PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Can obesity and physical activity predict outcomes of elective knee or hip surgery due to osteoarthritis? – A meta-analysis of cohort studies.
AUTHORS	Pozzobon, Daniel; Ferreira, Paulo; Blyth, Fiona; Machado, Gustavo; Ferreira, Manuela

VERSION 1 – REVIEW

REVIEWER	Ethan Kuperman University of Iowa United States
REVIEW RETURNED	26-Jun-2017

GENERAL COMMENTS	This is a well-written and thorough examination of the impact of obesity on elective arthroplasty outcomes. It adds to the current literature and would be useful within the orthopedic community. Addressing the following, generally minor, concerns might somewhat improve the paper: 1. The abstract does not provide clarification on the magnitude of the effect of obesity on pain, disability, and postsurgical complications. 2. I do not see a figure 1 in the attached files. 3. The number of significant figures displayed is too high on the I2 values (we do not need 3 decimal points for this number in the figures) and P values < 0.001 are typically not displayed as 0.000 even if very small (as in the short- and long-term pain differences). 4. The values of the standardized mean differences for most of the outcomes reported, while statistically significant, were of a generally small magnitude (most < 0.5). The authors interpreted these as both clinically and statistically significant results. Would it be possible to demonstrate, in terms of an absolute percentage of patients (or some other absolute quantity) the clinical significance of these findings? This would enhance the strength of the current conclusions. 5. I don't see where the results from the first sentence, second paragraph of discussion are derived: (e.g. 70% symptom improvement at 6 months). If this comes from an earlier work by the same group, the citation is missing.

	6. The comparison of the # of studies with Liu et al in the discussion is somewhat misleading--that team was only looking at hip arthroplasty, which may explain why this combined knee and hip study had a larger N. (in the "strengths and weaknesses in relation to other studies" paragraph of the discussion).

REVIEWER	Olalekan Uthman University of Warwick, UK
REVIEW RETURNED	19-Jul-2017

GENERAL COMMENTS	The manuscript reads well. The systematic review and meta-analysis was well performed and up to standard. However, my only concern was similar recent systematic reviews on the topic. This beg for why this additional meta-analysis was conducted. Though, the authors tried to justify why their meta-analysis is more comprehensive in the discussion section.

REVIEWER	Nick Clement Freeman Arthroplasty Unit Newcastle Upon Tyne UK
REVIEW RETURNED	17-Aug-2017

GENERAL COMMENTS	The authors should congratulate on an excellent study. I have read this paper several times and have enjoyed it; learning something new each time. I am unable, despite my best efforts, to find any major flaws to prevent publication in the Journal. There is only two small points I would like to highlight for amendment: In the methods the authors state an exact methodology for identification of the literature through specific search engines. Then in the results the authors state they found 26 additional studies from elsewhere. This sounds like they have included them by choice. I feel either these 26 are not included or amend the methods to allow inclusion by whatever search criteria they were found. Second: tables 4 and 5 – Ollivier reference has 20012 should be 2012

VERSION 1 – AUTHOR RESPONSE

Reviewer #1

1. The abstract does not provide clarification on the magnitude of the effect of obesity on pain, disability, and post-surgical complications.

Response: We have edited the abstract and added the requested information.

Results: 63 full papers were included in this systematic review. From these, 31 were included in the meta-analyses.
Our meta-analysis showed that non-obese participants tended to suffer less pain at both short (SMD -0.43; 95%CI: -0.67 to -0.19; p<0.001) and long term (SMD -0.36; 95%CI: -0.47 to -0.24; p<0.001), less disability at long term (SMD -0.32; 95%CI: -0.36 to -0.28; p<0.001) and report fewer post-surgical complications at short (OR: 0.48; 95% CI: 0.25 to 0.91; p<0.001) and long term (OR: 0.55; 95% CI: 0.41 to 0.74; p<0.001) and less post-surgical infections after hip arthroplasty (OR: 0.33; 95% CI: 0.18 to 0.59; p<0.001), and particularly when compared to morbidly obese participants after knee arthroplasty (OR: 0.42; 95% CI: 0.23 to 0.78; p=0.006).

