Author's response to reviews

Title: Prognostic Factors in Sciatica: A Systematic Review

Authors:

Julie Ashworth (j.ashworth@cphc.keele.ac.uk)
Kika Konstantinou (k.konstantinou@cphc.keele.ac.uk)
Kate M Dunn (k.m.dunn@cphc.keele.ac.uk)

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Author's response to reviews: see over
For the attention of:

Ms. Abigail Quiniquini
Journal Editorial Office
BioMed Central
BMC Musculoskeletal Disorders

Re: MS: 8626309875528135
Prognostic Factors in Sciatica: A Systematic Review
Julie Ashworth, Kika Konstantinou and Kate M Dunn

Dear Ms Quiniquini,

Thank you for offering us the opportunity to revise the above manuscript in light of the reviewers’ comments. We have set out a point by point response in the table below and have made the corresponding revisions in the revised manuscript highlighting the changes in red, along with some other minor amendments to the wording to enable the manuscript to remain within the permitted 2500 word limit. A Figures list and a Tables section have also been added to the manuscript.

We hope our revisions are acceptable to the reviewers.

Yours sincerely

Julie Ashworth

**Reviewer #1: Vicki Kristman**

1. **Methods, Methodological quality assessment:** A 17-item checklist was used to assess methodological quality where high quality studies were those that met all but two of the assessment criteria. Checklists can be used as a guideline for what to examine in studies, but should not be used to score quality. A global evaluation of study quality indicating belief in results would be a better indicator.

2. **Methods, Methodological quality assessment:** Studies were not excluded on the basis of methodological quality. This is fine for presenting in Tables such as Table 3 that give an overview of all studies published on the topic; however, it is not appropriate to be including poor quality or fatally flawed studies in evidence tables, such as Table 6. Poor studies do not provide good evidence and their inclusion may make a reader believe there is more evidence for or against an association than there really is.

1. We fully agree with reviewer that checklists used for assessing methodological quality do not necessarily guard against bias. However we feel the method is quite transparent and enables readers to assess for themselves the possible levels of bias. With the aim of making this clearer, we have amended Table 2 to include the details of the scoring for all the studies on the checklist we utilised. We hope that this is satisfactory for the reviewer given that a global evaluation of a study, although absolutely appropriate, may lead to bias as well.

2. We fully agree with reviewer. However sometimes the poor quality of a study is a function of poor reporting as opposed to poor methodology. This is the only reason we decided not to reject studies of seemingly poor quality. There is only one study of poor quality in our review and we have now, in line with the reviewer’s recommendation, removed it from the analysis presented in Table 6 (now Table 5) and added a comments to that effect in the methods section. The study remains in Table 5 (now Table 4) but with a note in the comments section regarding the poor methodological quality. We hope this acceptable to
3. Methods, Review Process: There is discrepancy between the text and Figure 1. The text indicates that all 3 authors reviewed all 23 potentially eligible articles, while the figure suggests that all 3 authors were only involved for disagreements where consensus was required.

4. Methods, Data extraction and analysis, second sentence: P-values are not that informative and are susceptible (always significant) to large sample sizes. Would be more useful to present findings for all prognostic factors examined in each study and provide effect estimates and 95% confidence intervals around those estimates, so readers can get a better idea of how study sample size influenced the findings.

5. Methods, Data extraction and analysis, third sentence: Didn’t all studies included have to have multivariate analyses as per the exclusion criteria?

6. Results, Tables 5 and 6: As stated earlier, poor quality or fatally flawed studies should not be included in these tables, especially table 6 as this provides a false level of evidence.

These two tables are also problematic because many diverse outcomes were measured (pain, function, disability, recovery or psychosocial measures) and all of these may not be influenced similarly by the prognostic factors under study. Therefore, Tables 5 and 6 should define the outcome under study for the particular factor listed.

7. Minor Essential Revisions
Methods, Exclusion criteria, first sentence: I don’t think the authors meant to exclude “studies evaluating a single prognostic factor” but rather those studies that evaluated a single factor in

the reviewer. The overall conclusion of the review remains unchanged; therefore we feel that this particular study does not contribute to misleading information.

3. We have corrected the text in Figure 1. All 3 authors independently reviewed the papers and the figure is now consistent with the main text.

4. We fully agree with the reviewer about the problems with p-values. Where possible, we have extracted and provided effect estimates and CIs, however this has not been possible for all studies, as the authors did not report this information and only provided p-values. We have made a point (which is now highlighted red) in the discussion about the limited value of p-values in prognostic studies.

5. The exclusion criterion relates to studies evaluating prognostic factors in isolation. All included studies looked at multiple predictor variables, however a few of the studies included did not use multivariate analyses. We have reported the statistical methods used for each study in Table 5 (now Table 4). We hope this is clearer now.

