PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Hip abductor muscle strength in patients after total or unicompartmental knee arthroplasty for knee osteoarthritis or avascular necrosis: a systematic review and meta-analysis protocol
AUTHORS	Kvarda, Peter; Nüesch, Corina; Egloff, Christian; Appenzeller-Herzog, Christian; Mündermann, Annegret; Ismailidis, Petros

VERSION 1 – REVIEW

REVIEWER	ARCHIT AGARWAL ESI BASAIDARAPUR, NEW DELHI, INDIA
REVIEW RETURNED	05-May-2020

GENERAL COMMENTS	The study is trying to find answer to a important question. But, to include both UKA and TKA is doubtful as both affect the knee bio-mechanics differently, consequently affecting the hip in a different manner. Also, the subtypes of TKA like PS, CR , BCS can have different effects. Thus it would be better to narrow down inclusion criteria. - The reviewer provided a marked copy with additional comments. Please contact the publisher for full details.

REVIEWER	Michael Masaracchio Long Island University - USA
REVIEW RETURNED	05-May-2020

GENERAL COMMENTS	Thank you for the opportunity to review this paper. I agree that this paper is an important topic and a timely one with the continued increase seen in TKA/UKA. I want to applaud the authors for their time and dedication to this protocol manuscript thus far. I have personally been involved with large systematic reviews and I completely understand the time it takes to develop them. I have reviewed the registration on PROSPERO as well and find it to be consistent in my opinion with this protocol manuscript. I have included some questions/suggestions for the reviewers below. ABSTRACT I believe in the sentence that says "We will search articles published between 1/1/90... there should be the word "to" added before the. INTRODUCTION Well done, with pertinent literature. I think the first paragraph is extremely important to set the stage and I would recommend some tightening up of the language to make it read and flow more

	clearly. I would also encourage one full proof read of the manuscript as there are some places where grammar and syntax, as well as word smiting would clean up the language. METHODS Under methodological consideration, the first sentence is important and to me it doesn't make sense the way it is written. Please clearly articulate what measures of AB strength will/will not be included. Others thoughts for the methodology are the following: 1. have you considered to search clinical trials.gov to assess fully for publication bias. It will fit in nicely with the GRADE. 2. I would like to know why the NOS was chosen as the tool to assess bias? Why not consider the Cochrane Risk of Bias tool for the RCTS? Please explain further. 3. It states that all case designs will be included. I am assuming this is because of the lack of research in this area. An explanation on why case studies, etc will be included would be helpful. 4. I would encourage the authors to consider when performing meta-analysis to separate the RCTs from prospective cohort studies. I would also suggest if there are retrospective studies to not perform meta-analysis. I understand this is a protocol paper, but these decisions up front, if possible, will help plan out the data analysis and make it clearer. 5. Please discuss how heterogeneity will be assessed? The I squared statistic, other means. Thank you for the opportunity to review this paper. I look forward to seeing it again, as well as the formal systematic review.

REVIEWER	David Snowdon Monash University Australia
REVIEW RETURNED	06-May-2020

GENERAL COMMENTS	Thank you for the opportunity to review this manuscript. My main concern with the protocol is that the question that this proposed systematic review intends to answer is not defined. It is also unclear what gap (in the literature) this proposed systematic review aims to address. There are also some issues with the proposed methods, which require clarification. However, the methods are difficult to review due to lack of clarity around the question. Below are some dot points for each section of the manuscript. Abstract: 1. The aims of this systematic review have been stated as ‘to collect all available primary research reporting hip abductor strength following TKA/UKA and conduct a meta-analysis’. I suggest revising the aims of the systematic review to reflect the intended outcome. For example: To determine hip abduction strength and the factors that influence hip abduction strength following TKA/UKA. 2. Will you be including studies that investigate hip abduction strength following revision TKA, or only primary TKA? 3. The methods should be restructured to improve the flow of reporting. Specifically, you state:

