PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Quality of life, sleep and rheumatoid arthritis (QUASAR): A protocol for a prospective UK mHealth study to investigate the relationship between sleep and quality of life in adults with rheumatoid arthritis
AUTHORS	Druce, Katie; Cordingley, Lis; Short, Vicky; Moore, Susan; Hellman, Bruce; James, Ben; Lunt, Mark; Kyle, Simon; Dixon, Will; McBeth, John

VERSION 1 – REVIEW

REVIEWER	Ingo Fietze Charité - Universitätsmedizin Berlin Germany
REVIEW RETURNED	26-Aug-2017

GENERAL COMMENTS	The paper 'Quality of life, sleep and rheumatic arthritis (QUASAR): A protocol for a prospective mHealth study' describes the study protocol and design of one prospective study. The topic chosen is extremely interesting and therefore much appreciated. Hereby I want to mention a few remarks for the study design: Quiality of sleep is planned to be assessed. However a standard tool to assess quality of sleep is not incluced. One such suggestion would be the standard questionnaire for insomnia, such as the insomnia severity index, ISI. Or alternatively for assessment of sleepiness, this could be the Epworth Sleepiness Scale, ESS. However none was mentioned, neither at baseline nor during follow-up visits. Actigraphy recordings do not allow an assessment of sleep quality. They allow an assessment of sleep duration and sleep efficiency. This is definitely different. What do you mean by circadian-sleep-rest-parameter? You also forgot to mention all details regarding the evaluation of actigraphy. There are many details which might differ from one study to another one. Where at the subjects, will the actigraphy be applied? It should be the wrist of the non dominant arm or it should be attached at the body at the same position in all subjects. Please specify. Another problem is the potential bias when selecting study participants.

	It can be assumed that those patients are interested to participate in this study, which do have sleep problems. and these patients will not only be those who suffer from secondary insomnia due to rheumatic arthritis, but also those who suffer from primary insomnia, being idiopathic or psychophysiological (10% from all subjects), or occasional or frequent bad sleepers (30% of subjects), or RLS patients (5-10%.), or even patients with obstructive sleep apnea. Unfortunately specific questionnaires for the assessment of RLS, obstructive sleep apnea and, as mentioned, primary insomnia, are missing for the baseline investigation of study participants.

REVIEWER	Laure Peter-Derex Centre for Sleep Medicine and Respiratory Disease Hospices Civils de Lyon LYON FRANCE
REVIEW RETURNED	22-Sep-2017

GENERAL COMMENTS	The question of the impact of sleep on quality of life in rheumatoid arthritis is original, relevant and worthy of investigation. The authors propose a protocol for a prospective cohort study. Informations about the disease, quality of life, various symptoms and important events occurrence will be collected, as well as sleep diary and actigraphy. The design study seems appropriate to answer the questions. I have some concerns about - The selection biais, as the author expect that of all patients that will receive the information about the study, 5% will enroll (probably patients comfortable with the use of connected device, or suffering from sleep disturbances …) - Study duration: is a 30 days period sufficient to assess quality of life fluctuations? - The choice to include patients with known sleep disorders (Sleep apnea syndrome, restless leg syndrome). Informations about of treatment, if any, and residual symptoms of these conditions should be assessed. - Which actographic variable will be used to assess sleep disturbances (sleep efficiency ? Total sleep time? Sleep fragmentation?) Minor points: - Discrepancy in the number of expected participants between abstract “350 people with RA” and sample size section “a total of 175 participants” - Many syntax issues: (for example: Introduction: “Occurrence between …the condition”, “Although there are…but…well-being”, Methods, Day 60: “participants wil be prompted…uMotif” etc…).

REVIEWER	Awat Feizi Isfahan University of Medical Sciences
REVIEW RETURNED	30-Sep-2017

GENERAL COMMENTS	The reviewer provided a marked copy with additional comments. Please contact the publisher for full details.

REVIEWER	Agnieszka Pac Jagiellonian University Medical College
REVIEW RETURNED	07-Oct-2017

GENERAL COMMENTS	This paper describes the study protocol of ongoing study. The paper was prepared very precisely and in details. The authors have not described exactly the study dates. However they described the dates of planned beginning of consecutive study waves. The 3rd aim of the paper/study is about "possible" intervention - I would like to find out in the introduction section what kind of intervention can be undertaken in this situation. The authors have not specify also the target effect they would like to achieve by "hypothetical successful intervention". The plan for the statistical analysis was prepared correctly. To answer the second aim two different method were planned - first SEM to identify the hypothesized association as well as mediation role of age and sex. The second one will allow to use fool set of information collected to confirm the associations from the SEM analysis.