2. I do not see a figure 1 in the attached files.

Response: We apologise for the missing figure. We will make sure all the relevant appendixes files are correctly uploaded on the submission process of the reviewed version.

3. The number of significant figures displayed is too high on the I2 values (we do not need 3 decimal points for this number in the figures) and P values < 0.001 are typically not displayed as 0.000 even if very small (as in the short- and long-term pain differences).

Response: We have accepted the reviewer's suggestion and changed the decimals in all figures to just 2 decimal points.

4. The values of the standardized mean differences for most of the outcomes reported, while statistically significant, were of a generally small magnitude (most < 0.5). The authors interpreted these as both clinically and statistically significant results. Would it be possible to demonstrate, in terms of an absolute percentage of patients (or some other absolute quantity) the clinical significance of these findings? This would enhance the strength of the current conclusions.

Response: We accept the suggestion and added a sentence to the data analysis section to describe how we quantified the standardized mean differences on our results.

Page 8 (paragraph 1)
Between-study heterogeneity was calculated using I2 (I2 <25%: small heterogeneity; 25% 75%: large heterogeneity).(19) We have defined a standardized mean difference (SMD) smaller than 0.2 as a clinically small difference, between 0.3 and 0.7 as clinically moderate difference and greater than 0.8 as a clinically large difference.(20)

5. I don't see where the results from the first sentence, second paragraph of discussion are derived: (e.g. 70% symptom improvement at 6 months). If this comes from an earlier work by the same group, the citation is missing.

Response: We apologise for the lack of clarity. These results derive from our fractional polynomial analyses. The information has been added to the results section, as follows:

Page 21 (paragraph 2)
Our results from the fractional polynomial analysis have also shown that patients experience a favorable course of pain and disability post-surgery, with decreases in symptoms from baseline of approximately 70% at 6 months and 75% at 12 months for pain and 55% at 12 months and 67% at 120 months for disability.

6. The comparison of the # of studies with Liu et al in the discussion is somewhat misleading--that team was only looking at hip arthroplasty, which may explain why this combined knee and hip study had a larger N. (in the "strengths and weaknesses in relation to other studies" paragraph of the discussion).

Response: We have altered the discussion to better address the differences between previous studies and ours.

Page 21
Strengths and weaknesses in relation to other studies
Our meta-analysis results regarding the association between obesity and post-surgical complications found that obese patients present higher complication rates than non-obese patients. These results are consistent with the findings of previous systematic reviews of Hofstede,(21) Samson(22) and Liu.(23) Our meta-analysis results regarding the association between obesity and post-surgery disability also agreed with the findings of Buirs et al(24) and Samson et al(22) which found that obesity (defined as having BMI over 30 kg/m2), was associated with worst postsurgical functional score. The only previous review which has performed a meta-analysis on the association between obesity and post arthroplasty pain or disability limited its inclusion criteria to hip joint.(23) That review included a total of 15 studies in their meta-analysis and found that obesity increases the risk of post-surgical complications (RR: 1.68, 95% CI 1.23 to 2.30, P = 0.0004) and is associated with worse disability scores following surgery (MD: -2.75, 95% CI -4.77 to -0.6; P = 0.07). Our study has included 33 cohorts of hip arthroplasty participants in the qualitative analysis, 16 in the meta-analyses, and confirms past findings that obesity is associated with worse outcomes in terms of not only disability and complications, but also pain at both short and long term periods following surgery. Hofstede et al(21) have also conducted a systematic review of the literature on pre-operative predictors of surgical outcomes after hip replacement in patients with osteoarthritis. Although those authors included 35 studies, only 5 studies investigated the effect of obesity on post-surgical pain, disability and quality of life.(21) No meta-analysis was performed.

Reviewer #2
The manuscript reads well. The systematic review and meta-analysis was well performed and up to standard. However, my only concern was similar recent systematic reviews on the topic. This beg for why this additional meta-analysis was conducted. Though, the authors tried to justify why their meta-analysis is more comprehensive in the discussion section.