6. As mentioned previously, we have excluded the one study of poor quality (Komori et al 2002) from Table 6 (now Table 5) and altered the main text accordingly using track changes. This does not seem to change the overall conclusion much.

We fully appreciate that not all factors influence all outcomes equally. However, as is evident from the description of outcomes measured presented in Table 3, nearly all studies used a composite measure of recovery including a number of outcomes such as disability and pain in one scale so it is not possible to separate the effect of each predictor on each single outcome. We have however included details of the outcomes with the results in Table 5 (now Table 4)

7. We have corrected this in the text using
isolation, without consideration of other important factors. Sentence should be reworded.

**8. Abbreviations:** Should CT be Computed Tomography and not Quality of Life?

**9. Discretionary Revisions**

**Title:** May be helpful to indicate the non-surgical population in the title.

**Table 3:** If possible, would be easier for reader if Table 4 could be incorporated into Table 3 using one column titled “Sciatica definition”.

**10. Results, Tables 5 and 6:** After removal of poor quality or fatally flawed studies, it would be useful for readers to see the results stratified by methodological quality.

I don’t refer to methodological quality as the score calculated from the scoring tool, but rather more of a Phase analysis as suggested below:

Phase 1 studies are exploratory, hypothesis generating studies characterized by descriptive explorations and demonstration of crude (unadjusted) associations.

Phase 2 studies are also exploratory, but employ matching, stratification or multivariable analyses to identify independent risk or prognostic factors.

Phase 3 studies are confirmatory studies that test a priori hypotheses that test one or more factors as independent predictors of outcome (risk or prognosis).

These studies include explicit control for confounding factors.

**Reviewer #2: Frederieke Schaafsma**

**1.** I was surprised that the authors could find only such a limited number of studies that deal with the prognosis of sciatica. I was also a bit surprised that there was only one article that had to be excluded because it dealt with a combination of LBP and sciatica patients. I always thought that for the most part these were combined in the literature.

**1.** We agree with the reviewer that most studies refer to mixed populations of LBP and sciatica, but for any such study to be eligible for this review, results would have had to be reported separately for patients with sciatica. The reasons for excluding studies are detailed in the flow chart in Figure 1, most of the mixed cohorts were excluded in the earlier stages of the selection process and we assume the reviewer is referring to the only one excluded at the last stage of the study selection process.

In addition, we did not include studies exploring prognostic factors in surgical cohorts for the reasons explained in the text. We think that these are the reasons that we identified only a limited number of studies fitting the criteria of the review.
Discretionary Revisions:

1. I know that there are experts in the field who make a difference between severe sciatica (with motor mall function or sever nerve root irritation; e.g. paresis of foot lifters) or mild sciatica. When reading the definitions as described in the selected articles there is quite a mixture but no division between severe and mild sciatica. Further, in the literature regarding positive SLR testing there are authors who differ between very positive e.g. after 30 degrees or mildly positive.

2. The authors used a more general definition for sciatica, but I would like to know if they feel that some division in severity may have added value and may differ in terms of prognosis?

3. Although, the authors mention in the results section that there was some difference about the definition of sciatica in the included studies, I did not read a recommendation for future studies that they should all use the same definition. I think this would be a good recommendation?

4. The same issue goes for the different types of outcome measures. This makes it difficult to compare study results. From the literature in low back pain we know that people still suffering from low back pain may already have returned to their usual daily activities and returned to work. There are different factors that may influence these different outcomes. As is mentioned by the authors there is a huge amount of literature partly from occupational health studies. For returning to your work a good relationship with your manager and having the possibility to organize your work yourself is of big influence for a quick return to work. It would be interesting to know if this also goes for people suffering from sciatica.

5. The authors found one study studying the influence of heavy work but could not find an association. This is an interesting finding because in the literature there are studies reporting that heavy work may cause sciatica: Sørensen IG et al. Occupational and other predictors of herniated lumbar disc disease – a 33-year follow-up in The Copenhagen Male Study. 2011 Spine. There is also another interesting article about this issue:

1. It is possible that in clinical practice the differentiation between severe sciatica with significant neurological deficits and mild sciatica is made, however the studies described do not make such an explicit differentiation and do not describe the population according to these symptoms. However, a number of studies evaluate neurological deficits or SLR for their contribution to outcome (prognostic factors), we feel that this is the appropriate analysis for these factors in prognostic studies.

2. It was not possible to extract data on degrees of severity. We do feel however that if the data that denote severity, such as pain, SLR, neurological deficits are evaluated as prognostic factors then their contribution is explored and described in statistical terms. We hope this is satisfactory to the reviewer.

3. We fully agree with the reviewer on the point of consistency in definition of sciatica. We have made this clearer in the discussion and added a recommendation to the conclusion. The definition of sciatica now appears in Table 3 with the other study characteristics rather than in a separate Table – at the suggestion of reviewer 1.