REVIEWER	George A. Kelley West Virginia University USA
REVIEW RETURNED	09-Oct-2017

GENERAL COMMENTS	GENERAL COMMENTS The purpose of this proposed prospective cohort study is to examine the association between sleep and health-related quality-of-life in adults with rheumatoid arthritis using the mHealth approach. While this may be a worthy study to conduct, there is a lack of rationale provided by the authors to convince me of such. In addition, a lack of detail is provided on the proposed instruments to be used as well as potential limitations. Furthermore, the sample size justification given the proposed statistical analysis plan does not seem to be appropriate. Finally, the manuscript does not seem to have been proofread very well. My specific comments appear below with page numbers referring to those listed in the top left and right corners of each page of the pdf document I reviewed. SPECIFIC COMMENTS * Page 3, Strengths and Limitations – Please list limitations of your study. For example, some of the biases associated with self-report, loss to follow-up, etc. * Page 4, Introduction – Suggest that you cite and describe previous studies that have conducted research similar to your planned study and why your proposed study is needed. In other words, what gap exists that your study aims to fill. Ideally, it would seem that a systematic review on this topic should have been conducted to help justify the currently proposed study. If no previous research exists on this topic, then a statement from the authors that they are not aware of such “to the best of their knowledge” would seem appropriate. * Page 4, line 5 – Insert “prospective” before “cohort” * Page 4, line 11 – Here and throughout the rest of the manuscript, I believe the reference is placed after a period or comma versus before a period or comma.

	* Page 4, lines 12 and 13 – Please rewrite the sentence that begins with “Occurrence…” In the same sentence, suggest that you list the proportion(s) of women with RA who stop working as a result of the condition. Also, if there is any data on the economic costs associated with women who stop working due to RA, I would suggest that you include such. * Page 4, line 22 – Suggest that you delete the word “but” * Page 4, lines 27 and 28 – Suggest that you rewrite the sentence that begins with “But sleep…” * Page 5, line 11 – Delete “and” after the word “fatigue” * Page 6, line 43 – Suggest that you replace “are” with “will be” * Page 6, line 49 – Suggest that you place a comma after “criteria” * Page 6, line 52 - Suggest that you replace “are” with “will be” * Page 7, line 20 – Delete “a” before the word “three” * Page 7, line 54 – Suggest that you replace “is” with “will be” after the word “consent” * Page 8, line 5 – Suggest that you replace “is to” with “will” * Page 8, line 11 – Suggest that you insert the word “to” after the word “agree”. The same thing on line 14. * Page 8, line 41 – Suggest that you replace “are” with “will be” after “Participants”. On the next line, delete the comma after “on” and place a comma after “Initially”. * Page 8, line 57 – Delete “is completed” * Page 9, line 3 – Suggest you replace “are” with “will be” * Page 8, line 57 – Delete “is completed” * Page 9, line 3 – Replace “are” with “will be” * Page 9, line 11 – Place a period after Table 1”. * Page 10, Table 1 – Suggest that you add current physical activity level as well as nutrition intake and state the instruments used to assess such. * Page 11, line 19 – Delete “the” before the word “provided”. * Page 11, line 46 – Replace “are” with “will be” before the word “immediately”. * Page 12, line 25 – Replace “responses” with “responded”. * Page 12, line 36 – Please provide validity and reliability data as well as the rationale for using the MotionWatch 8 versus another device. * Pages 12 and 13 – Please rewrite the last sentence on page 12 and the first sentence on page 13. * Page 13, line 17 – Replace “as” with “is” before the word “highlighted”. * Page 13, line 40 – Replace “are” with “will be” after the word “Participants”. * Page 15, line 43 – Replace “are” with “will be” after the word “reminders”. * Page 15, lines 47 through 51 – For all instruments used, please provide (1) a rationale for the selection of each (2) validity and reliability data, and (3) how each instrument is scored. * Page 16, line 31 – Replace “are” with “will be” after the word “participants”. * Page 16, line 44 – Replace “are” with “will be” after the word “copy”. * Page 16, line 45 – Delete “are” before the word “automatically”. * Page 16, line 55 – Insert “the” before the word “top”. * Page 17, Table 3 – For all instruments used and not previously described, please provide (1) a rationale for the selection of each (2) validity and reliability data, and (3) how each instrument is scored.

