

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Hospital readmission after anterior cruciate ligament reconstruction: protocol for a systematic review and meta-analysis
<b>AUTHORS</b>	Shao, Long; Wu, Di; Li, Jia-Ying; Wu, Xiangdong; Qiu, Gui-Xing; Zhou, Xi; Luo, Changqi; Xiao, Peng-Cheng; Liu, Jia-Cheng; Huang, Wei

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Adam Culvenor La Trobe University, Australia
<b>REVIEW RETURNED</b>	05-May-2020

<b>GENERAL COMMENTS</b>	<p>Thank you for the opportunity to review this systematic review protocol paper evaluating hospital readmissions after ACL reconstruction. It is an important topic that is well justified in the background and it is generally well written. The authors appear to use all of the appropriate checklists (eg. MOOSE, PRISMA) in their systematic review design and reporting plans. I have some comments below to help strengthen the paper.</p> <p>General Comments</p> <ol style="list-style-type: none"> <li>1. My major comment is whether ACLR revision surgery and total knee arthroplasty will be included in the hospital readmission data. These two re-surgeries are two of the most common reasons for hospital readmission after an ACLR. The rate of revision surgery is upwards of 20% in young athletes, while ACLR is a one of the major contributors to the TKR numbers. Obviously, these reasons for hospital readmission may be longer-term, but nowhere in the protocol was a maximum length of follow-up defined, so they should be included.</li> <li>2. Will only primary ACLR be included to evaluate the hospital readmission rates, or will secondary, tertiary etc ACLR data leading to hospital readmissions also be included?</li> <li>3. A couple of times throughout the manuscript, ACL reconstruction is referred to as the current “gold standard” treatment for ACL injuries. Just because there are a lot of ACLRs done around the world doesn’t mean it is the gold standard. The current best-available evidence from high-quality clinical trials is that ACLR is not superior to non-operative management in most cases (Frobell et al., NEJM 2010). I suggest rewording these sections to reflect this.</li> <li>4. The inclusion criteria suggest that studies need to focus in hospital readmissions. Does this mean that hospital readmissions need to be the primary outcome for the study to be included?</li> <li>5. Regarding study results being summarised in a forest plot, do the authors need to qualify this statement that results will be summaries in a forest plot “if possible” or “if sufficient data exist”.</li> </ol>
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	<p>As it may not be possible to pool data in a forest plot, depending on the nature of the studies and the heterogeneity.</p> <p>6. Are dollar values reflective of USD?</p> <p>7. For the evaluation of preventive measures for readmission, will only clinical trials be included? If including revision ACLR, then preventive measures such as completing rehabilitation/passing return to sport criteria need to be included as these are closely linked to re-rupture rates which are the primary reason for hospital readmission for revision surgery.</p> <p><b>Specific Comments</b>  <b>Abstract</b>          - Suggest including all databases to be searched in the abstract          - There is some mix up of past and present tense in the abstract</p> <p><b>Strengths and Limitations of the study – final dot point page 6 –</b>          how do the authors know that heterogeneity of the included studies will be a limitation prior to undertaking the review?</p> <p><b>Introduction</b>          Page 7 – perhaps qualify that ACLR is a safe and effective treatment option “in the right patient”.          Page 8 – sentence starting “Although the hospital readmission rate after ACLR was not high...” suggest rewording for clarity as it is difficult to read as it is.</p> <p><b>Methods</b>          Page 10, line 4 – systematic reviews should not be plural here.</p> <p>Page 12 under study selection – although it states that screening will be done according to inclusion/exclusion criteria, there are actually no specific inclusion/exclusion criteria listed anywhere in the paper.</p> <p>Page 13 under quality assessment section – Is it appropriate to dichotomous the risk of bias scores? Many guidelines now recommend this approach. To evaluate the influence of risk of bias on the study outcomes, an alternative to subgroup analysis would be to conduct a meta-regression using the continuous risk of bias score.</p> <p>Page 14 under data synthesis section – there is no mention of how preventive measure data will be synthesised and evaluate treatment effects</p> <p>Page 15 under subgroup analysis section – as mentioned above, it may be more appropriate to perform meta-regression analyses for continuous data rather than dichotomising data in subgroups.</p> <p>Discussion section – should include some content regarding the re-rupture and TKR risks and that these are major causes of readmission.</p>
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<b>REVIEWER</b>	Richard F O'Connor HSE West, Ireland
<b>REVIEW RETURNED</b>	11-May-2020

