PEER REVIEW HISTORY

This paper was submitted to a another journal from BMJ but declined for publication following peer review. The authors addressed the reviewers' comments and submitted the revised paper to BMJ Open. The paper was subsequently accepted for publication at BMJ Open.

(This paper received three reviews from its previous journal but only two reviewers agreed to published their review.)

ARTICLE DETAILS

TITLE (PROVISIONAL)	Delays between the onset of symptoms and first rheumatology consultation in patients with rheumatoid arthritis in the UK: an observational study
AUTHORS	Stack, Rebecca; Nightingale, Peter; Jinks, Clare; Study Syndicate, DELAY; Shaw, Karen; Herron-Marx, Sandy; Horne, Rob; Deighton, Chris; Kiely, Patrick; Mallen, Christian; Raza, Karim

VERSION 1 – REVIEW

REVIEWER	Claire Barber University of Calgary, Calgary, Alberta, Canada
REVIEW RETURNED	02-Jun-2018

GENERAL COMMENTS	The authors have conducted a study to investigate the causes in delays in assessment of patients with RA in England and Scotland. They have surveyed patients with new onset RA or unclassified IA. Overall I feel this is an important study but have a few comments that I would like the authors to address if possible. 1. In the methods, the authors state that the Early Rheumatoid Arthritis Network and Clinical Research Network were used to identify rheumatology centers to participate in this study. For those of us unfamiliar with these networks could a brief description and/or link to a reference or website be included. 2. I was curious about the rheumatology centers, in the methods it says they were secondary care based with one operating clinics in both hospital and community settings. Perhaps a few additional details about the setting would be helpful for the context (e.g. numbers of rheumatologists on average in each setting, whether there was a central triage in place for the settings as this may affect waiting times and referral patterns). Such information could be included in an appendix if there isn't space to summarize. 3. Are some of the questionnaires used available to be included in an appendix or could they be made available on request? It was a bit unclear if the survey on "actions taken in relation to their symptoms to seeking help in primary care" was a published survey. There is a ref at the end of the paragraph but if it is a published survey that was used it would be helpful to clarify. 4. Were inflammatory markers and serology captured? In other waiting time studies (ie for JIA these impacted speed of referral). If this wasn't available it should be included as a limitation. 5. For table reviewing actions taken before seeking help from a

	GP were other types of healthcare providers considered: e.g. physiotherapists, occupational therapists, massage therapists, naturopaths etc. 6. Make sure A&E abbreviation explained as may not be understood by some audiences 7. While postal codes were used to create an IMD score, was there any data on geographic distance from the rheumatology center as this has also been shown to be a predictor of access/delays to care in other studies. 8. In discussion can't recall if abbreviation NOA was previously defined, if not please define. 9. In discussion "Unlike some other studies conducted in the UK, we found that GP delay was the largest contributor"… could the authors state what the largest contributor to delay was in the other studies? It might be helpful to describe and discuss why the results here might be different (e.g. different methods perhaps?) 10. In your discussion about longer delays with individuals of different ethnic minorities and a family hx of RA it seems you could mention further work with qualitative analysis could be useful…. I also wonder if any implicit bias on the physician end could be at play in delayed referrals in although I appreciate this could be a tricky point to discuss…

REVIEWER	Rene Westhovens Rheumatology University Hospitals Leuven.
REVIEW RETURNED	05-Jun-2018

GENERAL COMMENTS	This research group looked for relevant data of treatment delay, an issue that deserves more attention and is important in improving outcome of RA treatment. In general I have no major remarks. Well designed study and correctly evaluated and discussed. I have some additional question that might be discussed: differences in disease perception at a societal level and how these might be changed to improve referral. I mean thoracic pain will rarely lead to late referral because it is 'the heart'!! Some minor points - In discussion "Unlike other some previous studies conducted in the UK,we found that ... should be rephrased - references 20 and 40 are identical, note that first author is De CocK D.