	* Page 17, lines 47 through 54 – Since it appears that you propose to conduct structural equation modeling as your primary analysis, I would suggest that you re-estimate your sample size based on structural equation models. This includes (1) the anticipated effect size, (2) desired statistical power level, (3) number of latent variables, (4) number of observed variables, and (5) probability level. * Page 18, line 10 – In the abstract you list a sample size of 350 but here you say 175. Please clarify. * Page 18, line 16 – Delete the comma after “study” and insert “and” * Page 18, line 18 – Delete the repeated “in”. END OF REVIEW

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: Ingo Fietze
Institution and Country: Charité - Universitätsmedizin Berlin, Germany Please state any competing interests: None declared

Please leave your comments for the authors below

Comment: The paper ‘Quality of life, sleep and rheumatic arthritis (QUASAR): A protocol for a prospective mHealth study’ describes the study protocol and design of one prospective study.
The topic chosen is extremely interesting and therefore much appreciated.
Hereby I want to mention a few remarks for the study design:
Quiality of sleep is planned to be assessed. However a standard tool to assess quality of sleep is not incluced. One such suggestion would be the standard questionnaire for insomnia, such as the insomnia severity index, ISI. Or alternatively for assessment of sleepiness, this could be the Epworth Sleepiness Scale, ESS. However none was mentioned, neither at baseline nor during follow-up visits. Actigraphy recordings do not allow an assessment of sleep quality. They allow an assessment of sleep duration and sleep efficiency. This is definitely different.

Response: Thank you for raising this. We have not been clear about the sleep measures collected. To clarify:
We measure the Pittsburgh Sleep Quality Index (PSQI), the most widely used measure in the field, at baseline and 60 day follow-up (Table 1;Table 3). Sleep quality is also assessed daily within the consensus sleep diary. We have better emphasised this within the text (Pg 11 line 46 onward; Pg 19, line 19).

With respect to the collection of information about insomnia, we do use the Sleep Condition Indicator (SCI), which measures “insomnia disorder” and reflects contemporary sleep nosologies which do not distinguish between primary vs. secondary insomnia. The SCI (Table 1) is the only validated and widely used insomnia measure that indexes insomnia disorder against contemporary criteria (ICSD-3; DSM-5). We have included more information about this in a paragraph (Pg 10, line 39-48)

Comment: What do you mean by circadian-sleep-rest-parameter?

Response: We have used the wrong terminology here and should have said circadian rest-activity rhythms. This has been edited throughout.

Comment: You also forgot to mention all details regarding the evaluation of actigraphy. There are many details which might differ from one study to another one. Where at the subjects, will the actigraphy be applied? It should be the wrist of the non dominant arm or it should be attached at the body at the same position in all subjects. Please specify.

Response: Thank you, we have included this information in a paragraph (Pg 15, line 53 onwards). along with some information requested by our other reviewers.

Comment: Another problem is the potential bias when selecting study participants. It can be assumed that those patients are interested to participate in this study, which do have sleep problems. and these patients will not only be those who suffer from secondary insomnia due to rheumatic arthritis, but also those who suffer from primary insomnia, being idiopathic or psychophysiological (10% from all subjects), or occasional or frequent bad sleepers (30% of subjects), or RLS patients (5-10%.), or even patients with obstructive sleep apnea.

Response: With respect to the collection of information about insomnia, we do use the Sleep Condition Indicator (SCI), which measures “insomnia disorder” and reflects contemporary sleep nosologies which do not distinguish between primary vs. secondary insomnia. The SCI (Table 1) is the only validated and widely used insomnia measure that indexes insomnia disorder against contemporary criteria (ICSD-3; DSM-5).

Comment: Unfortunately specific questionnaires for the assessment of RLS, obstructive sleep apnea and, as mentioned, primary insomnia, are missing for the baseline investigation of study participants.

Response: We agree that specific questionnaires to assess RLS and OSA would have been interesting, however we needed to make a pragmatic decision about which questionnaires to collect in order to balance availability of data and participant burden. We do however record RLS and OSA as co-morbidities and we also acknowledge that the PSQI has items related to RLS and OSA (and other attributions for sleep disturbance) which we will use to characterise our sample. To reflect these important points we have written new paragraphs (Pg10, line23-48) to discuss the data collected at baseline and elaborated on these decisions.

Reviewer: 2
Reviewer Name: Laure Peter-Derex
Institution and Country: Centre for Sleep Medicine and Respiratory Disease, Hospices Civils de Lyon, LYON,FRANCE Please state any competing interests: None to declare

Please leave your comments for the authors below The question of the impact of sleep on quality of life in rheumatoid arthritis is original, relevant and worthy of investigation.