<b>GENERAL COMMENTS</b>	<p>Overall a good protocol which could make for an interesting systematic review.</p> <p>Points for improvement:</p> <ol style="list-style-type: none"> <li>1. The rationale in the introduction could be improved with additional referencing to strengthen the basis for the study.</li> <li>2. Are studies which included longer term/ later readmissions (e.g readmissions after 9 months or after 2 years) to be included? It appears based on the inclusion/ exclusion criteria that they will be included. Their inclusion will be useful, and in that case there should be consideration of reinjury of the ACL in the introduction and throughout the protocol since reinjury is an important complication following ACLR. Re-injury, which is not uncommon, has very significant implications for rehabilitation, morbidity, later readmission, and financial cost.</li> <li>3. In the Methods section there is a description of the types of observational studies that will be eligible. The author also states that "There will be no specific restrictions on the study design, but most of the studies are expected to (be) retrospective observational studies." I agree that most of the studies will be observational but it should be stated more clearly as to whether randomised controlled trials will also be included or whether they are excluded. If RCTs are to be included is there a protocol in place for assessment of their quality?</li> <li>4. The flow and accuracy of the English language needs to be improved very significantly, particular attention is needed in the introduction where there are several errors. If the language/ grammar/ accuracy was addressed and the introduction improved then this protocol could be an excellent review. The following lines of notes require attention, this list is not exhaustive: Page 7 Line 22, 33, 48-59; Page 8 Line 17-33, 43-49; Page 9 Line 35, 43; Page 10 Line 38, Page 13 Line 20.</li> </ol>
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### VERSION 1 – AUTHOR RESPONSE

Comments from Reviewers:

Reviewer: 1

Reviewer Name: Adam Culvenor

Institution and Country: La Trobe University, Australia

Please state any competing interests or state 'None declared': None declared.

Please leave your comments for the authors below

Thank you for the opportunity to review this systematic review protocol paper evaluating hospital readmissions after ACL reconstruction. It is an important topic that is well justified in the background and it is generally well written. The authors appear to use all of the appropriate checklists (eg. MOOSE, PRISMA) in their systematic review design and reporting plans. I have some comments below to help strengthen the paper.

Response: Thank you, Prof. Culvenor, for your encouraging and positive comments on our manuscript. According to your helpful suggestions, we have revised the manuscript thoroughly.

#### General Comments

Comment 1: My major comment is whether ACLR revision surgery and total knee arthroplasty will be included in the hospital readmission data. These two re-surgeries are two of the most common reasons for hospital readmission after an ACLR. The rate of revision surgery is upwards of 20% in young athletes, while ACLR is one of the major contributors to the TKR numbers. Obviously, these reasons for hospital readmission may be longer-term, but nowhere in the protocol was a maximum length of follow-up defined, so they should be included.

Response: Thank you for your kind and instructive suggestions. We apologize for the lack of description of the types of participants. Just as mentioned above, we will include hospital readmission after both primary ACLR surgery and ACLR revision surgery, regardless of the types of re-surgeries (e.g., ACLR revision surgery, total knee arthroplasty) after readmitted to the hospital. Accordingly, we have revised the manuscript as follows.

Change in the text:

Types of participants

Also, to enhance the clinical significance of this study, both primary ACLR and ACLR revision surgery will be included.

Comment 2: Will only primary ACLR be included to evaluate the hospital readmission rates, or will secondary, tertiary etc ACLR data leading to hospital readmissions also be included?

Response: Thank you for your additional suggestion. We apologize for the confusion. Just as mentioned above, we will include hospital readmission after both primary ACLR surgery and ACLR revision surgery, regardless of the ACLR revision surgery is a second or tertiary surgery. It is conceivable that either secondary or tertiary ACLR surgery is typically treated as ACLR revision surgery in original studies, and hospital readmissions after both primary ACLR and ACLR revision surgeries will be included. According to your kind suggestion, we have rephrased this section as follows.

Change in the text:

Types of participants

Also, to enhance the clinical significance of this study, both primary ACLR and ACLR revision surgery will be included.

Comment 3: A couple of times throughout the manuscript, ACL reconstruction is referred to as the current “gold standard” treatment for ACL injuries. Just because there are a lot of ACLRs done around the world doesn’t mean it is the gold standard. The current best-available evidence from high-quality clinical trials is that ACLR is not superior to non-operative management in most cases (Frobell et al., NEJM 2010). I suggest rewording these sections to reflect this.

Response: Thank you for your professional comment. We apologize for the inappropriate description. Accordingly, we have revised our manuscript as below.