REVIEWER	Jette Primdahl University of Southern Denmark and King Christian X's Hospital for Rheumatic Diseases, Graasten, Denmark
REVIEW RETURNED	13-Jun-2018

GENERAL COMMENTS	The paper reports an interesting cross-sectional survey study on delays between the onset of symptoms and first rheumatology consultation in patients with rheumatoid arthritis in the UK. The study reports on a large number of patients with newly diagnosed rheumatoid arthritis or undifferentiated arthritis, but there are parts that need more detailed descriptions to achieve transparency. In the following, some major and minor issues that need to be

	addressed before the study can be considered for publication in BMJ Open are described. Major issues How should we identify persons in risk of developing inflammatorisk arthritis based on this research? Please clarify as this is included in the limitations p. 3. Introduction section The argumentation for a specific study in the UK is NOT quite clear. How and why is the UK expected to differ from previous results? Aim The aim of the study is rather vague and it does not reflect and match the later analyses. Also, please state the a priori hypotheses the study seems to test. Methods section Please add information about how long time there were between first and second visit for those patients who were included at the second visit – or at least discuss whether this could have affected the data (patients recall) (p 7) It seems strange that CRP or ESR were not part of the inclusion criteria. Please clarify if this was the case (p 7) The description of the two questionnaires, who collected the data and the three phases included in the data collection are a little hard to follow. Please rephrase (p 7-8). Also, other articles use the terms patient delay, physicians delay and hospital delay. It may be relevant to consider using the same expressions instead of defining similar with new names? (i.e. Palm and Purinszky, 2005; Raza et al., 2011; Villeneuve et al., 2013, Mølbæk et al., 2015) You describe the development of an additional questionnaire and that the questions were validated and assessed for reliability (p. 8). Please elaborate a little bit on this – which issues were included in the questionnaire and what part is included in this study – and what about the rest of the data? The description of the data collection lacks detail in several parts. I.e. How was patient delay reported, how was palindromic onset and acute onset defined and were they mutually exclusive? In Table 1 you report the number and percentages of the two types of onset of symptoms, but later (p 18) you also mention insidious arthritis in 64,4% of the patients. How did you reach this number and how does this link to palindromic and acute onset? On p. 15 you mention both mode of onset and rapidity of onset – so were there two different questions? Please ensure consistency and details in the description and reporting of these variables which is fundamental for the study. How was education reported? Part of the analysis section is hard to follow too, but maybe this will be more clear if the variables are described in more detail. Why were all ten explanatory variables retained in the multi-variate analyses if they were not significant in the univariate analyses? Maybe I misunderstand the description, but then please consider If

	it is possible to improve the description a bit. Also it seems as if the analyses include multiple testing. Please consider if correction for this is needed. On p. 14 you describe that an interaction was found between mode of onset and gender – but it is not until next sentence it becomes clear which type of onset you refer to – and do you mean a significant interaction? Which variables were included in the multivariate analysis regarding patient delay? In the multivariate analyses regarding GP delay, were ethnicity created as dummy variables in order to obtain the specific results? Mid p. 15 – which interactions were not found? Did the results differ between patients first diagnosed with RA and UA? On page 13 additional results are reported (use of telephone helpline i.e.) Please consider to include these results in Table 2. The formulation is a bit unclear i.e. "…in the vast majority of cases…" please provide the details instead. Also, "3.7 % sought help in the workplace…" – was this 3.7% of those in paid work or 3.7% of all the patients? What does the abbreviation A&E mean (p.13). Please clarify. Discussion section You find other results than previous UK studies regarding GP delay. Please elaborate a bit on possible reasons for this. Also on p. 16 you mention "Research is underway…." Please clarify what you mean. Do you mean that you have another study and what is the aim of that study? Who is going to be educated – patients, GPs, common public? On p 17 you mention that "a number of factors were found to influence GP delay", and you mention deprivation although in the Results section only ethnicity is reported to be significant. Please clarify. You refer to previous qualitative studies regarding help-seeking and delay, but does not include the most recent studies (i.e. Mølbæk et al, 2015; Tiwana et al 2015 (your own), Simons et al 2015(your own)) What do you mean by "a number of guidelines were published" as part of the limitation? How do you think this has affected the study? Please elaborate. Why do you think that another UK study is necessary? Why not an European study? (p 19) The very last sentence (p 20) stands alone and needs some further discussion. What does it mean in relation to the present study. Please add a conclusion to the study. Minor issues Abstract The objective of the study is formulated rater vaguely. In the result section of the abstract, please clarify in the formulation – took longer and delayed longer than what? Please consider to include the type of study in the title of the article