The authors propose a protocol for a prospective cohort study. Informations about the disease, quality of life, various symptoms and important events occurrence will be collected, as well as sleep diary and actigraphy. The design study seems appropriate to answer the questions.
I have some concerns about

- The selection biais, as the author expect that of all patients that will receive the information about the study, 5% will enroll (probably patients comfortable with the use of connected device, or suffering from sleep disturbances …)

Response: Thank you for raising this issue. We have amended the section about recruitment to clarify what we expect about people who enrol to clarify the numbers discussed. We have also mentioned that we will be assessing for sample bias based on age and sex within the analyses paragraph (Pg 22, line 20; Pg 22 line 27).

- Study duration: is a 30 days period sufficient to assess quality of life fluctuations?

Response: This is an interesting point. People with RA describe daily fluctuations in pain, fatigue, mood and sleep problems. These factors are known to impact on quality of life and it reasonable to hypothesise associated short term changes in quality of life. This is certainly the case in juvenile arthritis (e.g. Klotsche et al, 2014: doi: 10.1002/acr.22112). While there is scant data available in adults that addresses this, there is support. For example, in-patients with rheumatoid arthritis reported significant improvements in quality of life over a 2 week period and that improvement was detected by the WHOQoL-BREF (Taylor et al, 2004; DOI 10.1002/art.20398).

- The choice to include patients with known sleep disorders (Sleep apnea syndrome, restless leg syndrome). Informations about of treatment, if any, and residual symptoms of these conditions should be assessed.

Response: We have now included discussion of this in a paragraph (Pg10, line23-48). We will adjust for diagnoses and treatment in our analysis.

- Which actographic variable will be used to assess sleep disturbances (sleep efficiency ? Total sleep time? Sleep fragmentation?)

Response: Thank you, we have included this information in paragraphs (Pg 15, line 53 onwards) along with some information requested by our other reviewers.

Minor points:
- Discrepancy in the number of expected participants between abstract “350 people with RA” and sample size section “a total of 175 participants”

Response: Thank you, we have revised the sentence and inserted a key statement which was missing. We do aim to recruit 350, but we envisage only 50% (n=175) will give us sufficient data. (Pg 22, line 20 onwards.)

- Many syntax issues: (for example: Introduction: “Occurrence between …the condition”, “Although there are…but…well-being”, Methods, Day 60: “participants wil be prompted…uMotif” etc…).

Response: Thank you, we believe we have amended all instances of these syntax issues.

Reviewer: 3
Reviewer Name: Awat Feizi
Institution and Country: Isfahan University of Medical Sciences Please state any competing interests: There is no competing interests

Please leave your comments for the authors below Please see attached file, you will find my comments on the body of submitted manuscript

Page 3 Line 10 - The title of manuscript should reflect content of study as possible, according to your study's objective that you have stated here
Response:Thank you, revised.

Page 3 Line 14 - majority of latent variable models need more participants, accordingly it is suggested to recruit more ones
Response: Thank you, please see our response below about our sample size.

Page 3 Line 29 - interrelationship is more appropriate, also the trajectory over time should be reflected in interrelationship evaluations
Response: Thank you, we have amended the sentence to reflect your comments.

Page 3 Line 32 - some primary descriptive finding should be presented as common in published protocols of studies
Response: Thank you for this, but we currently have no data to provide about our study participants.

Page 4 line 49 - how affect the different dimensions of HRQoL" is more appropriate for clarifying the study objective
Response: Thank you, we have amended the sentence to reflect your comments.

Page 5 Line 10 - this objective is not a generic one, you can follow it through conducting the objective 1, by stratified analyses based on age and gender, i suggest to consider an important and valuable aspect of current study i.e. the time varying evaluations and interrelationships

Response: Thank you for highlighting this. Objective 1 should have been listed as two separate objectives “Describe baseline….” And “Determine relative contributions….” This was a formatting issue and has now been amended. (Pg 5, line 31)

Page 5 Line 15 - I do not think the current study could follow this objective
Response: By identifying the factors which explain the most variance in HRQoL it will be possible for intervention mapping activities to take place. We reference this in the paragraph on Pg 25, lines 7-14. For example, if disrupted circadian pathways were found to be important drivers of poor QoL these can be advanced or delayed using phototherapy. It is likely that multiple pathways (e.g. sleep-wake cycle; sleep-wake cycle and pain; sleep-wake cycle and mood) will impact on QoL and an intervention “package” will be developed based on those pathways.