Reviewer #3
There is only two small points I would like to highlight for amendment:

In the methods the authors state an exact methodology for identification of the literature through specific search engines. Then in the results the authors state they found 26 additional studies from elsewhere. This sounds like they have included them by choice. I feel either these 26 are not included or amend the methods to allow inclusion by whatever search criteria they were found.
Response: We have clarified the methods we used for identification of the literature (page 5, paragraph 2) and the result of these studies on the screening process (page 8, paragraph 3):

Page 5, paragraph 2
Data sources and searches
The first screening of potentially relevant records was conducted by one author (DP) based on titles and abstract, and two authors (DP and GM) independently performed the final selection of included trials based on full-text evaluation. A third reviewer arbitrated in case of disagreement (MF).

Response: Moreover, the reference lists of included studies were checked for potential studies. An additional 26 references were screened, none of which met our inclusion criteria. No restriction was applied on language.

Page 8, paragraph 4
Results
Our search strategy identified 11,990 studies. Twenty-six additional studies were identified through other sources and were included for screening. After removing 381 duplicates, 11,220 studies were screened and excluded based on keywords, titles, and abstracts. All the remaining 389 studies were written in English and were assessed by reading the full text, of which 327 were excluded, yielding 62 studies included in the systematic review. From these, 31 presented enough data to be included in at least one of the meta-analyses (Figure 1).

Second: tables 4 and 5 – Ollivier reference has 20012 should be 2012
Pages 18 and 19

Response: The typos on the tables 4 and 5 were corrected.

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VERSION 2 – REVIEW

REVIEWER	Ethan Kuperman University of Iowa Carver College of Medicine United States
REVIEW RETURNED	11-Oct-2017

GENERAL COMMENTS	My previous concerns have been addressed to my satisfaction. While there are some minor typos (e.g. First bullet under strengths and limitations: "themost" should be separated into two words) I believe this manuscript is nearly ready for publication.

REVIEWER	Nick Clement Orthopaedics and Trauma Freeman Hospital Newcastle UK
REVIEW RETURNED	19-Oct-2017

GENERAL COMMENTS	The authors should be congratulated on the quality of their work. This is a well written manuscript. The subject of paper is highly topical at the moment and would be of interest to the wider readership. My only suggestion or question is: would it be possible to look at change in score? It is well recognised that the post op score is worse compared to non-obese patients. However, the overall improvement is often equal to non-obese patients. Just though this might help give the reader insight, and not simply assume joint replacement should not be done in the obese. As far as am aware their is no literature showing a satisfaction difference according to weight. Hence, it is likely no the absolute post op score but the change relative to pre op function that is the most important factor.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1
My previous concerns have been addressed to my satisfaction. While there are some minor typos (e.g. First bullet under strengths and limitations: "themost" should be separated into two words) I believe this manuscript is nearly ready for publication.

Response: The manuscript was thoroughly read by the leading author and typos corrected.

Reviewer: 3
Reviewer Name: Nick Clement
The authors should be congratulated on the quality of their work. This is a well written manuscript.

Comment: The subject of paper is highly topical at the moment and would be of interest to the wider readership. My only suggestion or question is: would it be possible to look at change in score? It is well recognised that the post op score is worse compared to non-obese patients. However, the overall improvement is often equal to non-obese patients. Just though this might help give the reader insight, and not simply assume joint replacement should not be done in the obese.
As far as am aware there is no literature showing a satisfaction difference according to weight. Hence, it is likely no the absolute post op score but the change relative to pre op function that is the most important factor.

Response: We appreciate and thank the reviewer's suggestion, unfortunately we cannot present results based on change scores, as included studies did not provide measures of variability (e.g. SD) for change scores. These are necessary for the pooled analyses. We have added the following sentence to page 21, discussion section:

"We also highlight that although non-obese patients experience further improvements in pain and disability compared to obese participants, both groups improved significantly following surgery as depicted in figure 2."

VERSION 3 – REVIEW

REVIEWER	Nicholas Clement Department of Orthopaedics Royal Infirmary of Edinburgh UK
REVIEW RETURNED	22-Nov-2017

GENERAL COMMENTS	I congratulate the authors on their work in a very topical area at the moment.