	Introduction section Please consider to rephrase the sentence regarding reduced life expectancy, as this is not confirmed in more recent inception-cohorts or at best, the results differ. Page 5, Is it rather the time to initiation of effective treatment you mean is vital, rather than just to see a rheumatologist? I am aware that you probably imply that to see a rheumatologist will help ensure initiation of treatment

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Comment: The authors have conducted a study to investigate the causes in delays in assessment of patients with RA in England and Scotland. They have surveyed patients with new onset RA or unclassified IA. Overall I feel this is an important study.
Response: We would like to thank the reviewer for this comment.

Comment: In the methods, the authors state that the Early Rheumatoid Arthritis Network and Clinical Research Network were used to identify rheumatology centers to participate in this study. For those of us unfamiliar with these networks could a brief description and/or link to a reference or website be included.
Response: We have added a reference for the Early Rheumatoid Arthritis Network (Garwood W. The Early Rheumatoid Arthritis Network (ERAN). Musculoskeletal Care. 2004;2(4):240-4). We have expanded the term “Clinical Research Network” to “the National Institute for Health Research Clinical Research Network” and added a reference to a weblink (https://www.nihr.ac.uk/about-us/how-we-are-managed/managing-centres/crn/ (accessed 16th August 2018))

Comment: I was curious about the rheumatology centers, in the methods it says they were secondary care based with one operating clinics in both hospital and community settings. Perhaps a few additional details about the setting would be helpful for the context (e.g. numbers of rheumatologists on average in each setting, whether there was a central triage in place for the settings as this may affect waiting times and referral patterns). Such information could be included in an appendix if there isn’t space to summarize.
Response: We have reported which Trust operated in both primary and secondary care settings. Unfortunately, data were not collected on the details of each participating site as requested above. This has been included as a limitation in the discussion and it has been highlighted that future work should address this. Specifically we have added: “Similarly, a number of secondary care related variables may have influenced the extent of secondary care delay including the number of rheumatologists at each Trust, whether a dedicated early arthritis clinic was in place and approaches taken to the triage of referrals. Data relating to these variables were not collected though future work addressing issues of delay should address these important issues.”

Comment: Are some of the questionnaires used available to be included in an appendix or could they be made available on request?
Response: Yes, we will make the questionnaires available on request and have indicated this in the text in the Methods section.

Comment: It was a bit unclear if the survey on “actions taken in relation to their symptoms to seeking help in primary care” was a published survey. There is a ref at the end of the paragraph but if it is a published survey that was used it would be helpful to clarify.

Response: Data were collected via two questionanires. The first was completed by the Healthcare professional and is described in the paragraph beginning “Data were collected using two questionnaires (available on request). First, following consent, the recruiting healthcare professional completed a brief questionnaire that captured data on extents of delays between…”. The second was completed by the patient and is described in the paragraph beginning “Patients were asked to provide data on actions taken in relation to their symptoms prior to seeking help in primary care as part of a separate patient completed questionnaire”. That patient reported questionnaire has been previously published (Stack RJ, Mallen CD, Deighton C, Kiely P, Shaw KL, Booth A et al. The development and initial validation of a questionnaire to measure help-seeking behaviour in patients with new onset rheumatoid arthritis. Health Expect 2014; Jun(3):1-10). Only a small proprtion of the data from that pateint completed questionanire (specifically the data related to patient actions) is reported in the current manuscript. We will be reporting the majority of the data frokm that questionnaire (e.g. in relation to why patients chose certain behaviours) via a separate manuscript.

Comment: Were inflammatory markers and serology captured? In other waiting time studies (ie for JIA these impacted speed of referral). If this wasn’t available it should be included as a limitation.
Response: We agree that it would have been very helpful to have access to results tests performed in primary care to assess whether levels of inflammatory markers or RA related autoantibodies measured in primary care influenced the rapidity of referral from primary care. Indeed we have recently competed a quantitative study in primary care which suggests that these results may influence GP behaviour (Ian C Scott, Navjeet Mangat, Alex MacGregor, Karim Raza, Christian D Mallen, Samantha L Hider; Primary care challenges in diagnosing and referring patients with suspected rheumatoid arthritis: a national cross-sectional GP survey, Rheumatology Advances in Practice, Volume 2, Issue 1, 1 January 2018, rky012, https://doi.org/10.1093/rap/rky012). Unfortunately, we were not able to collect results of tests from primary care and have included this as a limitation.