Page 7 Line 13 - more appropriate and more sensitive exclusion criteria should be considered, such metal problems that affect both QoL and sleep quality and so on , this section needs completion
Response: We wish to apply only minimal exclusion criteria to recruit a broad spectrum of participants. The reason why we exclude people who participate in shift work is because the mobile app we use cannot account for persons who follow an alternate sleep wake cycle.

Page 7 Line 19 - from this point forward more relevant headings for covering their contents are required , the presented tools should be accompanied by relevant references
Response: We have included the information about the study tools requested in paragraphs (Pg 9, line 37 – Pg 12, line 54) along with some information requested by our other reviewers.

Page 10 line 28 - it is very subjective, it is suggested to use more objective tools and manners if available
Response: We seek to understand the strength with which people endorse the belief that sleep affects HRQoL. There are no other tools available to measure this.

Page 10 line 47 - all presented instrument should be referenced and I suggest to consider a section with heading "study instruments" and briefly introduce them along with their reliability and validities
Response: We have included the information requested in paragraphs (Pg 9, line 37 – Pg 12, line 54) along with some information requested by our other reviewers.

Page 17 line 48 - this section needs major revisions, it is not based on relevant references , also it does not consider the main statistical models that have been planed to use i.e. SEM, The sample size determination should be based on, it is not clear and based on which reference effect size=0.2 and for which variables has been considered, the estimated sample size should be capable to handle stratified analyses more relevantly
As highlighted in our sample size section, our sample size calculation was based on the SEM analysis proposed. We used a method that has been proposed to determine a minimum sample size for SEM (Westland 2010; Soper 2012). For this method, we assumed a minimum expected effect size (defined as correlations between pairs of latent variables) of 0.2 (rated as small). Based on our hypothesised model using baseline and 60 day measurements containing 13 observed variables and 4 latent variables, with a significance level of 5% and power of 80%, a minimum sample size of 166 at is required.

In error, we omitted the references used to calculate this sample size. We now include the references and have provided some additional details about the formula used. We have also incorporated a section about the latent growth models in this section.

Page 19 Line 18 - please consider the relevant references
Response: Thank you, we have included two example references.

Page 19 Line 32 - how about the quantitative variables presentations, presentation based on subgroups such as gender, age, ...this subsection needs expansion
Response: Thanks you, we have expanded this section to detail the groupings of age and socioeconomic level which will be used in paragraphs Pg 24, line 4)

Page 20 Line 3 - please consider the repeated structure of data or multilevel structure according latent growth or trajectory models

Figure 5 displays a simple model of proposed relationships (highlighted in the caption). As discussed in the paragraph below this we do plan to account for multi-level data structure and conduct multi-level growth models. Pg 24, line 44 onwards.

Page 20 Line 23 - the considered sample size in current study could not provide the this situation , it is few for identifying meaningful class , also you should this important point regarding to stratified analyses in the considered subgroups and other potential subgroups that these latent variable models that need relatively large sample size are encountered with challenges

Based on the discussion of Curran et al (2010: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3131138/) we believe that our proposed sample size is sufficient for these analyses and have added mention of this into our sample size paragraphs (Pg 22, line 8-14)

Page 20 Line 38 - presenting some primary and descriptive findings from study participants, it is suggested to consider a section
Response: Thank you for this, but we currently have no data to provide about our study participants.

Page 20 Line 55 - How about the discussion section, limitations and strengths, although the current format is related to an undone study however it is common these sections in published protocols
Response: We have completed the protocol with respect to BMJ Open's minimum items required for study protocols (http://bmjopen.bmj.com/pages/authors/#studyprotocols). The strengths and limitations section (amended in line with the comments of other reviewers) is positioned immediately after the abstract. As requested a discussion section has been added.

Reviewer: 4
Reviewer Name: Agnieszka Pac
Institution and Country: Jagiellonian University Medical College Please state any competing interests: None declared

Please leave your comments for the authors below

Comment: This paper describes the study protocol of ongoing study. The paper was prepared very precisely and in details. The authors have not described exactly the study dates. However they described the dates of planned beginning of consecutive study waves.

The 3rd aim of the paper/study is about "possible" intervention - I would like to find out in the introduction section what kind of intervention can be undertaken in this situation. The authors have not specify also the target effect they would like to achieve by "hypothetical successful intervention".

Response: The target of a future intervention would be improvement in QoL since this is the outcome of interest here. There are many pathways that could potentially be targeted, and that will necessarily be dependent on the outcome of the analyses. For example, if disrupted circadian pathways were found to be important drivers of poor QoL these can be advanced or delayed using phototherapy. It is likely that multiple pathways (e.g. sleep-wake cycle; sleep-wake cycle and pain; sleep-wake cycle and mood) will impact on QoL and an intervention "package" will be developed based on those pathways.