	‘We will search articles published between January 1, 1990 the date of our last search. Only articles in English or German language will be considered for inclusion. The assessment of quality and risk of bias will be performed with the modified Newcastle-Ottawa scale (NOS). Studies reporting manually measured muscle strength or measurements performed at hip abduction angles other than 0° will be excluded. References will be screened by two reviewers independently. Where necessary, a third author will make the final decision.’ I recommend moving the assessment of quality and risk of bias sentence to the end of the search strategy and inclusion/exclusion criteria reporting (i.e. following explanation of the screening process). Introduction: 1. The introduction provides a good overview of functional knee biomechanics, how this relates to the hip and how this is affected by OA. However, further information is required to justify the need for the review question. - What is the evidence gap that this systematic review addresses? - How can this influence management of TKA/UKA? - What are the functional-based limitations after TKA/UKA that are associated with reduced hip abductor muscle strength? - Is there anything previously known on this topic and/or any previous systematic reviews related to this topic? 2. The aim of the systematic review protocol is stated in the introduction. However, the aim of the systematic review is stated in the abstract. The aim of the systematic review should be stated in both sections (rather than the aim of the systematic review in one section and the aim of the protocol in another). Further, according to the PRISMA-P guidelines an explicit statement of the question(s) the review will address (with reference to PICO) must be provided. Instead of stating an aim, the reviewers should consider presenting the question and follow with an aim(s) as they see fit. Methods: 1. Consider re-structuring the inclusion and exclusion criteria using the heading ‘eligibility criteria’ as per the PRISMA-P guidelines. Sub-headings for the PICO components would also help (i.e. report on the inclusion/exclusion criteria for each component of the PICO question using a separate sub-heading). 2. What type of studies will you be including in this review? Be more specific as this will dictate what quality assessment tool you use. For example, the tool you have selected is for cohort studies. Will you also include intervention studies (e.g. Randomised Controlled Trials)? 3. Will you include primary and revision TKA/UKA? Or only primary TKA?

	4. Page 5, line 49: ‘Studies reporting hip abductor strength measurements by isokinetic/isometric dynamometers and at a 0° hip abduction angle will be considered for inclusion because manual measurements because the results are not reliable and not directly comparable with studies using electronic dynamometers and abduction angle other than 0° do not show relevant muscle function/strength during walking and standing.‘ Re-word ‘…because manual measurements because the results are not reliable and not directly comparable…’ 5. Why limit the search strategy to 1990? In the abstract you state that this is the date of your previous search. Has this search (presumably part of a previous systematic review) been published? If it has not been published, why not search prior to this date? Further justification for this decision is required. 6. How will you screen the citations? What will you use to perform citation tracking (e.g. Google Scholar)? 7. On page 6, line 28: ‘In order to find possible additional studies, we will screen the bibliographic references of all included articles as well as the citations. Data from the full texts will be extracted and entered into a standardized excel data entry form by PK and PI based piloting extractions. The study selection process will be presented in form of a PRISMA diagram. The information to be extracted can be found in Table 2. We will contact principal investigators and/or corresponding author(s) twice by email, in case of conference abstracts, in order to collect their results.’ You explain the study selection process, and then move onto the data extraction process, and then return to the study selection process with ‘The study selection process will be presented in form of a PRISMA diagram’. I suggest moving this statement to the end of the study selection (record screening) explanation. Reporting the data extraction process after this statement. 8. Page 7, line 21: ‘To minimise bias, articles that meet the inclusion criteria will be checked by two reviewers (PK and PI) independently according to a modified version of the NOS (Supplementary c).’ Re-word this sentence, removing the word ‘checked. For example, ‘Risk of bias of included studies will be assessed independently by two reviewers using…’. Also, write out ‘Newcastle-Ottawa Scale’ in full prior to abbreviating in the full text. I note that this is abbreviated in the abstract, however, the full text should be able to be interpreted by the reader without having to read the abstract first (and vice versa). 9. On page 7, line 36 you state that you will be extracting qualitative data. This is incorrect unless you plan on including data from interviews and focus groups (non-numerical data). Note that ‘qualitative data’ does not refer to ‘descriptive’ quantitative data. 10. The time points of outcome measurement need to be clarified in the eligibility criteria section (i.e. there will be no limitation on timing of outcome measurement).

	11. Contacting authors regarding missing data and methods relating to data extraction are not usually reported in the data synthesis section. Instead, these should be reported in the data extraction section. 12. What type of meta-analysis will be used? (e.g. inverse variance, fixed vs. random effects). 13. Please expand on the GRADE approach. What criteria will be used to downgrade (or upgrade) the quality of cumulative evidence? 14. Please expand on how you will assess for publication bias. Will you use funnel plots?