Change in the text:

#### ABSTRACT

Anterior cruciate ligament reconstruction (ACLR) has been widely performed as a safe and effective treatment for ACL injuries.

#### INTRODUCTION

However, the ACL has a limited intrinsic healing capacity due to the lack of vascularization,<sup>1</sup> and ACL reconstruction (ACLR) has been widely accepted as a safe and effective treatment option for many patients, which aims to restore the functional stability of the knee and allow patients to return to pre-injury functionality.

Comment 4: The inclusion criteria suggest that studies need to focus in hospital readmissions. Does this mean that hospital readmissions need to be the primary outcome for the study to be included?

Response: We apologize for the confusion. Although this study mainly focuses on hospital readmissions after ACLR., it does not mean the included original study needs to focus on hospital readmissions or hospital readmissions should be the primary outcome of the included studies. Instead, studies will be screened for eligibility only if the original study reported hospital readmissions, regardless of whether the hospital readmissions is the primary or second outcome. We might have used the inappropriate phrase “focus on,” and we have replaced it with “reported” to avoid any confusion.

Change in the text:

Eligibility criteria

Types of studies

Studies that reported hospital readmission or explored the associated causes and risk factors for hospital readmission after ACLR will be potentially eligible, which mainly including prospective cohort studies, retrospective cohort studies, case-control studies, and cross-sectional studies. There will be no specific restrictions on the study design, and eligible clinical trials will also be included, but most of the studies are expected to be retrospective observational studies.

Comment 5: Regarding study results being summarised in a forest plot, do the authors need to qualify this statement that results will be summaries in a forest plot “if possible” or “if sufficient data exist”. As it may not be possible to pool data in a forest plot, depending on the nature of the studies and the heterogeneity.

Response: Thank you for your kind and instructive suggestion. We agree entirely with you.

Accordingly, we have corrected the sentence as follows.

Change in the text:

ABSTRACT

If possible, study results will be summarized in a Forest plot, and heterogeneity will be tested by using the Cochran's Q and I2 statistics.

METHODS AND ANALYSIS

If sufficient data available, the outcome data will be further pooled and reported in a forest plot to summarize the results of each study visually.

Comment 6: Are dollar values reflective of USD?

Response: Thank you for your kind suggestion. The symbol “\$” denotes USD, as this dollar value has been widely used in literature, we did not replace this symbol “\$” with USD.

Comment 7: For the evaluation of preventive measures for readmission, will only clinical trials be included? If including revision ACLR, then preventive measures such as completing rehabilitation/passing return to sport criteria need to be included as these are closely linked to re-rupture rates, which are the primary reason for hospital readmission for revision surgery.

Response: Thank you for your constructive and thoughtful comments. We are very sorry for our use of vague expressions. There will be no specific restrictions on the study design, and eligible clinical trials will also be included. Although most of the evaluation of preventive measures for readmission is likely reported in clinical trials, which does not mean only clinical trials will be included. In fact, although there will be no specific restrictions on the study design and most of the included studies are expected to be retrospective observational studies, eligible clinical trials will also be included. We will include studies reported hospital readmissions after primary or revision ACLR, and thanks to your professional suggestion, preventive measures such as completing rehabilitation/passing return to sport criteria will be included. Accordingly, we have corrected the sentence as follows.

Change in the text:

Eligibility criteria

### Types of studies

Studies that reported hospital readmission or explored the associated causes and risk factors for hospital readmission after ACLR will be potentially eligible, which mainly including prospective cohort studies, retrospective cohort studies, case-control studies, and cross-sectional studies. There will be no specific restrictions on the study design, and eligible clinical trials will also be included, but most of the studies are expected to be retrospective observational studies.

### Data extraction and management

The following information will be collected: first author, publication year, country where the study was carried out, study design, study period, the database type, number of patients, patient characteristics, surgical procedure, the definition and time frame of readmission (e.g., 30-day readmission, 90-day readmission, 1-year readmission), number of readmissions, causes of readmission (e.g., all-cause, VTE, infection) and how they were identified (e.g., ICD-9-CM (International Classification of Diseases, Ninth Revision, Clinical Modification)), number and types of complications (e.g., wound infection), risk factors for readmission, and preventive measures for readmission (e.g., complete rehabilitation programs, pass return to sport criteria).

### Specific Comments

#### Abstract

Comment 8: Suggest including all databases to be searched in the abstract

Response: Many thanks for your careful review and kind suggestions regarding our manuscript.

Accordingly, we have added all databases that will be searched in the Abstract.

Change in the text:

Electronic databases, including PubMed, Embase, and The Cochrane Library, will be systematically searched from inception to June 2020.