The plan for the statistical analysis was prepared correctly. To answer the second aim two different method were planned - first SEM to identify the hypothesized association as well as mediation role of age and sex. The second one will allow to use fool set of information collected to confirm the associations from the SEM analysis.

Reviewer: 5
Reviewer Name: George A. Kelley
Institution and Country: West Virginia University, USA Please state any competing interests: None declared'

Please leave your comments for the authors below

GENERAL COMMENTS
The purpose of this proposed prospective cohort study is to examine the association between sleep and health-related quality-of-life in adults with rheumatoid arthritis using the mHealth approach. While this may be a worthy study to conduct, there is a lack of rationale provided by the authors to convince me of such. In addition, a lack of detail is provided on the proposed instruments to be used as well as potential limitations. Furthermore, the sample size justification given the proposed statistical analysis plan does not seem to be appropriate. Finally, the manuscript does not seem to have been proofread very well.

My specific comments appear below with page numbers referring to those listed in the top left and right corners of each page of the pdf document I reviewed.

SPECIFIC COMMENTS
* Page 3, Strengths and Limitations – Please list limitations of your study. For example, some of the biases associated with self-report, loss to follow-up, etc.
Response: Thank you, revised.

* Page 4, Introduction – Suggest that you cite and describe previous studies that have conducted research similar to your planned study and why your proposed study is needed. In other words, what gap exists that your study aims to fill. Ideally, it would seem that a systematic review on this topic should have been conducted to help justify the currently proposed study. If no previous research exists on this topic, then a statement from the authors that they are not aware of such "to the best of their knowledge" would seem appropriate.
Response: We have expanded the introduction to better highlight that although some studies have investigated the association between sleep and QoL, there have been a number of methodological challenges which mean that the data are not satisfactory to draw conclusions. Page 4-5.

* Page 4, line 5 – Insert "prospective" before "cohort"
Response: Amended

* Page 4, line 11 – Here and throughout the rest of the manuscript, I believe the reference is placed after a period or comma versus before a period or comma.
* Page 4, lines 12 and 13 – Please rewrite the sentence that begins with "Occurrence…"
Response: Amended

In the same sentence, suggest that you list the proportion(s) of women with RA who stop working as a result of the condition. Also, if there is any data on the economic costs associated with women who stop working due to RA, I would suggest that you include such.
The message conveyed in the original version of the protocol was not accurate due to various typographical errors. We have amended this section to reflect that RA impacts on the employment status of both men and women. We have amended our mention of the proportion to be more specific, but there are no reliable estimates of the true economic costs relevant to this available for citation in this paper.

* Page 4, line 22 – Suggest that you delete the word “but”
Response: Amended

* Page 4, lines 27 and 28 – Suggest that you rewrite the sentence that begins with “But sleep…”
Response: Amended.

* Page 5, line 11 – Delete “and” after the word “fatigue”
Response: Amended

* Page 6, line 43 – Suggest that you replace “are” with “will be”
Response: Amended

* Page 6, line 49 – Suggest that you place a comma after “criteria”
Response: Amended

* Page 6, line 52 - Suggest that you replace “are” with “will be”
Response: Amended

* Page 7, line 20 – Delete “a” before the word “three”
Response: Amended

* Page 7, line 54 – Suggest that you replace “is” with “will be” after the word “consent”
Response: Amended

* Page 8, line 5 – Suggest that you replace “is to” with “will”
Response: Amended

* Page 8, line 11 – Suggest that you insert the word “to” after the word “agree”. The same thing on line 14.
Response: Amended

* Page 8, line 41 – Suggest that you replace “are” with “will be” after “Participants”. On the next line, delete the comma after “on” and place a comma after “Initially”.
Response: Amended

* Page 8, line 57 – Delete “is completed”
Response: Amended

* Page 9, line 3 – Suggest you replace “are” with “will be”
Response: Amended

* Page 9, line 11 – Place a period after Table 1”.
Response: Amended

* Page 10, Table 1 – Suggest that you add current physical activity level as well as nutrition intake and state the instruments used to assess such.
Response: Thank you for this suggestion, however the study is already being undertaken and it is not possible to add in these additional items.

* Page 11, line 19 – Delete “the” before the word “provided”.

