BMJ - Decision on
Manuscript ID
BMJ.2018.043530.R
1

Body:

27-May-2018

Dear Mr. Palmer,

Manuscript ID BMJ.2018.043530.R1 entitled "Arthroscopic Hip Surgery compared with Physiotherapy and Activity Modification for the Treatment of Symptomatic Femoroacetabular Impingement: A Multi-Centre Randomised Controlled Trial"

Thank you for sending us your revised paper. We sent it back to the original peer reviewers and our statistician. Our statistician has some remaining concerns that we hope you will be able to address in another revision.

We are looking forward to reading the revised version and, we hope, reaching a decision.

Very truly yours,

Elizabeth Loder, MD, MPH
eloder@bmj.com

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** Comments from the external peer reviewers**

Reviewer: 1

Recommendation:

Comments:
I believe the authors have satisfactorily addressed reviewers' comments. This is an important study to the field. I look forward to seeing its publication soon.

Additional Questions:
Please enter your name: Yun Peng

Job Title: Research Fellow

Institution: Orthopaedic Surgery, Massachusetts General Hospital

Reimbursement for attending a symposium?: No

A fee for speaking?: No

A fee for organising education?: No

Funds for research?: No

Funds for a member of staff?: No

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Reviewer: 2

Recommendation:

Comments:
The authors responded very well to my comments. I think this is a relevant and well executed study.

Additional Questions:
Please enter your name: Sita Bierma-Zeinstra

Job Title: Professor

Institution: Erasmus MC - University Medical Center Rotterdam

Reimbursement for attending a symposium?: No

A fee for speaking?: No

A fee for organising education?: No

Funds for research?: Yes

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and Development, Dutch Arthritis Foundation, CZ, Nuts Ohra, and Stichting Coolsingel.
My university received consultancy fees based on my expertise of Infirst Healthcare.

Reviewer: 3

Recommendation:

Comments:
BMJ.2018.043530.R1 entitled "Arthroscopic Hip Surgery compared with Physiotherapy and Activity Modification for the Treatment of Symptomatic Femoroacetabular Impingement: A Multi-Centre Randomised Controlled Trial" for BMJ

I thank the authors for their revision and detailed response to my comments. Upon re-reading, I have some additional suggestions. Many relate to the same points as previously.

1) I did not understand the following sensitivity analysis "Primary analysis was also repeated with the baseline 'expectation' HOS ADL as a covariate" – what is the expectation of the baseline value and how was it calculated? Why is this needed over and above a simple adjustment for observed baseline value?

2) As mentioned before, the pre-defined subgroup analyses categorise age and baseline value at arbitrary cut-points. This loses information, and renders the investigation meaningless. E.g. those at age 39 cannot really be that different from those age 41, and yet the cut-point of 40 is used. Indeed, this age analysis identifies a difference in those above and below aged 40 – but how can we interpret this? The treatment effect does not truly jump when moving from 39 to 40 year old. Better would be to consider age and other continuous variables their original continuous scale, and even allow a spline (non-linear) function.

I asked the authors about this upon first revision, and they do not revise the manuscript in this regard. They do explain to me that they did do some other analyses (e.g. with age as linear), but do not include them. However "they would be agreeable to including this data at your request". I would like this to be addressed please. They argue against including age as linear saying that "We have concerns over the robustness of this observation due to the limited data in older age groups, the dataset not being sufficiently powered for this analysis, and the likelihood that the effect of age may not be adequately modelled by a linear relationship"

- however, I do not find these arguments as concerning as choosing the 40-year cut-point (which is meaningless as mentioned, and loses about 1/3 of the power when age is modelled as continuous). There are many references on the need to handle continuous variables as continuous, such as refs 1 2 An excellent blog on this subject is here: http://biostat.mc.vanderbilt.edu/wiki/Main/CatContinuous

3) The authors note that the observed difference 'exceeded the MCID'. I would not use the MCID abbreviation for minimally-important clinical difference. Moreover, the CI for the true treatment effect (6.4 to 13.6) contains values below 9 (the defined MCID), and so – if the authors truly want to make a strong statement about whether the effect is above the value of 9 – it would seem important to also state that some of the evidence is in accordance with a value below 9. This is often not mentioned, however.

Therefore, there is a tension in the current manuscript about whether there is strong evidence of an important treatment effect here, or actually whether it is inconclusive.
The authors often draw attention to the effect being greater than 9, but do not draw attention to the CI containing values < 9.

This issue was raised in the first review. But it remains prominent (e.g. see abstract, results, and start of discussion) in many places without a more balanced view. The authors have added a note in their conclusion at the end of the Discussion saying: "However, further research is required to identify patients most likely to benefit from intervention given a significant proportion of patients did not achieve a clinically important improvement". Though potentially true, this is not the same issue. Variability in patient responses may indeed make some patients respond with a smaller improvements than other patients. However, the main focus of the original MCID is on whether the overall (mean) effect (across all patients) is at least 9. Therefore, the main question is whether the mean effect is clinically important, let alone whether all patients would always get a big improvement themselves.

The further discussion about whether all patients achieve a clinically important benefit is a further complication. In their response it is stated that "However, only 51% patients receiving arthroscopic surgery exceeded this MCID (assuming the MCID of 9 points is valid for our cohort). " – but I do not see how 9 is derived for an individual patient. The MCID relates to a 9 mean point improvement in one group compared to another. But at the patient level, there is no direct comparator. So we cannot say this patient did 9 better than if they had been in another group. So, do the researchers refer here to a patient improving by at least 9 to be important (without comparison). But why is 9 points relevant as both an absolute change (for the individual) and a difference (in the mean difference in one group compared to another)? More clarity is needed.

May I suggest that the authors revisit all their discussion about clinically important differences in the paper. I understand why MCID are useful in sample size calculations, but I find the current emphasis on this in the results and interpretation to be quite confusing and I sense other Editors do too.

4) Given the large missing data (e.g. only 80% were complete in the physio group), it would seem important to have a clear sub-section in the results about the findings when missing data were handled through imputation and other approaches. That is, at the moment it is just mentioned in a brief sentence and the supp material that missing data analyses did not change the findings. But this needs more prominence I feel. Related point is that more details are needed about exactly how the multiple imputation was done in the methods, and also to explain what the 'rctmiss command in Stata' is actually doing/ assuming. The response gives good details, but not the revision. May I also ask whether the outcome values were included in the imputation model, as recommended (e.g. see 3)
5) The results per centre in the response are interesting, and the forest plot would be welcome addition to the supplementary material.

I am confident the authors can address these points in their second revision, especially as their response document was very clear.
Best wishes, Richard Riley

Reference List

1. Altman DG, Royston P. Statistics notes: The cost of dichotomising continuous variables. BMJ 2006;332::1080.
2. Royston P, Altman DG, Sauerbrei W. Dichotomizing continuous predictors in multiple regression: a bad idea. Stat Med 2006;25(1):127-41.
3. Moons KG, Donders RA, Stijnen T, et al. Using the outcome for imputation of missing predictor values was preferred. J Clin Epidemiol 2006;59(10):1092-101.

Additional Questions:
Please enter your name: Richard Riley

Job Title: Professor of Biostatistics

Institution: Keele University

Reimbursement for attending a symposium?: No

A fee for speaking?: No

A fee for organising education?: No

Funds for research?: No

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