Author’s response to reviews

Title: Predictors of Pain and Use of Pain medications following Primary Total Hip Arthroplasty (THA): 5,707 THAs at 2-years and 3,289 THAs at 5-years

Authors:

Jasvinder A Singh (jasvinder.md@gmail.com)
David G Lewallen (david.lewallen@mayo.edu)

Version: 2 Date: 17 April 2010

Author’s response to reviews: see over
We thank the reviewers for their comments. Below are our point-by-point responses to each comment.

Reviewer's report
Title: Predictors of Pain and Use of Pain medications following Primary Total Hip Arthroplasty (THA): 5,707 THAs at 2-years and 3,289 THAs at 5-years
Version: 1 Date: 23 March 2010
Reviewer: Roger Componovo
Reviewer's report:

Discretionary Revisions
1) Outcomes of Interest, last paragraph. Why did you group oral steroid users in with “none” in terms of pain medication usage. It seems that if they are using steroids, they are having pain. It should be lumped in with one of the other categories.

A: We made an a priori decision to lump steroids with none category due to three reasons: (1) a very small proportion of patients used steroids (<1% each for 2- and 5-year cohorts), therefore it was not large enough a category to perform any analyses-addition ; (2) Due to small numbers (<1%), we determined it was unlikely to impact the reference group of “no medications (>85% of cohort) due to difference in size by more than 80 times; and (3) oral steroid used for treating joint or systemic inflammation could be related to pain indication in some but not in other patients.

“Oral steroids are used for reducing joint and/or systemic inflammation, usually but not always associated with significant pain and some patients may be chronically steroid-dependent. Additionally, only a small fraction of patients reported oral steroid use, making it impossible to analyze as a separate outcome.”

2) Page 9 first line- Our findings suggest that screening for depression prior to surgery…” I think we need to be careful about the conclusions regarding depression in this study. The trend at 2 years did not carry over at 5 years. The authors don’t make any explanations for this. To me, since the trend did not carry over to 5 years, I can’t really say the conclusions at 2 years are valid. Furthermore, it should be pointed out that those who are depressed may score their pain in a higher category based on their psychiatric illness rather than actual pain.

A: We have added the statement regarding depression and pain perception as suggested.

The 2-year associations were significant, not trends -p-values <0.01 for moderate severe pain and p=0.02 for opioid medication use. We have clarified that significant associations were seen only at 2-years.

We agree that at 5-years the association was not significant. We have now added a statement and discussion pertaining to this. The revised portion indicates these changes.

“Our findings suggest that screening for depression prior to surgery may help identify patients at-risk for poorer pain outcomes and opioid use 2-years after THA. One of the potential explanation of baseline depression with 2-year outcomes may be higher pain perception and
reporting by those with depression than those without depression. Further studies need to examine if treatment of depression in the pre- or post-operative improves pain outcomes and opioid medication use 2-years after THA. At 5-years, these associations were not significant. The lack of significance with 5-year outcomes may be due to smaller sample size at 5-years compared to 2-years, longer duration since depression diagnosis or simple lack of any association at 5-years. “

3) Summary Paragraph- I don’t agree with second sentence. I don’t think we can really conclude much about the depression data

A: We have now modified the statement to reflect that depression associations with moderate-severe pain were significant only at 2-year follow-up and insignificant at 5-years. A much smaller sample size at 5-years compared to 2-years may be responsible for lack of association at 5-years, which is still in the same direction as the 2-year (odds ratio higher than one), but not significant.

“In summary, we studied pain severity and use of pain medications 2- and 5-years primary THA in a large cohort of patients. We noted significant impact of BMI on moderate-severe pain and use of pain medications 2- and 5-years after THA. Associations with depression with moderate-severe pain were significant at 2-years, but not at 5-year follow-up.”

General Comments
1) Some good points raised here. I am always cautious about conclusions from Regression Analysis studies, but I do think that the study is well done and that it accomplishes its goals.

A: We thank the reviewer.

2) The prevalence of pain reported 8.1% at 2 years and 10.8% at 5 years is quite interesting. I don’t think that most of us counsel our patients preoperatively about this. We all talk about failure rates and infection, etc, but this is a very important finding that should be a part of any preop counseling session.

A: We agree and have added a sentence in discussion based on the comment from the reviewer.

“In this large sample of patients, we provide estimates of moderate-severe pain at intermediate-term follow-up after primary THA. This information can be provided at pre-operative counseling so that patients have realistic expectations from the procedure.”

3) The response rates of 62% and 53% are very concerning. This could have a tremendous affect on the data in this study.