Response: Amended

* Page 11, line 46 – Replace “are” with “will be” before the word “immediately”.
Response: Amended

* Page 12, line 25 – Replace “responses” with “responded”.
Response: Amended

* Page 12, line 36 – Please provide validity and reliability data as well as the rationale for using the MotionWatch 8 versus another device.
Response: We have incorporated a paragraph detailing sources of validation data for the MW8 and our justification for selecting the MW8, based on the features it offers and the preference of patient focus group participants. Paragraphs (Pg 15, line 53 onwards)

* Pages 12 and 13 – Please rewrite the last sentence on page 12 and the first sentence on page 13.
Response: Thank you. We hope the amendments made improve the clarity.

* Page 13, line 17 – Replace “as” with “is” before the word “highlighted”.
Response: Amended

* Page 13, line 40 – Replace “are” with “will be” after the word “Participants”.
Response: Amended

* Page 15, line 43 – Replace “are” with “will be” after the word “reminders”.
Response: Amended

* Page 15, lines 47 through 51 – For all instruments used, please provide (1) a rationale for the selection of each (2) validity and reliability data, and (3) how each instrument is scored.
Response: Thank you, we have included these data within an expanded discussion of the baseline questionnaire measures (Pg 9, line 37 – Pg 12, line 54) and also include more information about the CSD (Pg 19, line 16-26)

* Page 16, line 31 – Replace “are” with “will be” after the word “participants”.
Response: Amended

* Page 16, line 44 – Replace “are” with “will be” after the word “copy”.
Response: Amended

* Page 16, line 45 – Delete “are” before the word “automatically”.
Response: Amended

* Page 16, line 55 – Insert “the” before the word “top”.
Response: Amended

* Page 17, Table 3 – For all instruments used and not previously described, please provide (1) a rationale for the selection of each (2) validity and reliability data, and (3) how each instrument is scored.
Response: Thank you, we have included these data within an expanded discussion of the baseline questionnaire measures (Pg 9, line 37 – Pg 12, line 54) and also include information about the CSD (Pg 19, line 16-26)

* Page 17, lines 47 through 54 – Since it appears that you propose to conduct structural equation modeling as your primary analysis, I would suggest that you re-estimate your sample size based on structural equation models. This includes (1) the anticipated effect size, (2) desired statistical power level, (3) number of latent variables, (4) number of observed variables, and (5) probability level.
Response: As highlighted in our sample size section, our sample size calculation was based on the SEM analysis proposed.

* Page 18, line 10 – In the abstract you list a sample size of 350 but here you say 175. Please clarify.
Response: Thank you, we have revised the sentence and inserted a key statement which was missing. We do aim to recruit 350, but we envisage only 50% (n=175) will give us sufficient data. (Pg 22, line 20 onwards.)

* Page 18, line 16 – Delete the comma after "study" and insert "and"
Response: Amended

* Page 18, line 18 – Delete the repeated "in".
Response: Amended

END OF REVIEW

VERSION 2 – REVIEW

REVIEWER	Laure Peter-Derex Sleep Medicine and respiratory Disease Center Hospices Civils de Lyon France
REVIEW RETURNED	16-Nov-2017

GENERAL COMMENTS	The paper has been improved. The authors have provided answers to many of my questions. Minor concern: - Abstract: The authors assume that rest/activity rhythm measured by actigraphy will be circadian, which is not sure. Moreover, they will have access to other information (sleep latency, sleep efficiency, total sleep time, wake after sleep onset) than rest/activity rhythm: I think the sentence "This study will identify sleep/wake rhythm-associated parameters that predict HRQoL in patients with RA" could be more appropriate. Most syntax issues have been addressed, there are some left (for example: Introduction "less total sleep time, unrefreshing sleep and…" instead of "less total sleeping time and etc…" or "studies which have been investigated…sleep and HRQol in RA") I have no further comments.

REVIEWER	Awat Feizi Isfahan University of Medical Sciences Iran
REVIEW RETURNED	29-Nov-2017

GENERAL COMMENTS	Thank you, as the last comment; Please complete the last section of manuscript with a short conclusion too

REVIEWER	Agnieszka Pac Jagiellonian University medical College
REVIEW RETURNED	27-Nov-2017

GENERAL COMMENTS	Description of the analysis of the last aim – effect of potential successful intervention is not described precisely. The model for this analysis should be indicated directly. The text should be checked carefully for some typo.