VERSION 1 – AUTHOR RESPONSE

Reviewers' Comments to Author:

Reviewer: 1
Reviewer Name: ARCHIT AGARWAL
Institution and Country: ESI BASAIDARAPUR, NEW DELHI, INDIA
Please state any competing interests or state 'None declared': none declared

Comment 1: The study is trying to find answer to a important question. But, to include both UKA and TKA is doubtful as both affect the knee bio-mechanics differently, consequently affecting the hip in a different manner. Also, the subtypes of TKA like PS, CR , BCS can have different effects. Thus it would be better to narrow down inclusion criteria.

Response 1: The reviewer raised a very important point. Although we agree that different type of implants may affect joint biomechanics in different ways, limited evidence is available. In order to capture as much data as possible, we extended our inclusion criteria to TKA/UKA regardless of implant type. If sufficient data can be extracted from the literature, we will perform a subgroup analysis to answer the question raised by the reviewer, which we would not be able to address if we included only one subtype of prostheses.

Reviewer: 2
Reviewer Name: Michael Masaracchio
Institution and Country: Long Island University - USA
Please state any competing interests or state 'None declared': None declared.

Thank you for the opportunity to review this paper. I agree that this paper is an important topic and a timely one with the continued increase seen in TKA/UKA. I want to applaud the authors for their time and dedication to this protocol manuscript thus far. I have personally been involved with large systematic reviews and I completely understand the time it takes to develop them. I have reviewed the registration on PROSPERO as well and find it to be consistent in my opinion with this protocol manuscript. I have included some questions/suggestions for the reviewers below.

ABSTRACT

Comment 1: I believe in the sentence that says "We will search articles published between 1/1/90... there should be the word "to" added before the.

Response 1: Thank you for noting this oversight. We have corrected this sentence in the manuscript.

Comment 2:

INTRODUCTION
Well done, with pertinent literature. I think the first paragraph is extremely important to set the stage and I would recommend some tightening up of the language to make it read and flow more clearly. I would also encourage one full proof read of the manuscript as there are some places where grammar and syntax, as well as word smiting would clean up the language.

Response 2: Thank you. We have carefully copy-edited the manuscript regarding wording, grammar and syntax.

Comment 3:

METHODS
Under methodological consideration, the first sentence is important and to me it doesn't make sense the way it is written. Please clearly articulate what measures of AB strength will/will not be included.

Response 3: We have rephrased this sentence to improve clarity.

Others thoughts for the methodology are the following:
Comment 4. have you considered to search clinical trials.gov to assess fully for publication bias. It will fit in nicely with the GRADE.

Response 4: We have carefully considered the reviewer's suggestion. We will include funnel plots to address publication bias. It is very unlikely to find studies reporting on negative results on clinicaltrials.gov especially considering the very limited number of publications in this area as determined in our pilot search. In response to reviewer 3, using funnel plots enables the correct assessment of publication bias.

Comment 5. I would like to know why the NOS was chosen as the tool to assess bias? Why not consider the Cochrane Risk of Bias tool for the RCTS? Please explain further.

Response 5: In the process of defining this systematic review, we reviewed several risk of bias tools. We are aware of the Cochrane Risk of Bias tool for RCTs. However, while this systematic review will consider RCTs, our main interest is not on comparison between different treatments. Hence, several of the criteria listed in risk of bias tools for RCTs are not applicable for assessing the quality of studies regarding muscle strength in patients undergoing TKA/UKA. Hence, we chose the modified

Newcastle-Ottawa Scale to assess risk of bias in individual studies. We have applied the same tool in a previous systematic review on hip abductor strength in patients undergoing hip arthroplasty and deemed this tool also suitable for the purpose of the current study. Furthermore, as we are writing in the manuscript, it does not make sense to specifically assess the quality of RCTs (using a suitable tool), since we do not extract estimates of treatment differences from RCTs but merely use them as a source for observational data.

Comment 6. It states that all case designs will be included. I am assuming this is because of the lack of research in this area. An explanation on why case studies, etc will be included would be helpful.