Comment 9: There is some mix up of past and present tense in the abstract

Response: Thank you for your additional helpful suggestion. We are deeply sorry for the mistakes.

Accordingly, we have revised the Abstract as follows.

Change in the text:

#### ABSTRACT

**Introduction** Anterior cruciate ligament (ACL) injury is one of the most common injuries of the knee. Anterior cruciate ligament reconstruction (ACLR) has been widely performed as a safe and effective treatment for ACL injuries. As there is an increasing trend in the incidence of ACL injury, hospital readmission after ACLR has attracted renewed attention for the financial burden to both patients and the healthcare system. However, information about hospital readmission after ACLR remains fragmented. Therefore, we plan to systematically review the literature to investigate the rate of, causes, and risk factors for hospital readmission after ACLR, and summarize interventions to reduce hospital readmission. This article is to provide the protocol for an upcoming systematic review and meta-analysis on this important issue.

**Methods and analysis:** Reporting of this protocol follows the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) checklist. Electronic databases, including PubMed, Embase, and The Cochrane Library, will be systematically searched from inception to June 2020. No language restrictions will be applied. Studies will be included if they reported hospital readmission or explored the associated potential causes and risk factors for hospital readmission after ACLR. The primary outcome will be the number and time frame of hospital readmission after ACLR. Secondary outcomes will be reasons for readmission, number and types of complications, risk factors for readmission, and preventive measures for readmission after ACLR. Quality assessments will be performed by using the Newcastle-Ottawa Scale. If possible, study results will be summarized in a Forest plot, and heterogeneity will be tested by using the Cochran's Q and I<sup>2</sup> statistics.

**Ethics and dissemination:** No ethical approval is required because our study is not related to patients or animals. The results will be published in a peer-reviewed journal.

PROSPERO registration number: CRD42020058624.

Comment 10: Strengths and Limitations of the study – final dot point page 6 – how do the authors know that heterogeneity of the included studies will be a limitation prior to undertaking the review?

Response: Many thanks for your kind suggestion. We are very sorry for the improper use of a positive tone. Considering there will be no specific restrictions on the study design, based on the literature we have reviewed, most of the eligible studies of this systematic review and meta-analysis are expected to be retrospective observational studies. Compared with clinical trials, the heterogeneity among observational studies, especially clinical heterogeneity, tends to be more significant. Accordingly to your insightful comments, we have revised the final dot as follows.

Change in the text:

Strengths and limitations of this study

□ This study may be limited by heterogeneity, especially the clinical heterogeneity, which might introduce some bias and decrease the reliability of the conclusion.

Introduction

Comment 11: Page 7 – perhaps qualify that ACLR is a safe and effective treatment option “in the right patient”.

Response: Thank you for your professional suggestion. Accordingly, we have amended the sentence as follows.

Change in the text:

INTRODUCTION

However, the ACL has a limited intrinsic healing capacity due to the lack of vascularization, and ACL reconstruction (ACLR) has been widely accepted as a safe and effective treatment option for many patients, which aims to restore the functional stability of the knee and allow patients to return to pre-injury functionality.

Comment 12: Page 8 – sentence starting “Although the hospital readmission rate after ACLR was not high...” suggest rewording for clarity as it is difficult to read as it is.

Response: Thank you for your careful and constructive suggestions. Accordingly, we have rephrased this sentence as follows.

Change in the text:

As such, there is a considerable amount of patients encountered postoperative adverse events associated with readmission after ACLR, suffered significant morbidity, experienced severely impaired quality of life, and expended higher costs.

Methods

Comment 13: Page 10, line 4 – systematic reviews should not be plural here.

Response: Thank you for your helpful suggestions. Accordingly, we have revised it as follows.

Change in the text:

This study protocol will be amended and updated in conjunction with the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P).

Comment 14: Page 12 under study selection – although it states that screening will be done according to inclusion/exclusion criteria, there are actually no specific inclusion/exclusion criteria listed anywhere in the paper.

Response: Thank you for your careful review and kind suggestion. We are very sorry for our inaccurate description. As the inclusion/exclusion criteria have been described in the Eligibility criteria section, we did not further list inclusion/exclusion criteria one-by-one. According to your kind suggestion, we have revised the sentence as follows.

Change in the text:

First, duplicate records will be removed. Second, two reviewers (X-DW and J-YL) will independently screen the titles and abstracts according to the eligibility criteria. They will develop a screening form and label each record as relevant, irrelevant, or indeterminate, and remove the records that did not fulfill the eligibility criteria. Third, the full text of the potential eligible records will be obtained and analyzed by two reviewers.