Comment: For table reviewing actions taken before seeking help from a GP were other types of healthcare providers considered: e.g. physiotherapists, occupational therapists, massage therapists, naturopaths etc.
Response: These response options were not provided in the patient questionnaire.

Comment: Make sure A&E abbreviation explained as may not be understood by some audiences.
Response: This has been corrected.

Comment: While postal codes were used to create an IMD score, was there any data on geographic distance from the rheumatology center as this has also been shown to be a predictor of access/delays to care in other studies.
Response: This is an interesting point. In order to address issues related to distance and delay across all elements of delay we would have to have recorded postcodes of GP practices to assess relations between delay and distance between the patients’ homes and GP practice and home or GP practice and hospital. Whilst we collected data on patient postcodes other postcodes were not collected and so we are not able to report this.

Comment: In discussion can’t recall if abbreviation NOA was previously defined, if not please define.
Response: This has been corrected. In fact the abbreviation “NOA” in the Discussion was a typographical error. This should have read “NAO” (and an explanation for that abbreviation is given in the Introduction).

Comment: In discussion “Unlike some other studies conducted in the UK, we found that GP delay was the largest contributor”… could the authors state what the largest contributor to delay was in the other

studies? It might be helpful to describe and discuss why the results here might be different (e.g. different methods perhaps?).
Response: We have rephrased the relevant section to read “Unlike our previous study conducted at a single centre in the UK where patient delay accounted for the largest element of delay, we found that GP delay was the largest contributor to overall delay; patient delay was less than we had previously reported in our single centre study”.

Comment: In your discussion about longer delays with individuals of different ethnic minorities and a family hx of RA it seems you could mention further work with qualitative analysis could be useful…. I also wonder if any implicit bias on the physician end could be at play in delayed referrals in although I appreciate this could be a tricky point to discuss…
Response: We have added “Qualitative approaches may be helpful to address some of these issues in the future.”

Reviewer: 2

Comment: This research group looked for relevant data of treatment delay, an issue that deserves more attention and is important in improving outcome of RA treatment. In general I have no major remarks. Well designed study and correctly evaluated and discussed.
Response: We would like to thank the reviewer for these positive comments

Comment: Differences in disease perception at a societal level and how these might be changed to improve referral. I mean thoracic pain will rarely lead to late referral because it is 'the heart'!!
Response: Thank you for highlighting this. We agree that this is an interesting and important concept which we have previously explored (Simons G, Belcher J, Morton C, Kumar K, Falahee M, Mallen CD, Stack RJ, Raza K. Symptom recognition and perceived urgency of help-seeking for rheumatoid arthritis and other diseases in the general public: a mixed method approach. Arthritis Care Res. 2017;69:633-641.) We have addressed this in the Discussion.

Comment: In discussion "Unlike other some previous studies conducted in the UK,we found that ... should be rephrased.
Response: We have rephrased this.

Comment: References 20 and 40 are identical, note that first author is De CocK D.
Response: We have corrected this.

Reviewer: 3

Comment: How should we identify persons in risk of developing inflammatorisk arthritis based on this research? Please clarify as this is included in the limitations p. 3.
Response: As the reviewer points out we have stated that “future research should examine those at risk and follow their journey to diagnosis to avoid the limitations of retrospective data collection”. We acknowledge that this is a challenging issue. One approach to this would be a longitudinal observational study of the first degree relatives of patients with RA (who are known to be at increased risk of RA) to track the development of symptoms and the relationship between that, GP consultation, GP referral and secondary care assessment. An observational study of first degree relatives is currently taking place in the UK (PREVENT-RA). One of the challenges with this, of course, is that the mere fact of being involved in such a study may influence subsequent patient and GP behaviour. Our understanding of this “Limitations of this study” section is that the limitations should be presented as a brief sentence. We have thus expanded on this issue in the Limitations section of the Discussion and have simplified what we have included under “Limitations of this study” on page 3.