Response 6: We thank the reviewer this valuable comment. We did not include case studies but only cross-sectional and longitudinal cohort studies as well as randomized clinical trials. We have revised the protocol accordingly.

Comment 7. I would encourage the authors to consider when performing meta-analysis to separate the RCTs from prospective cohort studies. I would also suggest if there are retrospective studies to not perform meta-analysis. I understand this is a protocol paper, but these decisions up front, if possible, will help plan out the data analysis and make it clearer.

Response 7: We appreciate this comment of the reviewer. We agree that in this case heterogeneity is a limitation of this study. Because our primary goal is not to compare the efficacy of different treatments, pooling data from different study designs is appropriate. In our methods section, we clearly stated inclusion and exclusion criteria, which aims to obtain and present comparable data. And included RCTs will merely be used as a source for observational data, which provides a rational not to separate RCTs from cohort studies in meta-analysis.

Comment 8. Please discuss how heterogeneity will be assessed? The I squared statistic, other means.

Response 8: We thank the reviewer this relevant comment. We will assess heterogeneity between studies with visual inspection of forest plots and using I^2-test.

Thank you for the opportunity to review this paper. I look forward to seeing it again, as well as the formal systematic review.

Reviewer: 3
Reviewer Name: David Snowdon
Institution and Country: Monash University, Australia
Please state any competing interests or state ‘None declared’: None declared

Thank you for the opportunity to review this manuscript. My main concern with the protocol is that the question that this proposed systematic review intends to answer is not defined. It is also unclear what gap (in the literature) this proposed systematic review aims to address. There are also some issues

with the proposed methods, which require clarification. However, the methods are difficult to review due to lack of clarity around the question. Below are some dot points for each section of the manuscript.

Abstract:

Comment 1. The aims of this systematic review have been stated as 'to collect all available primary research reporting hip abductor strength following TKA/UKA and conduct a meta-analysis'. I suggest revising the aims of the systematic review to reflect the intended outcome. For example: To determine hip abduction strength and the factors that influence hip abduction strength following TKA/UKA.

Response 1. Thank you for this valuable comment. We have adjusted the aim of the study on the Abstract and Introduction sections.

Comment 2. Will you be including studies that investigate hip abduction strength following revision TKA, or only primary TKA?

Response 2: We will include only primary TKA/UKA. Studies reporting measurements following revision surgery will be excluded. Please find our statement regarding this question in the section: "Eligibility criteria – inclusion criteria and exclusion criteria.

Comment 3. The methods should be restructured to improve the flow of reporting. Specifically, you state:

'We will search articles published between January 1, 1990 the date of our last search. Only articles in English or German language will be considered for inclusion. The assessment of quality and risk of bias will be performed with the modified Newcastle-Ottawa scale (NOS). Studies reporting manually measured muscle strength or measurements performed at hip abduction angles other than 0° will be excluded. References will be screened by two reviewers independently. Where necessary, a third author will make the final decision.'

I recommend moving the assessment of quality and risk of bias sentence to the end of the search strategy and inclusion/exclusion criteria reporting (i.e. following explanation of the screening process).

Response 3. We would like to thank the reviewer for this suggestion. We have moved the assessment of quality and risk of bias sentence to the end of the search strategy and inclusion/exclusion criteria reporting.

Introduction:

Comment 4. The introduction provides a good overview of functional knee biomechanics, how this relates to the hip and how this is affected by OA. However, further information is required to justify the need for the review question.

- What is the evidence gap that this systematic review addresses?

- How can this influence management of TKA/UKA?
- What are the functional-based limitations after TKA/UKA that are associated with reduced hip abductor muscle strength?
- Is there anything previously known on this topic and/or any previous systematic reviews related to this topic?

Response 4: We thank the reviewer for the valuable comments and suggestion. We have revised the Introduction section and provide additional information on all points listed.

Comment 5: The aim of the systematic review protocol is stated in the introduction. However, the aim of the systematic review is stated in the abstract. The aim of the systematic review should be stated in both sections (rather than the aim of the systematic review in one section and the aim of the protocol in another).