Comment 15: Page 13 under quality assessment section – Is it appropriate to dichotomous the risk of bias scores? Many guidelines now recommend this approach. To evaluate the influence of risk of bias on the study outcomes, an alternative to subgroup analysis would be to conduct a meta-regression using the continuous risk of bias score.

Response: Many thanks for your professional and constructive suggestions. Accordingly, we have revised this section as follows.

Change in the text:

Studies will be considered to be of high-quality if they score  $\geq 7$  and low-quality if they score  $< 7$ .

Comment 16: Page 14 under data synthesis section – there is no mention of how preventive measure data will be synthesised and evaluate treatment effects

Response: Thank you for your kind suggestion. Accordingly, we have revised the data synthesis section as follows.

Change in the text:

For the preventive intervention for hospital readmission, we will qualitatively synthesize the findings from included studies.

Comment 17: Page 15 under subgroup analysis section – as mentioned above, it may be more appropriate to perform meta-regression analyses for continuous data rather than dichotomising data in subgroups.

Response: Thank you for your insightful suggestion. We totally agree with you. Accordingly, we have revised the subgroup analysis section as follows.

Change in the text:

Subgroup analysis and sensitivity analysis

If the number of included studies is sufficient, subgroup analyses and meta-regression analyses will be conducted to investigate the underlying source of heterogeneity.

Comment 18: Discussion section – should include some content regarding the re-rupture and TKR risks and that these are major causes of readmission.

Response: We fully agree with your thoughtful and constructive suggestions. Accordingly, we have added some content regarding the re-rupture and TKR risks and that these are major causes of hospital readmission after ACLR, as follows.

Change in the text:

#### DISCUSSION

Hospital readmission rates have been recognized as an essential indicator of patient clinical outcome and healthcare system performance.<sup>4</sup> Hospital readmissions after ACLR always associated with adverse postoperative outcomes and numerous publications have investigated the causes for readmission.<sup>17,24-27</sup> The findings indicated that in the short term, readmissions are often attributed to certain medical complications (e.g., infection) or surgical complications (e.g., stiffness of the knee joint);<sup>17,24-27</sup> while in the long term, readmissions are usually caused by the ACL graft failure and degenerative knee osteoarthritis, which necessitate subsequent operations like ACLR revision surgery and total knee replacement.<sup>45,46</sup> Though previous studies have identified some causes and related risk factors for readmission after ACLR, there remains a lack of synthesis of the current evidence. Therefore, we believe this proposed systematic review and meta-analysis is feasible, attainable, and timely.



Thank you very much for your positive appraisal and constructive suggestions for our manuscript. In the revision, we have thoroughly amended the Manuscript, aiming to enhance the clinical significance and make it understandable. If you have any suggestions, please let us know.

Reviewer: 2

Reviewer Name: Richard F O'Connor

Institution and Country:

HSE West,

Ireland

Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below

Overall a good protocol which could make for an interesting systematic review.

Response: Thank you, Prof. O'Connor, for your positive and encouraging comments on our manuscript. Based on your insightful and constructive suggestions, we have modified our manuscript, as described below.

Points for improvement:

Comment 1: The rationale in the introduction could be improved with additional referencing to strengthen the basis for the study.

Response: Thank you for your insightful and professional comments. We fully agree with you that the introduction section could be improved with additional referencing to strengthen the basis for the study. According to your kind suggestion, we have revised the introduction section thoroughly and added additional references. We sincerely hope that all these changes will improve the readability of the manuscript and will make the manuscript acceptable for publication in BMJ Open. Once again, thank you so much for your positive comments and helpful suggestions.

Comment 2: Are studies which included longer term/ later readmissions (e.g readmissions after 9 months or after 2 years) to be included? It appears based on the inclusion/ exclusion criteria that they will be included. Their inclusion will be useful, and in that case there should be consideration of reinjury of the ACL in the introduction and throughout the protocol since reinjury is an important complication following ACLR. Re-injury, which is not uncommon, has very significant implications for rehabilitation, morbidity, later readmission, and financial cost.

Response: Thank you for your professional comment. We apologize for our unclear expression. Studies that reported longer-term or later readmissions (e.g., readmissions after 9 months or after 2 years) after ACLR will also be included. As mentioned above, these studies are informative and useful, which has significant implications for postoperative rehabilitation, morbidity, later readmission, and financial cost. According to your kind suggestion, we have revised the Eligibility criteria section as follows.