Comment: The argumentation for a specific study in the UK is NOT quite clear. How and why is the UK expected to differ from previous results?
Response: We do not believe that a specific study in the UK has benefits over an international study. We were funded by the UK National Institute for Health Research to conduct this study in the UK and we believe that the resulting data are valuable but we agree that an extension of this work in the context of an international study would be highly valuable and we have included this as future potential research ("an international study would be particularly helpful."

Comment: The aim of the study is rather vague and it does not reflect and match the later analyses. Also, please state the a priori hypotheses the study seems to test.
Response: We have revised the Aim section and hope that this is now clearer.

Comment: Please add information about how long time there were between first and second visit for those patients who were included at the second visit – or at least discuss whether this could have affected the data (patients recall) (p 7).
Response: These data were not collected. The manuscript highlights issues associated with reliance on patient recall and we have further expanded on this in the Discussion.

Comment: It seems strange that CRP or ESR were not part of the inclusion criteria. Please clarify if this was the case (p 7).
Response: Inflammatory markers were not part of the inclusion criteria. We aimed to include patients with newly presenting inflammatory arthritis of the rheumatoid type or that was unclassified. Suggesting that CRP or ESR should be part of the inclusion criteria suggests that there would be an expectation that for patients to be included in this study they should have a CRP or ESR above a predefined threshold. Since it is know that patients with inflammatory arthritis can have normal inflammatory makers we did not wish to have inflammatory marker levels as an inclusion criterion for this study but rather to focus on the clinical features of synovial inflammation.

Comment: The description of the two questionnaires, who collected the data and the three phases included in the data collection are a little hard to follow. Please rephrase (p 7-8).
Response: We have rephrased this as requested.

Comment: Also, other articles use the terms patient delay, physicians delay and hospital delay. It may be relevant to consider using the same expressions instead of defining similar with new names?
Response: We would like to thank the reviewer for this comment. We agree that consistent terminology across the published literature would be helpful. We have elected to use the terms "patient delay", "general practitioner delay" and "hospital delay" throughout (consistent with terminology in our previous publications e.g. Kumar et al Rheumatology 2010;49:1005–1012; Kumar et al Rheumatology 2007;46:1438–1440). We have elected to avoid the term "physicians delay" as we are concerned that there may be some ambiguity regarding whether the "physician" being referred to was the primary care physician (i.e. the General Practitioner) or the secondary care physician (i.e. the Rheumatologist).

Comment: You describe the development of an additional questionnaire and that the questions were validated and assessed for reliability (p. 8). Please elaborate a little bit on this – which issues were included in the questionnaire and what part is included in this study – and what about the rest of the data?
Response: As described above only a small proportion of the data from this additional patient questionnaire have been presented in this manuscript. Another manuscript reporting on psychosocial variables explaining patient delay will be reported separately.

Comment: The description of the data collection lacks detail in several parts. I.e: How was patient delay reported.
Response: We have now clarified this – the dates of symptom onset and first presentation to a healthcare professional in primary care were obtained from the patient and relied on patient recall.
Comment: How was palindromic onset and acute onset defined and were they mutually exclusive?
Response: This has now been clarified. Palindromic onset and acute onset were not mutually exclusive terms.
Comment: In Table 1 you report the number and percentages of the two types of onset of symptoms, but later (p 18) you also mention insidious arthritis in 64,4% of the patients. How did you reach this number and how does this link to palindromic and acute onset?
Response: In table 1 we reported that 35.9% of patients had an acute onset and on page 18 we reported that "In our national sample 64.1% of people describe an insidious onset of RA". Onset is categorised as either acute (35.9%) or insidious (64.1%) and palindromic (42.8%) or non-palindromic (57.2%).

Comment: On p. 15 you mention both mode of onset and rapidity of onset – so were there two different questions? Please ensure consistency and details in the description and reporting of these variables which is fundamental for the study.
Response: Yes these were different variables. We hope our answers above have helped clarify this.

Comment: How was education reported?
Response: Education was reported as Highest educational achievement either [1] no qualification; [2] GCSE or equivalent; [3] A levels or equivalent; [4] Higher education.