Further, according to the PRISMA-P guidelines an explicit statement of the question(s) the review will address (with reference to PICO) must be provided. Instead of stating an aim, the reviewers should consider presenting the question and follow with an aim(s) as they see fit.

Response 5: Thank you for this comment. We now state the aim of the systematic review in the Abstract and Introduction sections. We have also listed open research questions that will be address in the proposed systematic review.

Methods:

Comment 6. Consider re-structuring the inclusion and exclusion criteria using the heading ‘eligibility criteria’ as per the PRISMA-P guidelines. Sub-headings for the PICO components would also help (i.e. report on the inclusion/exclusion criteria for each component of the PICO question using a separate sub-heading).

Response 6: We have included the heading eligibility criteria as suggested. We had designed study question using the PICOS. Please find the detailed PICOS description of our study in Table 1.

Comment 7. What type of studies will you be including in this review? Be more specific as this will dictate what quality assessment tool you use. For example, the tool you have selected is for cohort studies. Will you also include intervention studies (e.g. Randomised Controlled Trials)?

Response 7: We thank the reviewer this comment. Case studies will not be considered for inclusion. No other restrictions on study design will be applied. Please find this statement in the section “Inclusion criteria”. Only human based clinical studies will be considered for inclusion.

Comment 8. Will you include primary and revision TKA/UKA? Or only primary TKA?

Response 8. We would like to thank the reviewer for this relevant question. We will include only primary TKA/UKA. Studies reporting measurements following revision surgery will be excluded.

Please find our statement regarding this question in the paragraph: “Eligibility criteria – inclusion criteria and exclusion criteria”.

Comment 9. Page 5, line 49: ‘Studies reporting hip abductor strength measurements by isokinetic/isometric dynamometers and at a 0° hip abduction angle will be considered for inclusion because manual measurements because the results are not reliable and not directly comparable with studies using electronic dynamometers and abduction angle other than 0° do not show relevant muscle function/strength during walking and standing.‘

Re-word ‘…because manual measurements because the results are not reliable and not directly comparable…’

Response 9: We have corrected the sentence in our manuscript accordingly.

Comment 10. Why limit the search strategy to 1990? In the abstract you state that this is the date of your previous search. Has this search (presumably part of a previous systematic review) been published? If it has not been published, why not search prior to this date? Further justification for this decision is required.

Response 10. Thank you for noting this mistake. The sentence containing this statement was incomplete as also raised by reviewer 1. The intended and correct statement is: “We will search articles published between January 1, 1990 and the date of our last search.” We limited the time period based on our search experience of a similar systematic review on muscle strength deficits in patients after total hip replacement, where we retrieved a significant number of methodological inadequate/inappropriate abstracts prior to 1990. To avoid this problem, we limited the publication time period.

Comment 11. How will you screen the citations? What will you use to perform citation tracking (e.g. Google Scholar)?

Response 11: We will use Scopus and/or Web of Science for citation tracking. We have added this information into our manuscript in the section `Study record: data management, selection process and data extraction`

Comment 12. On page 6, line 28: ‘In order to find possible additional studies, we will screen the bibliographic references of all included articles as well as the citations. Data from the full texts will be extracted and entered into a standardized excel data entry form by PK and PI based piloting extractions. The study selection process will be presented in form of a PRISMA diagram. The information to be extracted can be found in Table 2. We will contact principal investigators and/or corresponding author(s) twice by email, in case of conference abstracts, in order to collect their results.’

You explain the study selection process, and then move onto the data extraction process, and then return to the study selection process with ‘The study selection process will be presented in form of a PRISMA diagram’. I suggest moving this statement to the end of the study selection (record screening) explanation. Reporting the data extraction process after this statement.

Response 12: Thank you for this suggestion. We have modified the order and now report data extraction after the study selection process.

Comment 13. Page 7, line 21: ‘To minimise bias, articles that meet the inclusion criteria will be checked by two reviewers (PK and PI) independently according to a modified version of the NOS (Supplementary c).’

Re-word this sentence, removing the word ‘checked. For example, ‘Risk of bias of included studies will be assessed independently by two reviewers using…’.

Also, write out ‘Newcastle-Ottawa Scale’ in full prior to abbreviating in the full text. I note that this is abbreviated in the abstract, however, the full text should be able to be interpreted by the reader without having to read the abstract first (and vice versa).