A: We acknowledge non-response bias in the limitations section. However for large surveys of this size average response rates of 60% have been reported in a meta-analysis of response rates, as we quote. We presented the characteristics of non-responders and discussion of how the characteristics in which responders and non-responders differ could bias findings. These biases make our study prone to make conservative estimates, i.e., the associations noted in our study may in fact be stronger, had all patients responded.
“Our study has several limitations. Non-response and referral bias may limit generalizability to
general populations. The response rate of 62% at 2-years and 53% at 5-years, is similar to the
average response rate of 60% in large surveys of this size (37). A higher response rate is
always more desirable. The estimates of association in this study are conservative, since non-
responders were more likely to be younger, have ASA class III-IV and live >100 miles away
from the medical center, same categories that also reported more pain.”

4) Areas to strengthen the study:
   Report pain as a score based on a visual analog scale.
   Record how many patients took narcotics before surgery.
   Record how many had moderate/severe pain before surgery. Although we
   presume this was an indication for surgery, we don’t know how the patient would
   have categorized their pain based on this scale.

   A: As requested by the reviewer, we now provide the number of patients who had
   moderate/severe pain before surgery. This was 95% for both 2-year and 5-year cohorts. The
   pain data were collected on a categorical scale, not visual analog scale. We do not have record
   of narcotic use before surgery.

   “95% of patients each from 2-year and 5-year follow-up cohorts reported moderate-severe pain
   in the index hip at pre-surgery evaluation.”

   Level of interest: An article of importance in its field
   Quality of written English: Acceptable
   Statistical review: No, the manuscript does not need to be seen by a
   statistician.
   Declaration of competing interests:
   I declare that I have no competing interests

Reviewer's report
Title: Predictors of Pain and Use of Pain medications following Primary Total Hip
Arthroplasty (THA): 5,707 THAs at 2-years and 3,289 THAs at 5-years
Version: 1 Date: 16 April 2010
Reviewer: Alison Rosemary Harmer
Reviewer's report:
Is the question posed by the authors well defined?
Yes, authors propose to examine pain and predictors of use of pain medications
after THA; and this is what is reported in Methods and Results.

A: We thank the reviewer.

Are the methods appropriate and well described?
1. Methods are appropriate; however, a minor point is that method of calculation
   of odds ratio needs to be explicit; or an appropriate reference quoted.

A: We have added an explanation of odds ratio as suggested.
“The odds ratio defines the risk of an outcome in those with the risk factor compared to those without, such that a number >1 indicates higher occurrence of the outcome in those with each specific risk factor. “

Are the data sound?
2. Yes. Although a retrospective analysis (and hence detailed analysis of depression/anxiety not available – as the authors acknowledge), the existing data were collected prospectively. Survey response rate is somewhat poor (but typical) at 5 years, especially considering that participants were telephoned if they did not respond to mailed surveys or did not attend follow-up clinics. Reasons for non-response are not detailed. However, given the size of the cohort and the fact that non-responders possessed characteristics that were typically associated with worse pain (and hence data represent conservative estimates), I do not believe that response rate is a major issue of concern in this study.

A: We agree with the comment and have this as a study limitation.

Does the manuscript adhere to the relevant standards for reporting and data deposition?
3. Minor essential revisions: The authors do not report the cut-off date for their cohort ‘recruitment’, i.e.. all patients undergoing THA since 1993 appear to be included; however, no end date is specified. Exclusion criteria are not specified. One of the reference papers (Rand et al, 2003; Ref 18), which reports upon total knee replacement, specifies exclusion of patients with malignancy, partial or revision replacements; however, these criteria can only be partially applicable to the THA cohort presented here. Although the authors state the response rate in the present analysis, and hence it is possible to calculate the total number of patients who underwent THA, there is no statement regarding actual numbers of patients who were eligible to be included in this retrospective study. Eligibility is discussed in other recent publications by the authors (Refs 22-25); however, these are all in relation to patients who have had TKA, not THA. Albeit a retrospective analysis, a flowchart or at least a statement regarding patient numbers, exclusion criteria, number excluded (and reasons), etc would assist with clarity for the reader in the present paper.

A: WE clarify the time-frame, the number eligible and eligibility criteria as requested by the reviewer.

“The study cohort consisted of all patients who underwent primary THA at the Mayo Clinic, Rochester between 1993 and 2005 and were alive at the 2- or 5-year follow-up. We did not restrict by age group or diagnosis. A total of 9,154 THAs at 2- and 6,243 THAs at 5-year were eligible for the study.”

“The characteristics of responders at 2- and 5-years were similar, as described in Table 1. The survey response rate was 62.3% (5,707/9,154) at 2- and 52.7% (3,289/6,243) at 5-years post-primary THA. In this study, we studied 5,707 primary THAs at 2-years and 3,289 primary THAs at 5-years.”
Are the discussion and conclusions well balanced and adequately supported by the data? Yes.
Are limitations of the work clearly stated? Yes.
Do the authors clearly acknowledge any work upon which they are building, both published and unpublished? Yes, quoted.
Do the title and abstract accurately convey what has been found? Yes: title; Yes: abstract.