REVIEWER	George A. Kelley West Virginia University, USA
REVIEW RETURNED	21-Nov-2017

GENERAL COMMENTS	GENERAL COMMENTS Thank you for the opportunity to review this revised manuscript. Overall, the authors have done a good job in responding to my comments. However, I have one minor concern as well as one major concern, the latter of which was not identifiable in the original submission. First, I had previously suggested that the reference numbers should probably be placed after a period or comma, it was stated that this was done, but in my revised copy, this suggested error still appears as in the original manuscript. Second, I had suggested in my initial review that the assessment of current level of physical activity as well as nutrition intake, including the instruments to assess such, be added to the protocol and included in Table 1. However, in the authors' response, it was stated that the study is already underway and therefore, it's not possible to add these items. If the study is already underway, then I'm confused as to why a protocol was submitted for review and potential publication. This is especially true given that one of the very reasons for submitting a protocol for review is to actually try and improve the planned study and not just publish what was originally planned. This is very different than disagreeing with a reviewer about their suggestions. END OF REVIEW

VERSION 2 – AUTHOR RESPONSE

Reviewer: 2
Reviewer Name: Laure Peter-Derex
Institution and Country: Sleep Medicine and respiratory Disease Center, Hospices Civils de Lyon, France Please state any competing interests: None declared

Please leave your comments for the authors below

The paper has been improved. The authors have provided answers to many of my questions.

Minor concern:
- Abstract: The authors assume that rest/activity rhythm measured by actigraphy will be circadian, which is not sure. Moreover, they will have access to other information (sleep latency, sleep efficiency, total sleep time, wake after sleep onset) than rest/activity rhythm: I think the sentence "This study will identify sleep/wake rhythm-associated parameters that predict HRQoL in patients with RA" could be more appropriate.

Response: Thank you, we have amended this sentence and replace all other mentions of "circadian rest/activity parameters" with "sleep/wake rhythm-associated parameters".
Page 2, lines 10-11, 30-31.
Page 4, lines 24, 34, 39. 44
Page 24, lines 22, 27

Comment: Most syntax issues have been addressed, there are some left (for example: Introduction "less total sleep time, unrefreshing sleep and…" instead of "less total sleeping time and etc…" or "studies which have been investigated…sleep and HRQol in RA")

Response: we cannot locate the phrases "less total sleep time, unrefreshing sleep and…", nor "studies which have been investigated…sleep and HRQol in RA" in the revised document we submitted. No changes have been made.

I have no further comments.

Reviewer: 3
Reviewer Name: Awat Feizi
Institution and Country: Isfahan University of Medical Sciences, Iran Please state any competing interests: NO

Please leave your comments for the authors below

Comment: Thank you, as the last comment; Please complete the last section of manuscript with a short conclusion too

Response: We note the above recommendation from the Editorial team that this comment can be disregarded when writing the revisions.

Reviewer: 4
Reviewer Name: Agnieszka Pac
Institution and Country: Jagiellonian University medical College Please state any competing interests: None declared

Please leave your comments for the authors below

Comment: Description of the analysis of the last aim – effect of potential successful intervention is not described precisely. The model for this analysis should be indicated directly.
Response: Thank you we have revised the paragraph to be more specific about the methods we will use.
Page 25, lines: 13-27

Comment: The text should be checked carefully for some typo.

Response: Thank you we have had our manuscripts proof-read and have made the relevant corrections.

Reviewer: 5
Reviewer Name: George A. Kelley
Institution and Country: West Virginia University, USA Please state any competing interests: None declared.

Please leave your comments for the authors below
GENERAL COMMENTS Thank you for the opportunity to review this revised manuscript. Overall, the authors have done a good job in responding to my comments.

Comment: However, I have one minor concern as well as one major concern, the latter of which was not identifiable in the original submission. First, I had previously suggested that the reference numbers should probably be placed after a period or comma, it was stated that this was done, but in my revised copy, this suggested error still appears as in the original manuscript.

Response: Thank you for pointing out this oversight. We have now made these changes in the uploaded manuscript.

Second, I had suggested in my initial review that the assessment of current level of physical activity as well as nutrition intake, including the instruments to assess such, be added to the protocol and included in Table 1. However, in the authors' response, it was stated that the study is already underway and therefore, it's not possible to add these items. If the study is already underway, then I'm confused as to why a protocol was submitted for review and potential publication. This is especially true given that one of the very reasons for submitting a protocol for review is to actually try and improve the planned study and not just publish what was originally planned. This is very different than disagreeing with a reviewer about their suggestions.

Response: We have submitted this article to help prevent duplication of work and highlight the most up-to-date research on-going in this area. We note that BMJ Open guidance states that "Protocol manuscripts should report planned or ongoing research studies. If data collection is complete, we will not consider the manuscript".
We also note the above recommendation from the Editorial team that this comment can be disregarded when writing the revisions.