Comment: Part of the analysis section is hard to follow too, but maybe this will be more clear if the variables are described in more detail. Why were all ten explanatory variables retained in the multi-variate analyses if they were not significant in the univariate analyses? Maybe I misunderstand the description, but then please consider If it is possible to improve the description a bit.
Response: The reviewer is correct in noting that all ten explanatory variables were retained (as main effects) in the multivariate analysis. As our sample size is large enough to support estimation of a model with this many variables, we preferred to retain them all in the model, as removing variables purely on the basis that they are not significant in the initial univariate analysis can be detrimental (Heinze G, Dunkler D. Five myths about variable selection. Transplant International 2017; 30: 6–10.)

Comment: Also it seems as if the analyses include multiple testing. Please consider if correction for this is needed.
Response: For each multivariate analysis (patient delay, GP delay and hospital delay) we performed a single backward stepwise analysis. Such analyses are usually performed with no correction for multiple testing, but we have used a p value of 0.01 rather than the usual 0.05 as the significance level for the two-way interactions.

Comment: On p. 14 you describe that an interaction was found between mode of onset and gender – but it is not until next sentence it becomes clear which type of onset you refer to – and do you mean a significant interaction?
Response: We thank the reviewer for pointing this out and have reworded this as follows: "An interaction was found between palindromic onset and gender ($F=45.658$, $P<0.01$); men with a palindromic onset waited significantly longer before seeking help."

Comment: Which variables were included in the multivariate analysis regarding patient delay?
Response: The same variables were used in all three multivariate analyses. We have now made this clear in the Analysis section: "For each of the outcomes patient delay, general practitioner delay and hospital delay a general linear model was used with main effects and two-way interactions for the

following explanatory variables: gender, ethnicity, IMD score, age, education, employment status, mode of onset, rapidity of onset, patient reported family history of RA and RA vs. UA. For each outcome any two-way interactions which were not significant were removed in a backwards stepwise fashion, with the pairings with the highest p values being removed first. All main effects were retained, so that the final model for each outcome included all ten explanatory variables and any significant two-way interactions ($p<0.01$). All significant main effects and interactions are reported in the Results section."

Comment: In the multivariate analyses regarding GP delay, were ethnicity created as dummy variables in order to obtain the specific results?
Response: Ethnicity was included in the general linear model as a categorical variable with the four categories Black British, South Asian, White British and Other. As the ethnicity variable in the model for GP delay was statistically significant, pairwise comparisons were then performed.

Comment: Mid p. 15 – which interactions were not found?
Response: As there are ten variables in the multivariate model, the backwards stepwise approach started with a model containing 45 two-way interactions (i.e. all the possible pairs of variables). None of the 45 was significant, so the final model contained ten main effects and no interactions.

Comment: Did the results differ between patients first diagnosed with RA and UA?
Response: The variable RA vs. UA was included as a main effect in all three models but was not significant in any of them (and there were no significant interactions involving this variable).

Comment: On page 13 additional results are reported (use of telephone helpline i.e.) Please consider to include these results in Table 2.
Response: The variables reported in Table 2 derive from a section of the patient completed questionnaire entitled "These questions ask about the things you may have done to manage your symptoms before you first saw your GP". The additional results derived from a section of the questionnaire entitled "These questions ask about other people you may have spoken to about your symptoms before you first saw your GP. Did you seek help or information from…". It is for this reason that we do not report these results together. The formulation is a bit unclear i.e. "…in the vast majority of cases…" please provide the details instead. For simplicity we have removed the phrase "Whilst, in the vast majority of cases, the GP was the first healthcare professional consulted by the patient…" Also, "3.7 % sought help in the workplace…" – was this 3.7% of those in paid work or 3.7% of all the patients? This was 3.7% of all patients.

Comment: What does the abbreviation A&E mean (p.13). Please clarify.
Response: This has been clarified

Comment: Discussion section: You find other results than previous UK studies regarding GP delay. Please elaborate a bit on possible reasons for this.
Response: We have expanded on this in the Discussion. Results of our previous UK study were derived from only a single centre.