Response 13: We would like to thank the reviewer this comment. We have revised these sentences accordingly.

Comment 14. On page 7, line 36 you state that you will be extracting qualitative data. This is incorrect unless you plan on including data from interviews and focus groups (non-numerical data). Note that ‘qualitative data’ does not refer to ‘descriptive’ quantitative data.

Response 14: We thank the reviewer for highlighting this point. We have revised this sentence accordingly.

Comment 15. The time points of outcome measurement need to be clarified in the eligibility criteria section (i.e. there will be no limitation on timing of outcome measurement).

Response 15: We are thankful for this comment. We have revised the inclusion criteria of the eligibility criteria section.

Comment 16. Contacting authors regarding missing data and methods relating to data extraction are not usually reported in the data synthesis section. Instead, these should be reported in the data extraction section.

Response 16: We would like to thank the reviewer to highlight this mistake. We have moved this sentence into the “Study records: data management, selection process and data extraction” section.

Comment 17. What type of meta-analysis will be used? (e.g. inverse variance, fixed vs. random effects).

Response 17: We will perform the meta-analysis based on random effects depending on availability of the appropriate data and will generate forest plots.

Comment 18. Please expand on the GRADE approach. What criteria will be used to downgrade (or

upgrade) the quality of cumulative evidence?

Response 18: We have added information on our approach according to the GRADE system. Please find more precisely in the 'Confidence in cumulative evidence' section.

Comment 19. Please expand on how you will assess for publication bias. Will you use funnel plots?

Response 19: We would like to thank the reviewer the importance of this section. We will use funnel plots to asses publication bias and Egger's regression test to assess the asymmetry of the plot. We have added this information in the revised manuscript.

VERSION 2 – REVIEW

REVIEWER	David Snowdon Monash University, Australia
REVIEW RETURNED	09-Jun-2020

GENERAL COMMENTS	I thank the authors for their detailed response to my comments. I have a couple more minor comments/suggestions as follows: Introduction: Line 120 – Do you mean the only effective treatment? Please provide a reference to support this statement. Line 120 – 'Despite of extensive efforts of alternative treatment…' Please refer the first 'of'. Methods: Line 266 – The strength of the Newcastle-Ottawa Scale is that it can be used to assess the bias of all study designs. The GRADE approach may also have to be applied across a variety of study designs. However, you have listed criteria for downgrading randomised controlled trials and criteria for upgrading non-randomised controlled trials. Therefore, I recommend describing an approach that can be applied across all study designs (not one for RCTs and one for non-RCTs). This is because the GRADE approach will be applied to synthesised findings from the review, which may include synthesis of findings from different study designs.

VERSION 2 – AUTHOR RESPONSE

Reviewer's Comments to Author:

Reviewer: 3
Reviewer Name: David Snowdon
Institution and Country: Monash University, Australia
Please state any competing interests or state 'None declared': None declared.

I thank the authors for their detailed response to my comments. I have a couple more minor comments/suggestions as follows:

Comment 3: Introduction:
Line 120 – Do you mean the only effective treatment? Please provide a reference to support this statement.
Line 120 – 'Despite of extensive efforts of alternative treatment...' Please refer the first 'of'.

Response 3: We would like to thank the reviewer for this comment. We corrected this statement. Non-surgical management options try to control symptoms in different stages of knee osteoarthritis. If these methods fail or the knee osteoarthritis is severe and in advanced stage, the only effective method is joint arthroplasty.

Comment 4: Methods:
Line 266 – The strength of the Newcastle-Ottawa Scale is that it can be used to assess the bias of all study designs. The GRADE approach may also have to be applied across a variety of study designs. However, you have listed criteria for downgrading randomised controlled trials and criteria for upgrading non-randomised controlled trials. Therefore, I recommend describing an approach that can be applied across all study designs (not one for RCTs and one for non-RCTs). This is because the GRADE approach will be applied to synthesised findings from the review, which may include synthesis of findings from different study designs.

Response 4: We thank the reviewer for commenting on this point and raising attention to this topic. We would like to emphasize, that we use the same criteria for downgrading or upgrading for all the investigated studies. We corrected it in our manuscript.