4. We fully agree with the reviewer on the point of outcomes. However, most studies used composite measures to define recovery and as such some basic comparisons can be made amongst studies. We agree that work issues influence return to work. It will be an interesting research question for original research studies. We have now included the outcome measures used alongside the individual study findings in Table 4 (previous Table 5).

5. This review’s timeframe is 1980 to December 2010 and of the studies referred to by the reviewer were published after that date. On looking at the Sorensen et al study, it seems to investigate risk factors for first onset sciatica and as such it would have been excluded from our review anyway as our review includes only papers evaluating prognostic factors for persistence. Jensen’s recent paper is interesting, although it
| Predictors of vocational prognosis after herniated lumbar disc: a two-year follow-up study of 2039 patients diagnosed at hospital. By Jensen LD et al. Spine 2011 | deals only with vocational rather than clinical outcomes  
Maybe the authors could elaborate some more on this in their discussion?  
6. In the conclusion section authors should change no into not; first sentence. |
| --- | --- |
| We have added a comment to the discussion to reflect the fact that overall results from this review may change as new studies are published.  
6. We have now changed the wording of this sentence. |
| Reviewer #3: Freek Lötters | |
| Although the systematic approach of the review seems alright, the conceptionalization is what I’m worrying about. I will elaborate on this in my general remarks.  
General remarks.  
1. It starts with the rather broad definition of sciatica used in the review “pain down the leg which spreads below the knee”. It is questionable whether this is an accurate definition of sciatica. Medical anamneses and physical examination on neurological signs (eventually followed by radiological findings) will yield a much more accurate and valid definition. Than solely built on selfreported symptoms.  
2. Besides summing up the different definitions used by the included studies, the authors need to address this more in their manuscript. I have a bit a problem with the fact that the prognoses for sciatica is not well conceptualized. Prognosis says something about recovery. However the definition of recovery is broad as we can distinguish: medical recovery (i.e. diminished radiating leg pain; prolap withdrawal etc.), or functional recovery (i.e. persistent disability in daily life, being able to work etc.). So taken recovery in a broad sense makes it difficult to interpret the data in an accurate and valid way. The authors need to address this I there manuscript.  
3. In this respect it remains unclear what the authors mean with a ‘good outcome’ and a ‘poor outcome’. In table 6 only the poor outcomes found in at least three studies are addressed, however the study by Jensen (assessed as a high quality study) does show some significant good outcomes (defined by a combination of diminished pain intensity and functional disability). However these results are not are not considered further in the |
| 1. We fully agree with reviewer that self-reported sciatic symptoms are the least accurate definition. However, only one of the included studies relied on self-report. We have also discussed further now the role of definition and its effect on population selection with the condition of interest in the discussion and conclusion. We hope the reviewer finds this acceptable.  
2. Almost all the included studies used a composite measure of recovery which reflects their efforts to address various aspects of recovery. In recent times patient outcomes tend to dominate, such as pain, disability, return to work or a global improvement of recovery that may or may not include a medical assessment of physical symptoms and outcome. We have pointed out in the discussion that the variation in outcome measure causes difficulties in interpretation and recommended in our conclusion that future studies should consider using at least a number of core outcome so comparisons and pooling of results from different studies is achievable.  
3. The definition of ‘poor’ or ‘good’ outcome is not defined by the authors of this review. It is taken as it is stated in the studies included. Most authors reported predictors of poor outcome whereas Jensen reported predictors of good outcome. These are mentioned in the text and are now highlighted. We hope this is satisfactory. |
4. The background paragraph is very short. I miss the context of the research. Why is it important to know what the prognostic factors are for sciatica? And what perspective is been taken? The perspective of the medical doctor, societal perspective, treatment perspective? Now it looks like they are all taken into account, resulting in a review with heterogenic studies. This is related to my foregoing remark on the kind of recovery that is taking into account.

Whether patients got a treatment or even the kind of treatment was not in the inclusion criteria. Only chirurgical procedures where excluded. However, the kind of treatment (even usual care) might influence the prognoses of sciatica. In all studies except one there was some kind of treatment applied. The authors need to say something about treatment influencing the prognosis. Also hospitalization was no inclusion or exclusion criteria, whereas this might be an indication of severity of complaints. People with high pain intensity or high functional disability tend to visit a medical specialist more often. Although most study included were on hospitalized patients, some were not and this might obscure the results of the review.

5. An other issue that is omitted in the manuscript is the natural course (or prognosis) of radiculopathy; approximately 80% will be free of symptoms after 3 months. Medical guidelines also state not to interfere (except for pain killing) in first weeks and advice patients to stay active as much as possible. So, it would be appropriate to know what prognostic factors are for those with neurological signs due to a disc prolaps after 3 months of onset of the complaints. However, this aspect is not addressed in the manuscript.