Comment: Also on p. 16 you mention "Research is underway…." Please clarify what you mean. Do you mean that you have another study and what is the aim of that study?
Response: We had added the following as clarification: "For example, a questionnaire has been developed and validated to capture such symptoms in patients presenting with joint symptoms which by history are suggestive of an underlying inflammatory cause [31] and data are currently being collected from such patients in secondary care based longitudinal observational cohort studies to identify symptoms that may predict RA development. Furthermore an assessment of primary care databases has identified a range of symptoms including hand related joint symptoms, morning

stiffness and carpal tunnel syndrome type symptoms as being ones with which patients frequently present to the GP in consultations prior to the one in which the GP refers the patient to a Rheumatologist or records a diagnosis of RA [32]"

Comment: Who is going to be educated – patients, GPs, common public?
Response: We have made extensive changes to the Discussion section and hope that this comment has now been satisfactorily addressed.

Comment: On p 17 you mention that "a number of factors were found to influence GP delay", and you mention deprivation although in the Results section only ethnicity is reported to be significant. Please clarify.
Response: We have removed the phrase "and deprivation" from the Discussion and apologise for this error.

Comment: You refer to previous qualitative studies regarding help-seeking and delay, but does not include the most recent studies (i.e. Mølbæk et al, 2015; Tiwana et al 2015 (your own), Simons et al 2015(your own).
Response: We have now added these references.

Comment: What do you mean by "a number of guidelines were published" as part of the limitation? How do you think this has affected the study? Please elaborate.
Response: The issue we were aiming to highlight was that we were not able to report on the relationship between the publication / adoption of RA management guidelines and patterns of presentation, referral and further assessment. We have amended the relevant paragraph.

Comment: Why do you think that another UK study is necessary? Why not an European study? (p 19)
Response: We agree that a European / other international study would add value in this area and have added the following: "A study comparing delays and referral patterns between hospitals with local policies and practices which may influence the time between onset and first consultation would be useful and an international study would be particularly helpful."

Comment: The very last sentence (p 20) stands alone and needs some further discussion. What does it mean in relation to the present study.
Response: In the originally submitted version of the manuscript the very last sentence read "However, a previous study addressing delay in patients with RA, has highlighted the accuracy of patient recollection by comparing patient accounts of their journey to first rheumatology consultation against medical records." We included this sentence as data from the study we referred to in that sentence validates our approach to gathering data related to dates of the onset of symptoms and initial GP consultant from patients (i.e. replying on patients'' memories). We have amended the relevant section to "Fourthly, data relating to the dates of onset of symptoms and initial GP consultation were gathered from patients' histories, and therefore relied on patient recollection with a possible associated error. However, a previous study addressing delays in the assessment of patients with RA, compared patient accounts of their journeys to first rheumatology consultation against medical records and highlighted the accuracy of patient recollection in relation to dates found to be documented in primary care records40. This validates our approach of using patient memory to define the dates of symptom onset and initial GP presentation".

Comment: Please add a conclusion to the study.
Response: We have changed the order in the Discussion so that the "limitations" section is not the final section but rather the penultimate section and that the Discussion section now ends with a conclusion.

Comment: Minor issues: Abstract: The objective of the study is formulated rather vaguely.
Response: The original objective read “To investigate delays to rheumatology assessment for patients with a new onset of rheumatoid arthritis (RA)”. We have reformulated this to “To investigate delays from symptom onset to rheumatology assessment for patients with a new onset of rheumatoid arthritis (RA) or unclassified arthritis.”

Comment: In the result section of the abstract, please clarify in the formulation – took longer and delayed longer than what?
Response: We have clarified this.

Comment: Please consider to include the type of study in the title of the article.
Response: We have added “an observational study” to the title

Comment: Introduction section: Please consider to rephrase the sentence regarding reduced life expectancy, as this is not confirmed in more recent inception-cohorts or at best, the results differ.
Response: We acknowledge this and have removed the phrase “and reduced life expectancy”.

Comment: Page 5, Is it rather the time to initiation of effective treatment you mean is vital, rather than just to see a rheumatologist? I am aware that you probably imply that to see a rheumatologist will help ensure initiation of treatment.
Response: The reviewer is absolutely correct in this. We have changed the relevant sentence from “Therefore, it is vital that patients are seen by Rheumatologists rapidly following the onset of RA symptoms” to “Therefore, it is vital that patients are seen by Rheumatologists rapidly following the onset of RA symptoms to allow the rapid introduction of disease modifying anti-rheumatic drug treatment.”

