<0.05$ was reached. Confusing currently.

The sentence in the results section relating to CRP has been made clearer (page 8 lines 6-8) (see also Reviewer 1 point 7) and states that there was a trend towards higher $\text{BMD}_a$ in those with a CRP level above 10 mg/L though this association did not attain statistical significance. This has also been clarified in the discussion (page 10, lines 17-19).