A: We thank the reviewer.

Is the writing acceptable?
Needs minor essential revisions for typos and expression as detailed here:
Abstract
4. Conclusion, first line: Insert a semi-colon after “pain”, i.e. “moderate-severe pain;...”
A: Done as suggested

Introduction
5. Paragraph 2, line 1: Insert “pain” before “outcomes after THA?”
A: Done as suggested

6. Paragraph 3, line 1: Change “in” to “of”, i.e. “Non-modifiable factors of interest...”
A: Done as suggested

7. Paragraph 3, line 2: Remove the word “pain” occurring between “outcomes pain post-primary...”
A: Done as suggested

8. Paragraph 3, line 3: References (7, 12) (9) should all be included within one bracket, i.e. (7, 9, 12).
A: Done as suggested

9. Page 4, first 2 lines: missing words. “…female gender associated with less post-operative pain...”
A: Done as suggested

10. Page 4, paragraph 2, line 3: missing word. “…associated with worse pain outcomes...”
A: Done as suggested

Methods
11. Page 4, para 3, last sentence: The authors refer to their previous publications, stating that the questionnaires were administered to patients with both knee and hip replacement, however, all these references (Refs 22-25) report on data for patients after total knee replacement. Please revise this sentence.

A: We have added reference for hip questionnaire as suggested, apologize for the overlooking.

12. Page 4, last paragraph, line 6: insert a semi-colon after “…is moderate-severe hip pain; …”

A: Done as suggested

13. Page 5, line 2: uncapitalise the ‘e’ of “and (3) Even…”

A: Done as suggested

14. Page 5, para 2, line 1: Change the ampersand to “and”

A: Done as suggested

15. Page 5, para 2, line 3: missing words. “…operated hip? Responses could include…”

A: Done as suggested

16. Page 5, para 2, line 4: Why was oral steroid use considered as a reference response? Oral steroids are sometimes used for pain (albeit not for hip pain); perhaps a brief sentence could clarify this for the reader.

A: Done as suggested

“…Oral steroids are used for multiple conditions including lung disease usually without pain, arthritic conditions with pain such as rheumatoid arthritis and immune conditions without pain such as lupus or vasculitis without significant pain. In addition, small fraction of patients reported oral steroid use, making it impossible to analyze as a separate outcome.”

17. Page 6, para 2, 4th last sentence: Remove “is” from “…Mayo Clinic is provides…”

A: Done as suggested

18. Page 6, para 2, 4th last sentence: Insert italicized words/letter and change comma to semi-colon between “…expectation, both…” “…since the Mayo Clinic provides THA as a primary medical center for the local residents, but is also a referral center for patients traveling from afar, who may have different severity of disease and different level of expectation; both can impact pain outcomes.”

A: Done as suggested

19. Page 6, para 2, 2nd last line: please confirm how odds ratios were calculated.
A: Odds ratio were calculated in the standard fashion using logistic regression analyses. We have added a statement as suggested by the reviewer.

20. Page 6, para 2, last line: Should it be “excluding one”? (However, a few of the results presented in the Tables do have a lower bound that equals one...so perhaps should remove “excluding” and instead write #1.)

A: Done as suggested

Results
21. Table 1. Legend. “Legg Parthe’s” should be corrected to “Legg-Calvé-Perthe’s”

A: Done as suggested

22. Table 2. Anxiety and Depression in left-hand column both have a surplus comma after Ref; and it would be clearer to the reader to title the reference category as “none”, rather than “no”. (The latter comment also applies to Table 3.)

A: Done as suggested

23. Table 3. BMI > 40. Data need to be bold for both 2- and 5-year results. Ditto for Depression at 5 years.

A: Done as suggested

24. Table 4. Legend under Table 4 differs in configuration from other tables.

Discussion
A: Done as suggested

25. Page 9, para 2, 2nd last sentence: Remove “and” from “…WHO classification (27), and since…”

A: Done as suggested

26. Page 10, para 3, line 5: Insert “i.e., the” between “…center, same…”

A: Done as suggested

27. Page 10, 2nd last line: Insert semi-colon after “…questionnaires”

A: Done as suggested

28. Page 11, para 2, line 1: Insert “after” following “…2- and 5-years…”; and remove the hyphenation from 2- and 5-years.

A: Done as suggested
29. Page 11, para 2, line 3: Insert “are” between “factors amenable”.

A: Done as suggested

Level of interest: An article of importance in its field
Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:
I declare that I have no competing interests.