Change in the text:

Types of participants

Additionally, there will be no specific restrictions on the time frame, which means that studies focused on either short-term (within one year after surgery) or long-term (more than one year after surgery) readmissions after ACLR would be eligible.

Comment 3: In the Methods section there is a description of the types of observational studies that will be eligible. The author also states that "There will be no specific restrictions on the study design,

but most of the studies are expected to (be) retrospective observational studies." I agree that most of the studies will be observational but it should be stated more clearly as to whether randomised controlled trials will also be included or whether they are excluded. If RCTs are to be included is there a protocol in place for assessment of their quality?

Response: Thank you for your thoughtful and constructive suggestions. We apologize for our unclear expression. There will be no specific restrictions on the study design, most of the studies are expected to be retrospective observational studies, but eligible clinical trials will also be included. Further, if RCTs were included in this systematic review and meta-analysis, the appropriate quality assessment tools (e.g., Cochrane risk of bias tool) will be used. Accordingly, we have revised the text as follows.

Change in the text:

Eligibility criteria

Types of studies

There will be no specific restrictions on the study design, and eligible clinical trials will also be included, but most of the studies are expected to be retrospective observational studies.

Quality assessment

Moreover, if other types of studies were included (e.g., randomized controlled trials), the appropriate quality assessment tools will be used accordingly.

Comment 4: The flow and accuracy of the English language needs to be improved very significantly, particular attention is needed in the introduction where there are several errors. If the language/ grammar/ accuracy was addressed and the introduction improved then this protocol could be an excellent review. The following lines of notes require attention, this list is not exhaustive: Page 7 Line 22, 33, 48-59; Page 8 Line 17-33, 43-49; Page 9 Line 35, 43; Page 10 Line 38, Page 13 Line 20.

Response: Thank you for your careful review. We fully agree with you that there are a number of problems, although we tried our best to rephrase this article. According to your kind suggestion, our team members reviewed and revised the entire manuscript repeatedly. We also asked our co-author, whose native language is English, to rewrite the content of our manuscript, eliminate any potential grammatical and spelling errors, improve the quality of the language, and enhance the clarity and readability of the manuscript. We sincerely hope that the resulting changes will render the manuscript acceptable for publication in BMJ Open. Once again, thank you for all your helpful suggestions.

Finally, we would like to reiterate how much we appreciate the editor's and reviewers' kind and constructive suggestions about our manuscript.

#### VERSION 2 – REVIEW

<b>REVIEWER</b>	Adam Culvenor La Trobe University
<b>REVIEW RETURNED</b>	27-Jul-2020

<b>GENERAL COMMENTS</b>	The authors have done a commendable job of addressing reviewer comments. I still have some remaining concerns. 1. My original comment (and I also note, that of the second reviewer) regarding whether hospital readmissions due to secondary ACLR surgery and total knee replacement would be included as outcomes appears to have been misinterpreted. I was trying to convey that I think secondary (and tertiary) ACLR revision and total knee replacement are causes of hospital readmission and should be considered as an outcome (alongside infection rates etc), rather than as an exposure. So instead of stating that hospital readmissions after revision ACLR will be reported, actually
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	<p>treating revision ACLR as the hospital readmission. Including these outcomes would likely strengthen the review, and would also require some modification to the background to include these outcomes. The addition of the following text in the revised manuscript does not address my original comments: “Also, to enhance the clinical significance of this study, both primary ACLR and ACLR revision surgery will be included.”</p> <p>2. Following on from my first point above, perhaps the search strategy could be strengthened by including specific terms causing readmission, because some eligible papers may not specifically use the word “readmission”. Including terms such as infection, revision may ensure no studies are missed?</p> <p>3. It was a little unclear in the response, will a meta-regression of the risk of bias scores (as a continuous variable) be used (where possible) to explore the influence of risk of bias on study results (as opposed to simple dichotomous risk of bias score analysis)?</p> <p>4. Page 7, line 54 – “repair” should probably be “reconstruction”.</p> <p>5. Page 11, line 31 – how will you define “complicated surgery”</p> <p>6. Page 13, line 56: “If RCTs are included other quality assessment tools will be used.” Please define which quality assessment tools will be used in these instances.</p>
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## VERSION 2 – AUTHOR RESPONSE

Comments from Reviewers:

Reviewer: 1

Reviewer Name: Adam Culvenor

Institution and Country: La Trobe University

Competing interests: None declared

Please leave your comments for the authors below

### General Comments

The authors have done a commendable job of addressing reviewer comments. I still have some remaining concerns.