Discussion.
6. Comparing studies on non-specific LBP and sciatica (specific LBP) is (in my opinion) evaluating the difference between apples and pears. Sciatica (radiating pain below the knee) is due to specific pathology in the lower back (disc prolap). Long lasting sciatica is approached much

4. The relevance of knowing prognostic factors in sciatica presentations is related to the possibility of tailoring treatment that may optimise outcome as oppose to ‘one size fits all’. It may be that patients with certain characteristics for example very severe pain or disability or prolonged duration of symptoms may be more at risk of a poor outcome (however this outcome is defined; in most cases it is disability, time off work etc). And it may be that in these patients more treatment or early treatment or specific types of treatment may be more effective. We have tried to make this more explicit in the text.

We fully agree with the reviewer that treatment may influence outcome. With the exception of one study which was population based (Miranda et al), in all other studies treatment was applied. The nature of the treatment is given for each study in Table 3. In the literature in general, with the exception of one study only (Weber et al), all studies involving sciatica patients (or LBP patients) tend to describe clinical course and prognostic factors on clinical cohorts (either receiving surgical interventions or conservative treatment only or both) rather than the natural history.

5. We did not feel that natural course of radiculopathy in the first 3 months was one of the aims of our review, although we fully agree with the reviewer’s comments about natural course and guidelines’ recommendations in terms of active treatment. The shortest follow-up period of an included study is 3 months, therefore all included studies deal with prognosis beyond 3 months. The specific question of the reviewer about prognostic factors in patients with neurological signs due to a disc prolapse was simply not one of the aims of this review. However, we agree it is an interesting question and perhaps a question one could address in future studies or reviews.

6. We agree with the reviewer that Sciatica and non-specific LBP and rather different conditions. The comparison with LBP studies was made simply to illustrate the disparity in terms of the volume and breadth of evidence available in terms of prognostic factors for these 2 conditions. To date it would appear that there is little evidence one way
more medically (eventually with surgery) whereas long lasting a-specific low back pain is approached from a cognitive behavioural way. In this regard it is recognized that the prognostic factors are different. As said before, the rational of knowing prognostic factors should be addressed more, also in the discussion.

Tables.

7. In the result section you mentioned that also in the study of Carregee et al. radiological findings were used. However this is not mentioned in table 4.

8. In table 5 (and also in the result section) the strength of association for the study by Carregee et al is presented as $R=0.50$. Why did you present $R$ and not an OR as measure of association? The authors of that study conducted logistic regression analysis, hence probably presented their result with ORs.

9. Also in table 5 the results of the study by Hasenbring et al. are presented by Beta (coming from the multiple regression analysis). However in this way it is hardly informative. You need to know the measurement level and model as a whole in order to be able to interpret these data. Moreover you described that pain intensity was the only outcome in that study. Was pain intensity the dependent variable in the regression analysis? If so how does the analysis contribute to the knowledge on sciatica prognosis? Pain intensity itself is not synonymous for sciatica.

10. In table 6 you mentioned that the study by Miranda et al. did show no association between smoking and a poor outcome of sciatica. However in table 5 you presented a significant OR of 2.3 for the factor ‘ex-smoker’. You need to check this.

or the other regarding the influence of psychosocial factors in conservatively managed sciatica cohorts so it is difficult to say, on the basis of the current literature, how much the two populations differ in that regard. We have highlighted why we feel the study of prognostic factors is important in the text.

7. We have amended the table accordingly, although this information is now contained within Table 3 rather than in a separate Table 4. The patients were selected for phase 1 of the study (which looked at disc morphology) based clinical symptoms and signs of sciatica, but all patients did have an MRI scan and those with a normal scan were excluded prior to phase 2 which is the part of the study dealing with prognosis.

8. We agree with the reviewer that odd ratios should be reported as a measure of association but unfortunately the authors did not report odds ratios, they reported only $R$ and a $p$ value.

9. Again we agree with the reviewer regarding the issue of odds ratios but the authors presented only beta values. In the absence of any odd ratios, we included the beta (rather than B) values because they are standardised regression coefficients (i.e. they do not have a unit of measurement) so they at least give us an idea of the relative importance of the various predictors. We also agree that pain intensity is inadequate as the sole outcome measure in sciatica, although we do feel that pain intensity is a valid measure of one aspect of outcome. Unfortunately the authors did not include any other outcome measures relating to function, but the paper met our inclusion criteria and given that the outcome measures used are given along with the study characteristics and the results we hope this acceptable.

10. We were also surprised by the Miranda study which found that neither current smoking nor being a life-long non-smoker was predictive of poor outcome but that being an ex-smoker did predict poor outcome with an odds ratio of 2.3.