Comment: Authors must include a statement in the methods section of the manuscript under the sub-heading 'Patient and Public Involvement'.
Response: We have now added this to the Methods section. “Patient and public involvement was an important element of this study. Patient representatives from Sandwell and West Birmingham Hospitals NHS Trust were involved in the study design, advised on the content of patient facing materials including participant information sheets and consent forms and the content of questionnaires including questions related to actions taken by patients prior to consulting their GPs. Patients were members of the Project Management Group reviewing study recruitment and supporting the Group in developing approaches to ensure that recruitment proceeded to time and target”. We have thanked our patient partners for their support in the acknowledgment section.

VERSION 2 – REVIEW

REVIEWER	Claire Barber University of Calgary, Canada
REVIEW RETURNED	01-Oct-2018

GENERAL COMMENTS	I have no further comments for the authors.

REVIEWER	Rene Westhovens Rheumatology KU Leuven, Belgium
REVIEW RETURNED	25-Sep-2018

GENERAL COMMENTS	The authors did an excellent job in dealing with reviewers concerns. No further issues

REVIEWER	Jette Primdahl King Christian X's Hospital for Rheumatic Diseases, Graasten, Denmark and University of Southern Denmark, Odense, Denmark
REVIEW RETURNED	13-Oct-2018

GENERAL COMMENTS	I am happy with the changes made in the revised manuscript, but I do have a few minor comments to the revised version of the manuscript: 1: Reviewer 1 comments on whether patients saw other types of health care professionals before referral to a rheumatologist and the possible influence regarding distance between the patients home and the rheumatologist. These issues should be included as additional limitations. 2: There is no information regarding informed consent, ethical issues, safe storage of data etc. 3: It may not be clear to the reader what the difference is between insidious onset and palindromic onset. The authors explain the different categories in the response letter, but this information needs to be included in the manuscript as well. 4: In the revised text in the Discussion section, some new references are missing. The text says (add ref.) and (ref) If these issues are taken into consideration, I do not need to see the manuscript again.

VERSION 2 – AUTHOR RESPONSE

Comment 1: Reviewer 1 comments on whether patients saw other types of health care professionals before referral to a rheumatologist and the possible influence regarding distance between the patients home and the rheumatologist. These issues should be included as additional limitations.
Response to comment 1: *The following sentences have been added. " In addition, this study did not examine the distances between patients' homes and their local GP surgeries, and hospital and so we were unable to assess whether physical distance between the patient's home and the GP surgery or hospital influenced delay." Added to page 17.*

Comment 2: There is no information regarding informed consent, ethical issues, safe storage of data etc.
Response to comment 2: *Information related to ethical approval is contained in a separate section at the request of the publication. The section is entitled "ethical approval information". However, this comment has encouraged us to expand the statement to include information about safe storage of information. The statement now reads "**Ethical approval information** Ethical approval was obtained from South Birmingham Research Ethics Committee (reference no. 10/H1207/98) and all participants gave written informed consent. Paper and electronic data were stored in secure locations and protected by relevant security systems as approved by the study Sponsor and research ethics committee.*

Comment 3: It may not be clear to the reader what the difference is between insidious onset and palindromic onset. The authors explain the different categories in the response letter, but this information needs to be included in the manuscript as well.
Response to comment 4: *The definitions of terms was included in the methods section which currently reads "clinical variables including the mode of symptom onset (palindromic (defined as intermittent symptoms) vs. non-palindromic (defined as persistent symptoms)), rapidity of symptom onset (acute vs. insidious; an acute onset was typically viewed as an onset of symptoms which came on rapidly over 24-48 hours)"*
However, to support readers' understanding of the data presented in the results section, the following sentence has been added to the paragraph which describes the interaction between delay and symptom onset "Palindromic onset was defined as intermittent symptoms, while non-palindromic was defined as persistent symptoms. Acute onset was defined as symptoms which came on rapidly over

24-48 hours, while insidious onset was defined as symptoms which developed slowly over extended longer period of time."

Comment 4: In the revised text in the Discussion section, some new references are missing. The text says (add ref.) and (ref) If these issues are taken into consideration, I do not need to see the manuscript again.
Response to comment 4: We apologise for this error in the tracked version of the manuscript, the clean version did not have this error. We have checked the current version and the required references have been added.