Response: Thank you for your insightful and professional comments. According to your kind suggestions, we have revised our manuscript thoroughly.

### Major Comments

Comment 1: My original comment (and I also note, that of the second reviewer) regarding whether hospital readmissions due to secondary ACLR surgery and total knee replacement would be included as outcomes appears to have been misinterpreted. I was trying to convey that I think secondary (and tertiary) ACLR revision and total knee replacement are causes of hospital readmission and should be considered as an outcome (alongside infection rates etc), rather than as an exposure. So instead of

stating that hospital readmissions after revision ACLR will be reported, actually treating revision ACLR as the hospital readmission. Including these outcomes would likely strengthen the review, and would also require some modification to the background to include these outcomes. The addition of the following text in the revised manuscript does not address my original comments: "Also, to enhance the clinical significance of this study, both primary ACLR and ACLR revision surgery will be included."

Response: We appreciate your kind and detailed suggestion. Truth be told, we did misunderstand your previous suggestion, which mainly due to our pre-conceived idea that we will all kinds of hospital readmission after ACLR, regardless of the causes (e.g., caused by secondary (and tertiary) ACLR revision and total knee replacement). However, as you just figured out, we failed to state this point clearly. Accordingly, we have revised this section as follows.

Change in the text:

Additionally, there will be no specific restrictions on the time frame and causes of hospital readmission. That is to say, studies focused on either short-term (within one year after surgery) or long-term (more than one year after surgery) readmissions after ACLR, no matter caused by infection, re-surgery (e.g., caused by secondary or tertiary ACLR revision, or total knee replacement) or other causes, would be potentially eligible.

Comment 2: Following on from my first point above, perhaps the search strategy could be strengthened by including specific terms causing readmission, because some eligible papers may not specifically use the word "readmission". Including terms such as infection, revision may ensure no studies are missed?

Response: Thank you for your constructive and thoughtful comments. We totally agree with you. Accordingly, we have revised the search strategy in consultation with a second research librarian. The revised full search strategy for all databases is now presented in Table 1.

#### Table 1 Search strategy

##### PubMed Search Query

#1 "Patient Readmission"[Mesh]

#2 Readmission[Title/Abstract]

#3 Re-admission[Title/Abstract]

#4 Readmission\*[Title/Abstract]

#5 Readmit\*[Title/Abstract]

#6 Re-admit\*[Title/Abstract]

#7 Rehospitalization[Title/Abstract]

#8 Rehospital\*[Title/Abstract]

#9 Re-hospital\*[Title/Abstract]

#10 "Reoperation"[Mesh]  
 #11 Reoperation[Title/Abstract]  
 #12 Re-operation[Title/Abstract]  
 #13 Resurgery[Title/Abstract]  
 #14 Re-surgery[Title/Abstract]  
 #15 "Infections"[Mesh]  
 #16 "Wound Infection"[Mesh]  
 #17 "Surgical Wound Infection"[Mesh]  
 #18 Infection\*[Title/Abstract]  
 #19 Wound Infection[Title/Abstract]  
 #20 Surgical Wound Infection[Title/Abstract]  
 #21 Graft failure[Title/Abstract]  
 #22 Graft rupture[Title/Abstract]  
 #23 Reinjury[Title/Abstract]  
 #24 Re-injury[Title/Abstract]  
 #25 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR  
 #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24  
 #26 "Anterior Cruciate Ligament"[Mesh]  
 #27 "Anterior Cruciate Ligament Reconstruction"[Mesh]  
 #28 Anterior Cruciate Ligament[Title/Abstract]  
 #29 ACL[Title/Abstract]  
 #30 #26 OR #27 OR #28 OR #29  
 #31 #25 AND #30  
 Embase Search Query  
 #1 'hospital readmission'/exp  
 #2 readmission:ti,ab,kw  
 #3 re-admission:ti,ab,kw  
 #4 readmission\*:ti,ab,kw  
 #5 readmit\*:ti,ab,kw  
 #6 re-admit\*:ti,ab,kw

#7 rehospitalization:ti,ab,kw  
#8 rehospital\*:ti,ab,kw  
#9 re-hospital\*:ti,ab,kw  
#10 'reoperation'/exp  
#11 reoperation:ti,ab,kw  
#12 re-operation:ti,ab,kw  
#13 resurgery:ti,ab,kw  
#14 re-surgery:ti,ab,kw  
#15 'infection'/exp  
#16 'wound infection'/exp  
#17 'surgical infection'/exp  
#18 infection:ti,ab,kw  
#19 wound infection:ti,ab,kw  
#20 surgical infection:ti,ab,kw  
#21 graft failure:ti,ab,kw  
#22 graft rupture:ti,ab,kw  
#23 reinjury:ti,ab,kw  
#24 re-injury:ti,ab,kw  
  
