

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

TITLE (PROVISIONAL)	Natural corollaries and recovery after acute ACL injury – the NACOX cohort study protocol
AUTHORS	Kvist, Joanna; Gauffin, Håkan; Tigerstrand Grevnerts, Hanna; Ardern, CL; Hagglund, Martin; Stålmán, Anders; Frobell, Richard

VERSION 1 – REVIEW

REVIEWER	Shahnaz KLOUCHE, MD Clinique du Sport, AP-HP, Paris, France
REVIEW RETURNED	19-Dec-2017

GENERAL COMMENTS	Well done. Will you please have a longer follow-up to assess the osteoarthritis after 5 years?
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REVIEWER	Mohammad A Yabroudi Assistant Dean, Assistant Professor Department of Rehabilitation Sciences Faculty of Applied Medical Sciences Jordan University of Science and Technology Irbid - Jordan
REVIEW RETURNED	17-Feb-2018

GENERAL COMMENTS	<p>This paper is well written and the study protocol is well done. I have only some concerns and questions that were not very clear.</p> <p>Page 7, line 40. Serious concomitant knee injury is not clear. Do concomitant ligaments injury; cartilage or meniscus injuries that required surgery are considered serious injuries? If no, are they going to be considered in the analysis of predictors for OA and return to sports??</p> <p>Page 12, line 26. Quality of life assessment is not clear. Why the author chooses only these time points?? 24 months could be also important, as patients may not maintain their activity level after 12 months, which may have an impact on their quality of life!!</p> <p>Page 12, line 33. Problems during physical activity will be only assessed for non-ACL patients from month 6- 11. This was not clear. Why not for patients with ACLR?? I think this needs to be clarified in the text page 11, line 14.</p> <p>Page 20, line 10. Regression analysis can be more specific to logistic regression analysis.</p> <p>Page 21, line 39. Sample size calculation for regression analysis is not clear. The author needs to clarify whether the sample size of 130 subjects was based on arbitrary decision or based on statistical</p>
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	<p>method!!</p> <p>Page 22, line 7. The author stated that the recruitment started in October 2016 and will continue until June 2018 that is equal to 20 months. However, the author mentioned on page 7, line 24 that the recruitment will be over approximately 12 months. I think this needs to be modified or clarified.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

COMMENT: Well done. Will you plan a longer follow-up to assess the osteoarthritis after 5 years?

RESPONSE: Thank you for your time reviewing the manuscript, and your positive comments. We plan additional follow-up, specifically to evaluate osteoarthritis with imaging and patient-reported outcomes at 10, 15 and 20 years. We have not specified these follow-up points in the protocol because we do not yet have ethical approval (we intend to apply for ethics approval for longer-term follow-up at an appropriate time).

Reviewer: 2

COMMENT: This paper is well written and the study protocol is well done. I have only some concerns and questions that were not very clear.

RESPONSE: Thank you for your thoughtful, constructive comments. We appreciate the time you have taken to help us improve our manuscript.

COMMENT: Page 7, line 40. Serious concomitant knee injury is not clear. Do concomitant ligaments injury; cartilage or meniscus injuries that required surgery are considered serious injuries? If no, are they going to be considered in the analysis of predictors for OA and return to sports??

RESPONSE: We have clarified that patients with posterior cruciate ligament ruptures will be excluded. We will not exclude patients with meniscus or articular cartilage injuries, or those with collateral ligament injuries. However, we have clarified in the statistical analysis that we will include concomitant injury to other knee structures at index ACL injury as predictor variable(s) in our multilevel modelling approach (study objectives A, D and E).

COMMENT: Page 12, line 26. Quality of life assessment is not clear. Why the author chooses only these time points?? 24 months could be also important, as patients may not maintain their activity level after 12 months, which may have an impact on their quality of life!!

RESPONSE: Thank you for the opportunity to clarify our patient-reported data collection. We have specified in Figure 2 that we will collect quality of life data using the ACL-Quality of Life scale at 4 weeks and 3 and 12 months follow-up, and using the Knee Injury and Osteoarthritis Outcome Score (KOOS) quality of life subscale at 24 and 36 months follow-up.

COMMENT: Page 12, line 33. Problems during physical activity will be only assessed for non-ACL patients from month 6- 11. This was not clear. Why not for patients with ACLR?? I think this needs to be clarified in the text page 11, line 14.

RESPONSE: Thank you for picking this up. This was a pragmatic decision to reduce respondent burden, given we are already asking a lot of our participants with detailed longitudinal data collection. These questions about physical activity participation (from the Oslo Sports Trauma Research Centre questionnaire) are most relevant once a patient has returned to sport. We expect patients with ACL

reconstruction to return to sport later than those with non-surgical treatment, and this is the rationale for collecting these data at different time points.

COMMENT: Page 20, line 10. Regression analysis can be more specific to logistic regression analysis. RESPONSE: Thank you for the opportunity to clarify the regression analysis – we agree, logistic regression is the appropriate approach here.

COMMENT: Page 21, line 39. Sample size calculation for regression analysis is not clear. The author needs to clarify whether the sample size of 130 subjects was based on arbitrary decision or based on statistical method!!

RESPONSE: We estimated the required sample size based on Tabatchnik & Fidell's¹ rule of thumb ($N \geq 50 + 8m$, where m is the number of independent variables).

COMMENT: Page 22, line 7. The author stated that the recruitment started in October 2016 and will continue until June 2018 that is equal to 20 months. However, the author mentioned on page 7, line 24 that the recruitment will be over approximately 12 months. I think this needs to be modified or clarified.

RESPONSE: Thank you for identifying this discrepancy. We have clarified that recruitment will be conducted over a period of approximately 20 months.

FORMATTING AMENDMENTS (if any)

REQUEST 1: Please remove figure 1 in your main document and upload each of them separately under file designation 'Image' (except tables and please ensure that Figures are of better quality or not pixelated when zoom in). NOTE: They can be in TIFF or JPG format and make sure that they have a resolution of at least 300 dpi. Figures in PDF, DOCUMENT, EXCEL and POWER POINT format are not acceptable.

RESPONSE: We have removed Figure 1 and Figure 2 from the manuscript file and uploaded each as a separate TIFF file in the online submission system.

REQUEST 2: Please include Figure legends at the end of your main manuscript.

RESPONSE: Please find the legends for Figures 1 and 2 listed in the manuscript file.

REQUEST 3: Table 1 format

RESPONSE: We have reformatted the previous Table 1 as an image file (Figure 2), and amended how we refer to it in the text.

REQUEST 4: Please make sure that your Tables are on editable format.

RESPONSE: We have checked that all tables are embedded in an editable format.

Reference

¹Tabatchnik BG, Fidell LS. Using multivariate statistics. 4th edn. Needham Heights, MA: Allyn & Bacon, 2001.