#25 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR  
#14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24  
  
#26 'anterior cruciate ligament'/exp  
#27 'anterior cruciate ligament reconstruction'/exp  
#28 'anterior cruciate ligament':ti,ab,kw  
#29 acl:ti,ab,kw  
#30 #26 OR #27 OR #28 OR #29  
#31 #25 AND #30  
  
Cochrane Search Query  
#1 MeSH descriptor: [Patient Readmission] explode all trees  
#2 Readmission:ti,ab,kw  
#3 Re-admission:ti,ab,kw

#4 Readmission\*:ti,ab,kw  
#5 Readmit\*:ti,ab,kw  
#6 Re-admit\*:ti,ab,kw  
#7 Rehospitalization:ti,ab,kw  
#8 Rehospital\*:ti,ab,kw  
#9 Re-hospital\*:ti,ab,kw  
#10 MeSH descriptor: [Reoperation] explode all trees  
#11 Reoperation:ti,ab,kw  
#12 Re-operation:ti,ab,kw  
#13 Resurgery:ti,ab,kw  
#14 Re-surgery:ti,ab,kw  
#15 MeSH descriptor: [Infections] explode all trees  
#16 MeSH descriptor: [Wound Infection] explode all trees  
#17 MeSH descriptor: [Surgical Wound Infection] explode all trees  
#18 (Infection\*):ti,ab,kw  
#19 Wound Infection:ti,ab,kw  
#20 Surgical Wound Infection:ti,ab,kw  
#21 Graft failure:ti,ab,kw  
#22 Graft rupture:ti,ab,kw  
#23 Reinjury:ti,ab,kw  
#24 Re-injury:ti,ab,kw  
#25 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24  
#26 MeSH descriptor: [Anterior Cruciate Ligament] explode all trees  
#27 MeSH descriptor: [Anterior Cruciate Ligament Reconstruction] explode all trees  
#28 Anterior Cruciate Ligament:ti,ab,kw  
#29 ACL:ti,ab,kw  
#30 #26 or #27 or #28 or #29  
#31 #25 and #30

Comment 3: It was a little unclear in the response, will a meta-regression of the risk of bias scores (as a continuous variable) be used (where possible) to explore the influence of risk of bias on study results (as opposed to simple dichotomous risk of bias score analysis)?

Response: Many thanks for your careful review and kind suggestions regarding our manuscript. We are very sorry for our use of vague expressions, mainly due to the uncertainty about whether we could conduct a meta-regression of the risk of bias scores to explore the influence of risk of bias on study results. According to your kind suggestion, we have rewritten the sentence as follows.

Change in the text:

If the number of included studies is sufficient, subgroup analyses and meta-regression analyses will be conducted (e.g., on the risk of bias scores, follow-up periods) to investigate the underlying source of heterogeneity.

Comment 4: Page 7, line 54 – "repair" should probably be "reconstruction".

Response: Thank you for your helpful suggestions. Accordingly, we have corrected it in the revised version.

Comment 5: Page 11, line 31 – how will you define "complicated surgery"

Response: Thank you for your additional suggestion. We apologize for the confusion, since "complicated surgery" is a broad term. Accordingly, we have replaced this term with "multi-ligament reconstruction".

Change in the text:

However, studies will be excluded if patients suffered from multi-ligament knee injuries and received multi-ligament reconstruction.

Comment 6: Page 13, line 56: "If RCTs are included other quality assessment tools will be used." Please define which quality assessment tools will be used in these instances.

Response: Thank you for your additional suggestion. We are very sorry for the unclear description. Accordingly, we have edited this sentence to make it more readable.

Change in the text:

Moreover, if other types of studies were included, the appropriate quality assessment tools (e.g., Cochrane risk of bias tool for randomized controlled trials) will be used accordingly.

Finally, we would like to reiterate how much we appreciate the editor's and reviewer's kind and constructive suggestions about our manuscript. If you have any suggestions, please let us know.

Thank you for your further consideration of our manuscript



### VERSION 3 – REVIEW

<b>REVIEWER</b>	Adam Culvenor La Trobe University, Australia
<b>REVIEW RETURNED</b>	09-Sep-2020
<b>GENERAL COMMENTS</b>	Thank you for addressing the comments. I have nothing further to add.